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ABSTRACTS
**Nanogenerators for Powering Implantable Medical Devices and Self-powered Sensors**

Zhong Lin Wang  
Georgia Institute of Technology, United States

Self-powered system is a system that can sustainably operate without an external power supply for sensing, detection, data processing and data transmission. Nanogenerators (NG) were first developed for self-powered systems based on piezoelectric effect and triboelectrification effect for converting tiny mechanical energy into electricity, which have applications in internet of things, environmental/infrastructureal monitoring, medical science, environmental science and security. NGs have three major application fields: micro/nano-power source, self-powered sensors and blue energy. We will present the applications of the NGs for harvesting body motion energy that will be used for medical science and bioengineering.

**Mechanosensitve Ion Channels Play a Crucial Role in Substrate Rigidity Sensing in Mesenchymal Stem Cells**

Masahiro Sokabe, Takeshi Kobayashi  
Nagoya University Graduate School of Medicine, Japan

Cells can sense substrate rigidity through mechanical interaction at focal adhesions (FAs) that involve integrins, talins, and a variety of receptor tyrosine kinases, and link to the actin cytoskeleton connected to the nucleus. The rigidity sensing is the highlight in basic mechanobiology because it regulates fundamental cell functions, including cell migration, proliferation, differentiation and cell death. Rigidity sensing can be done by sensing the force (tension) required for fixed length stretching of the substrate by the contractile actin cytoskeleton stress fibre (SF). Thus mechanosensitive elements that can feel tension in the SF, including receptor tyrosine kinases and even the nucleus pore, are thought to be able to convert substrate rigidity into biochemical signals. However, little is known for the involvement of mechanosensitive ion channels (MSCs) in this process.

MSCs are the major player in cell mechanosensing. Among them, bacterial MSCs have been the best studied ones owing to their resolved 3D crystal structures. They are activated exclusively by tension in the membrane and contribute to the cell volume control against hypo-osmotic challenge, suggesting that they sense global tension in the cell membrane. By contrast, eukaryotic MSCs are known to be linked to the actin cytoskeleton SF anchored to FA, and activated by tension in SFs. Sparse distribution of SF/FA/MSC complex in the ventral cell surface suggests that it can sense local force in the membrane. Actually, in Ca2+-permeable MSCs in endothelial cells, force conducting along a single SF induces a localized increase in the intracellular Ca2+ concentration ([Ca2+]i).

The SF/FA/MSC complex has another important function called “active-touch sensing”, in which SF contraction pull the cell substrate via FA to activate linked MSCs. As changes in stress in SF/FA/substrate complex in response to a fixed length SF contraction depend on the substrate stiffness, the MSCs can transduce local substrate stiffness into the amount of localized Ca2+ influx across the MSCs. Actually, we observed spontaneous [Ca2+]i increases (Ca2+ sparks) mediated by spontaneous SF contraction in a variety of cultured cells including mesenchymal stem cells, in which amplitude and frequency of the Ca2+ sparks strictly depended on substrate stiffness. The Ca2+ sparks were nearly perfectly inhibited by extracellular Ca2+ depletion, GsMTx4, a generic MSC inhibitor, or a ROCK inhibitor that inhibits SF contraction. Furthermore, a TRPV4-antagonist or TRPV4-knockdown strongly inhibited the Ca2+ sparks, suggesting that SF/FA/TRP complex can act as a mechanosensor to detect not only global (μm scale) but also local (nm scale) substrate stiffness. More importantly, inhibition of the TRP channel largely reduced YAP translocation to the nucleus which is a major rigidity dependent response in mesenchymal cells.
Results and Conclusions: The intracellular actin cytoskeleton and nucleus were found to be elongated and aligned in the direction of zero normal strain (i.e. with respect to the stretch direction) in an actomyosin tension-dependent manner. The nuclei of the stretched cells were dramatically compressed by the reorganized actin stress fibers located on their apical and both sides, and a significant increase in the intranuclear DNA density was observed. Intercellular tension, as assessed with live cell AFM imaging, also increased following exposure to cyclic stretch. The UV radiation-induced DNA damage, estimated from the fluorescence intensity of the phospho-histone γ-H2AX, significantly decreased in these stretched cells. These results indicate that the cyclic stretch-induced morphological changes in the nucleus may improve the UV radiation resistance of cells, probably owing to the intracellular force-induced condensation of chromatin.

In conclusion, we found that cyclic stretching dramatically induced the actin-nucleus orientation and nucleus compression in an actomyosin tension-dependent manner. Such mechanical changes in the nucleus improved chromatin condensation and UV radiation resistance of intranuclear DNA. To our knowledge, this is the first study to demonstrate the inhibition of UV radiation-induced DNA damage by mechanical stimulation.

Abstract Number: ICBME1302

Identifying Cell Mechanical Changes in Cancer Invasion

Huabing Yin, Giulia Spennati, Dominika A. Rudzka, Louise Mason, Ya-Hua Chim, Manlio Tassieri, Michael Olson
University of Glasgow, UK

The life-threatening characteristic of deadly cancers derives principally from their ability of metastasis. Although a plethora of insights have been made on the biochemical aspects of cancer metastasis, only in recent years, the importance of the mechanical properties of cells in pathological conditions has been recognized. This imposes an urgent need of advanced technological platforms to investigate how cancer cells respond mechanically (e.g. structure, stiffness) to its environment to enable its migration.

In recent years, we have developed several Atomic force microscopy (AFM)-based methods to study cell mechanical properties and cell-matrix interactions. These include a novel “one-step” AFM-micro rheology (AFM2) as well as single cell force microscopy technologies. The AFM2 method measures the viscoelastic properties of living cells at precisely defined location, over a wide range of continuous frequencies, from a simple stress-relaxation nanoindentation. This reveals respective elastic and viscous responses of living cells to imposed stresses, leading to the discovery of a characteristic transitions of the loss tangent (i.e. viscos moduli/elastic moduli) in the low frequency range (0.005 Hz ~ 0.1 Hz) that indicates the capability for cell restructuring of F-actin network.

These new technologies in combination with advanced imaging and omics studies allowed us to investigate the role of biomechanical properties in cancer progression. Here, I will present one recent study aiming at identifying key changes in biomechanical properties that facilitate tumor cells passing through confined spaces in three-dimensional extracellular matrix. By examining micropore-selected human MDA MB 231 breast cancer and MDA MB 435 melanoma cancer cells, membrane fluidity and nuclear elasticity were excluded as primary contributors. Instead, reduced actin cytoskeleton anisotropy, focal adhesion density and cell stiffness were characteristics associated with efficient passage through constraints. Together transcriptomic studies, it was found that increased Ras/MAPK signaling was linked with cytoskeleton rearrangements and cell softening. MEK inhibitor (Trametinib) treatment reversed the cytoskeleton, focal adhesion and viscoelasticity changes. These results reveal that MAPK signalling, in addition to tumour cell proliferation, has a significant role in regulating cell biomechanics.

Abstract Number: ICBME1366

Hydrostatic Pressure Induces Magnitude-Dependent Changes in Endothelial Cell Behavior

Daisuke Yoshino
Tohoku University, Japan

Introduction: Blood pressure – the force exerted by circulating blood against the vascular wall – is an important factor in both maintenance and breakdown of homeostasis in the living body. Vascular endothelial cells (ECs) are constantly exposed to blood pressure, and therefore play an important role in the physiological and pathological events. The mechanical forces due to blood pressure are well known to regulate endothelial functions leading to those events. Although hydrostatic pressure has been particularly shown to elicit physical and chemical responses, we have the knowledge limited to answer how ECs change their responses to the magnitude of hydrostatic pressure. Here we show endothelial dynamics leading to the physiological or pathological responses to hydrostatic pressure exposure.

Methods: Confluent cultured human umbilical vein ECs were exposed to hydrostatic pressure (up to 500 mmHg) for 30 min, 1, and 24 hours. We first focused on early-stage dynamics in ECs exposed to hydrostatic pressure. Phase-contrast images were captured every one minute for 30 minutes, and changes in the cell structure was quantified by PIV using the time-series phase-contrast images. We also analyzed protein expressions and their localization, which are related to the observed dynamics in the ECs exposed to hydrostatic pressure, by immunofluorescence staining and immunoblotting. After 30 min, 1, or 3 h of exposure to hydrostatic pressure, the cells were fixed with 4% paraformaldehyde, and the target proteins were stained with primary and secondary antibodies. Fluorescence images of the stained cells were captured with confocal laser microscopy. The cells were also collected by SDS buffer after 30 min, 1, or 3 h of pressure exposure, and the collected proteins were analyzed by SDS-PAGE and immunoblotting. We second conducted live/dead assay to observe late-stage mechaonresponsess of ECs to hydrostatic pressure exposure.

Results and Discussion: Exposure to hydrostatic pressure did not affect elongation, orientation, and tortuosity, which indicate morphological changes in ECs. In contrast, following exposure to hydrostatic pressure, the cellular structure rounded up toward their middle. This result suggests that exposure to hydrostatic pressure induces cell contraction. This notion is supported by the following findings; (1) After 1 h of exposure, intercellular junction protein VE-cadherin exhibited wedge-like structures between
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neighboring cells; (2) exposure to hydrostatic pressure induced the development of actin stress fibers at the cell periphery and actomyosin contractility. The tendency of those responses was more significant depending on the increase in pressure magnitude. In addition, hydrostatic pressure up to 150 mmHg has no effect on the viability of ECs, while the pressure of 500 mmHg induced EC apoptosis after 24-h exposure.

Summary: We investigated the pressure magnitude-dependent changes in endothelial cell behavior. We demonstrated that hydrostatic pressure causes actomyosin-mediated EC contraction in the early-stage exposure. We also confirmed the apoptosis of ECs in the late-stage exposure to high hydrostatic pressure. These responses might be induced by water efflux from the ECs, which caused EC contraction due to the hydrostatic pressure stimulation.

A space-filling algorithm, based on Constrained Constructive Optimization, for generation of 3D printable models of biomimetic vascular networks. Currently there is no method for automatic generation of 3D printable vascular networks for arbitrary scales and spaces. The proposed method accounts for physical constraints (flow conservation, pressure consistency), physiological constraints (minimum network volume, Murray’s law, no short-circuit intersections), and manufacturing constraints (minimum feature sizes, infill prevention).

A method for production of three-dimensional and hierarchical vascular networks in ECM-like hydrogels, using sacrificial 3D printing and cellular co-cultures.

Abstract Number: ICBME1347

Generation of Vascular Invasion Model of Colorectal Cancer with the Three-Dimensional Culture Method

Kiminori Yanagisawa, Masamitsu Konno, Tsunekazu Mizushima, Taroh Satoh, Michiya Matsuaki, Masaki Mori, Yuichiro Doki, Hideshi Ishii
Graduate School of Medicine, Osaka University, Japan

Objectives: For translational research, new research tools with structural materials and tissue engineering are necessary to reflect the precise condition of patients. The incidence of colorectal cancer tends to increase, and Stage IV has a five-year survival rate of 30% and a poor prognosis, and thus, progress in treatment is required.

In three-dimensional (3D; three-dimensional) culture using human cells, cell-cell interaction is maintained, and it resembles a living body more than monolayer culture. It is becoming an alternative tool for in vivo experiments and the need for 3D culture techniques is growing. The purpose of this study is to apply these 3D cultures to create a vascular invasion model of colon cancer and to clarify the invasion and metastasis mechanism of colorectal cancer.

Methods: We cultured human umbilical vein endothelial cells (Huvec) in a gel made with collagen microfiber, fibrinogen and thrombin. A colon cancer cell line (HT29) was cocultured with Huvec. Huvec was fluorescently labeled with GFP, and HT29 was also labeled with RFP. A confocal fluorescence microscope was used to observe samples. In addition, to investigate whether exosomes affect vascular infiltration, colon cancer cell lines derived exosomes were recovered by ultracentrifugation. These exosomes were exposed to Huvec and cocultured with colon cancer cell lines in gel.

Result: We were able to confirm the vascular network by Huvec inside the gel with a microscope. Histologically, it was confirmed that the blood vessel retained the lumen. In co-culture with cancer cells, when the cancer cells and blood vessels are in contact, the cancer cells enter the blood vessels. It has been confirmed that cancer cells migrate and proliferate in blood vessels. In the model using Huvec exposed to exosomes, more vascular infiltration of colon cancer cell lines was observed.

Conclusion: We succeeded in creating a vascular invasion model of cancer, and it was suggested that exosomes enhance the vascular invasion phenomenon of colon cancer. The advantage of this model is that it allows the observation of cell dynamics in real time, which
Bioprinting of Human Endometrial Stem Cell (eMSC) on 3D Melt Electrospun Meshes Induce Anti-Inflammatory Response Following Tissue Regeneration in a Mouse Model

Kallyanashis Paul, Saeedeh Darzi, Gordon Mcphee, Mark Del Borgo, Jerome A Werkmeister, Caroline E Gargett, Shayanti Mukherjee
Monash University, Australia

Objectives: Pelvic Organ Prolapse (POP) affects 1 in every 4 women in the world. While there is no optimal treatment at present, the transvaginal meshes for POP surgery have recently been banned in countries like Australia, New Zealand and USA. Recent reports have associated inflammation and prolonged foreign body response to non-degradable meshes to their adverse effects. This study aims to 3D print a degradable poly ε-caprolactone (PCL) mesh bioprinted with eMSCs to promote tissue integration and anti-inflammatory response.

Methods: The degradable PCL was melt electrospun following a CAD model; MES mesh. eMSCs were identified using our established SUS02 marker following m-Cherry gene transduction. An Aloe Vera-Sodium Alginate (AV-ALG) composite hydrogel was used to bioprint mCherry+eMSCs. The MES/eMSC interaction was studied in vitro using electron and atomic force microscopes. The in vivo acute inflammation and foreign body response through pro-inflammatory, (F4/80+CCR7+, M1) and anti-inflammatory (F4/80+CD206+, M2)macrophages were identified histologically at 1 week. Tissue integration and in vivo mesh fate was assessed by electron microscopy and histologic staining. Statistical analysis was performed using Graph Pad Prism V 7.0.

Results: The MES mesh morphology study revealed the highest open pore diameter (47.22 ± 11.42 µm), strand thickness (118.5 ± 46 µm) and favourable eMSC attachment at 100°C and speed (20 mm/sec). AV-ALG hydrogel was optimised to a 1:1 mixture (1%AV-1%ALG) and supported significant proliferation (p<0.0001) of eMSCs in an MTS assay. The inflammatory cell response to the implanted meshes revealed significantly fewer cells in eMSCs/MES (p=0.0002) compared to MES alone, and significantly higher compared to MES/hydrogel (p<0.0001). The anti-inflammatory response of eMSCs/MES meshes demonstrated a significantly higher number of M2 macrophages compared to MES and MES/hydrogel groups (p<0.0001 for both). The high influx of M2 macrophages altered an enhanced tissue integration of eMSCs/MES constructs as revealed from collagen staining and scanning electron microscopy images.

Conclusions: This study demonstrates alternative treatment strategies degradable polymers fabricated by MES and bioprinted eMSCs. Our study clearly illustrates that the retention of eMSC with MES mesh significantly lowered the pro-inflammatory and increased the anti-inflammatory wound-healing macrophages; therefore, enhanced collagen deposition leading to successful tissue integration. Considering the limitation of non-degradable and high stiffness meshes, this study highlights the potential of MES meshes as a novel transvaginal mesh for POP treatment."

Stereo lithography (SLA) 3D Printed Templates for Engineering Perfusable Biomimetic Vasculatures in Alginate-Gelatin Hydrogel

Terry Ching, Yi-Chin Toh, Michinaho Hashimoto
Singapore University of Technology and Design, Singapore

This paper reports a method to engineer complex, hierarchically branching biomimetic vasculature of perfusable alginate-gelatin networks by using stereolithography (SLA) 3D printed templates. Design and fabrication of effective biomimetic vasculature constitutes a biologically relevant and yet unsolved challenge. At present, fabrication of biomimetic vasculatures mostly revolves around extrusion-based 3D printers, where attainable scaffolds often lack the intricate branching geometries of native microvasculature. SLA printing may offer avenues to engineer biomimetic vasculatures as it provides better print resolutions and less topological restrictions than extrusion-based 3D printers. However, there has been limited demonstration to fabricate biomimetic vasculatures via SLA due to the lack of suitable photocurable biomaterials with adequate mechanical and biological properties. Poly(ethylene glycol) diacrylate (PEGDA) and gelatin methacrylamine (GelMA) are commonly used hydrogels in SLA. PEGDA possesses suitable mechanical properties to support SLA printed structures, but does not favor cell adhesion and cell motility, limiting applications in bioengineering. On the other hand, GelMA has suitable biocompatibility but has suboptimal mechanical properties.

Herein, we report a novel two-step method to fabricate complex biomimetic vasculatures. We used SLA-printed PEGDA as a template to form perfusable cell-laden networks of hydrogels. A mold consisting of PEGDA with network of biomimetic microchannels was printed with a SLA printer. This mold was then used as a template to cast alginate-gelatin (Alg-Gel) hydrogel to form a perfusable network. The casting of Alg-Gel hydrogel was achieved by perfusing calcium chloride (CaCl2) solution into the microchannel network, allowing time for the calcium ions to sufficiently diffuse into the PEGDA matrix. After rinsing the microchannel with buffer solution, solution of sodium alginate and gelatin mixture was perfused into the channel. The calcium ions within the PEGDA matrix prompted ionic crosslinking of the alginate-containing solution, forming a thin-layer (~200 µm) of Alg-Gel hydrogel along the wall of the microchannel network.

Depending of the intricacy of the PEGDA mold, we successfully fabricated perfusable, cell-laden Alg-Gel networks with varying complexity. We fabricated a hierarchically branched network that subdivides from a single inlet to three microchannels before converging to a single outlet. Additionally, the Alg-Gel network could be removed from the template of PEGDA to form a free-standing perfusable network. The developed method circumvents the limited availability of photocurable biomaterial in SLA that are favorable for cell culture. These demonstrations highlighted a simple route to engineer perfusable biomimetic vasculatures in cell-laden alginate-containing hydrogels. The biological properties of alginate hydrogels can be tuned by blending with other bioactive gels. The alginate component, which is biologically inert, can also be dissolved using chelating agents.
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To conclude, we developed a method to engineer complex biomimetic vasculature in relevant biomaterials using SLA-printed fluidic networks as templates. The developed technology permits fabrication of free-form, cell-laden vascular models for various applications in tissue engineering, regenerative medicine, drug screening and fundamental studies in vascular biology.

Wearable Sweat Sensors for Personalized Health Monitoring

Wei Gao
California Institute of Technology, USA

The rising research interest in personalized and precision medicine promises to revolutionize traditional medical practices. This presents a tremendous opportunity for developing wearable devices toward predictive analytics and treatment. In this talk, I will introduce fully-integrated flexible biosensors for multiplexed in-situ perspiration analysis, which can selectively and accurately measure a wide spectrum of sweat analytes (e.g., metabolites, electrolytes, heavy metals, drugs and other small molecules). This platform allows us to gain real-time insight into the sweat secretion and gland physiology. I will also demonstrate an integrated wearable sweat extraction and sensing system which can be programmed to induce sweat on demand with various secretion profiles. To demonstrate the clinical value of our wearable sweat sensing platform, human subject studies were performed toward fitness monitoring, physiological monitoring, cystic fibrosis diagnosis and drug monitoring. These wearable and flexible devices open the door to a wide range of personalized monitoring and diagnostic applications.

Obstacle Detector and Qibla Finder for Visually Impaired Muslim Community

Aaron Raymond See, Dwi Sudarno Putra, Kristine Mae Dunque, Bo-Yi Li, Rong Da Lin
Southern Taiwan University of Science and Technology, Taiwan

Vision impairment remains a serious global health problem in poor and developing countries. Indonesia has the second highest rate of people with blindness in the world and the highest percentage of people with blindness in the Southeast Asian region with roughly 3.0 million visually impaired persons. Subsequently, a great deal of study was conducted on wearable devices for the visually impaired population but only a few assistive technologies are specifically tailored for the Muslim blind society. Salah which means worship is a religious duty for every Muslim individual observed five times a day and performed in a whole series of movement. It requires them to face the direction of the qibla that is oriented towards the Ka’ba in the city of Mecca. In this research, a lightweight assistive device placed in a traditional Muslim head wear Peci or Hijab would help them to not only avoid head collisions but also determine the correct direction of the qibla.

The module would incorporate obstacle detection, direction finder, and notification devices. First, the ultrasonic sensor will be placed in front of a Peci for obstacle detection. Second, a digital compass and GPS module will be utilized to determine the orientation of the person and used to calculate the direction of the qibla. Third, control and feedback will be done through the use of a button or voice control for qibla determination or obstacle detection. Fourth, notification is done through a vibration motor. Fifth, a mobile application will provide family members the real-time location of the visually impaired person.

The proposed system is portable, lightweight, and custom-made suitable for the Muslim blind community and the algorithm was programmed and embedded in the microcontroller. Obstacles were detected and the user is notified in advance to avoid head collisions. It was also able to determine the qibla direction and assist the users during their prayer time. Calibration of the system were done through the angle deviations compared to the known qibla directions at different mosques. An additional test will be conducted to verify the mobile application which will help the family members track their visually impaired loved one.

The device will provide millions of visually impaired Muslim to navigate their surroundings independently. The obstacle detector has been validated to assist in ensuring safety when moving around and during their worship time. Subsequently, the Qibla finder provides a convenient way for them to find the right direction to face in time of worship.

Development of Wearable Device for Blood Pressure Estimation Based on Pulse Rate Measurement: Feasibility Study

Soshi Kuroe, Toshiyuki Hayase, Suguru Miyauchi, Daisuke Ito, Shunkei Pak, Osamu Iwamoto
Tohoku University, Japan

Blood pressure is an important vital signal. Currently, the number of people with hypertension is increasing all over the world, and according to WHO’S World Health Statics of 2015, 24.0% of men and 20.5% of women were diagnosed as hypertension among adults over 18 years old. Since hypertension is a risk factor for many diseases such as cerebrovascular disease, heart disease, and arteriosclerosis, early detection and improvement of lifestyle habits are desired. There are various sphygmomanometers. However, it is difficult to measure daily continuous blood pressure with existing devises. The authors have developed a wearable blood pressure estimation device to obtain continuous blood pressure estimation by using pulse rate measurement data and simulation program of a simplified circulatory system taking account of a circulatory control system. The accuracy of the blood pressure estimation by this device has not been verified sufficiently. The purpose of this presentation, therefore, is to examine the feasibility of the device by a fundamental verification experiment. The experiment was carried out for 10 subjects of 20’s according to the ethical codes of Tohoku University. Pulse rate was measured with the wearable device every other day for a total of 3 days. For the verification, blood pressure measurement was performed with an automatic sphygmomanometer in every hour in the daytime, and with a mercury manometer three times by two nurses, respectively, between 2 p.m. and 3 p.m. After all measurements were finished, computation for the blood
pressure estimation was performed by a personal computer. Parameters of the blood pressure estimation algorithm were determined for each subject based on the measurement data with the automatic sphygmomanometer and corresponding analysis results on the first day. Measurement results of the automatic sphygmomanometer on the second and third days were used to verify the accuracy of the estimated blood pressure for each subject. Comparison was also made between the results of estimation, automatic sphygmomanometer, and mercury manometer. In the experiment, good correlation was found between the systolic and diastolic pressures of the estimated blood pressure of the wearable device and those of the measured blood pressure of the automatic sphygmomanometer for all subjects. In conclusion, fundamental verification experiment was carried out for 10 subjects to verify the accuracy of the wearable blood pressure estimation device. Good correlation was found between the estimated blood pressure of the device and the measured one of the automatic sphygmomanometer for all subjects showing the effectiveness of the device. Since the number of subjects of the present fundamental study was limited, more complete feasibility study is necessary in the future work.

Abstract Number: ICBME1368

Smart Landmark Navigation Cane for People with Visual Impairment (PVI)

Wai Ming Kong, Shi Shao, Jiang Huizing, Lim Woon Yong, Tan Tsu Soo, Nazirah Hassan, Wong Chin Sae Raymond, Kassim Bin Sa‘at, Ang Wei Sin, Cheryl Yeo, Simone Oh, Tan Hwei Lan
Nanyang Polytechnic, Singapore

Objectives: The project aims to develop a smart landmark navigation cane system to help the PVI travel independently in the outdoor and indoor environments. The system improves upon the traditional landmark navigation method by providing direction guidance and accurate position data to help the PVI travel. The smart cane can be produced at low cost and does not require building floorplans and infrastructure investment.

Method: The system makes use of a route recorder phase and a navigation guidance phase. In the route recording phase, a mobility instructor will accompany the PVI to record the route information needed for the PVI to travel independently to reach a destination. During recording phase, the system will remember landmarks and the distance/direction travelled will be recorded using gyroscope sensor and an omnidirectional wheel attached to the white cane. After the route is recorded, the navigation guidance system is capable of providing verbal guidance to the user to navigate to the destination using the location data from the smart cane.

Result: Trial tests were conducted at the Tampines MRT station with the help of 2 PVI volunteers. In the trial tests, the smart cane is able to guide the PVI to successfully navigate to 7 out of 8 landmarks.

Conclusion: The smart cane system will be very useful to the PVI community as it is able to provide accurate outdoor navigation as well as indoor navigation for all buildings in Singapore without the need to draw building floorplans and additional infrastructure investment for indoor navigation.

Session: 1.4: Human Disease Diagnosis & Therapy 1
Date: 9 December 2019, Monday
Time: 1045 - 1215
Venue: EA-06-03

Abstract Number: ICBME1472

Nucleic Acid Based Bioengineering and Organic Electrochemical Transistor Based Flexible Bioelectronics

I-Ming Hsing
Hong Kong University of Science and Technology, Hong Kong

Rapid and Sensitive diagnostics of nucleic acid based molecular markers are in critical needs for countries/regions in the South East Asia. Over the years, our laboratory has developed a number of non-optical (e.g., electrochemistry) based sensing strategies with or without analyte amplification procedures, with or without the use of probe immobilization, and with or without the incorporation of enzyme (e.g., polymerase, or exonuclease). In the first half of my talk in nucleic acid based bioengineering, I will discuss platform strategies to achieve rational design of electrochemical DNA biosensors for point of care applications. In particular, the emphasis will be given to our recent approaches exploiting thermodynamics and kinetics of DNA self-assembly to achieve a molecular diagnostic platform that is sensitive, without the use of enzyme and flexible in integrating to various transduction platforms (1-3). In the rest of my presentation, I will introduce organic electrochemical transistor arrays (OECT) for extracellular electrophysiological recording of polarized and excitable cells and discuss the use of this OECT based flexible probe for brain research (4-5).

References

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**Lupus Affects Total Hip Arthroplasty Outcomes**

Jasvinder Singh, John D. Cleveland
*University of Alabama at Birmingham, USA*

**Objectives:** Hip osteonecrosis and hip osteoarthritis are common causes of severe hip disease in lupus, treated successfully with a total hip arthroplasty (THA). Comprehensive analyses for complications after THA are lacking. Our objective was to assess the risk of specific post-THA outcomes, i.e., infection, transfusion, revision and mortality and associated health care utilization, associated with lupus.

**Methods:** We used the 1998–2014 U.S. National Inpatient Sample data. Multivariable-adjusted separate Cox proportional hazard regression models assessed the association of lupus with post-operative complications (infection, transfusion, THA revision and mortality) and health care utilization outcomes (total hospital charges, discharge to inpatient facility, length of hospital stay) post-THA, adjusting for demographics, underlying diagnosis, comorbidity, insurance payer, and hospital characteristics, using hazard ratios (HR) and 95% confidence intervals (CI).

**Results:** Among 4,116,485 primary THA hospitalizations, 22,557 (0.5%) were in lupus patients. Patients with lupus were younger, more likely to be female, African-American or Hispanic and, have higher comorbidity, Medicaid insurance payer, lower income, or living in the South. In multivariable-adjusted analyses, lupus was associated with a significantly higher risk of infection, transfusion, hospital charges above the median ($37,658) and discharge to inpatient facility, length of hospital stay) post-THA, adjusting for demographics, underlying diagnosis, comorbidity, insurance payer, and hospital characteristics, using hazard ratios (HR) and 95% confidence intervals (CI).

**Conclusions:** Lupus was associated with a higher risk of infection and transfusion and higher hospital charges post-primary THA. Insight into modifiable factors associated with these outcomes may improve outcomes in lupus patients undergoing THA.

Abstract Number: ICBME1022

**Adopting a Three-Dimensional Beads Array Design for Quick Isolation of Circulating Tumor Cells**

Sung-Chi Tsai, Doong Howard
*LifeCode Biotech Co., LTD, Taiwan*

We report a novel microfluidic platform which accomplishes a rapid circulating tumor cell (CTCs) isolation process. This new microfluidic platform, named CTC SCANNER, features extremely low limit of detection, high specificity and low cost. Adopting an automatic three dimension column like microfluidic channels, CTCs from human whole blood can be easily separated out in our device.

Circulating tumor cells have been extensively explored as a potential tool for diagnostics and prognostics of cancers. Among all the CTC isolation instruments, Cell Search™ system is the first company to get FDA approval. However, false positive issue still remains a big challenge in beads-based positive selection [1]. In addition, isolated cancer cells may not survive and cells could be injured after a long-time incubation and mixing. To resolve these problems, we had presented two novel microfluidic platforms for CTC isolation in the 2017 MicroTAS conference [2]. We now focus on high throughput dynamic flow and how to increase limit of detection. Furthermore, we create curved channels to promote disturbing flows to let cells roll and interact with the beads. Since this process does not require blood sample pretreatment, it will save time and prevent cell damages due to long-term incubation.

In this study, we report a microfluidic platform to isolate CTCs directly from human whole blood. We design a micro-ladder to lock the EpCAM-coated polystyrene beads in the mixing chamber and the beads form arrays in the microfluidic channel. The curved, wavy design will enhance the rolling and mixing of the cells, which results in high capture efficiency. Figure 1 illustrates how CTCs can be retained on the beads surface in the microfluidic chip. The novelty of this microfluidic chip is to increase CTC recovery rate using static beads arrays to capture CTCs from dynamic flow in an automatic fashion (Figure 2). The photos show MCF-7 cancer cells are captured by beads arrays which was taken by a high speed CCD camera. In brief, we confirm our structure design can increase the chances for cells to roll across to all beads surface. This method can reduce non-specific binding, only cancer cells are retained on the beads surface and blood cells may keep flowing away.

To optimize the recovery efficiency of CTCs and increase cell survival rate, vacuum pump used as a power supply source in this experiment. The recovery rate and survival rate of the CTCs under different pressure have been tested in Figure 3. Most importantly, we have demonstrated significant improvement of detection limits and lower down false positive rate of CTCs from a testicular cancer patient (figure 4). Our data shows that the microfluidic device we designed captured less white blood cells compared with using other platform (2 vs 528 cells) [3-4], indicating that our instrument has a lower false positive rate. Table 1 summarizes the CTC limit of detection tests we conducted. The entire process is completed automatically with our CTC SCANNER platform.

Abstract Number: ICBME1092

**Cryocompression for Preventing Chemotherapy-Induced Peripheral Neuropathy**

Aishwarya Bandla, Gayathiri Magarajah, Lee Soo Chin, Einar Wilder-Smith, Nitish Thakor, Raghav Sundar
*National University of Singapore, Singapore*

**Objectives:** Severe chemotherapy-induced peripheral neuropathy (CIPN) is a common dose-limiting toxicity of several chemotherapeutics, with no effective treatment. Recent studies suggest that limb hypothermia is neuroprotective in CIPN. Current methods such as ice packs are unable to achieve deep and continuous hypothermia, limiting efficacy. Here, in a 2-phased study, we investigated the optimal method of limb
hypothesis and assessed the safety and tolerability in healthy subjects and then in breast cancer patients, prior to assessing its efficacy in preventing CIPN. We compared the following modalities of limb hypothermia – continuous-flow cooling vs cryocompression. The proposed hypothesis represents a novel, non-invasive, non-pharmacological therapy to prevent CIPN.

Methods: Healthy subjects underwent limb hypothermia of 3h for temperature thresholding and assessing safety and tolerability. Continuous-flow cooling was tested between coolant temperatures 25-21°C and cryocompression between 21-10°C at low cyclic compression (5-15 mmHg). Skin temperatures were monitored and tolerability was evaluated using various clinical scores. Subsequently, a proof-of-concept study was conducted in breast cancer patients receiving adjuvant taxane chemotherapy. Limb hypothermia was carried out concomitantly with every chemotherapy cycle (3h) for a maximum of 12 cycles, at temperatures determined optimal from the healthy volunteer studies. Skin temperature and tolerance scores were monitored. Neuropathy was assessed using nerve conduction studies (NCS) conducted before (NCSpre), after (NCSpost) and 3-months post chemotherapy (NCS3m).

Results: In phase 1, 15 healthy subjects and 14 cancer patients aged between 21-70 years were recruited to undergo 3h continuous-flow limb cooling. In the healthy subjects, we achieved a minimum tolerated coolant temperature of 22°C. Following on, 14 breast cancer patients underwent a total of 168 cycles of cooling. A mean skin temperature drop of 2.2±1.1°C was achieved in the cooled limbs. Tolerability scores were well within limits with no early termination of cooling. Minimal discomfort, numbness and skin discoloration was reported with no lasting adverse effects in all cohorts. In phase 2, 36 healthy volunteers and 28 cancer patients were recruited to undergo cryocompression therapy. Coolant temperatures as low as 11°C were well tolerated continuously over 3h with no long-lasting adverse effects. Twenty-eight patients then underwent a total of 320 cycles of cryocompression administered at 11°C (moderated according to tolerance). Mean skin temperature reduction of 4.7±1.0°C was achieved in the cooled limbs and was well tolerated. Only 8 out of 28 patients required an intra-cycle temperature increase, with no early termination of cryocompression. NCS analysis showed significant preservation of motor amplitudes at NCS3m compared to baseline. Sensory nerve amplitudes showed a reduction at NCSpost compared to baseline but continued to be preserved at NCS3m.

Conclusions: Limb hypothermia is safe and well-tolerated by healthy subjects and breast cancer patients. Cryocompression permitted hypothermia delivery at significantly lower temperatures compared to continuous-flow cooling, with similar safety profile. In breast cancer patients, multiple cycles of 11°C cryocompression lasting the duration of chemotherapy were safe, well tolerated and showed initial efficacy signals of motor nerve preservation. Cryocompression may provide greater efficacy in preventing CIPN, with clinical trials currently ongoing (NCT03248193).

Abstract Number: ICBME1378

Prediction of Evolving Readmission Risk in Heart Failure Using Multivariate Clinical Time Series Data

Guo Yang, 1Shao Chuen Tong, 2Fahimi Fatemeh, 3Angela Ng, 4Oh Hong Choon, 4Wai Leng Chow, 4Michael R. Macdonald, 4Sheldon Lee, 4Savitha Ramasamy*, 4Pavitra Krishnaswamy*
1 Machine Intellgence Department, Institute for Infocomm Research, Singapore
2 Health Services Research, Changi General Hospital, Singapore
3 Health Management Unit, Changi General Hospital, Singapore
4 Department of Cardiology, Changi General Hospital, Singapore
5 Machine Intellgence Department, Healthcare Division, Institute for Infocomm Research, Singapore

Congestive heart failure (CHF) is a leading cause of hospitalization among the rapidly growing elderly demographic. A high proportion of hospital visits are return visits due to exacerbation, with over 25% of discharge patients readmitting within 30-180 days of discharge in many systems. In order to address these challenges, clinical systems are increasingly investing in data-driven models to predict risk of hospitalization to enable proactive target treatment and optimization of care management. Despite much progress in this field and well-known clinical predictors, developing robust and actionable risk prediction models remains an unmet need.

One challenge is that readmission risk models developed at one point in the disease progression may not generalize well as the patient stage evolves. Further, many previous readmission risk prediction studies merely analyze data from the most recent assessment or one admission episode, resulting in suboptimal performance. To address these limitations, we investigate the use of longitudinal clinical time series data for dynamic prediction of utilization risk in CHF patients.

We base our study on retrospective clinical time series data acquired longitudinally during every hospital visit for 1268 CHF patients during 2012-2017. The dataset comprises fixed socio-demographic and clinical history information, as well as multivariate time series features including vitals, cardiovascular and renal biochemical markers, cardiovascular investigation results, and administrative records. Overall, we have tens of thousands of variable length trajectories comprising multivariate time series features from 13, 220 hospitalization events for this cohort over the study duration. The prediction task comprises mapping the input data features to the output risk of 180-day readmission events over time. To account for the temporal correlations and evolution, we employ deep recurrent neural networks, such as Long Short Term Memory (LSTM) networks for this problem. The output of the model is a trajectory of evolving 180-day readmission risk for each patient.

We demonstrate feasibility for this dynamic prediction task and quantify performance using AU-ROC, AU-PRC and accuracy. We find that predictions made using clinical time series data are more accurate than predictions that use data from one-off episodes. Our results have implications for improving the relevance of risk predictions for patient stratification and treatment targeting across a variety of conditions.
Robot-Assisted Therapy Improves Task and Motor Performance in the Upper Extremities of Chronic Stroke Patients

Hsien-Yun Hsu
National Cheng Kung University, Taiwan

Restoring the upper limb motor function is the best practice recommendation for post-stroke rehabilitation. Recently published guidelines propose high-intensity and high-repetition rehabilitation program is optimal for restoring upper extremity motor functions in stroke survivors. Robot-assisted rehabilitation, a kind of augmented motor learning technique, has been shown to help patients develop effective encoding strategies. The experience of normal proprioceptive feedback and neurophysiological adaptation through repetitive and intensive movement practice can help restore patients’ motor capability in affected upper limbs. Moreover, robot-assisted therapy increases the amount of rehabilitation time without requiring additional therapist manpower. At present however, evidence is insufficient to integrate a robot-assisted therapy for the paretic upper extremity into stroke rehabilitation with a view to improving upper extremity motor impairments or disabilities.

In the first part of the talk, I introduce the fundamentals of robot-assisted therapy for the paretic upper extremity. In the second part, the effects of training program delivered using an end effector and an exoskeleton upper extremity robotics are demonstrated. And then, a portable, easy-to-wear and affordable 3D printed exoskeleton robotic device for tenodesis-grip training for the stroke patients developed by Motion Analysis Laboratory of National Cheng Kung University are illustrated in the third part.

Abstract Number: ICBME1495

Toward the Soft Robotic Hand for Stroke Rehabilitation

Zheng Li, Kelvin Holam Heung, Zhiqiang Tang, Raimond Kaiyu Tong
Chinese University of Hong Kong, Hong Kong

Objectives: Stroke is the second leading cause of death and the third leading cause of disability. Impaired hand function is the most frequently persisting consequences of stroke. Recovery of motor control after the stroke occurs most rapidly during the first 3 months and usually plateauing by 6 months. This requires the easy access of hand rehabilitation and quantitative feedback to the training effects. Commercial hand rehabilitation robots are expensive and the hand function recovery is mostly by subjective evaluation, such as the ARAT and MAS score. In this work, we intend to propose a low cost robotic hand that could assist the repetitive training tasks as well as quantitatively evaluate the patient’s hand condition simultaneously.

Methods: A soft robotic hand contains five finger actuators is developed. The finger actuator design follows the serial elastic composite actuator (SECA), which contains a silicon body and an elastic torque compensating layer for extending the spastic finger. The flexion is achieved by pneumatic pressure supplied to the silicon body. Both the finger actuator and the finger are modeled as the second order system. They are controlled with the model based online learning adaptive control algorithm. At the end of the training, the finger model is extracted from the learned dynamic model for evaluating the finger condition. Six subjects were recruited, including three normal subjects and three stroke subjects. The index finger is used for evaluation.

Results: The 3D printed soft robotic hand is lightweight and cost effective. Under a pressure of 160 kPa, the overall bending angle could reach 137° (76° for MCP segment and 61° for PIP segment). The force generated at the fingertip is 2.45 N. By applying the finger actuator to a wooden finger (MCP stiffness 1.03 Nm/rad, initial angle 26°; PIP stiffness 1.25 Nm/rad, initial angle 50°), the MCP returns to 4° and the PIP was brought back to 10°. The stiffness term in the dynamic model is used to evaluate the finger condition. For the three normal subjects, the average stiffness term (N/(kg*m*radian)) for MCP and PIP are 105.77 and 74.04 respectively. For the three stroke subjects the average stiffness term for MCP and PIP are 356.56 and 246.56, which showed significant difference compared with that of normal subjects (p<0.005).

Conclusions: The developed soft robotic hand could effectively extend and flex the spastic finger for repetitive training tasks. Moreover, it could quantitatively evaluate the stiffness condition of the finger after the training. This paves the way for training effect online evaluation and would lead to a smart rehabilitation robot.

Abstract Number: ICBME1510

Affordable Assistive Devices for Movement Disability

Sujatha Srinivasan
Indian Institute of Technology Madras, India

The TTK Center for Rehabilitation Research and Device Development (R2D2) headed by Prof. Sujatha Srinivasan in the Department of Mechanical Engineering at IIT Madras focuses on the development of orthotic, prosthetic and assistive devices that are biomechanically and economically suited to lifestyles and conditions in low-resource settings. Her talk will describe some of the devices currently being developed and field-tested, and present a model for affordable commercialization. Devices under development include a standing wheelchair, a prosthetic knee, a body-motion wheelchair, an add-on that converts a regular wheelchair into an outdoor mobility device, and rehabilitation robots for the upper limb. The standing wheelchair is ready for production and will be launched soon. Prof. Srinivasan’s group collaborates extensively with medical professionals, organizations working in the disability sector, and industry. Her work is supported by grants from government funding agencies, alumni, the Wellcome Trust, UK and industries such as the TTK group, among others. More details are available at https://home.iitm.ac.in/r2d2.
Rehabilitation Robotics
Vincent Crocher
University of Melbourne, Australia

Upper-limb neurorehabilitation is challenging due to the biomechanical complexity of the upper extremities and the variety of tasks at hand. Robotics devices have been developed and introduced into clinical practice for a number of years. These robotics devices are often either planar manipulanda (end-effector based devices) with limited exercise options or exoskeletons with a relatively complex design and an intrinsically challenging biomechanical compatibility. To overcome the usability problem of exoskeleton type systems while preserving their versatility, we have explored the potential of 3D printing in the design of robotic devices to overcome the limitations of traditional exoskeletons. This talk will focus on the potential use of these 3D printed assistive technologies in healthcare applications.

Abstract Number: ICBME1500

Wearable Sensors and Nanogenerators for Healthcare Applications
Chengkuo Vincent Lee
National University of Singapore, Singapore

Healthcare monitoring and rehabilitation treatment in both clinical and non-clinical environment have been envisioned for a long time. Wearable electronic systems have been demonstrated to be a promising technology allowing people to be monitored during their daily activities and help them by providing healthcare services such as medical monitoring, environmental monitoring, and rehabilitation treatment in daily life. Textiles with unique and promising advantages of flexibility, deformability, breathability, comfortability, and unobtrusiveness have been demonstrated to be promising for body sensor networks. Here we report a simple and large-scale immersion-coating method of the conductive polymer directly on commercial textile to create an energy harvesting textile based on the triboelectric mechanism with versatile functions. This textile-based triboelectric nanogenerator can scavenge waste energy from different body sites and provides diversified applications.

Abstract Number: ICBME1521

EsoGlove - Soft Robotics for Hand Rehabilitation
Raye Yeow Chen Hua
National University of Singapore, Singapore

The world is facing an ageing population, with a corresponding increase in number of patients suffering from age-related diseases, such as stroke. Hand motor impairment is very prevalent, particularly for stroke. The common rehabilitation approach for stroke patients involves standard physical therapy, which is both time and labour-intensive. We developed the EsoGlove which is a soft robotic glove system, capable of providing automated rehabilitation through robot-assisted hand/finger flexion-extension. This system enables the users to carry out activities of daily living and acts as an adjunct to occupational therapists in carrying rehabilitation, thus improving their productivity, especially given limited manpower and growing greying population. In this talk, I will present the design and characterization of the different generations of EsoGlove, and the associated clinical trials that demonstrated its efficacy. I will also cover the evolution of EsoGlove into a viable rehabilitation product adopted by hospitals around the world.

Abstract Number: ICBME1518

A Robotic Platform Integrated with FES for Gait Rehabilitation
Haoyong Yu
National University of Singapore, Singapore

This talk presents a novel omnidirectional platform for gait rehabilitation of people with hemiparesis after stroke. The mobile platform, henceforth the “walker”, allows unobstructed pelvic motion during walking helps the user maintain balance and prevents falls. The system aids mobility actively by combining three types of therapeutic intervention: forward propulsion of the body’s center of mass, controlled body weight support, and functional electrical stimulation (FES) for compensation of deficits in angular motion of the joints. FES is controlled using gait data extracted from a set of inertial measurement units (IMUs) worn by the user. The resulting closed-loop FES system synchronizes stimulation with the gait cycle phases and automatically adapts to the variations in muscle activation caused by changes in residual muscle activity and spasticity. A pilot study was conducted to determine the potential outcomes of the different interventions. One chronic stroke survivor underwent five sessions of gait training, each one involving a total of 30 minutes using the walker and FES system. The patient initially exhibited severe anomalies in joint angle trajectories on both the paretic and the non-paretic side. With training, the patient showed progressive increase in cadence and self-selected gait speed, along with consistent decrease in double-support time. FES helped correct the paretic foot angle during swing phase, and likely was a factor in observed improvements in temporal gait symmetry.

Abstract Number: ICBME1528
In conclusion the talk introduces wireless battery free sensors and stimulators that match mechanical and physical properties of biological systems to deliver clinical grade data streams and stimulators and inhibitors will be highlighted. These highly miniaturized systems enable untethered, operation for behavioral studies that eliminate motion constraints and enable new experimental paradigms in a range of complex 3D environments and contexts (e.g. social interactions) that cannot be explored with conventional technologies. We extend this concept to devices with capabilities in multimodal stimulation of the brain and the peripherals resulting in a broad suite of modulation and recording tools for the nervous system and major organs such as the heart.

In this talk, I will describe our work on wireless technologies for bioelectronics and their applications in medicine. I will present our approaches to wirelessly power and extract data from deeply implanted microdevices that are not accessible by conventional means, and discuss how these technologies can enable new therapies, including a targeted form of cancer treatment based on the wireless delivery of light. I will also highlight our approach to efficiently and securely interconnect wireless networks of wearable sensors using metamaterial textiles, inspired by the way that light propagates on metallic surfaces.”

Abstract Number: ICBME1048

Soft, Wireless and Battery Free Sensors and Photonics for Broad Application in the Assessment and Stimulation of Biological Systems

Philipp Gutruf
University of Arizona, USA

Recent advances in materials and fabrication concepts for the creation of soft electronics coupled with miniaturization of wireless energy harvesting schemes enable the construction of high-performance electronic and optoelectronic systems with sizes, shapes and physical properties matched to biological systems. Applications range from continuous monitors for health diagnosis to minimally invasive exploratory tools for neuroscience.

This talk presents science and engineering aspects for the creation of soft devices with near field power transfer and data communication capabilities and discusses application in imperceptible body-worn devices for the assessment of hemodynamics, sweat and thermal properties of the skin. Here sensor performance with distinct improvement in sensor fidelity with respect to rigid counterparts is shown alongside resistance to motion, resulting in an attractive platform for the use in digital health applications.

Building on these advances in resonant power transfer opportunities for highly miniaturized embodiments for the deployment as subdermal neuroscience tools for wireless recording and stimulation of genetically targeted indicators, stimulators and inhibitors will be highlighted. These highly miniaturized systems enable untethered, operation for behavioral studies that eliminate motion constraints and enable new experimental paradigms in a range of complex 3D environments and contexts (e.g. social interactions) that cannot be explored with conventional technologies. We extend this concept to devices with capabilities in multimodal stimulation of the brain and the peripherals resulting in a broad suite of modulation and recording tools for the nervous system and major organs such as the heart.

In this talk, I will describe our work on wireless technologies for bioelectronics and their applications in medicine. I will present our approaches to wirelessly power and extract data from deeply implanted microdevices that are not accessible by conventional...
Abstract Number: ICBME1499

Applications of Wireless Technology for Biomedicine

Sanghoek Kim
Kyung Hee University, Korea

Recent development of wireless interfaces in biomedical applications using electromagnetic wave are reviewed. First, the talk introduces the analytical bound on the efficiency of wireless power transfer to a miniature implant and its implementation. The optimal source is physically synthesized using a slot array structure whose performance is quite close to the theoretical bound. The development of highly efficient power delivery system miniaturizes a cardiac neurostimulator to a millimeter scale, removing energy storage from the device. The neurostimulator is demonstrated on a rabbit. As a second example of wireless interfaces for biomedical applications, this talk demonstrates a method to assess ones abdominal fatness using electromagnetic waves. It shows the feasibility that the thickness of the fat can be estimated by measuring the frequency where the wave reflection is minimized.

Abstract Number: ICBME1044

3D Printing of Functional Electronics and Ingestible Biomedical Devices

Yong Lin Kong
University of Utah, USA

My research group focuses on the development of 3D printing technologies to create multifunctional structures and devices that cannot be fabricated with conventional fabrication methods. We seek to advance the scientific understanding of the assembly and processing of functional nanomaterials to functionalize a wide range of constructs. We develop a multi-scale, multi-material additive manufacturing approach that is fundamentally free from the constraint of the conventional two-dimensional, top-down fabrication methodologies to achieve a seamless integration of a diverse classes of materials. The freeform fabrication approach could overcome the geometrical, mechanical and material dichotomies between conventional manufacturing technologies and a broad range of threedimensional systems. As an example, I will first highlight the development of 3D printed quantum-dots light-emitting diode, which extended the reach of 3D printing and demonstrated that active electronic materials and devices can be entirely 3D printed. In the second part of the talk, I will highlight the latest development of a 3D printed gastric resident electronics system, which leverage the significant space and immune-tolerant environment available within the gastrointestinal tract to circumvent the potential complications associated with surgically placed medical implants. Ultimately, we strive to address unmet clinical needs by creating tailor able three-dimensional free-form biomedical devices with 3D printing technologies.

Abstract Number: ICBME1331

Body Area Network: Connecting Things Together Around the Human Body

Jerald Yoo
National University of Singapore, Singapore

Body Area Network (BAN) connects on/in body sensors, and this is an attractive method for realizing healthcare, medical or multimedia applications. RF-based wireless standards such as Bluetooth, Medical Implant Communication Service (MICS) are not ideal for medical/healthcare BAN applications due to their limited data rate, high power consumption, and most importantly, body shadowing effects: the human body absorbs the majority of energy in GHz range. Body Coupled Communication (BCC) utilizes the human body itself as a transmission medium, and it provides higher data rate (~10Mbps), has low power consumption and is free from Line-of-Sight (LoS) requirement.

There are largely three mechanisms in BCC: 1) galvanic, 2) magnetic resonance and 3) capacitive coupling. In galvanic coupling, both TX and RX sides have two electrodes each; the differential signal then induces a galvanic current that propagates through the skin. This method is resilient to external environmental variation. However, due to its high path-loss, this is applicable when the communication distance is less than a foot.

Magnetic resonance coupling adopts two resonant coils around the body. As far as the magnetic resonance is kept constant, this is an energy efficient method thanks to lower channel pathloss. However, due to the TX/RX coil form factor may not be suitable to be applied on the torso.

In capacitive coupling, TX and RX each have a signal electrode (no explicit ground electrode is present). The forward path is through the body, and return path is formed by parasitic ground of TX / RX as well as body in between. This is more energy-efficient when compared to galvanic signaling, but the return path formed by parasitic ground means a huge fluctuation in RX receiving signal strength, and is a challenge. The capacitive coupling is preferred choice if transmission distance should cover from an entire body, or the form factor requirement does not allow two electrodes (galvanic) or a coil around the point (magnetic resonance).

All three BCC mechanisms are affected by varying channel gain and environmental change, although there is a trade-off between coverage over channel reliability. In specific, channel gain may vary over the subject, posture, and communication distance. Therefore, proper compensation is needed. It is also important to note that in galvanic and capacitive coupling, electrodes are attached to the human body, and the attaching strength affects the channel gain. Therefore, the skin-electrode impedance monitoring and TX/RX adaption may be necessary.

When it comes to BAN, we should note that a PHY TRX energy efficiency does not necessarily directly translate into BAN system energy efficiency; this is because of the MAC/ network layer also affects the systemwise efficiency significantly. For In BCC BAN, it is found that the simple star network consumes less overall energy than the ad-hoc counterpart.
Nanobiodevices, Quantum Technology, and AI for Precision Medicine and Future Healthcare

Yoshinobu Baba
Nagoya University, Japan

We have devolved nanobiodevices, quantum technology, and AI for biomedical applications and healthcare, including single cell cancer diagnosis for cancer metastasis, circulating tumor cell (CTC) detection by microfluidic devices, nanopillar devices for ultrafast analysis of genomic DNA and microRNA, nanopore devices for single DNA and microRNA sequencing, nanowire devices for exosome analysis, single-molecular epigenetic analysis, AI-powered nano-IoT sensors, quantum switching intra vital imaging of iPS cells and stem cells, and quantum technology-based cancer theranostics. Immuno-wall microfluidic devices realized the fast and low invasive “from blood to analysis” type biomarker detection of cancer with fM detection sensitivity within 2 min. Additionally, nanopillar nanofluidic devices give us ultrafast separation of DNA and microRNA within 60 μs and nanopillar-nanopore integrated nanobiodevice enables us ultrafast single molecular DNA sequencing. Nanowire devices are extremely useful to isolate extracellular vesicles from body fluids and vesicle-encapsulated microRNA analysis. The device composed of a microfluidic substrate with anchored nanowires gives us highly efficient collections of extracellular vesicles in body fluids and in situ extraction for huge numbers of miRNAs (2,500 types) more than the conventional ultracentrifugation method. Nanowire devices gave us the miRNA data for several hundred patients and machine learning system based on these miRNA data enabled us to develop the early-stage diagnosis for lung cancer, brain tumor, pancreas cancer, liver cancer, bladder cancer, prostate cancer, diabetes, heart diseases, and Parkinson disease. Nanowire-nanopore devices combined with AI (machine learning technique) enable us to develop mobile sensors for PM2.5, bacteria, and virus in the environment. Quantum dots and nanodiamonds with nitrogen-vacancy centers are applied to develop quantum-biodevices for single cancer cell diagnosis, single molecular epigenetic analysis, quantum switching intra vital imaging for iPS cell (induced pluripotent stem cells) based regenerative medicine, and quantum photo-immuno-therapeutic devices for cancer diagnosis/therapy.

Abstract Number: ICBME1506

Single Cell Biosensors for Dynamic Multigene Analysis in Complex Tissue Environments

Pak Kin Wong
Penn State University, USA

Objective: Heterogeneity is a common feature of biological systems. The heterogeneity across multiple...levels collectively drives a variety of biological processes, such as tissue morphogenesis, cancer invasion, and microbial host interactions. Conventional biosensing approaches for characterizing molecular and cellular heterogeneity, however, are often limited due to the requirement of a large number of cells. Furthermore, the existing single cell analysis techniques often require physical isolation or lysis of cells to “snapshot” RNA and protein biomarkers in a small subset of cells. Features of the complex microenvironment, such as hierarchical organization and dynamic cellular processes, are inherently lost by studying cells in isolation, fixation, and lysis.

Methods: To address this challenge in biomedical research, we are developing a nanobiosensing platform to enable dynamic single cell gene expression analysis in complex tissue environments.

Results: In particular, we design nanoengineered probes that enable endocytic uptake for real-time, dynamic intracellular detection of mRNA/miRNA, protein, and small molecules in living cells. In this keynote presentation, I will discuss the application of the nanobiosensing platform for probing leader cell formation during wound healing and bladder cancer heterogeneity.

Conclusion: The ability of the single cell nanobiosensor to perform multigene analysis in live cells will provide a valuable tool for deciphering the regulation of collective cell migration during tissue regeneration and wound healing.

Abstract Number: ICBME1197

Production of Extracellular Matrix Mimic with Tunable Stiffness and Its Use for Cancer-On-a-Chip Applications

Jyothsna Vasudevan, Lim Chwee Teck, Javier Gomez Fernandez
Singapore University of Technology and Design, Singapore

Tumor growth and progression has been widely known to be influenced by the mechanics of its microenvironment. In comparison to healthy tissues, there is an abnormal increase in the stiffness of tumor extracellular matrix (ECM) owing to increased deposition of proteins and enhanced crosslinking density of collagen fibrils. It is important to understand how tissue stiffening increases the invasiveness of the tumor to develop novel therapeutic interventions targeting this mechanotransduction machinery. Current 3D tissue mimics explore concurrent effects of crosslinking density, ligand
concentrations and matrix pore sizes on tumor cell invasion. This convolution of parameters often makes it challenging to precisely understand the contribution of matrix stiffness, which is known to independently and significantly contribute to tumorigenesis. In this study, we aim to decipher the effects of stiffness of Gelatin Methacylate (GelMA) hydrogel based artificial ECM mimics on breast cancer cell behavior. We aim to precisely control the stiffness of the artificial ECM matrices, independently of other variables, by fine-tuning their degree of cross-linking with micrometric control of geometry. GelMA hydrogel variants were synthesized with varying degrees of functionalization (DoF). Fabrication of 3D matrices with elasticity spanning a more physiologically relevant range of ECM stiffness was achieved by varying the DoF. Long term cell viability of breast adenocarcinoma cells (MCF7) was observed regardless of the degree of chemical modification. Cells exhibited lamellipodial protrusions in matrices of low and intermediate elastic modulus as opposed to those embedded in matrices of higher elasticity, suggesting strong influence of matrix biophysical cues on cell behavior. Real time cell tracking analysis revealed higher migration rates in hydrogels of lower stiffness in comparison to gels of higher stiffness. Our findings can aid in the development of mechanically tunable materials to unravel the biophysical factors that contribute to cancer cell migration phenomena in physiologically relevant 3D tumor models.

Abstract Number: ICBME1037

Increased Hydrostatic Pressure Affects Vascular Endothelial Cell Behavior

Satomi Hirose, Kenichi Funamoto, Daisuke Yoshino
Tohoku University, Japan

Introduction: Chronic hypertension induces vascular endothelial dysfunction, leading to serious vascular diseases such as arteriosclerosis. However, the detailed mechanism underlying vascular endothelial dysfunction due to hypertension remains unclear. Influences of increased blood pressure on vascular endothelial morphology and function is also incompletely understood. Here, we show different behavior of vascular endothelial cells depending on the magnitude of hydrostatic pressure.

Methods: Human umbilical vein endothelial cells (HUVECs) from the fifth to ninth passages were cultured in Medium 199 containing 20% heat-inactivated fetal bovine serum (FBS), 10 µg/L human basic fibroblast growth factor, and 1% penicillin/streptomycin (P/S) to reach confluence. HUVECs were then exposed to hydrostatic pressure using our previously reported system filled with Medium 199 containing 10% FBS and 1% P/S. The cells were exposed to a hydrostatic pressure of 0, 50, 100, or 150 mmHg. We first examined morphology in HUVECs after exposure to hydrostatic pressure. After 24-h exposure to each pressured condition, cell nuclei were stained with Hoechst 33342, and areas of the whole cell and nuclei were measured with an inverted phase-contrast and fluorescence microscope. We next analyzed changes of protein expression in HUVECs by hydrostatic pressure applied in the present study. Expression level of retinoblastoma protein, which has a crucial role in regulating the cell cycle, was significantly decreased after the HUVECs were cultured under the pressured conditions for 24 h. In addition, an expression level of endothelial nitric oxide synthase (eNOS) was significantly decreased after 3-h exposure to the pressure of 150 mmHg. These indicate that HUVECs exhibited the opposite morphological responses with increasing pressure and changes in expression of eNOS might be related to regulating them.

Conclusion: This study showed hydrostatic pressure loading affects behavior of vascular endothelial cells. In particular, the increased pressure (150 mmHg) induced different vascular endothelial morphology in comparison with physiological levels of hydrostatic pressure (50-100 mmHg). These results provide important information for elucidating the mechanisms underlying vascular endothelial dysfunction due to hypertension.

Abstract Number: ICBME1257

Emerging Oscillation in Confined Collective Cell Motion Due to Geometry-Defined Polarization

Jing Yu, Pingqiang Cai, Xiaodong Chen
Nanyang Technological University of Singapore, Singapore

Biological processes such as morphogenesis, angiogenesis or embryogenesis involves group of cells coordinating their movements collectively to achieve specific functions, in a constricted fashion. Unlike single cell, collective cellular motions, which involve intercellular coordination, are much more complex and largely remain mysterious. Variances in environment could easily lead to changes in cell behaviors; factors such as chemical, physical or mechanical signals are common regulators in guiding cell migration. Among these factors, topological cue is a critical, yet easily neglected factor. Different from most benchside scenarios, in which migrations are allowed on infinite surfaces, the physiological microenvironment of cellular migration is usually confined.

Here we show that motion of cell cohort could be modeled through topological cues and confinement. In our experiment, geometrical confinement are established to modulate collective cell motions. Madin-Darby Canine Kidney (MDCK) cells was cultured on confined micropatterns, with both different geometrical patterns and varying aspect ratios. On such patterns, cell cohorts manifested coherent motions with persistent oscillations in orthogonal directions, which was best observed on patterns with the aspect ratio of 1. Increased aspect ratios resulted in diminished coherency, whilst the oscillation behavior persists. With the pattern size increasing, discrete small clusters started to emerge in the cell monolayer and each cluster move coherently and independently. This formation of smaller cell cohorts disrupted the coordinated collective motion and led to sluggish oscillations. Mechanical analysis revealed that this phenomenon seemed correlated with the effect of collective polarization: cells on smaller patterns were more structurally and mechanically polarized, due to higher degree of constrain; they were highly aligned and thus tended to move according to their packing direction.
Initial Metastatic Pattern of Three-Dimensional Bladder Multicellular Tumor Spheroid at Heterogeneous Matrix Interface

Ting-Yuan Tu, Roger D. Kamm, Jean Paul Thiery
National Cheng Kung University, Taiwan

Objectives: The ability to mimic physiological cancer microenvironment and tumor three-dimensional (3D) structures may be critically important in the study and prevention of the various processes in metastasis. In fact, tumor cells that metastasized in patients have been discovered to favor migration in existing bone cavities or between adipocyte, indicating that the ECM structural arrangement may aid cell dissemination. Thus, this study aims to establish an in vitro model for 3D multicellular tumor spheroids (MCTS) invasive hydrogel platform that captures part of the bladder histological arrangement for studying BC cell migration at heterogeneous matrix interface. Considering that BC metastasis is initiated by cell dispersion from a solid tumor through different tissue layers of the bladder, this approach allows the study of how ECM architectural and compositional context affect the initial process of cancer delamination. Understanding the early metastatic pattern and the factors influencing different modes of cell migration may further provide insights to the development of BC metastasis.

Methods: T24 bladder cancer cells were formed into size-controlled 3D MCTS in four days, followed by collection and mixing with type I collagen. The MCTS-embedded collagen gel was then placed on top of a PDMS surface to create an artificial matrix interface. The initial position of the MCTS was located near the interface after gel polymerization at 37ºC.

Results: The process of an early metastatic pattern of a BC MCTS is shown. The upper layer of the MCTS faced the ECM region that exhibited persistent radial cell invasion from 12 h onwards; the lower part faced the matrix interface, where the MCTS displayed a more prominent migratory behavior. Formation of a ring structure was observed in the lower part of the MCTS at 12 h, in which a few cells were arranged into a circular shape along with some cells extended protrusions. ECM structure integrity was concurrently visualized by reflectance imaging, indicating that the matrix disruption (void space) was appeared at 6 h prior to cell invasion at 12 h. By comparing the occupied area in degraded matrix vs invaded cells, a rapid disruption, potentially through cell contractions, can be observed in the ECM at 6 h which corresponds to the “ring” formation, and then slowly followed by the later invasion.

Conclusions: A preliminary experimental model for studying the BC MCTS invasion at heterogeneous matrix interface was demonstrated to be potentially useful for studying the process of early metastatic pattern of BC development. Further investigations may shed light on identifying new strategies for the prevention of early BC metastasis.
Background: Current medicine, which is predominantly based on small molecule drugs, has only taken us so far in beating disease and tissue degeneration. Extracellular vesicles (EVs), which are highly specialized, yet ubiquitous nanoscale messengers secreted by cells have emerged as the new generation of medicine. The problem is, their power cannot be harnessed because they are heterogeneous, and little is known about them.

Aim: To determine the molecular composition of individual EVs, populations, and subpopulations and define the correlation between the molecular composition of EVs and their therapeutic efficacy for tissue repair and regeneration.

Method: To characterize what is inside individual vesicles we developed a methodology that utilizes the ultra-high-resolution capability of atomic force microscopy nano-infrared spectroscopy (NanoIR). Our study showed that EVs isolated from different types of placental stem cells, which are exposed to the different level of oxidative stress, have major differences in protein, RNA/DNA and lipid contents. We further cross validate AFM-IR technique with the nanoflow analyzer (nanoflow cytometry, NanoFCM) to determine the concentration of nucleic acids (RNA/DNA), proteins and membrane lipids of EVs. We also studied the effects of different purifications of EVs using ultracentrifugation, tangential flow filtration, and size exclusion column, and indeed we demonstrated that the molecular composition, i.e. protein, is substantially different for EVs depending on purification method. Analyzing these variations at the nanoscale may also provide robust evidence of pathological processes – diagnostic applications.

Taken together, there is a potential for AFM-IR coupled with NanoFCM to be utilized as highly sensitive, precise and relatively fast measurement of EV structure and composition to determine the most effective EVs purification protocols as well as to gain new knowledge how they are produced to be able to harness their power for diagnostic and therapeutic applications.

Keywords: Extracellular vesicles, AFM-IR, Nano FCM, nano-characterization, EV therapeutics.

Abstract Number: ICBME1188

Comparative in Vivo Evaluation of Perivascular Silk Fibroin Microneedle Meshes for Inhibiting Neointima Formation

Jiyong Lee, Jae Ho Kim, Eui Hwa Jang, Jung-Hwan Kim, Young-Nam Yoon, WonHyoung Ryu
Yonsei University, Korea

Objectives: Endothelium damages of blood vessel after coronary/peripheral bypass graft surgery often cause abnormal proliferation of smooth muscle cells (SMCs) in tunica media, resulting in the decreased arterial lumen space. In order to prevent restenosis or occlusion caused by such neointima (NI) formation, perivascular microneedle (MN) devices including MN cuff and flexible MN meshes have been developed. Both MNs showed significantly reduced NI formation by restricting the excessive proliferation of SMCs of the injured blood vessel as well as improved drug delivery efficiency to the tunica media. However, tensile properties of MN devices needed to be modified to minimize mechanical constriction to the blood vessel. To improve the vascular safety of MNs with localized and secure drug delivery, we have developed highly stretchable MN meshes using natural biocompatible silk fibroin (SF). SF MN meshes could be wrapped around the external surface of vessels and the anti-proliferation drug, Sirolimus (Sir), was released from the MNs into injured vascular tissue. After comparative in vivo animal study, we evaluated the efficacy and safety of perivascular SF MN meshes for inhibiting NI formation.

Methods: SF from bombyx mori cocoon was dissolved in LiBr solution and dialyzed. Aqueous SF solution, mixed with Sir, was cast in MN molds and attached on a lyophilized SF mesh using a transfer molding method. In order to demonstrate the efficacy and safety of SF MN meshes for reducing NI formation, a total of 18 New Zealand white rabbits were prepared for in vivo experiments. Abdominal aorta of rabbit was exposed and de-endothelialized by balloon injury for 3 times. Subsequently, SF MN mesh was conformably wrapped around the lesion of vessel and fixed with a surgical clip. Three animal groups were classified for case-control study. Group A was treated with SF MN mesh without drug. Group B was treated with 1 μg of drug loaded SF mesh without MN structure. Group C was treated with 1 μg of drug loaded SF MN mesh. After 4-week follow up, every lesion of abdominal aorta was harvested and prepared for histopathological/immunohistochemistry analysis.

Results: We fabricated 2 × 4 array of SF MNs with 640 μm of height on a porous and highly-stretchable SF mesh with thickness of 400 μm. Each SF MN mesh was gently applied around the injured blood vessel. As a result of in vivo study, NI was significantly reduced in group C (10.8 %) compared to group A (28.6 %) and B (21.4 %). The results indicated prominent efficacy of Sir for NI formation and high drug delivery efficiency of MNs compared to meshes even though the same amount of drugs were loaded. Additionally, immunohistochemistry analysis showed the negative activities of inflammation in blood vessel as well as positive vascular endothelialisation.

Conclusions: We developed SF MN meshes for reducing NI formation by supressing the proliferation of SMCs. After 4-week animal study, excellent drug delivery efficacy as well as safety of SF MN meshes for inhibiting NI formation were concisely evaluated.

Abstract Number: ICBME1299

Influence of Surface Modification of Polystyrene Using Spectrum-Controlled UV Radiation on Mouse Embryonic Stem Cell Culture

Yuma Yamanoi, Shogo Miyata
Keio University, Japan

Pluripotent stem cells such as embryonic stem cells (ESCs) and artificial pluripotent stem cells (iPSCs) are important resource for regenerative medicine due to their self-renewal ability and pluripotency. For culturing pluripotent stem cells to maintain their pluripotency, feeder cell layers or cell adhesion matrix coated on culture substrate is required. However, these culture methods include risks such as cell contamination and require high-cost reagents. In this study, we focused on surface modification of cell culture plastics using UV radiation to improve adhesion and proliferation of pluripotent stem cells. In previous study, polystyrene dishes were modified by UV radiation of low
pressure mercury lamps to increase adhesion of mouse ESCs (mESCs). However, the UV light spectrum was not optimized for surface modification for the ESCs, because the UV light spectrum could not be changed to evaluate the effect of change in the spectrum of UV light on polystyrene modification for cell culture. The purpose of this study is to develop a device to control UV light spectrum and to evaluate the effect of surface chemistry of polystyrene on adhesion and proliferation of mESCs.

The UV radiation system using arrayed excimer laser lamps with three wave-length (172, 222, and 308 nm) was developed. The cell culture polystyrene dishes were exposed to different UV light spectrum using to modify surface molecular structure. Mouse ESCs were cultured on the modified polystyrene for 3 days, and the amount of total DNA was measured to evaluate the effect of surface modification on cell adhesion and proliferation. Pluripotency of mESCs was also evaluated by alkaline phosphatase staining. In addition, changes in molecular structure of the modified polystyrene surfaces were evaluated by X-ray photoelectron spectroscopy (XPS) and Time-of-Flight Secondary Ion Mass Spectrometry (ToF-SIMS). The Partial Least Squares (PLS) regression analysis was performed to determine the relationship between the total DNA amount and the amount of functional groups measured by ToF-SIMS.

As a result, mESCs could be cultured on the surface-modified polystyrene dishes under feeder-free, matrix-free conditions. The DNA amount of cultured cells on the dishes exposed to the combined UV lights of 172 nm and 222 nm wave-length was larger than that on the dishes treated by UV lights with a single wavelength (172, 222, 308 nm). Furthermore, mESCs cultured on the surface-modified dishes were considered to be undifferentiated because they stained positively by alkaline phosphatase staining. The ratio of the functional group expressed on the polystyrene dish was different depending on the respective UV wavelength conditions. The expression amount of C=O was increased in the group irradiated with the UV light of 172 nm and 222 nm in combination. The PLS model suggested several ions derived from the surface modification was assumed to affect the adhesion and proliferation of mESCs.

In conclusion, the spectrum-controlled UV radiation could develop the different surface structure for cell-culture polystyrene dishes. The UV radiation combined with the wave-length of 172 nm and 222 nm increased the amount of C=O group to promote the adhesion and proliferation of mESCs.

Loss of functional motor skills are common and often require patients to undergo rehabilitation so that they have a chance at motor recovery. Advancement in technology has seen to arise in the use of robotic technology in conducting rehabilitative exercises that are traditionally carried out by physiotherapists. In recent years, soft robotic exoskeletons, using pneumatics-based actuation in particular, have gained much interest due to their compliant characteristics and safe operating conditions. In order to carry out complex task-based rehabilitative exercises, these soft pneumatic actuators must ideally be able to move with multiple degrees of freedom or minimally, in a bidirectional motion. Majority of the research covering soft actuators can only achieve finger flexion with some providing passive finger extension. Non-invasive intent detection in the control of these exoskeletons is also lacking in sensing both finger flexion and extension. In this paper we present our work on a fold-based bidirectional 3D printed intent-sensing soft pneumatic actuator (ISPA) that can achieve bidirectional motion and provide intent detection for finger flexion and extension for application in upper limb rehabilitative exoskeletons. We have outlined our design and fabrication approach of the ISPA used in the exoskeleton. When compared to our proposed mathematical model, the sensing mechanism is shown to have an error of <2%. Characterization of the ISPA used in the hand exoskeleton was conducted and intent detection sensitivity of the ISPA towards finger flexion and extension is reported to be less than 10% change in MVC values. We hence show that minimal muscular strength is needed in our intent detection algorithm; this may be especially useful for stroke patients with weak muscular strength, wherein the exoskeleton detects the movement intent and assists with the completion of the movement accordingly. Therefore, we make the following notable contributions 1) description of fabrication steps towards an intent-sensing soft pneumatic actuator (ISPA) for bidirectional bending 2) a novel printable finger flexion-extension intent detection mechanism that has high sensitivity with low computational costs in an electronic valve control system.

**Abstract Number: ICBME1036**

**3D Printed Soft Pneumatic Actuators with Intent Sensing for Hand Rehabilitative Exoskeletons**

**Benjamin Ang**

National University of Singapore, Singapore

**Abstract Number: ICBME1479**

**Soft Robotics in Biomedical Applications**

**Cecilia Laschi**, Matteo Cianchetti, Egidio Falotico

Scuola Superiore Sant’Anna, Italy

Largely inspired by the observation of the role of soft tissues in living organisms, the use of soft materials for building robots is recognized as one of the current challenges for pushing the boundaries of robotics technologies. The study of living organisms sheds light on principles that can be fruitfully adopted to develop additional robot abilities. Though responding to fundamental research questions in science and in technology, soft robotics is finding its way towards a variety of application scenarios. Soft robotics technologies are especially well-suited for biomedical applications, for the compliance and the mechanical properties of soft robots. They allow various levels of interaction with the human body, spanning from soft tools for surgery and diagnosis, to wearable and assistive devices, prostheses, artificial organs, up to tissue-mimicking active simulators for training and biomechanical studies. Biocompatibility and biomimicry of the soft materials used in robots become key aspects in this field. A real step forward would be the combination of materials science with tissue engineering approaches, paving the way for biohybrid soft robots.
Abstract Number: ICBME1143

Novel Autonomous Magnetic Actuated Endoscope for Single Port Surgery

Truman Cheng, Weibing Li, Calvin Ng, Philip Chiu, Li Zheng
The Chinese University of Hong Kong, Hong Kong

Objective: Laparoscopes are controlled through long, rigid bodies. In single port surgery, the laparoscope is inserted parallel to other instruments. As such, they offer limited perspectives, and can interfere with other instruments. These problems are even more pronounced in procedures with narrow operation space, such as video assisted thoracoscopic surgery (VATS). To overcome these challenges, researchers have explored remote controlled endoscopes. One example is magnetic anchored and guided systems (MAGS), where magnetic linkage replaces the physical shaft of endoscopes. The endoscope is anchored under the abdominal or chest wall, and is free to move about the surface. This provides more perspectives, improve triangulation with an elevated view and avoid collision with instruments. However, many existing MAGS rely on imprecise manual control. Some MAGS use internal motors to steer the endoscope, adding to bulk and weight. These issues have impeded clinical uptake of MAGS. We aim to develop compact magnetic actuated endoscope with intuitive, robot assisted control. This should enhance surgeons and patients experience in VATS and single port surgery.

Method: We developed a novel magnetic actuated endoscope with unique structural design to operate near the chest wall. Instead of motors, the endoscope is steered remotely by magnetic interaction with an external magnet. As such, the endoscope is lightweight (3.6g) and compact (4 cm long, 7 mm in diameter). We then developed a robotic control system, where a robot arm addresses 3 directional translation and 2-DOF rotation of the external magnet. It takes visual feedback from the endoscope, then automatically steers the endoscope to track color markers near center of view. This autonomous endoscope control can reduce risk from errors and fatigue of human assistant, and allow a solo surgeon to operate intuitively and independently.

Results: To evaluate the system, we conducted a tracking experiment with moving target. The system was tested both in controlled environment and in a human chest phantom. Test in controlled environment offer quantitative investigation of tracking speed and pixel errors. The phantom test verifies system feasibility in clinical settings. The moving target is a da Vinci surgical instrument tagged with color marker. It follows a path on a nine-point numbered grid, from step 1 through 9, then move back to grid center (point 1). In both settings, the system successfully tracks the instrument near endoscope center of view (n=3, both). In all cases, technical complications or lose of anchor (endoscope drop-off) did not occur. The task completion time is under 3 min. The average tracking time for each step is 17 s.

Conclusion: A novel autonomous magnetic anchored and actuated endoscope was developed for single port surgery, particularly VATS. Compared with conventional laparoscopes, it has the following advantages: 1) does not occupy space at the trocar; 2) provide much better triangulation and potential for panoramic view; 3) intuitive control with visual servoing and robot assistance. While the system shows success in experiments, issues such as lens cleaning and sterilization need to be resolved before the system can move towards clinical application.

Abstract Number: ICBME1199

Sensorized Soft Hands for Enhanced Grasping Applications

May Khin, Jin Huat Low, Marcelo H. Jr. Ang, Raye Yeow Chen Hua, Qian Qian Han
National University of Singapore, Singapore

In this project, we developed a sensorized soft robotic hand, which was designed to emulate the fundamental movement of a human hand. It was constructed with five Fabric-based Finger Actuators (FFAs), and flexible sensing components are embedded along the fingers and palm of the hand. This enabled the soft robotic hand to flex and extend its fingers in manlike motion and sensed the objects it was interacting with. A composite fabric skin was customized to house the finger components in a human-hand-like form factor. Its dorsal side was made with elastic fabric to facilitate the actuation and its palmar side was enhanced with anti-slip surface to improve the grasping performance. Two sensing components were used to sensitize the robotic hand. Dorsal surface of the hand was fitted with five sets of commercial flex sensors (Spectra Symbol, Salt Lake City, UT), and the palmar surface was fitted with one array of force sensor (4 by 4 array of taxels). The flex sensors measured flexion angle of each of its fingers and the force sensor measured the contact forces with objects of interaction. The force sensor array was fabricated using layers of printed electrode on polyethylene sheets and piezoresistive fabric. Application of compressive force on the sensor led to compression of semi conductive threads within the structure of fabric. This created subsequent change in the resistance of the piezoresistive fabric. Each array of piezoresistive sensor was of the dimension 17 mm by 17 mm and it consisted of 16 taxels, each of which measured to be 2 mm by 2 mm. Due to changes in resistance upon application of force, voltage output of the sensor changed from its ideal state. The extent of voltage drop depended on the characteristics of the applied load on the sensor. To mimic the varying length of human fingers, five sets of FFAs were fabricated to be of different actuation lengths and folds. The total weight of the hand was approximately 150 g. It is able to generate resistive grip force up to 7.1 N during horizontal pull test and 26.5 N during vertical pull test at 120 kPa, which is adequate for handling a variety of common household objects. The embedded sensors are used in closed-loop feedback control of the hand when it is grasping objects. This enables the hand to detect and prevent slippage of objects. The enhanced grasping capability of the hand can potentially be implemented in biomedical applications. The soft robotic hand can be used to provide assistive grasping functions for patients who have lost the ability to control the movement of their upper limbs. The sensory feedback system of the hand creates a path of possibility to develop smarter robotic hand which can adapt and adjust to the movement of the user to provide more suitable grasping strategy.
Day 1 – 9 December 2019, Monday

Session 1.8: Human Disease Diagnosis & Therapy 2
Date 9 December 2019, Monday
Time 1400 - 1530
Venue EA-06-03

Abstract Number: ICBME1118

Modular DNA-Enzyme Switches for Sensitive, Equipment-Free, and Visual Molecular Diagnostics

Nicholas Rui Yuan Ho, Noah R Sundah, Diana Lim, Tze Ping Loh, Huilin Shao
Agency for Science, Technology and Research, Singapore

Rapid, visual detection of nucleic acids has considerable utility in diagnostics, either through detecting the specific genome of viral, bacterial, and parasitic pathogens or host gene expression signatures. We have developed a modular platform for nucleic acid detection, consisting of independent recognition and signal amplification DNA-enzyme nanostructure elements that are coordinated to produce a colour signal for the naked eye when triggered by hybridisation of specific nucleic acid sequences. We named this technology enzyme-assisted nano-complexes for visual identification of nucleic acids (enVision). The series of enzyme reactions that make up enVision enables fast (< 2h), sensitive (< 10amol) and accurate nucleic acid sequence detection at room temperature. The amount of target sequence can also be calculated from the intensity of the colour readout, showing potential for portable smartphone-enabled quantitative diagnostics. As a demonstration of its utility for portable genetic diagnostics, we integrated the chemistry in a configurable microfluidic platform for pathogen detection. The modular nature of the technology means that it is easy to design new recognition elements to create assays for different targets with similar performance. The assay can also be configured for diverse target detection in a single reaction, chemical computers that produce different outputs for the same combination of targets. Using human papillomavirus (HPV) as a clinical model, we ran a proof-of-concept study using clinical samples and showed that enVision has a high concordance with a gold-standard clinical qPCR test and can improve subtype detection coverage.

Abstract Number: ICBME1088

Using a Pneumatic Microfluidic Chip with Enhanced 3D Mixing Capability to Increase the Isolation and Capture Efficiency of Circulating Tumor Cells

Sung-Chi Tsai, Doong Howard
LifeCode Biotech, Taiwan

Objectives: We have created a pneumatic microfluidic platform to isolate and capture circulating tumor cells (CTCs) from human blood with high purity and recovery rate. To accomplish this goal, we adopted a novel microfluidic design to promote cell mixing with the magnetic beads and an integrated pneumatic platform to increase CTC recovery rate and to reduce false positive ratio. The main process includes cell mixing and sorting, CTC detection and cell counting. All the procedures can be manipulated automatically in a single microfluidic device.

Methods: Our device uses microfluidic channels and dynamic flows to enhance the mixing efficiency of cells and magnetic beads. The purpose is to separate CTCs from other types of blood cells and each isolated cancer cell could be trapped by the magnetic field and moved into a microfluidic reservoir. In this device, the cell will remain in the reservoir and start to multiply. Dulbecco’s Minimum Essential Medium (DME, Thermo-Fisher, USA) containing 10% foetal bovine serum (FBS, Thermo-Fisher, USA) was used to culture cancer cells at 37°C with 5% CO2 in air. Compare to our previous work of CTC isolation from human whole blood, the new method minimizes the chance to damage cells by taking out the RBC lysis step, which results in the increase of cell survival rate and a reduction of processing time. The advantage of using this new device is that after CTC isolation from the whole blood, it will be easier to culture cancer cells successfully and afterward cancer genetic mutation detection by DNA sequencing.

Results: We demonstrates CTCs can be isolated from other human blood cells in the microfluidic chip. The novelty of this microfluidic chip is to increase CTC recovery rate using a series combination of micro-pumps, dynamic flow and microfluidic structure in an automatic fashion. We show that cancer cells (in green color) could be isolated using specific antibodies coated on the magnetic beads after RBC depletion. In contrast, WBCs would be removed by the dynamic flows generated in the device (WBCs do not interact with antibody-coated magnetic beads). Our data show that the microfluidic system could recover almost 84 % of cells when comparing to a 68% of recovery rate using benchtop process. The false positive ratio is extremely low based on only capture 2 white blood cell in our microfluidic chip.

Conclusions: We have demonstrated an automated and integrated microfluidic system for CTC detection and isolation through the processes of WBC removal and positive selection. Our experimental data show that the whole process of CTC isolation and cell culture could be achieved by using a single microfluidic device.

Abstract Number: ICBME1151

Subtyping of Circulating Exosome-Bound Amyloid B Reflects Brain Plaque Deposition

Carine Lim, Yan Zhang, Yu Chen, Haitao Zhao, Mary C. Stephenson, Nicholas R.Y. Ho, Yuan Chen, Jae-hoon Chung, Anthonin Reilhac, Tze Ping Loh, Christopher L.H. Chen, Huilin Shao
Institute for Health Innovation & Technology, Singapore

Current AD diagnosis and disease monitoring are subjective and late-stage. They are achieved through clinical and neuropsychological assessments using published criteria. New molecular assays are being developed, including cerebrospinal fluid measurements and brain amyloid plaque imaging through positron emission tomography (PET); however, these tests face limitations as they either require invasive lumbar punctures or are too expensive for wider clinical adoption. Despite intense interests in developing blood measurements of Alzheimer’s disease (AD), the progress has been confounded by limited sensitivity and poor correlation to brain pathology.

We present a dedicated analytical platform for measuring different populations of circulating amyloid β (Aβ) proteins – exosome-bound vs. unbound – directly from blood. The
technology, termed amplified plasmonic exosome (APEX), leverages in situ enzymatic conversion of localized optical deposits and double-layered plasmonic nanostructures to enable sensitive, multiplexed population analysis. It demonstrates superior sensitivity (~200 exosomes), and enables diverse target co-localization in exosomes. The technology is capable of direct detection of target markers from blood and is mass-production ready. Employing the platform, we find that prefibrillar Aβ aggregates preferentially bind with exosomes. We thus define a population of Aβ as exosome-bound and measure its abundance directly from AD and control blood samples. As compared to the unbound or total circulating Aβ, the exosome-bound Aβ measurement could better reflect PET imaging of brain amyloid plaques and differentiate various clinical groups.

Abstract Number: ICBME1183

A Path toward Safer Chelation Therapy: Developing a Wearable Microscale-Based Ex Vivo Device for the Removal of Toxic Excess Iron from Plasma

Jad Touma, Matthew Coblyn, Jaturavit Pantakitcharoenkul, Goran Jovanovic, Oregon State University, USA

Iron is a physiologically essential element involved in gas transport along other central biological functions. Additionally, its tight regulation in the body is critically important, given the ability of excess iron to form dangerous free radicals via the Fenton reaction. Unfortunately, following several clinical conditions such as thalassemia major, sickle cell disease, hemochromatosis, end-stage renal disease and diabetes mellitus, a toxic excess of serum iron known as non-transferrin bound iron (NTBI) can be generated, leading to a life-threatening accumulation of iron in the organs. Consequently, chelation therapy is initiated to reduce the iron amounts to physiologically safe levels. Despite their effectiveness and extensive clinical use, current subcutaneous and oral iron chelators are associated with severe adverse effects, including ocular and auditory complications, gastrointestinal disturbances, increased creatinine and hepatic enzymes. These undesired effects can negatively impact the patient’s adherence to therapy and quality of life.

Inspired by the promises of the ex vivo iron removal to reduce and prevent these adverse effects via avoiding the introduction of chelators into the circulatory system, we have designed, manufactured, and tested the i-Blood microfluidic platform. The i-Blood device is envisioned to serve as a wearable blood processing platform in various medical environments: research, clinical, emergency, and at home medical care delivery.

In this work we integrated the process intensification and miniaturization attributes of microfluidic technologies, with the biomedical potentials of surface functionalization, to develop a laboratory prototype of a safe, biocompatible and wearable microfluidic platform for the continuous removal of excess iron from plasma.

We have successfully immobilized Desferrioxamine (DFO), a widely used iron chelator, to capture excess plasma iron during its passage through the i-Blood device (mean residence times ≤ 60 s). For increased stability and reliability, DFO was covalently bonded to different biocompatible and porous polymeric matrices inserted in the platform. The loading capacity of DFO varied with the support used and the pertinent immobilization technique. Additionally, the anti-protein-fouling properties of the device were improved by tethering polymer ‘brushes’ to the support. A research version of the developed platform was subsequently assessed within relevant clinical and physiological requirements. We have shown that the device was able to completely remove iron from deionized (DI) water initially containing 10 μM of ferric citrate.

Moreover, when tested with equine plasma having the same inlet iron concentration, the i-Blood device exhibited a similar performance, with a complete iron removal from the plasma. The deployment of the promising anti-protein-fouling ‘brush’ layer was able to maintain iron removal activity in the presence of albumin and fibrinogen.

The successful development of a laboratory prototype of the wearable, ex vivo iron removal platform holds promising potentials for a safer, possibly cheaper and less distressing chelation therapy. It is worth noting that other device attributes such as maximizing the loading capacity, enhancing the control of iron removal rate, deploying more benign iron-removing molecules and maintaining the biocompatibility for extended treatment times are being currently pursued to reach a stand-alone operating platform.

Abstract Number: ICBME1382

A Real Time Analysis of PPG Signal to Measure the Hemoglobin Concentration

Shankarnath Suthakaran, Ajmal Abdul Azees, Mohammad Rizan Mohamed Athif, , E.H. Jayathunga, W.F. Shahana

University of Ruhuna, Sri Lanka

Hemoglobin concentration is a vital parameter which can be used to detect abnormalities of the human body, including anemia and polycythemia. Currently, invasive techniques are used for hemoglobin measurement despite their many disadvantages including discomfort and potential complications for the pregnant, elderly and pediatric patients. This research paper focuses on measuring the Hemoglobin level without withdrawing blood.

The non-invasive assessment of hemoglobin concentration in arterial blood is based on the absorption of light by oxyhemoglobin and deoxyhemoglobin in blood and the analysis of the resulting photoplethysmograph (PPG) signals. PPG wave is analysed using the modulation ratio (R) which is defined as the ratio of AC to DC components of the PPG signal from two different wavelengths of 660nm and 940nm. In this study, measurements were obtained from a total of 106 patients. A linear relationship (Hb = -3.626*R + 15.84) was obtained between hemoglobin concentrations (Hb) measured using the invasive technique and the modulation ratio (R) calculated by analysing PPG signal using the measurements from 84 patients.

Based on the mathematical model, a non-invasive screening tool was developed to determine hemoglobin concentration. A probe is used to transmit the IR and red light through the fingertip and to record the resulting PPG waveform at the fingertip. The fingertip was used since it is reported as the most accurate site in
the body for PPG measurement compared to other locations. The recorded PPG waveform is analysed using a microcontroller based processor built into the device. The device subsequently predicts the risk of anaemia in patients depending on the haemoglobin concentration, age, gender and pregnancy status. This device operates in three modes. Mode 1 is a standalone device. In mode 2, the device is connected to a desktop application that displays the real-time PPG waveforms and can generate a medical report. In mode 3, the device can be connected to a mobile application that facilitates the continuous monitoring of haemoglobin concentration remotely. The device was evaluated using 22 subjects. The performance was measured using the deviation percentage defined as the percentage difference between the actual and measured haemoglobin concentrations. An average deviation of 4.41%, a maximum deviation of 9.4% and a minimum percentage of 0.36% was observed for the tested patients.

Current haemoglobin measuring techniques do not facilitate continuous and remote monitoring. The proposed device has this main advantage in addition to the benefits of non-invasive measurement including the prevention of infections, physical pain, and the lack of operational or maintenance costs while being portable. The effect of confounding factors such as gender, age, pregnancy and environmental factors such as ambient light may cause slight variations in the proposed measurements. However, with the availability of data, improvements can be made into the model to capture such factors into the model.

**Session** | Special Symposium 3: Biomedical Nanotechnology
---|---
**Date** | 9 December 2019, Monday
**Time** | 1400 - 1530
**Venue** | EA-06-04

Abstract Number: ICBME1483

**Engineering Nanoplasmonic Materials for Optofluidic Biosensors towards Personalized Medicine**

Pengyu Chen  
*Auburn University, USA*

The framework of precision medicine envisions a world in which diseases are diagnosed not simply on the basis of a patient’s symptoms but on accumulated data that reveals the fundamental mechanistic bases of human diseases. This raises an emerging demand for transformative tools/biosensors that can measure the biochemical and biological markers to understand the dynamical response of the patient status in a rapid and accurate manner. Cytokines are well-studied proteins secreted by immune cells and essential for intercellular signaling to regulate the maturation, growth, and responsiveness of particular cell populations. Quantification of cytokine-based immune fingerprints provides clinically and immunologically useful information related to infectious diseases, cancer, autoimmune diseases, and allergy transplantation. This requires collecting time series data that could be on the order of seconds for ion transport, to hours for changes in cytokine levels, and to days for phenotypic changes in host body with sensor sensitivity from biological relevant concentration to single molecular level using minimum sample volume. In this talk, we will present a number of plasmonic nanomaterial based optofluidic biosensing platforms for rapid, high throughput, sensitive and multiplex cytokine detection from whole blood to single-cell level towards next-generation point-of-care immunoassays. The multi-scale research both experimentally and theoretically will bridge the gap in fundamental understanding of immune system and enhance the applicability, diagnosis and prediction power for immune system diseases. The developed platforms would ultimately gear the biologists and clinicians with capability to real-time monitor the immune status in patients, a transformative achievement that has enormous implications to fundamental research and clinical applications.

**References**


Abstract Number: ICBME1504

Metal Nanoparticle Radiosensitization for Improving Radiotherapy

Ivan Kempson
University of South Australia, Australia

Objectives: Metal nanoparticles have gained market approval for enhancing the effects of ionizing radiation in radiotherapy treatment of cancer. However, the mechanism of action of metal nanoparticles exerting their effect remains controversial and poorly elucidated. We have developed a methodology inspired by Quality-by-Design principals to investigate mechanisms and the structure-function relationship of nanoparticle parameters with radiobiological effect.

Methods: A cross-correlative methodology was developed to measure the number of DNA breaks in cells after irradiation with clinical X-ray sources coupled with quantitative analysis of the number of label-free nanoparticles in the same individual cells. Image processing was performed with an in-house application developed for analysing large sample sizes and to remove user bias. Statistically significant trends were then analysed in cell sub-populations across multiple cell-lines.

Results: Sub-cellular populations were identified and radiobiological response was determined for individual cells as a function of the number of nanoparticles in the same cells.

Conclusions: The data is continuing to reveal many insightful aspects of nanoparticle-cell interactions and the consequence these have on radiobiological response of cancer cells. Importantly, a number of biological mechanisms exist that not only sensitize cells but can actually de-sensitize cells. These mechanisms contravene the physical concepts of radiosensitization. Nanoparticle uptake is highly heterogeneous and the observations made in our research cannot be deduced by conventional bulk assays. Biological mechanisms, such as down regulating proteins involved in DNA damage repair, lead to preferential sensitization of the most radio-resistant S-phase cells which act as a negative prognostic factor for many indications. Despite metal nanoparticles entering clinical use, we highlight many questions that remain in how they exert their function. Our research is revealing these mechanisms and will enable optimization of radiosensitizer formulations.

Abstract Number: ICBME1482

Sensing While Heating in a Cell

Madoka Suzuki
Osaka University, Japan

Heat has been used for medical treatments. Recent advances in nanotechnology allow us to accumulate nanomaterials as small heat sources around targeted cells. The time and the duration of releasing heat is also controllable by stimuli-responsive nanomaterials that release heat by a specific type of external stimulus such as alternating magnetic field, light and ultrasound. However, while the total amount of heat released is measurable in bulk samples, how the heat propagates around the small heat sources in space and time remains unresolved, especially, at the single-cell level. The lack of these knowledges can cause side effects in untargeted cells surrounding targeted regions. Insufficient heating may induce unexpected responses in targeted cells as thermal sensing can occur at multiple scales from diffusion of signalling molecules, enzymatic activities to gene expressions. In other words, precise heating could have a chance to elevate the efficacy of thermal treatments, or may even be able to control cellular activities. One of our group’s interests has been to understand the mechanism of endogenous heat release in our bodies. For this purpose, we have developed luminescent nanoparticles and molecules for optical sensing of temperature changes in living cells. The luminescent intracellular nanothermometry is a useful means to combine with other methods to study cellular responses in real time [Front. Bioeng. Biotec., 6, 204 (2019)]. By taking this advantage, our methods have successfully been demonstrated to evaluate local temperature variations induced by stimuli-responsive nanomaterials [ACS Nano, 9(7), 7678-7689 (2015); ACS Nano, 11(3), 2494-2508 (2017)], and to shed light on a novel way of cellular thermal sensing [ACS Nano, 11(3), 2494-2508 (2017); J. Gen. Physiol., 151(6), 860-869 (2019)].

Abstract Number: ICBME1484

Acoustic Enhancement of Intracellular Delivery for Ex Vivo Autologous Cell Therapeutics

Leslie Yeo, Shwathy Ramesan, Amgad Rezk, Christina Cortez-Jugo
Royal Melbourne Institute of Technology (RMIT), Australia

Recent advances in gene editing and therapy have highlighted the potential of ex vivocell-based techniques to treat many diseases, wherein a patient’s cells are harvested, engineered to insert various therapeutic agents such as nucleic acids or proteins, and re-infused. Considerable challenges however remain in the ability not just to insert these agents into cells whilst retaining high levels of cellular viability, but also to ensure that they are not lysed within the cell.

Physical methods (e.g., electroporation, sonoporation, etc.), for example, allow efficient translocation of therapeutic cargo into the cell through the formation of pores in the cell membrane. This, however, afflicts some damage to the cells, leading to apoptosis of a considerable proportion of the cells. Biochemical methods, in contrast, rely on carriers such as nanoparticles, vesicles or viruses to facilitate greater endocytotic take-up. The endocytosis pathway nevertheless results in the concentration of the internalised cargo within the endosomal regions of the cell, almost all of which ends up in the lysosome where they are degraded. Strategies that allow them to escape the endosomal recycling path in order to enter the cytoplasm are therefore required if the cargo is to target the nucleus.

We show that exposure of the cells to high frequency (>10 MHz) order sound waves are able to enhance the uptake of nanoparticles, molecules and nucleic acids by several-fold, whilst retaining very high levels (>97%) of cellular viability. This is because the high frequency excitation, unlike sonoporation, does not result in the formation of physical pores in the cell membrane. Instead, the high frequency excitation sufficiently temporarily disrupts the structure of the lipids that make up the cell membrane, thus increasing the membrane permeability.
sufficiently to allow the therapeutic agent to diffuse through it. The effect, is however, transient such that the organisation of the lipid structure immediately returns to its original state upon relaxation of the acoustic excitation. Such immediate recovery of the cell is the reason for the high cell viability. As this internalisation mechanism does not involve endocytosis, we observe the therapeutic cargo to be distributed throughout the cell instead of being localised within the endosomes or lysosomes, thus facilitating a greater possibility for nuclear targeting and hence transfection. Indeed, with siRNA delivery into human embryonic kidney (HEK293-T) cells, we observe a two-fold knockdown in the gene expression.

Abstract Number: ICBME1076

Peptide Modification of Ferritin Nanocages for Intracellular Cholesterol Reduction in Atherosclerosis

Samyukta Ravishankar, Sierin Lim
Nanyang Technological University of Singapore, Singapore

Accumulation of lipid laden macrophages (foam cells) is characteristic of atherosclerosis development in the arterial walls. Reconstituted high density lipoprotein (HDL) molecules have been shown to reduce plaque area both in vitro and in vivo. Synthetically synthesized HDL has several components including multiple types of phospholipids and synthetic peptide chains to mimic the HDL molecules. The mimetics are composed of multiple components thus increasing the possibility of undesired interactions with other receptors or molecules when used in physiological systems. Synthetic HDL mimetic peptides are shown to be promising candidates for cholesterol reduction. However, there are challenges in terms of plaque localization due to the low hydrodynamic diameter and early protease degradation. Ferritin nanocages have been found to passively accumulate in the atherosclerotic plaque. We have shown 3-fold preferential localization of ferritin to foam cells is due to transferrin receptor mediated endocytosis process. We propose the use of the nanocages as a delivery vehicle of therapeutics such as peptides and small molecules. We have successfully genetically engineered the outer surface of the ferritin cage to display HDL mimetic peptides such as 4F and its variants. The conjugates are characterized using dynamic light scattering, circular dichorsim and transmission electron micrographs. Intact ferritin cage structures are obtained with enhanced alpha helical structures due to the modifications. Cholesterol sequestration efficacy is tested using in vitro foam cell models wherein murine macrophages are loaded with modified lipoproteins in serum starved conditions. Enzymatic assays used to quantify intracellular cholesterol levels shows up to 25% reduction in cells treated with the conjugates. Experiments to incorporate therapeutic small molecules along with the protein conjugates for enhanced sequestration efficacy are presently ongoing. The work highlights the potential of modifications of the ferritin nanocages with peptides and small molecules for future implications in the reduction of atherosclerosis plaques.

Abstract Number: ICBME1336

Myosin-Independent Regulation of Wavy Cell Structure and Nuclear Strain Transfer

Pen-Hsiu Grace Chao, Chin-Hsun Huang, Onnie Wu
National Taiwan University, Taiwan

Connective tissues have complex mechanical properties that are controlled by the chemistry and organization of its constituents. The most abundant extracellular matrix component, collagen, is often organized as parallel wavy fibers in tissues such as artery, ligament, and tendon. The resident cells are embedded in the wavy fibers and have wavy nuclei. The wavy structure allows easy extension at low strain and stiffens at higher strain to prevent overload and injury. Moreover, the wavy structure is cell instructive. When cultured in this biomimetic environment, fibroblasts have increased collagen and phenotypic expressions. To understand how the wavy structure regulates cell mechanosensing, we used microcontact printing to generate precise wavy patterns. Cells conformed to the fibronectin patterns and had actin structures that followed the long axis of the cell. Straight and wavy cells had similar spread area and elongation length. In the wavy pattern, strong actin arcs were seen in the concave edges, with fewer actin fibers on top of the nucleus. Nuclear shapes also followed the patterns, with increased curvature in the wavy cells. A concomitant increase in chromatin condensation index (CCI), as analyzed from the bright DAPI clusters, was found with increasing curvature. Wavy cells
also had reduced intracellular strain transfer when stretched, as seen with reduced nuclear strain using live imaging. Since morphology-associated strain transfer and nuclear changes have been attributed to actomyosin tension, we measured cell contractility with traction force microscopy. Significant increases in contractility was found in the wavy cells. Surprisingly, while myosin II inhibition with blebbistatin reduced contractility in both groups, it did not abolish the differences in contractility between the straight and wavy cells. Myosin II-inhibition also did not alter nuclear shape or organization. As previously reported, blebbistatin treatment reduced strain transfer in straight cells. However, myosin inhibition did not change nuclear strain transfer in the wavy cells. Our results revealed myosin II-independent cell and nuclear structures and mechanosensing mechanisms in the wavy cells. Future mechanotransduction studies need to consider the unique cell and nuclear structures in tissues with wavy organization.

Abstract Number: ICBME1240

Thermal-Disrupting Interface Inducing Survival Dichotomy of Bacteria and Host Cells for Accurate Topical Antibacterial Therapy

Benhui Hu, Chee Teck Lim, Xiaodong Chen
Nanjing Medical University, China

Objectives: Hospital-acquired infection, contracted from health care settings, occurs globally and is a significant burden for both patient and public health. Traditional treatment of these infections involving the worldwide misuse of antibacterial drugs has enhanced the antimicrobial resistance of these three pathogens and, even worse, increased the number of multi-drug resistant bacteria. Thermoblation has been emerging as an effective treatment modality against most popular pathogens even though the drug-resistance has been developed. To date, most of accurate photothermal therapies are accomplished by dispersing nanocomposite to target regions of interest in vivo, enlarging the risk of post-therapeutic toxicity due to the residual nanocomposite. An appealing strategy to circumvent the concern of residual toxicity is encapsulating these nanocomposites in matrix as dressing materials, which could effectively treat cutaneous disorders. However, the undesirable heat distribution during photothermal therapy could specifically harm the cohesion energy of skin tissue and inhibit the restoration of barrier function. Therefore, the thermal management regulating heat transfer at the biointerface between dressing matrix and cutaneous tissue remains a challenge.

Methods: Finite-Difference Time-Domain Simulation, Atomic Force Microscopy, Nanoindentation, micromechanical adhesion testing system

Results: A better solution for antimicrobial dressing managing infection is modifying the surface to enable both the disruption on biofilm and the elimination of engaged planktonic bacteria, and thus maintain a significant therapeutic efficiency. We demonstrated the microtopography of the film could manage thermal dissipation at the biointerface and thus realize accurate photothermal therapy at moderate temperature, minimizing the heat induced reduction on mechanical property of normal tissue. Animal tests show our strategy cures infection within 6 days following infrared irradiation for half an hour per day.

Conclusion: We have developed a hybrid biomimetic film that combines optimized biomimetic features with photothermal nano-therapy for antibacterial dressing with significant cyto compatibility. Upon infrared light irradiation with a modest dose (70 mW/cm²), the biomimetic films composed of raised regions and photothermal-agents-concentrated depressed regions, provide a spatial window (3 µm) to filter out larger objects from directly contacting the active depressed regions during photothermal therapy. Such a hybrid formulation integrates two soft materials into one robust system with topographically transformable properties that actively disrupt biofilms and more importantly, enables elimination of bacteria while sparing host cells.

Abstract Number: ICBME1541

Hypertension Meets Osteoarthritis: A Revisit to Vascular Aetiology

Chunyi Wen
Hong Kong Polytechnic University, Hong Kong

Vascular aetiology of osteoarthritis (OA) has been proposed for decades. It was once postulated that subchondral bone ischaemia, e.g. in hypertension, might jeopardize the gas and nutrition exchange in bone-cartilage functional unit, and ultimately contributes to destruction of entire joint in the pathogenesis of OA. However, the exact mechanism remains poorly understood until now.

Abstract Number: ICBME1469

Collective Migration and the Epithelial-Mesenchymal Transition in Engineered Microenvironments

Ian Wong
Brown University, USA

Collective behaviors emerge from coordinated cell–cell interactions during the morphogenesis of tissues and tumors. For instance, cells may display density-dependent phase transitions from a fluid-like “unjammed” phase to a solid-like “jammed” phase, while different cell types can “self-sort”. We use comprehensive single cell tracking to elucidate these spatially and temporally heterogeneous behaviors in the context of self-organizing patterns. First, we consider co-cultured mixtures of sheet-forming epithelial cells and dispersed mesenchymal cells, which show a composition-dependent “unjamming” transition. Second, we consider a gelation-like mechanism whereby cells at very subconfluent densities organize into spanning network architectures. Finally, we analyze the disorganization and dissemination of cells cultured in 3D matrix, which exhibit both collective and individual invasion phenotypes with distinct topological and traction signatures. These complex behaviors exhibit striking analogies with non-living systems, suggesting that these physical concepts may be applicable to understand development and disease.
Engineering of Cell Mechanical Microenvironment

Feng Xu
Xi’an Jiaotong University, China

Cells in vivo reside within a complex microenvironment that is rich in biological, chemical and mechanical cues, playing critical roles in regulating cellular activities both spatially and temporally. Although it is well accepted that biological and chemical cues can significantly influence cell functions, recent accumulating evidence has also shown that mechanical feedback from the cell microenvironment (e.g., stiffness of ECM, morphology, and tension force) also play an important role in controlling the fate of cells. Disequilibrium of mechanical microenvironment can cause a series of diseases, such as cancer migration and cell fibrosis. Thus, there is a pressing need to understand how cells transduce these mechanical cues in their native microenvironment, especially mechanical elements such as elasticity, viscosity and viscoelasticity, viscoplasticity into biochemical cues.

Using today’s micro and nanoscale technologies and novel biomaterials especially hydrogels, we have developed various approaches to create synthetic but native-like conditions to understand cell behavior. Most research involving human cell manipulation has been carried out on artificial two-dimensional (2D) substrates. However, recent studies showed that cells respond and behave differently in these 2D settings compared to in 3D intricate microenvironment that cells reside in. Therefore, we have developed innovative 3D in vitro cellular models with well-controlled mechanical microenvironment for re-creating distinct niches and in vitro cell modeling under well-defined and reproducible conditions.

Besides, we have also proposed some cellular mechanosensing mathematical models to describe three main mechanosensing processes including mechanosensing behaviors on the cell-ECM interaction, mechnochemical conversion in the cytoplasm and nuclear pore enlargement due to the increase of cellular tension: (i) The improved motor-clutch model and integrin clustering model to described the FA dynamics on the cell-ECM interface to sense the substrate the mechanical properties; (ii) The signaling pathway model to describe the cytoplasmic signal transduction and stress fiber reconstitution; (iii) an integrated mathematical model to describe the YAP/TAZ nucleocytoplasmic shuttling dynamics. These mathematical models are able to capture the breadth of mechanobiological responses known to govern the behavior of animal cells. By using today’s micro and nanoscale technologies (e.g., microfluidics, lithographic approaches and micromolding technologies), they will further instructionally contribute to engineering cell mechanical microenvironment in vitro to reconstruct the native cellular behaviors and functions for various applications, such as tissue engineering and regenerative medicine.

Abstract Number: ICBME1441

Electrostatic Switching of Nuclear Basket Conformations Provides a Potential Mechanism for Nuclear Mechanotransduction

Guy Genin
Washington University in St Louis, USA

Cells can respond to mechanical forces by changing gene expression. Changes to transport through pores in the nuclear membrane have been implicated in these responses, but the mechanisms by which stress-dependent, selective nuclear transport occur have not been elucidated. We identified a potential mechanism for this via stretch-dependent switching behavior in nuclear pore complexes (NPCs). NPCs, composed of proximal and distal rings connected by a “basket” of filaments within the nucleus, form channels for the selective transport through the nuclear membrane. Our simulations showed that the relatively narrow NPC distal ring, long believed to be responsible for channel gating and selectivity, cannot stretch to accommodate larger molecules. Instead, our results suggested that rapid phase transitions in nuclear basket filament conformations could serve to regulate large molecule transport. Nuclear basket conformations were bi-stable under certain conditions within the physiological range, enabling strong sensitivity to the mechanical state of the nuclear membrane, and suggesting a possible pathway for mechanosensitive nuclear gating.

Abstract Number: ICBME1502

Segmentation of Endothelial Cell Growth in a Swirling Well Plate Allows Investigation of the Shear-Dependent Release of Soluble Mediators

Kuin Tian Pang, Mean Ghim, Mehwish Arshad, Xiaomeng Wang, Peter D. Weinberg
Imperial College London, UK

Introduction: Endothelial cells (EC) sense the shear stress generated by the flow of blood over them and respond by altering their stiffness, morphology, junctions with neighboring cells and release of soluble mediators. A swirling well system has gained increasing attention in the study of the effect of shear stress on EC because it can induce complex flow with spatial variation in flow characteristics. However, there is a potential flaw in this method: EC release soluble mediators, a process that can depend on flow characteristics. Hence EC in one region may be responding to effects of flow in another region. To overcome this, we developed a method that allows the culture of EC at only specific region in a well.

Methods: Flow in a swirling 6-well plate was simulated in STARCCM+ and post-processed using MATLAB, to produce maps of shear stress. Human Umbilical Vein Endothelial Cells (HUVEC) were grown in a specific region by coating the region with fibronectin and passivating the remainder of the well with Pluronic. Sheared HUVEC were fixed and stained with DRAQ5 prior to confocal imaging. Cell alignment and number in tile scans were calculated using MATLAB and ImageJ. Calcein-AM-labelled THP-1 monocytes were incubated with previously-sheared and TNF-a-treated HUVEC that had been grown on a segmented or full well for 1 h in a static condition, prior to fixation and immunofluorescence imaging.

Results: The centre of the swirling 6-well plate exhibited Low Magnitude Multidirectional Flow (LMMF) whereas the edge
The number of dead cells in the compression groups increased. However, most cells in both groups were alive at 32 h of culture. The results of calcein-AM/PI fluorescent staining indicated that there was no significant difference between both groups at 32 h. However, there was no significant difference in the elongation of F-actin filaments compared to control groups. For the regression analysis, the number of dead cells highly correlated with the amount of melanin. In general, melanin is known as a factor that can promote cell death. It was speculated that the increased melanin synthesis evoked by the mechanical compression caused cell death.

Conclusions: We describe a simple and effective method to restrict cell growth to a specific region of well plates. This reduces the possibility of mediators being released from cells in one region of the well, exposed to a certain shear stress profile, and affecting cells in another region, exposed to a different shear profile. Funded by A*STAR and BHF.

Abstract Number: ICBME1320

Effect of Static Compression on Invasion Process of Malignant Melanoma Cells Within in Vitro Three-Dimensional Culture.

Takashi Morikura, Shogo Miyata
Keio University, Japan

Malignant melanoma in the plantar surface of the foot is subjected to various mechanical stimuli. Some studies have reported that mechanical compression affects the development and progression of melanoma. However, little is known about how mechanical compression affects the behavior of malignant melanoma cells in a physiological condition due to the complexity of the invasion mechanisms. In this study, we established an in vitro three-dimensional cell culture model in order to evaluate the effects of mechanical compression on the invasion process of malignant melanoma.

The in vitro three-dimensional cell culture model was prepared using mouse malignant melanoma B16F10 cells covered with type I collagen gel layer. To impose static compression (7.8×102 Pa) on the gel-covered cells, cell culture insert with a cylindrical weight was mounted on the gel layer. A malignant melanoma model without weights was also prepared in a similar manner as a control group. The cell invasion process was evaluated by the change in occupied area of cells in the phase contrast images which was measured by image processing and analysis software (ImageJ, NIH). To determine the effect of compression, the viability of cells and morphological change of F-actin was observed by calcein-AM/PI and rhodamine-phalloidin fluorescent staining. In addition, the amount of melanin in the malignant melanoma model were evaluated using the colorimetric analysis of microscopic images. Furthermore, the correlative relationship between the viability of cells and melanin concentration was evaluated by the regression analysis.

As a result, the change in the occupied area of cells in compression group was significantly larger than those in control group at 8 h. However, there was no significant difference between both groups at 32 h.

The results of calcein-AM/PI fluorescent staining indicated that most cells in both groups were alive at 32 h of culture. However, the number of dead cells in the compression groups increased significantly compared to the ones in the control groups at 32 h. Regarding the melanogenesis of B16F10 cells, the amount of melanin in compression groups at 32 h were significantly increased more than control groups. From the regression analysis, the number of dead cells highly correlated with the amount of melanin. In general, melanin is known as a factor that can promote cell death. It was speculated that the increased melanin synthesis evoked by the mechanical compression caused cell death.

From the result of rhodamine-phalloidin fluorescent staining, the B16F10 cells under the static compression of 8 h showed elongated F-actin filaments. It was suggested that the static compression caused elongation of actin filaments in cancer cells to promote cell migration.

In summary, our results suggest that the invasion of melanoma cells under the compressive stress for 8 h was promoted with the elongation of F-actin filaments compared to control groups, whereas there was no significant difference between both groups at 32 h with increasing cell death associated with hyperfunction of melanogenesis. The results of this study contribute to the elucidation of the invasion mechanisms of malignant melanoma caused by mechanical compression.

Abstract Number: ICBME1204

Mechanical Programming of Soft Pneumatic Actuators Using Embedded Endostructures

Ajinkya Bhat, Raye Yeow Chen Hua
National University of Singapore, Singapore

Soft Robotics has evolved as a domain for developing light, compliant and safe actuators. However, there is a lack of repeatable fabrication techniques as well as a lack of customizability that restricts application of soft robots. In this manuscript we present a novel fabrication technique and demonstrate the utility of this technique to develop highly customizable soft robots. Using sacrificial moulding, it is possible to fabricate the pneumatic channel in one piece, enabling fabrication of actuators that withstand higher pressure. We demonstrated that the proposed technique reduces the variance between performance multiple iterations of the same actuator. In addition, it is possible to use embedded endostructures to customize the behavior of the actuator by altering local mechanical characteristics. Since the endostructure used are manufactured using 3D Fused Deposition Modelling (FDM) printers, it is possible to fabricate varied structures to achieve a wide range of motions. Commonly used motions such as compression and expansion, bending as well as torsion and curling can be achieved using this technique. We envision that this technique could be used for developing complex soft robotic devices with programmable mechanical motions.
**Day 1 – 9 December 2019, Monday**

**Abstract Number:** ICBME1167

**Design, Fabrication and Characterization of a Modular Soft Robotic Arm with 3 Degrees of Freedom**

**Ahmed Khalil Khan, Liang Xinquan**  
National University of Singapore, Singapore

The advent of soft robotics has led to numerous developments to incorporate soft robotics in various fields. As compared to their traditional mechanical counterparts, soft robotics is much lighter in weight, offers greater degrees of freedom, is more cost effective and most importantly, poses very little risk to users due to its compliant and soft nature. One of the prominent applications of soft robotics is the soft robotic arm. The soft robotic arm has been developed for numerous industries, such as the manufacturing industry and the medical industry. Presently, soft robotic arms tend to either take a very long fabrication time or are very heavy. Moreover, modular soft robotic arms have yet to be commonplace and those that have been developed are heavy, is composed of soft and rigid mechanical components and have complex assemblies. These modular soft robotic arms also have wiring and tubes on the exterior which can be hazardous to users. In this paper, we propose the design, fabrication and demonstration of a modular soft robotic arm that is made of Nylon fabric that is pneumatically actuated. The aim of this design is to create a modular soft robotic arm that is lightweight, inexpensive, entirely soft that can be assembled in a safe and elegant manner.

The modular soft robotic arm is made of 3 arm sections, 3 joint sections and a gripper. Each section is made using Nylon fabric that is folded and heat-sealed to create an airtight bladder. The weight of each section is 14.85g, 23.86g and 39.74g respectively. The different sections overlap at the joints and are bound by cable tie. Each section is pneumatically actuated via silicon tubes that run internally along the length of the soft robotic arm. When fully assembled, the modular soft robotic arm weighs approximately 350g. When activated, the modular arm is pneumatically inflated at 20kPa in the arm sections and 40kPa in the joint sections.

Each joint section was inflated bidirectionally at 40kPa and bending was video recorded. Analysis of the bending angle capability of each joint was performed using Tracker software. Each joint section can bend up to 56.64° ±0.23 in the positive direction and up to 39.21° ±0.01 in the negative direction. When assembled, the modular soft robotic arm can bend up to 65.60° in the positive direction and up to 42.95° in the negative direction. The overall work space of the arm is approximately 108.55°.

The proposed design of a modular soft robotic arm has shown to be lightweight, entirely soft and can be assembled in safely. The arm possesses a good range of motion at each joint section and overall work space. We believe this design is a positive step in creating modular soft robotic arms that can be applied in various industries.  

**Abstract Number:** ICBME1155

**Shape Shifting Actuators with Controllable Constraints**

**Chao-Yu Chen, Raye Yeow Chen Hua**  
National University of Singapore, Singapore

**Objectives:** For the past few years, the concept of soft robots has shown to be applicable in medical and industrial applications. Compared to conventional robots built with rigid links and joints, soft actuators have the nature of manipulating multi-degrees of freedom and a safer interface between machine and humans. Nevertheless, the actuators that appear in recent studies are mostly constrained by pre-programmed patterns, which further limits the functionalities of individual actuators.

Recent studies show that soft actuators are capable of performing complex locomotion when an external stimuli vector field is applied. In particular, pneumatic actuators, which have been vastly investigated and studied over the past years, might overcome the limitation of lacking functionality by utilizing other controlling methods. In combination with the internal pneumatic net force and controllable external constraint, this article is intended as a proof of concept of the feasibility in controlling actuators with a more diverse and controllable actuating pattern.

**Methods:** The geometry of the actuator will be defined and simulated via commercial finite-element analysis software, ABAQUS. During fabrication process, controllable particles and structure are embedded inside the elastomer, Ecoflex 00-30 and Dragon Skin 10M (Smooth-on Inc.). The molding process is carried out in several parts depending on the geometry of the actuator. Subsequently, the parts are assembled. Several shapes of actuating will be achieved based on the pattern of the external and internal constraints. After all sets of shapes are noted, the maximum bending angle and a gripping force will also be measured.

**Results:** The actuators perform a non-linear motion with the mechanical properties dictated by the embedded structure and particles. Endocytosis inspired movements also allow the actuator to grip, manipulate objects and shape shift by imposing external induction forces.

**Conclusions:** This work shows the feasibility of combining pneumatic actuators with other sources of actuation. By this, we can extend this possibility to a controllable and universal unit of pneumatic actuator that can be specified with deformation and orientation by external vector forces.

**Abstract Number:** ICBME1071

**A Novel Modular Soft Robotic Arm towards Assisting Activities of Daily Living**

**Xinquan Liang, Raye Yeow Chen Hua, Chui Chee Kong**  
National University of Singapore, Singapore

**Objectives:** In this study, a novel soft robotic arm made from fabrics is designed and presented. This robotic arm contains a modular inflatable joint and two limbs. It is completely
Actuated by air and able to achieve a large bending range of ±120°. Benefiting from the fabrication materials, this soft robotic arm carries the advantages of being lightweight, low cost and excellent in compliance. The arm can be mounted on a wheelchair and assist users in daily living activities as demonstrated in this study.

Methods: The basic soft robotic arm contains an inflatable joint and two limbs. The inflatable joint consists of three airtight bladders. Thermoplastic polyurethane (TPU) coated nylon oxford fabrics are used to make the air bladders by heat sealing the boundaries of the fabrics. Three air bladders are fabricated then assembled together by cable ties. The inflatable limbs are made from rolling and heat sealing a planar bladder. After the limbs are fabricated, the inflatable joint is then inserted in the hollow of the limbs and fixed to the limb.

Results: Experiments were conducted to inflate the joint bladders in sequence to bend the arm. When two of the bladders are inflated, the maximum bending angle is about ±120°, which is sufficiently large for most of the applications. When all three bladders are inflated sequentially, the arm can achieve various bending profiles which is important to get a large workspace.

The soft robotic arm can be used for applications involving close human interactions due to its advantage of being soft, compliant and safe. A possible application of the soft robotic arm is to be mounted on a wheelchair and assist the user to retrieve objects from a distance. The design of the joints is the same as mentioned previously but the size is larger to suit this application. This soft robotic arm consists of three inflatable joints which lead to a much larger workspace, thus the robotic arm is very dexterous. The end-effector is a three-finger inflatable hand that is able to pick up light objects needed in daily life. Compared to rigid robotic arms mounted on wheelchairs, this soft robotic arm is more lightweight and also reduces safety concerns.

Conclusions: In this study, a novel soft robotic arm is presented and studied. The design of this soft robotic arm is modular so that it can be reconfigured for different applications. Experiments are conducted to characterize the bending profiles under different conditions and the results are discussed accordingly. At last, a demonstration is presented, where the soft robotic arm is mounted on a wheelchair and helps to fetch an object on the table. This study reveals the great potential of this for robotic arm to assist people in activities of daily living.

Abstract Number: ICBME1374

Multifunctional Soft Robots Based on Durian Thorn-Inspired Actuators
Luis Carlos Hernandez Barraza, Guo Jin, Jin Huat Low, Raye Yeow Chen Hua National University of Singapore, Singapore

Soft actuators are the main components of soft robots’ motion. Soft actuators can be stimulated by employing various methods, including actuation with the aid of electrical charges, chemical reactions, shape memory allows and pressurized fluids. One key feature of the soft pneumatic actuators is its easy process of fabrication, safe operation, high power to weight ratio, and low cost. However, most of their design is based on the primary geometrical shapes such as circle, square, triangle, rectangle, or any polygonal shape. Most of these shapes only allow one kind of motion. Therefore, we designed a novel actuator inspired by nature, especially on the characteristic shape of the durian-thorn. The durian thorn-inspired actuator (DTIA) allows programmable inflation from a two-dimensional stretchable flat surface into a three-dimensional structure under applied air pressure. The 3D inflated shape and direction are controlled by a specific network of rings embedded inside the silicone rubber plate. The DTIA started with the mold design using a 3D CAD software; once the design is done, the mold was printed using a 3D printer machine with veroclear used as a print material. After a polymer mold was fabricated using a polymer solution. One advantage is that the DTIA can be modified according to its application; this is done varying the arrangement of the ring generating a unique 3D inflated shape. For abstract purposes, we described two soft robots as a direct application of the novel actuator design (DTIA), namely self-motion and mobile-fruit. Each robot achieves different motions to perform specific actions.

The self-motion robot consists of a rectangular box (15cm, 9cm and 5cm) with two circular holes (3.5 cm diameter)placed on the bottom face. The DTIA were placed with a distance of 5 cm from each other. In order to perform the self-motion actuation, a circular tube of 40 cm and a diameter of 3 cm was used to guide the motion. The robot was placed over the tube, and each actuator was controlled through a valve to let-in/scape the air. The robot was able to move by itself and reach the end of the tube in a time of approximately 5 minutes. The second robot consists of a fruit mobile composed of 15 DTIA. In order to contain all the DTIA, a spherical 3D case was designed and printed using PLA as print material. The sphere resembles the durian shape, and it has a diameter of 21 cm. Each DTIA was activated individually to generate the motion in four directions. Through the two robots mentioned, we demonstrated the versatility and novelty of the DTIA.

Abstract Number: ICBME1053

DNA Sequence-Topology Assembly for Multiplexed Profiling (STAMP) of Subcellular Protein Distribution
Noah Riandiputra Sundah, Huilin Shao National University of Singapore, Singapore

Massively parallel DNA sequencing is established, yet high-throughput protein profiling remains challenging. Here, we report a barcoding technology that leverages the properties of DNA nanostructures for multiplexed, high-throughput profiling of the subcellular expression and distribution of proteins in whole cells. The technology, termed DNA sequence-topology assembly for multiplexed profiling (DNA STAMP), utilizes the combinatorial sequence content of DNA nanostructures for diverse protein identification and their programmed 3D structure to improve barcoding efficiency, through nanostructure-assisted enzymatic or chemical ligation. Leveraging this sequence-structure synergy, we couple DNA nanostructures with short localization
Smooth Microfluidic Media Recirculation Using Sinusoidal Peristaltic Action of Refreshable Braille Actuator Array

Tomohiro Sekiguchi, Kotaro Nishikata, Nobuyuki Futai
Shibaura Institute of Technology, Japan

Spontaneous microvascular network formation and its remodeling into optimized network in 3D culture is a crucial structure in so-called Organ-on-a-Chip that will grow into transplantable engineered tissue. It is also known that microfluidic media perfusion is a key factor of spontaneous microvascular network formation from 3D culture of vascular endothelial cells. Previously we developed an Organ-on-a-chip platform by combining an on-chip CO2 incubation that maintains freshness and pH of cell culture media, and a Braille actuator array that displaces elastomeric microfluidic channel and generates fluid flow in it. However, the fluid flow generated from peristaltic action of Braille pins is too pulsatile and has strong backflow resulting in cells that experience non-physiological flow.

Here, we have developed a method to alleviate the strong pulsatile flow and backflow by driving the Braille pins with high-frequency sinusoidal waves.

Our microfluidic system consists of 1) a poly (dimethylsiloxane) (PDMS) microchannel layer bonded to a glass slide with Braille dots printed on, 2) a PDMS reservoir filled with bicarbonate solution as a CO2 supply, and 3) a PMMA reservoir that contains medium and covers 1) and 2). The microfluidic channel has a 3 mm-long three-lane segment separated with pillars. The lane at the center is 2 mm-wide and to which gel matrix with cells is injected. Two lanes at the sides are connected to Braille-driven perfusion channels (width:300µm, depth:50µm). Three pins of a Braille cell (SC11, KGS) continuously displace the bottom of the perfusion channel driven with rectangular voltage waveform (switching 0V and +200V) and sinusoidal voltage waveform (Upstream and downstream: Vp-p = 50V, offset=+200V, Middle: Vp-p = 145V, offset=+55V). The pins placed up- and downstream should act as valves rather than s displacement pump. The frequency and phase difference among pins were ranging 10~160 Hz, and 90 degree, respectively.

The Braille pins follow the movement of the tip of piezoelectric bimorph benders. The bimorph benders were driven by piezoelectric amplifiers (SVR-3, Piezosystemjena). The input voltage waveforms were generated from digital-to-analog converters (NI9263, National Instruments). Fluorescent beads (4.8µm) were introduced to the inlet of the microchannel. The images of the beads were taken at 395 frame/s with an inverted microscope (DMi8, Leica with DMK33UX174, The Imaging Source). The images were binarized and the volumetric flow rate was calculated with PIVlab run on MATLAB software.

The volumetric flow rate per period generated by square wave-driven Braille actuators were 8.0 [nl/s] in forward direction and 5.8 [nl/s] in reverse direction. When the actuators were sinusoidal wave-driven at 80 Hz, the forward flow rates were increased to 11.2 [nl/s], whereas the backflow was decreased to 1.6 [nl/s]. The overall flow rate was about 10 [nl/s] when the channel was driven with sinusoidal wave ranging 60 ~ 160 Hz. The backflow/forward flow rate ratio was improved to 14% from 73 % when the sinusoidal wave drive was used instead of the square wave drive.

Abstract Number: ICBME1465

Microfluidic Perfusion Array: Applications in Oral Mucosal Drug Permeation Studies

Giridharan Muniraj, Massimo Alberti, Tong Cao, Zhiping Wang, Ruige Wu, Gopu Sriram
National University of Singapore, Singapore

Objectives: Evaluation of drug absorption through oral mucosa is conventionally tested on ex vivo porcine oral mucosal tissues and recently using in vitro reconstructed oral mucosal epithelium placed within a traditional Franz diffusion cell system. However, use of Franz cell system is laborious, require large piece of oral mucosal tissues, relatively expensive and low in throughout. Use of animal-derived tissues are associated with reproducibility issues and low physiological relevance to humans. On the other hand, reconstructed oral epithelial models are made of human cells, but lack underlying connective tissues and have weak barrier function. In this work, we present the development of full-thickness engineered human oral mucosa equivalents (hOME) integrated into a custom-made microfluidic permeation array (µFPA) device, to enable high-throughput transmucosal permeation of dental anaesthetics.

Methods: hOMEs were developed using human oral keratinocytes and human primary oral fibroblasts in three stages: (i) Human fibrin-based mucosal matrix containing oral fibroblast were fabricated; (ii) the oral keratinocytes were seeded on top of the mucosal matrix following which the co-culture was submerged in media supplements; (iii) this setup was exposed to air-liquid interface for two weeks to facilitate epidermal differentiation. µFPAs consisting of multiple testing chambers functioning as flow-through diffusion cells were designed and built, loaded with hOMEs and mounted on a bespoke fraction collector to identify the penetration kinetics of dental anaesthetics through oral mucosa.

Results: Histological analysis of hOME was suggestive of the formation of a non-keratinized stratified squamous epithelium representative of lining oral mucosa. The suitability of the µFPA for permeation experiments of topical anaesthetics was first validated by using silicone membranes as oral mucosa substitutes and different doses to determine cumulative amount profiles. Various experimental parameters such as steady state fluxes, permeability coefficients and lag times were measured. Dental anaesthetics permeation through hOME in the µFPA provided the cumulative amounts and permeability coefficients of the drugs.

Conclusion: hOME in combination with µFPA has the potential to serve as a promising alternative to animal-derived tissues
and conventional Franz cell-based systems for more accurate prediction on the safety and toxicity assessment pertaining to clinical applications.

Abstract Number: ICBME1543

Low Cost Spiral for the Separation of Cells

Danny van Noort, Massimo Alberti, Tong Cao, Zhiping Wang, Ruige Wu, Gopi Sriman
Ljubljana University, Slovenia

Methods: Single unsteered plane wave blood vector velocity imaging: according to the theoretical investigation of the PSF induced by dual steered PW (DSPW) emission, an SUPW emission scheme is designed to reduce the influences of sidelobe level and reverberations on blood velocity estimation. Directional beamform is used to obtain the flow velocity components in different directions and the corresponding vector velocity is derived by RSL reconstruction. The estimation error of the proposed SUPW method was examined using simulations of a 9-mm-radius rotating cylindrical phantom with an angular speed of 20 rad/s. Also, in vivo experiment on carotid artery was performed.

Abstract Number: ICBME1266

Biomedical Engineering Education Program for Graduate Students at TWIns, Waseda University

Mitsu Umezu, Kiyotaka Iwasaki, Yuki Matsushashi, Yusuke Tsuboko, Hiroshi Kasanuki
Waseda University, Japan

Objectives: “To promote medical innovation for the overall happiness of Japanese nations” is one of the special core policies proposed by Japanese Prime Minister, Mr. Shinzo ABE. Waseda faculty members in the field of biomedical science and engineering have conducted several trials to get on a “medical innovation” policy at TWIns, where TWIns is an abbreviation for Tokyo Women’s Medical University and Waseda University Joint Institute for Advanced Biomedical Science. We will introduce master’s and doctoral education programs related to biomedical engineering (BME) at TWIns.

Methods: In 2008, the TWIns building was constructed next to Tokyo Women’s Medical University Hospital and it became the first collaborative research institute between a school of medicine and a school of science and engineering in Japan. 750 researchers, including more than 300 graduate students share this facility. 20% of them have a mechanical engineering background and they belong to a department of “Integrative Bioscience and BME”. In addition, we opened a joint graduate school that offers the first government-approved PhD degree program in Medical Regulatory Science (RS), organized by both Waseda University and Tokyo Women’s Medical University.

Results: Sustainable growth of the medical instrument industry requires fruitful collaborations among engineers and medical doctors as well as new recruits hired from the BME graduate program. Around 30 BME students in the department of “Integrative Bioscience and BME” receive their master’s degree every year. Medical RS focuses on various medical problems by formulating guidelines for advanced medical treatment—based on the foundations of life and medical sciences or medical engineering. More than 100 PhD candidates were accepted to the 3-year RS education program of which 48 submitted doctoral theses and were awarded PhD degrees as a RS specialist throughout the last ten years.

Discussion: Invention of sophisticated medical technology calls for creative thinking to solve a wide array of design and construction problems in unconventional ways. As many OB/OG who graduated from the BME department have contributed to aforementioned field, it is confirmed that the TWIns BME Graduate program is designed to satisfy the present request. The RS specialists show a great aptitude in adjusting the criteria for determining value among diverse interested parties that may include scientists, medical practitioners, industrialists,
Day 1 – 9 December 2019, Monday

governments, lawyers, ethicists as well as patients. Their RS philosophy is effective to harmonize scientific and ethical standards to allow the proper judgements to be made in different circumstances.

Conclusions: Several trials to get on the government’s medical innovation policy have produced favorable environment, such as a setup of the dry-laboratories for non-clinical evaluation of innovative medical devices and treatments, and a development of human resources. These human resources being (1) practical bioengineers (Master of Engineering), having a valuable experience on true collaboration between Medicine and Engineering towards clinical application, and (2) medical RS specialists (PhD), having professional skills to propose future medical policies.

Abstract Number: ICBME1532

Internet of Things Education for Applications in Medicine and Healthcare

Ratko Magjarevic
University of Zagreb, Croatia

Medicine and healthcare have both become major application fields of Internet of Things (IoT) industry with a large economic impact and expectations of more than 50 billion IP devices connected by 2022. The specific case of connecting medical devices and applications from healthcare IT systems through online computer networks even got a dedicated name, Internet of Medical Things or IoMT. In addition of the enormous interest from industry, IoMT aroused interest in research community and in public sector. In this presentation, we analyze the latest IoMT applications and trends of IoMT in healthcare. We also discuss how education has changed from a knowledge-transfer centric and cost-effective care through sustainable technology-centric and content creation.

Abstract Number: ICBME1033

Driving Healthcare Innovation, the SUTD Way

Xiaojuan Khoo
Singapore University of Technology and Design, Singapore

Like many developed nations, Singapore faces a daunting challenge of a rapidly aging population and an associated burgeoning healthcare cost. As such, there has been a recent push to reinvent our healthcare system to deliver more patient-centric and cost-effective care through sustainable technology-enabled solutions.

The Singapore University of Technology and Design (SUTD), Singapore’s fourth autonomous university, was established in 2009 to advance knowledge and nurture technically grounded leaders and innovators to serve societal needs. Here, we will describe how SUTD uses a unique multidisciplinary design-thinking approach towards the undergraduate engineering curriculum to support and drive healthcare innovation.

Doing away with traditional schools and departments, SUTD provides students with a broad and rigorous grounding in the fundamental engineering sciences, active immersion in design, prototyping and fabrication, and multiple opportunities to connect and integrate their learning across courses and terms. We further leverage upon partnerships with Changi General Hospital, Duke-NUS Medical School, and other partners to develop specialized healthcare-centric undergraduate programs that facilitate collaboration, mentorship, and “cultural” exchange to boost innovation efforts. With such partnerships, students will also be able to gain deeper practical knowledge and experience of working in these industries, more research and development exposure, more internship opportunities, and ultimately better career prospects.

By taking a non-traditional approach to undergraduate biomedical and healthcare engineering education, SUTD aims to produce a new breed of engineer-innovators (i.e., engineer-designers, engineer-clinicians, and entrepreneurs) best positioned to harness technological advancements across disciplines to address a wide range of pressing healthcare challenges.

Session Special Symposium 5: Wearable Sensing Technology
Date 9 December 2019, Monday
Time 1600 - 1730
Venue EA-06-04

Abstract Number: ICBME1496

Stretchable Gold Nanowire Electrode – A New Wearable Electrochemical Biosensing Platform

Wenlong Cheng
Monash University, Australia

Next generation of electronic devices will be not only flexible but also stretchable, enabling applications impossible to achieve with existing rigid circuit board technologies. This needs new materials and new design principles. Among various materials of choices, gold has advantages of biocompatibility, chemical inertness and band-gap-matching with a lot of semiconductors materials. In this talk, I will discuss our newly developed standing gold nanowire electrochemical biosensing platform. The unique Janus structures, high surface area and facile surface modification offer novel features for next-generation wearable and implantable biodianostics.

Abstract Number: ICBME1539

Skin – The Ultimate Window to Your Health

Zee Upton
Agency for Science, Technology and Research (A*STAR), Singapore

Skin is the largest organ in the body. It is a complex tissue with key roles in barrier function, thermal regulation, homeostasis, immunity, etc., and is the second largest reservoir of blood in the body. This provides us with a unique opportunity to exploit these characteristics and develop new technologies that enable us to monitor our health and wellbeing through hyper-personalised monitoring of physical and metabolic changes in skin and their association with not only skin conditions such as
Eczema, Dermatitis, and pressure sores, but also the onset on chronic diseases and other conditions associated with ageing (Cardiovascular, Diabetes, Hypertension). This will enable us to better predict, monitor, manage and prevent disease and improve health and well-being. This is being progressed by development of: 1) Real-time continuous biochemical sensing capabilities to enable better stratification of skin anomalies and quantification of analytes and hydration levels; 2) Quantitative assessment using innovative non-invasive imaging modalities to effectively measure blood flow, microvascular circulation, vascular elasticity and perfusion pressure; and 3) Clinical decision support systems by using predictive modelling techniques based on AI/machine learning algorithms. This will lead to skin being patched with new multipurpose sensors and actuators, novel diagnostics, predictive tools, mobile apps, imaging technologies and therapy recommendations, and cost-saving changes in care delivery. This presentation will provide an overview of skin biology and how this can be exploited as a window to your health.

Abstract Number: ICBME1399

Multi-Physical Modelling of Soft PDMS-Liquid Metal Interdigitated Capacitors Sensor

Zhuangjian Liu, Yida Li, Aaron Voon-Yew Thean
Institute Of High Performance Computing, Singapore

Numerical models of multi-sensing capability soft-matter interdigitated (IDE) capacitors sensors are studied by using the 3D finite element method. With micro-channels of liquid-phase metals embedded in a flexible matrix, this type of sensors can undergo large deformations while sustaining adequate characters as comparison with conventional rigid electronics. Therefore, the sensor are easy employed and integrated with the human body and potentially extend to be used as skin-like electrical devices. In this study, we quantitatively verified this numerical model subjected to uniaxial load by using the comparison between simulation and experimental results at firstly. The capacitance increases with an increasing strain along the channel's axial direction. Excellent linearity between the capacitance and strain is shown. And more, the effect of bending and stretch strain with difference direction on the capacitance are analysed. Then, we demonstrate the capacitance change with a float electrode (human finger) placed at different distances from the capacitor. The capacitance is increased when the float electrode move towards the capacitor and decreased when float electrode away from the capacitor. It can be used for on-body respiratory sensing by utilizing the proximity effect, when the soft IDE capacitor sensor attached to a human chest with integrated a functional capacitance sensing chip. It is potentially used as a soft sensor suitable for use in wearables for health monitoring.

Abstract Number: ICBME1527

Stretchable Smart Device Using Liquid-State Electronics

Hiroki Ota
Yokohama National University, Japan

Stretchable devices have many potential applications in wearable electronics, robotics, health monitoring, and more. Mechanically deformable devices and sensors enable conformal coverage of electronic systems on curved and soft surfaces. Sensors utilizing liquids confined in soft templates as the sensing component present the ideal platform for such applications, as liquids are inherently more deformable than solids. A new approach utilizing the concept of “liquid-state electronics” with conductive liquids for stretchable sensors has been proposed. Here, we report the fabrication methods of the electronics, sensors and system integration using the electrodes.

In terms of fabrication methods, we show 2D and 3D fabrication based on micro fabrication technologies. The 2D fabrication methods are based on the soft lithography and describing by a dispenser. The surface of the liquid metal is oxidized and prevent the fine fabrication which is required to make sophisticated electric devices. In this presentation, we show the fabrication of high-resolution liquid metal electrodes.

Using these fabrication methods, we propose four sensors, pressure, temperature, humidity and light sensors in this report. In terms of a pressure sensor, current liquid-metal based pressure sensors are incapable of resolving small pressure changes in the few kPa range, making them unsuitable for applications such as heart-rate monitoring which require much lower pressure detection resolution. The developed capable of resolving sub-50 Pa changes in pressure with sub-100 Pa detection limits and a response time of 90 ms is demonstrated in this report. As examples of potential applications, a polydimethylsiloxane wristband with an embedded microfluidic diaphragm pressure sensor capable of real time pulse monitoring. Liquid-based devices such as pressure sensors have been limited to metal lines based on a single liquid (e. g. Liquid metal) component given the difficulty in the fabrication of liquid-based junctions due to intermixing. We demonstrate state-of-art microfluidic environmental sensors using liquid metal, temperature, humidity, oxygen and light sensors with mechanically robust liquid-liquid “heterojunction”.

In addition to the sensors, the system integration using 3D liquid metal electrodes is proposed. As a proof of the concept, we demonstrate a smart glove having resistive heater, “earable” device for real time detection of tympanic body temperature and wearable sensors for multi vital detection of newborn babies.

This report will present an important advancement towards the realization of liquid-state electronic systems.

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Abstract Number: ICBME1523

Exosomes and Mimetic Technologies for Therapeutics

Yong Song Gho
Pohang University of Science and Technology, Korea

Communication between cells and environment is an essential process in living organisms. The secretion of exosomes and exosome-mediated communication are universal cellular processes occurring from simple organisms to complex
multicellular organisms, including humans. Recent progress in this area has revealed that exosomes play multiple roles in intercellular and interspecies communication, suggesting that exosomes are NanoCosmos, i.e., extracellular organelles that play diverse roles in intercellular communication (http://evpedia.info). This presentation will briefly introduce the state-of-art exosome research and focuses on our recent progress in novel exosome-mimetic technologies for targeted drug delivery, theranostics, and epigenetic reprogramming as well as for adjuvant-free, non-toxic vaccine delivery system against bacterial infection. Future research directions on our exosome isolation technology ‘ExoLute’ for basic researches and clinical applications will be briefly introduced.

Extracellular Vesicles in Cross Species Communication and Cancer Progression

Suresh Mathivanan
La Trobe University Australia

Identification: Current medicine, which is predominantly based on small molecule drugs, has only taken us so far in beating disease and tissue degeneration. Extracellular vesicles (EVs), which are highly specialised, yet ubiquitous nanoscale messengers secreted by cells have emerged as the new generation of medicine. The problem is, their power cannot be harnessed because they are heterogeneous, and little is known about them.

The aim of our study was to determine molecular composition of individual EVs, populations and subpopulations and define the correlation between molecular composition of EVs and their therapeutic efficacy

Methods: To characterize what is inside individual vesicles we developed methodology that utilizes ultra-high-resolution capability of atomic force microscopy nanoinfrared spectroscopy (nanoIR) and nanoflow cytometry (nanoFCM).

Results: Our study showed that EVs isolated from different types of placenta stem cells, which are exposed to different level of oxidative stress, have major differences in protein, RNA/DNA and lipid contents. We further studied the effect of purification of EVs using size exclusion chromatography, and indeed we demonstrated that the molecular composition, i.e. protein, is substantially different for purified EVs. Analyzing these variations at nanoscale may also provide a robust evidence of pathological processes.

Discussion & Conclusions: Taken together, there is a potential for AFM-IR to be utilized as highly sensitive, precise and relatively fast measurement of EV structure and composition to determine the most effective EVs purification protocols as well as to gain new knowledge how they are produced to be able to harness their power for diagnostic and therapeutic applications.

Acknowledgements: University of Sydney SOAR Fellowship; European Respiratory Society for the ESR Fellowship.

Abstract Number: ICBME1517

Label-Free Isolation of Circulating Exosomes from Whole Blood Using Centrifugal Forces

Han Wei Hou
Nanyang Technological University of Singapore, Singapore

Background & Objectives: Extracellular vesicles (EVs), including exosomes (~50–200 nm) and microvesicles (~100 nm–1 µm), are produced by cells upon physiological or pathological cues and serve as key mediators for intercellular communications [1]. While circulating EV in blood are promising diagnostics biomarkers in diseases [1-2], isolation of blood-borne exosomes involves laborious ultracentrifugation [1] or commercial precipitation kits with high protein contamination [3]. Our group has previously developed a microfluidic technology termed High-resolution Dean Flow Fractionation (HiDFF) for sub-micron binary particle sorting [4]. Herein, we further developed the HiDFF technology into a novel multiplexed EV fractionation tool (ExoDFF), and demonstrated direct isolation of circulating exosomes from whole blood. Our label-free, low-cost EV purification approach is high throughput (~20 µL undiluted whole blood (WB)/min), scalable by device stacking, and offers higher EV yield as compared to differential ultracentrifugation.

Method: The spiral ExoDFF polydimethylsiloxane microdevice has a 4-outlet system with non-uniform outlet resistance configuration. Diluted WB (1:1) is introduced at channel outer wall, where smaller blood components (platelets and EVs, particle size (ap)/hydraulic diameter (Dh) <0.07) migrate laterally towards inner wall under the influence of Dean vortices. Near the inner wall, they occupy differential innermost transient (non-equilibrium) positions due to size-dependent wall-induced inertial lift force (FWL) for high-resolution size fractionation into inner outlets (O1–O3). Larger blood cells (RBCs and WBCs), experiencing significant Stoke’s drag, remain closer to the outer wall and exit via the outer outlet (O4).

Results: The device was first characterized using fluorescent microbeads (50 nm–1 µm) at an optimized flow rate to visualize streamline positions, and quantification by flow cytometry and scanning electron microscopy indicated high separation efficiency. For whole blood processing, high-speed imaging reflected efficient removal of platelets (~2–3 µm) and larger blood cells (~5–15 µm) via O3 and O4, respectively. The ExoDFF-sorted EVs (O1, O2) were then characterized using nanoparticle tracking analysis which showed higher EV yield in O1 as compared to ultracentrifugation. In addition, bioanalyzer analysis also indicated increased microRNA in ExoDFF O1, which is crucial for downstream RNA profiling. To further increase processing throughput, we stacked identical ExoDFF devices (3 layers) to achieve ~60 µL undiluted WB/min processing time with similar separation performance.
Conclusion: We have developed a low-cost and label-free microfluidic strategy for direct and scalable isolation of circulating exosomes from whole blood. The device is simple to use, requires minimal user operation, and can be readily translated to clinical settings to accelerate exosome biology research, and development of point-of-care exosome diagnostic tools.

References

Abstract Number: ICBME1513

MSC Exosome for Cell-Free Regenerative Joint Therapy: Escalating towards Clinical Application

Wei Seong Toh
National University of Singapore, Singapore

Mesenchymal stem/stromal cells (MSCs) are currently evaluated in clinical trials for treatment of several diseases including joint injuries and osteoarthritis (OA). Increasingly, the therapeutic efficacy of MSCs is attributed to the paracrine secretion, particularly small extracellular vesicles (sEVs) of 50-200nm. Exosomes are a specific class of sEVs of endosomal origin, and are thought to function primarily as intercellular communication vehicles to transfer bioactive lipids, nucleic acids and proteins between cells to elicit biological responses in recipient cells. For MSC exosomes, many of these biological responses translate to a therapeutic outcome in injured or diseased cells. Here, we developed a scalable manufacture of human MSC exosomes from an immortalized MSC line, and demonstrated that these exosomes displayed a modal size of 100nm and expressed the exosomal markers including CD81, ALIX and TSG101. In a rat osteochondral defect model, we observed that weekly intra-articular injections of MSC exosomes (100µg) effectively promoted osteochondral regeneration. Exosome-mediated osteochondral repair was associated with suppressed inflammation with increased M2 over M1 macrophage infiltration, enhanced cellular proliferation and matrix synthesis, and reduced apoptosis. This wide spectrum of activities could be attributed to the diverse protein cargo of MSC exosome. Among them, exosomal CD73/ecto-5´-nucleotidase was found to regulate chondrocyte survival, proliferation and migration through adenosine-mediated activation of AKT and ERK survival kinases. In escalating towards clinical application, we explored the combination with hyaluronic acid (HA) that is clinically used in viscosupplementation for joint injuries and OA, and performed further investigation in a rabbit model of osteochondral defect. We observed that three 1-ml injections of exosomes (200µg) and HA were effective in promoting sustained and functional cartilage repair. Defects treated with exosomes and HA showed enhanced functional cartilage repair with progressive improvements in gross appearance, histological scores and mechanical properties. By 12 weeks, the newly repaired tissues in defects treated with exosomes and HA composed mainly of hyaline cartilage that are mechanically and structurally superior to that of HA treated defects and demonstrated mechanical properties that approximated that of adjacent native cartilage. Collectively, our findings have provided the basis for development of an off-the-shelf cell-free therapy that can be escalated to a clinical protocol for joint repair in patients.

Abstract Number: ICBME1512

Nanosensor Technologies for Molecular Analyses of Circulating Exosomes

Huilin Shao
National University of Singapore, Singapore

Objectives: The growing emphasis on personalized medicine significantly increases the need to analyze key molecular markers. In comparison to tissue biopsies, circulating biomarkers (liquid biopsies) can be conveniently and repeatedly obtained from biofluids with minimal complications. In particular, exosomes have recently emerged as a promising circulating biomarker. Exosomes are nanometer-sized membrane vesicles actively shed off by cells and possess unique advantages: they abound in biofluids and harbor diverse molecular contents (e.g., proteins and nucleic acids).

Methods: In this talk, I will describe various nanosensor systems that we have developed for quantitative analyses of diverse exosome targets. These technologies integrate advances in molecular biology, nanomaterial sciences and device engineering.

Results and Conclusions: By enabling rapid, sensitive and cost-effective detection of circulating biomarkers, these platforms could significantly expand the reach of preclinical and clinical research, in informing therapy selection, rationally directing trials, and improving sequential monitoring to achieve better clinical outcomes.
Biomedical Signal Analysis of "Nihon Kendo Kata"

Kentaro Takahashi, Minato Kawaguchi
Kanto Gakuin University, Japan

A study was performed to analyze electromyographic (EMG) and electroencephalographic (EEG) levels during the motion of "Nihon Kendo Kata Ippon-me". The results suggested that EEG-EMG coherent intensity might serve as an index to differentiate the skill levels. There are three types of advancement in kendo, with being preemptive regarded as critical. Reports are available on the experiments of kendo-kata first move representing pre-advancement; however, there have been no reports on kendo-kata sixth move representing post-advancement. In this study, we simultaneously measured EEG and EMG levels during the motion of kendo-kata sixth move in the hope of clarifying the characteristics of skill levels among swordsmen.

The study involved five experienced kendo practitioners (1 seventh-dan, 1 fifth-dan, 1 fourth-dan, and 2 third-dan players) and one inexperienced layman. The participants were asked to perform Nihon Kendo Kata "Ippon-me" and "Rokuhon-me", uchitachi and shitachi move three times each. EEG and EMG levels were measured by "eego sports" software with the sampling frequency set at 1024 Hz. For EEG measurement, 32 ch was used based on the international 10/20 system, and power vector densities were calculated at α, β, and γ waves. From the measured EEG and EMG levels, EEG-EMG coherence values were extrapolated.

During the uchidachi sessions, the seventh-dan player exhibited high coherence values from the start of the motion toward the moment of the thrust. During the shitachi sessions, the seventh-dan player and the fifth-dan player showed high coherence values from the raising of the sword to the moment of the thrust. These results indicate that these players had their concentration heightened during these moments, thus enhancing the precision of the movement. During the uchidachi sessions, the dispersion of the minimum EEG-EMG coherence values was low among the highly ranked players. This may be because strong signals from the brain made it possible to repeat the movement with precision. Meanwhile, the shitachi motion requires the player to precisely handle the wooden sword and flexibly respond to subtle changes in the opponent’s movement. Therefore, the higher ranked player exhibited lower dispersal of mean EEG-EMG coherence values. These findings suggest that analysis of biomedical signals in "Nihon Kendo Kata" may make it possible to clarify the characteristics of skill levels by dan rank.

Analysis of Respiration Pattern and Frontal Brain Activity During the Aiming Period in Rifle Shooting

Minato Kawaguchi, Hiroshi Sato, Susumu Takemura, Kentaro Takahashi
Kanto Gakuin University, Japan

In some shooting competitions, the shooter is required to maintain physical and mental stabilities. Some investigations have shown a cardiac deceleration in shooters just before the timing of trigger pull since heartbeat, directly affected by the respiration, reflects both physical and mental stabilities. However, it has been not unclear whether this phenomenon can assess skill level. Thus, other portable methods that directly estimate cognitive status has been applied such as the electroencephalogram (EEG) and the near-infrared spectroscopy (NIRS). Although investigations have analyzed for the detection of the intention by the EEG, it has been unclear whether the NIRS can assess the shooting skill.

Our objective is to analyze whether the physiological signals derived from practically suitable methods can assess the skill in rifle shooting.

Four students participated in this study. Each participant demonstrated the task consisting of the rest (3 minutes), sighting shot, and the live shot (20 trials). During the shot tasks, the participant demonstrated the ISSF 10m air rifle. They have required the standing position and aimed at a target with a diameter of 45.5[m] and a distance of 10[m]. The respiratory pattern, the ECG, and the NIRS were recorded simultaneously with a sampling frequency of 200[Hz] (respiration and ECG, using “Polymate-II” (Miyuki Giken Co., Ltd., Japan)) or 10[Hz] (NIRS using “NIR-200NX” (Hamamatsu Photonics K.K., Japan)). The NIRS was applied for the prefrontal brain area. The time event of the trigger pull (ttrig) was further recorded during a live shot. The average score was compared by the multiple comparisons with the Bonferroni correction. The signals were split with the reference of the trigger event (from ttrig-20[s] to ttrig+1.5[s]) since all the intervals of triggering was longer than 20[s]. We calculated the root mean square of (RMS) respiration in the range from ttrig to ttrig+1.5[s] as an index of physical stability. The heart rate [bpm] was calculated from the ECG as inverting R-R intervals.

The results from the score showed that they were classified into three groups: one elite, two skilled, and one novice. The RMS in the elite was significantly lower than the other participants. The results of heart rate showed that heart rate [bpm] significantly decreased in only the elite, despite both elite and novice maintained exhausting until triggering. We could successfully observe that 1) the elite stabilizes the posture even after triggering and a respiration sensor can detect that, and 2) cardiac deceleration could be necessary, but there are other factors than respiration such as activity in the central nervous system. We will analyze the frontal brain activity. This study could accelerate our understanding of a mechanism for physical and cognitive coordination in shooting actions.

Analysis of the Muscle Activity and the 3-Direction Force During the Constant Work Rate Pedaling

Atsushi Iwashita, Yuto Konishi, Iori Arisue, Katsuya Tamaki, Toshio Kawanaka, Takeshi Fujinaga, Hiroki Okubo, Masaki Yoshida
Yamato University, Japan

Objectives: There is diversity in the combination of the loading and the pedaling rate when the constant work rate pedaling. So
Simulations were performed for a degeneration and arthroplasty studies. The effect of compressive loads that should be effectively supported by the human cervical spine to protect the spinal cord and maintain interrelationships among vertebrae. Different experimental studies have used various testing protocols to study the effect of a compressive load on the cervical spine. The objective of this study is to investigate the effect of such an in vivo compressive load on the range of motion (ROM) of the sub-axial column using a novel computational method. Endplate stresses (EPS) from physiological flexion-extension loading is examined under the intact condition for an improved understanding of internal mechanics with future applications in adjacent level degeneration and arthroplasty studies.

Methods: Ten subjects participated in the study. This study was approved by the Ethics Committee of the Nara city hospital. Ergometric cycling was performed under five pedaling rates (30, 50, and 70,90,110) into work rates (150W). We used the dynamic sensor built-in crank. We measured it every crank angle of 1° that the force in the rotational direction of the pedal(Fθ) and the force in the rotational axis direction of the crank from the pedal(Fr),the force in the direction in which the pedal shaft pushes the crank(Fz). We calculated the average 3-directon force for pedal during 15 revolutions for each pedaling rate. We measured crank angle and hip, knee and ankle angle on pedaling by 3D motion Analysis system. We used an active electrode, and the electromyography activity during ergometric cycling was measured in the vastus lateralis, semimembranous, gastrocnemius lateralis, and tibialis anterior, all bilateral. We calculated Averaged Mean New Value (ARV) and normalized with the maximum isometric contraction of each muscle taken as 100%, and expressed as% ARV. For statistical analysis, we used repeated measures One-way ANOVA and Fisher`s PLD.

Results and Conclusions: The force in the rotational direction of the pedal (Fθ) decreased as pedaling rate increased. The force in the rotational axis direction of the crank from the pedal(Fr) in the radial direction decreased as pedaling rate increased. The force in the direction in which the pedal shaft pushes the crank(Fz) shifted from the inside to the outside as pedaling rate increased. The muscle activity showed a minimum value at 50 rpm. In otherhand, the muscle activity of low rpm and high rpm speed showed a high value. These showed that the operation strategy of depressing the pedal is changed and the rotation is performed efficiently as pedaling rate increases.

Abstract Number: ICBME1294

Influence of Compressive Preloading on Range of Motion and Endplate Stresses in the Cervical Spine During Flexion/Extension

VIT University, Chennai Campus, India

Objective: The natural weight of the head, any head supported mass and various muscle forces result in eccentric compressive loads that should be effectively supported by the human cervical spine to protect the spinal cord and maintain interrelationships among vertebrae. Different experimental studies have used various testing protocols to study the effect of a compressive preload on the biomechanics of the cervical spine. The objective of this study is to investigate the effect of such an in vivo compressive load on the range of motion (ROM) of the sub-axial column using a novel computational method. Endplate stresses (EPS) from physiological flexion-extension loading is examined under the intact condition for an improved understanding of internal mechanics with future applications in adjacent level degeneration and arthroplasty studies.

Methods: An anatomically accurate and validated finite element model (FEM) of a human sub-axial spinal column (C2-T1) was used in this study. Material properties for all spine components were taken from literature. Cortical bone, cancellous core and intervertebral disks were modelled using linear isotropic elements. Ligaments were modelled using shell elements with non-linear material properties. External load was applied at the center of gravity of the C2 vertebrae through a kinematic coupling to account for the head mass.

An algorithm programmed using Python was interfaced with ABAQUS to calculate ROMs with nodal data extracted from its workspace. The code used nodal co-ordinates at the endplates to define physiological planes, and this process helped to calculate ROMs using a similar plane that was constructed for the deformed model. The ROMs was successfully computed using these definitions, and EPS was measured further across all the segmental units.

Results And Conclusion: Simulations were performed for a physiological sagittal moment of 2 Nm with a compressive preload of 100 N (head load with supported mass) with the appropriate boundary conditions. The effect of segmental response on the cervical spine was investigated and the ROM values verified with literature. ROMs in extension varied from 3-11 degrees while the maximum stress induced in the endplates varied between 2.02e-3 MPa and 2.072e-1 MPa. The ROM in flexion ranged between 6-15 degrees while the maximum stress induced in the endplates varied between 3.47e-3 MPa and 2.687e-1 MPa. These results indicate that extension loading with head supported mass induces greater ROM and stresses in endplates than flexion. A future research would be to incorporate active musculature and investigate occurrence of different grades of heterotopic ossification and bone remodeling after disc arthroplasty in patient-specific FEMs.

Acknowledgements: This study was supported by the Dassault Systemes Foundation, India; the Department of Neurosurgery, Medical College of Wisconsin; VIT, Chennai, India and Ganga hospitals, Coimbatore, India.

Abstract Number: ICBME1030

Biomechanical Analysis of Bone-Prosthesis Interface Micromotion for Cementless Talar Component Fixation in Preventing Aseptic Loosening Failure

1Desmond Y.R. Chong, Yu Shen Ong, Chin Tat Lim, Raye Yeow Chen Hua, Desmond Yok Rue Chong
2Singapore Institute of Technology
National University of Singapore, Singapore

Objective: Primary stability of a total ankle replacement (TAR) is essential in preventing long-term aseptic loosening failure, and could be analysed biomechanically in terms of bone-prosthesis interface relative micromotion. Clinical outcome studies have shown that aseptic loosening of the TAR is commonly due to the failure of the talar component. Hence it was of interest to
investigate the failure mechanism of the talar component when subjected to physiological loading conditions. The influence of different design features of the talar component on bone-prosthesis interface micromotion was also studied.

Methods: The commercially available STAR™ (Scandinavian Total Ankle Replacement) Ankle design and several additional divergence design features (including trabecular metal, side fin, double fin and polka-dot designs) were studied using finite element analysis (FEA). Bone-prosthesis interface micromotion and talar bone minimum principal stresses were examined and analysed. Different loading conditions consisting of three distinct events of a human walking gait cycle of heel strike, midstance and toe off were applied to the FEA models. The FEA models and results were also being validated with experimental cadaveric study.

Results: The predicted bone-prosthesis interface micromotion results have shown that the STAR™ Ankle talar component primary stability failure was mainly due to the de-bonding displacement (COPEN) and was highly concentrated within the posterior region of interest. Lower bone-prosthesis interface micromotions and comparable minimum principal bone stresses were predicted for the polka dot design and was consequently selected as part of the convergence study. The convergence study was focused mainly on the hemisphere features of the polka dot design with variations such as the diameter, length, shape and density. Length increment (to 3 mm pin length) and modified density (pin reduction in a crisscross manner) variations have generated encouraging FE results and therefore was used as part of the proposed final design. In validating the FEA models, the experimental and predicted max/min principal bone strains were fitted into regression models and showed good correlations. The correlation regression coefficients (R²) were 0.812 and 0.816 for the STAR™ Ankle and polka dot designs respectively. The measured bone-prosthesis interface micromotion of the polka dot talar component (19.50 µm to 43.10 µm) was found to be much lower than the STAR™ Ankle talar component (230.02 µm to 245.88 µm) across the three distinctive loading conditions.

Conclusions: High bone-prosthesis interface micromotion due to de-bonding was predicted for the STAR™ Ankle talar component at the posterior region which coincided with clinical observations of talar component loosening. The polka for talar component design that incorporated both the 3 mm pin length and pin reduction in a crisscross manner was found to be a favourable design with reduced bone-prosthesis interface micromotion and talus bone stress thereby reducing the risk of long-term aseptic loosening.

Abstract Number: ICBME1263

Identifying Hip Fracture-Related Critical “Weak-Links” Within the Femur by in Vivo microMRI-Based Finite Element Analysis

Lingyun Zhang, Yang Haisheng, Fu Ruisen
Beijing University of Technology, China

Objectives: Osteoporosis is a metabolic bone disease characterized by loss of bone density and deterioration of bone microstructure, inducing an elevated risk of fracture. Hip fractures are the most common type of osteoporotic fractures and over 90% of them are caused by sideways fall. Whereas dual-energy X-ray absorptiometry (DXA)-assessed areal bone mineral density (aBMD) is a standard clinic tool for estimating fracture risk, close to half of individuals with fractures have normal aBMD by DXA. DXA cannot capture bone microarchitectures and identify the regions at the highest risk of failure (“weak-links”) within the femur, particularly under a sideways fall condition. High-resolution micro-magnetic resonance imaging (microMRI) can be used in vivo to reveal detailed bone microarchitectures with low radiation effects [1]. The objective of the study was to investigate the micromechanics of the proximal femur under stance and sideway fall by microMRI-based finite element analysis (FEA) and identify critical weak-links of the microarchitectures related with hip fractures.

Methods: In vivo microMRI (resolution: 0.1875 mm) was performed on the proximal femurs of 12 subjects (50±16 years old; 5 males and 7 females). The proximal femur was segmented out from surrounding muscles and other soft tissues on the microMRI scans. MicroFE models were built by directly converting voxels into eight-node hexahedral finite elements. Each femoral FE model consists of about 9 million elements. Loading and boundary conditions were applied to each proximal femur to simulate the stance and sideway fall postures [2]. Large-scale linear elastic FEA was performed, from which stiffness (load/displacement) of the proximal femur as well as maximum and minimum principal stresses were determined. “Weak-links” regions were then identified as the microarchitectures that are highly stressed and therefore present a high risk of initial failure.

Results: Compared to the stance loading condition, the femoral stiffness under the sideway fall loading condition were decreased by 21% regardless of gender. The maximum or minimum principal stresses were greater for sideway fall than stance postures. In terms of stress distribution, the superior femoral neck was in compression and the inferior femoral neck was in tension for the sideways fall whereas this stress distribution was opposite for stance. Based on the overall stress distribution within the proximal femur, two regions of 10 X 10 X 10 mm3 within the femoral neck and trochanter were selected, respectively, to compare. The mean compressive or tensile strains were not significantly different between femoral neck and trochanter for the stance posture but 45.3% higher in the sideways fall than the stance postures (p<0.05 by paired t-test), indicating that the trochanter region may be a critical “weak-link” at a high risk of fracture initiation during sideway falls.

Conclusions: In vivo microMRI-based FEA revealed the trabecular bone nearby the great trochanter might serve as one of the “weak-links” of the femur under sideways fall. Identification of the “weak-links” may be important for fracture risk evaluation beyond BMD in clinic.

References
[1] Chang G et al., 2018 Radiology;

Abstract Number: ICBME1376

Dynamic 3D Imaging of Articular Cartilage under Repetitive Compression Measured by Phase-Contrast X-Ray CT

Takako Osawa, Tatsuhiro Aoki, Tomoya Konishi, Shinji Tatsumi, Masato Hoshino, Takeshi Matsumoto
Kindai University, Japan

Abstract Number: ICBME1376

Dynamic 3D Imaging of Articular Cartilage under Repetitive Compression Measured by Phase-Contrast X-Ray CT

Takako Osawa, Tatsuhiro Aoki, Tomoya Konishi, Shinji Tatsumi, Masato Hoshino, Takeshi Matsumoto
Kindai University, Japan
Articular cartilage is a connective soft tissue, which protects articulating bones by transferring and redistributing contact/impact loads. The cartilage has laminar structure varying across cartilage depth. This depth-dependent structure is deeply involved in mechanical property and behavior of cartilage. The cartilage degeneration disease such as osteoarthritis impairs primary functions, and the dysfunctions of cartilage decreases quality of active daily life seriously. In osteoarthritis, compositional and structural alterations of articular cartilage are sensitively detected through changes in the mechanical tissue properties. The evaluation of mechanical properties of cartilage may be useful for the diagnostics of early osteoarthritis. Essence of mechanical properties of cartilage under the dynamic environment is viscoelasticity. Thus, the dynamic 3D imaging technology is necessary to analyze the viscoelasticity of cartilage having inhomogeneous microstructure. The dynamic phase-contrast X-ray CT has much higher density resolution than absorption-based X-ray microtomography. In our previous study, a high-resolution phase-contrast X-ray CT of the inhomogeneous density distribution in pig knee joint cartilage was successfully carried out. The purpose of this study is to sophisticate this technique for the measurement of local deformation of cartilage under dynamic viscoelasticity test. Using SPring-8 synchrotron radiation as X-rays light source, pig knee joint cartilage tissue was imaged by dynamic phase-contrast X-ray CT under repetitive compression. The X-ray energy is set to 20keV. The phase-contrast reflecting the cartilage density difference was detected through using Talbot interferometer. The specimen was harvested from medial condyle and lateral condyle at a femur of an edible pig knee joint. The cartilage is thick in these regions. The cartilage tissue was manufactured into column specimens ranging in height from the upper subchondral bone layer to a cartilage surface layer (a diameter: 3mm, a thickness: 2-3mm). The specimen was placed in saline, its bottom was fixed, and the top was subjected to the repetitive compressive force. The repetitive compressive force was applied as the intermittent triangular form on the conditions of strain amplitude=10%, frequency=0.4Hz or 0.8Hz, and pre-load=0.4-0.6N, respectively. The artifact due to density differences between acrylic indenter and articular cartilage observed in the previous study was reduced by using a polypropylene indenter, thereby enabling the measurement of local deformation in the surface layer of cartilage. In both frequencies of 0.4Hz and 0.8Hz, a clear density distribution of cartilage was imaged (resolution: 4.4μm), showing that the dynamic phase-contrast X-ray CT is useful for assessing the local deformation of cartilage at each layer under the viscoelasticity test.

Abstract Number: ICBME1440

An Inverse Finite Element Method to Measure In-Vivo Biomechanical Properties of Human Iris

Satish Kumar Panda, Baskaran Mani, Aung Tin, Michael Girard
National University of Singapore, Singapore

Iris biomechanical properties play a significant role in the pathophysiology of primary angle-closure glaucoma which is one of the leading cause of blindness, especially in the Asian subcontinent. Over the past few decades, several experimental, e.g., tensile testing and indentation testing, and computational approaches, e.g., inverse finite element analysis and vector force analysis, have been made to compute these properties accurately. However, the experimental procedures are ex-vivo in nature, and also the post-mortem biological changes alter the tissue properties. Furthermore, the current computational approaches are not sufficient to extract true tissue properties. Here, we propose a novel non-invasive methodology to obtain the biomechanical properties of iris soft tissues from the in-vivo bio-medical images.

An optical coherence tomography machine was used to capture the constriction of the pupil as a series of images. The boundary of the iris was delineated for each image to obtain the temporal deformation pattern of the iris during spontaneous contraction. A finite element (FE) model was constructed using the information from the first image, whereas the other images were used for extraction of mechanical parameters. We loaded the sphincter region of the iris with active stress to initiate active contraction and then used an optimization algorithm to minimize the differences between the true and the FE iris boundary during spontaneous contraction. In this way, we were able to compute the ‘best-guessed’ mechanical properties of the iris tissue. We used both compressible and incompressible Mooney-Rivlin material for our simulation to determine the true nature of the tissue, and also examined the consequences of sphincter muscle location on the iris biomechanics. The normalized Young’s modulus, i.e., the ratio of Young’s modulus to the applied active stress, was found to be 0.8 which agrees well with the current literature.

We believe, the proposed methodology will provide an efficient way to compute the soft tissue stiffness from the in-vivo bio-images of iris movement.

Abstract Number: ICBME1056

Wirelessly Responsive and Highly Pliant Sutures for Post-Operative Wound Monitoring

Viveka Kalidasan
National University of Singapore, Singapore

Wirelessly responsive and highly pliant sutures for post-operative wound monitoring

Surgical sutures are passive medical devices which are used to appose tissue at the surgical site and hence provide a promising platform to build any multi-pronged monitoring and therapeutic strategy. Monitoring a surgical site deep within the body and under the bandage is involves expensive and not continuous imaging techniques like magnetic resonance imaging (MRI), computerized tomography (CT) etc., Moreover, invasive corrective interventions might be needed as the symptoms of post-surgical complications often appear very late. It is important to monitor surgical site for post-surgical complications, as it can help in early and non-invasive/minimally invasive corrective interventions. We have developed a class of wireless sensing (WISE) sutures to monitor the surgical site and communicate for post-surgical complications. WISE sutures are fabricated by coating commercial sutures with conductive polymer PEDOT: PSS and attaching ultra-miniaturized electronics on-board. The sensing module comprises of LC circuit and communication is
through Schottky diode while the conductive suture itself acts as a dipole antenna. Change in permittivity of the capacitor area, due to change in surgical environment causes a change in capacitance, which in-turn modulates a change in resonant frequency. Our proof-of-concept studies show that WISE sutures can monitor post-surgical complications like sudden bleeding/haemorrhage, bacterial infection through and compromise in suture integrity. As the capacitance of on-board ultra-miniaturized device changes during bleeding and infection, the resonant frequency shifts up to 200 MHz from the initial frequency. The power decreases up to 50 dBm when there is complete compromise in suture integrity. In vivo studies on skin (surface) and muscle (deep) tissue of rats over a period of 14 days show that the wound healing of surgical site using WISE suture is similar to that of medical grade sutures interms of material mechanics and biocompatibility and the wireless capabilities do not degrade over the time. The hematoxylin and eosin (H&E) and confocal micrographs of animal tissue sutured with WISE and medical grade silk sutures show the comparable expression of fibronectin, collagen and cluster of differentiation 3 (CD3) protein through the different phases of normal wound healing.

The resonant frequency of WISE sutures remains constant over a period of 14 days for both skin and muscle applications. WISE sutures thereby become the first-of-its kind ‘active’ sutures which can aid in improved patient-centred outcome. WISE sutures are the first step towards the next generation intelligent and holistic surgical approach from surgery to monitoring for post-surgical complications.

Abstract Number: ICBME1150

Tissue-Adhesive and Wireless Light-Emitting Device for Photodynamic Cancer Therapy

Kento Yamagishi, Izumi Kirino, Isao Takahashi, Hizuru Amano, Shinji Takeoka, Yuji Morimoto, Toshinori Fujie

Waseda University, Japan

For the development of light-based cancer therapy such as photodynamic therapy (PDT), the local delivery of sufficient light energy to target lesions in the body is crucially important. Especially, metronomic (low-dose and long-term) PDT (mPDT) for treating deeply-located lesions requires a long-term stable fixation of small, wirelessly-powered optical devices to the living internal tissue surfaces to enable continuous, local light irradiation. Surgical suturing or use of medical glue are the standard choices for the fixation of implantable devices, but such operations can be unsuitable in the presence of surrounding major nerves and blood vessels, as well as for organs or tissues that are fragile, change their shape or actively move. Therefore, attaching patch-type optical devices onto the surface of tissues or organs with the aid of the tissue-adhesive platform is the least invasive approach. In this study, we developed tissue-adhesive and wirelessly powered optoelectronic devices that can be secured onto the biological tissue surfaces without suture or glue in the animal body. Wirelessly-powered LED chips were encapsulated with polydopamine-modified polydimethylsiloxane ultrathin films (PDA-PDMA nanoshes, 650 nm thick). The devices were subcutaneously fixed, without any medical glue or suture operation, on the intradermal tumor model mice. LEDs were placed just beneath the tumors. After administration of a photosensitizer (photofrin) into the mice, the implanted optical devices locally irradiated the target tumors for 10 days at an approximately 1,000-fold lower intensity than conventional PDT. As a result, remarkable tumor regression including complete disappearance was observed. Such a fully-implantable and wireless LED-based mPDT system is expected to be applied for deeply located cancers that conventional laser-based optical devices could not reach.

Abstract Number: ICBME1170

Mechanical Loading Promotes the Expansion of Primitive Osteoprogenitors and Organizes Matrix and Vascular Morphology in Long Bone Defects

Chao Liu, Pamela Cabahug-Zuckerman, Christopher Stubbs, Martin Pendola, Cinyee Cai, Kenneth A. Mann, Alesha B. Castillo

Southern University of Science and Technology, China

Objective: Mechanical stimulation has crucial impact on bone formation [1] and has the potential to enhance bone repair [2]. The regulatory role that mechanical loading exerts on the osteogenic stem cell population and blood vessel morphology during bone repair is still unclear. Dynamic compressive loading after the onset of matrix deposition has been shown to enhance bone repair [3], we hypothesized that loading induces the expansion of the osteoprogenitor cell population within a healing bone defect, leading to increased osteogenic cell number. We further hypothesized that loading during the repair process regulates vascular and collagen matrix morphology and spatial interactions between vessels and osteogenic cells.

Methods: To address these hypotheses, we used a mechanobiological bone repair model in mice, which produces a consistent and reproducible intramembranous repair response confined in time and space. Bilateral tibial defects were created in adult C57BL/6 mice, which were subjected to axial compressive dynamic loading either during the early cellular invasion phase on post-surgical days (PSD) 2-5 or during the matrix deposition phase on PSD 5-8. Confocal and two-photon microscopy was used to generate high-resolution 3D renderings of longitudinal thick sections of the defect on PSD 10. Endomucin (EMCN)-positive vessels, Prx1+ Sca-1+ primitive osteoprogenitors (OPCs), and Osx+ preosteoblasts were visualized and quantified using deep tissue immunohistochemistry. New bone matrix was visualized with second harmonic generation autofluorescence of collagen fibers. Analysis method for 3D dataset was developed to measure the spatial co-localization and correlation between different cell populations. Orientations of blood vessels and collagen fibers were quantified using a convolutional approach, which was validated with fast Fourier transform analysis.

Results: We found that mechanical loading during the matrix deposition phase (PSD 5-8) increased vessel volume and number, and aligned vessels and collagen fibers to the load-bearing stress field within the defect. Furthermore, mechanical loading led to an increase in the proliferation and number of primitive OPCs with co-expression of Prx1 and Sca-1; but not Osx+ preosteoblasts within the defect. The vast majority of Osx+ preosteoblasts were within 20 microns of a blood vessel, and mechanical loading increased the number of preosteoblasts in contact with blood vessels.

Conclusions: Together, these data illustrate the adaptation of both collagen matrix and vascular morphology to better withstand mechanical load during bone repair; and the mechaanoresponse cells are the primitive osteogenic progenitors.
References

Abstract Number: ICBME1064

Wireless Biosensing System for Simplified Salivary Uric Acid Self-Check
Yuki Ikemoto, Yuki Hasegawa, Haruna Saito, Yoshiki Tójyo, Rina Tokuda, Hiroyuki Kudo
Meiji University, Japan

A wireless biosensing system for daily self-check of salivary uric acid (UA) was constructed and tested. Gout is a disease that causes acute arthritis associated with hyperuricemia. It is reported that gout attacks also occur in case of a sharp reduction of blood UA levels. Therefore, control of UA levels is promising for prevention and treatment of gout. However, it is still difficult to measure blood UA in daily life because blood sampling is required. We focused on salivary UA, which correlates with blood UA, as a reference of blood UA. Our UA sensing system consists of three elements: an electrochemical UA biosensor with a miniaturized reaction chamber formed using polydimethylsiloxane (PDMS), a wireless readout and control circuit and a disposable sampling device for saliva collection. The electrochemical UA biosensor was prepared by immobilizing uricase, which specifically oxidizes UA, and osmium-wired horseradish peroxidase (Os-HRP) which selectively in the PLTF. The biosensor was confirmed after insertion of the sampling device, onto his own sublingual gland. The current response of the UA biosensor showed a linear relationship in the range from 10 to 400 µM. The calibration range included the UA levels in saliva of both healthy people and gout patients. Thus, it is expected that the sensing system was useful for prevention and treatment of gout. The biosensor also showed sufficient selectivity towards UA (> 60) against possible substances found in saliva (glucose, creatinine, lactic acid and ammonia). Under the approval of Meiji University Ethical Committee (approval No.17-534), measurement of salivary UA was conducted. Saliva was collected by a healthy adult male volunteer by pressing the sampling device onto his own sublingual gland. The current response of the UA biosensor was confirmed after insertion of the sampling device, and the signal became steady state 180 seconds after insertion. As a result, typically salivary UA was estimated to be about 140 µM, which value was consistent with the range of salivary UA levels in the previous literature. Therefore, the proposed method is expected to be applicable for daily self-check. At the meeting, we will introduce detailed structure of the system and the results of measurement under conditions that assumed daily use.

Abstract Number: ICBME1304

CLeONs: Contact Lens-Coated Oxygen Nanosensors for Rapid pO2 Sensing in the Post Lens-Tear Film
Thanuja My, Tejaswini, Puttur Sujith Karanth, Amul Goge, Srivathsa M M, Rohan Anil Shet, Sachin Krishna Moger, Mahima N Bontadka, Prajna A, Sangly P Srinivas, Sudhir R Ranganath
Siddaganga Institute of Technology, Tumkur, India

Background: Background: Contact lens wear affects oxygen tension (pO2) in the post-lens tear film (PLTF), and thereby, influence oxidative metabolism in the cellular layers of the cornea. pO2 measurement underneath the tear film is important to assess corneal health. Currently, the phosphorescence lifetime of oxygen sensitive porphyrin (100-1000 µs) measured in the time domain gives a poor sampling speed of 1 sample per 10 s. Hence, rapid measurement of pO2 dynamics in the PLTF is still an unmet need and thus, we propose to employ O2-sensitive and silica-nanoparticle bound Ru phenanthroline.

Objectives: Preparation, surface functionalization and characterization of Ru-SiO2 nanoparticles (NPs) by microemulsion method. Coat the surface functionalized Ru-SiO2 NPs onto the posterior part of contact lenses. Investigate selectivity and sensitivity of CLeONs towards measuring pO2 dynamics.

Methods: Ru-SiO2 NPs were prepared by microemulsion method. To enhance binding of the NPs to the contact lenses, Ru-SiO2 NPs were surface functionalized with binders and coated on the posterior surface of contact lenses using drop-coating method. They were examined using SEM for surface morphology and coating. Fluorescence lifetime of Ru complex was 4-6 µs in the presence of oxygen and showed a significant increase upon exposure to N2.

Results and Discussion: The average size of surface functionalized Ru-SiO2 nanoparticles, which were spherical and possessed a smooth morphology, was 190 nm ± 50. Photoluminescence analysis showed fluorescence at 590 nm confirming the presence of Ru complex. SEM imaging of CLeONs confirmed the deposition of nanoparticles on the lens surface. Furthermore, Ru did not leach out from CLeONs. Fluorescence lifetime of Ru complex was 4-6 µs in the presence of O2 and showed a significant increase upon exposure to N2.

Conclusions: Based on these findings, we presume that CLeONs can be used as a sensor for measuring pO2 dynamics rapidly and selectively in the PLTF.
molecules of IL-6 in 6 hours stimulation, and its concentration in the surrounding medium became 180 pM.

Abstract Number: ICBME1542

Manufacturing Cell Therapies with Predictive Therapeutic Outcomes: Case Studies in Critical Quality Attributes for Tissue and Glial Stem Cell Therapies

Krystyn Van Vliet
Massachusetts Institute of Technology, United States

While cell therapies are poised to transform healthcare, there remain many outstanding scientific and technical challenges to realize significant global impact. Even with recently approved therapies, there exist key questions and uncertainties regarding production of cells for larger patient populations. Here we discuss the manufacturing bottlenecks and technology advances that afford new means to measure and to correlate properties of biological cells expanded in vitro with in vivo outcomes. These approaches to identify critical quality attributes – multivariate properties that designate some cell subpopulations as safe and/or effective medicine – require novel instrumentation for rapid and accurate product release, advanced data analytics, and creative thinking about how label-free attributes can enable care teams to qualify the cells provided to the patient. We illustrate examples of these advances over years of collaborative research in the US and in Singapore on several stem and progenitor cell types and distinct clinical indications, including hematopoietic recovery of bone marrow and glial stem cells for neurodegeneration that have moved toward clinical trials and commercialization.

Abstract Number: ICBME1047

Three-Dimensional Multiscale Surface Processing Methods to Create Bio-Inspired Surface

Yoshitaka Nakanishi, Kazuma Shibata, Yuta Nakanishi
Kumamoto University, Japan

Introduction: Three-dimensional (3D) multiscale surface processing methods have been developed. The methods provided few restrictions on the kind of materials that could be created on a bio-inspired surface, and reduced the pre- and post-treatments of the material surfaces. In this study, practical applications were also demonstrated.

Methods: A micro slurry jet (MSJ) was used for microscopic mechanical removal processing. The MSJ method involves wet blasting in which the slurry (water with alumina/diamond particles) is injected through a nozzle using compressed air. Additive Manufacturing (3D printing) or photolithography technology was used in microscopic masking processing in order to adjust the MSJ removal rate to increase machining accuracy.

Results: The 3D multiscale surface processing methods achieved ultraprecision machining on the order of nanometres in the orthogonal direction on the material surface. Machining accuracy on the order of micrometres was realized in the parallel direction. Sharp-edge and ultra-smooth surface profile was also obtained.

Abstract Number: ICBME1047

Design and Fabrication Methods of Micro/Nanofluidics for Biomedical Applications: Example for Cytokine Analysis from Single Living B Cell

Takehiko Kitamori
The University of Tokyo, Japan

Microfluidic devices which was pioneered in the 1990’s and established in the 2000’s have become tools for bio and medical researches. It may be a matter of time before diagnosis devices are put into practice in hospital and home. Many kinds of assay methods are very actively developed in the world now. CTC, exosome, disease marker proteins, DNA and RNA, they are the present main targets. Apmeters, padlock probes, and antibodies are the most popular probes. In most cases, these developments are single function. Of course, it is very important to develop CTC separation, selective exosome capture, and so on. However, after completing the development of a particular function on a chip, total integration of all the processes, like sampling, target molecule recognition, separation and purification of targets, and detection are needed.

In 1990, we developed many kinds of functions on chip, like cell culture, extraction, immunoassay and etc., and pioneered pressure driven microfluidics which is the mainstream of today’s microfluidics. These methods were summarized in the general design method using micro/nano unit operation MUO/NUO in 2002 and continuous flow chemical processing CFCP. Even very complicated multistep chemical and biomedical experiments can be designed as a micro/nano channel network which is similar to the electric circuit. The lecture will explain what is MUO/NUO, and how to draw the channel network as CFCP along to the procedures and protocols of the macroscale experiments. This method enables to design microfluidic and nanofluidic devices for almost all kinds of the experiments. Of course, the CFCP based on MUO/NUO is pressure driven, and therefore, this design method can be applied to any kinds of solvent and solutions. And our substrate of microfluidics and nanofluidics is glass, while many groups use PDMS. I will briefly mention about the comparison of the substrate materials: glass, PDMS, and plastics.

We published the world’s first microfluidic immunoassay in 1999, commercialized it in 2009 for medical and research uses, and innovated it to single cell immunoassay device. As one of the examples, micro/nanofluidic device for cytokine analysis at countable number molecules from living single B cell is introduced. In total, 24 steps of MUO/NUO for the cell handling procedure and the protein analysis procedure are integrated on a chip. The ultrasensitive detection method is our original photothermal optical phase shift (POPS) detector which is a powerful detector of light absorption by target molecules. The analyte was IL-6 from single living B cell by stimulation. The number of IL-6 molecules detected was 136 molecules in 6 hours stimulation, and its concentration in the surrounding medium became 180 pM.

Abstract Number: ICBME1507

Create Bio-Inspired Surface

Three-Dimensional Multiscale Surface Processing Methods to Create Bio-Inspired Surface

ICBME1047

Abstract Number: ICBME1047

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Takehiko Kitamori
The University of Tokyo, Japan

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Abstract Number: ICBME1507
The bio-inspired surface of a Co-Cr-Mo alloy as a counterface material of polyethylene in an artificial joint increased the polyethylene particle size and reduced the total wear, preventing adverse tissue reactions. The wettability of a processed surface on a glass was changed to prevent the retention of sebum and fingerprints on the surface. The developed process could remove microscopic cracks and other microstructural defects on a dental ceramic, resulting in improved bending properties and a smoother ceramic.

**Discussion:** Although the surface processing accuracy of the system will be lower than that of a nanoimprint technology, the system will be able to create a texture design on a variety of materials and will be applicable for a large-scale 3D surface. The system will contribute towards the application of a bio-inspired surface design onto a variety of industrial products.

Abstract Number: ICBME1201

**Controlled Oxygen Tension Regulates Vascular Endothelial Cell Migration through P21-Activated Kinase Signaling**

Yugo Tabata, Naoyuki Takahashi, Daisuke Yoshino, Kenishi Funamoto
Tohoku University, Japan

Hypoxic environment in vivo contributes to maintenance of homeostasis, but an abnormal oxygen tension in blood vessel is a trigger that leads to onset and progression of various diseases. Vascular endothelial cell monolayer has been shown to increase permeability and collective cell migration speed, resulting from the cell-cell junction lessened by hypoxic exposure. However, the underlying mechanisms are not fully understood yet. Here, we investigated signal transduction which relates to the changes in collective cell migration of vascular endothelial cells under hypoxic condition. Especially, a contribution of p21-activated kinase (PAK), which is a protein involved in motility of the cells and vascular permeability, was examined under controlled oxygen tension.

We first evaluated several proteins involved in a change of collective cell migration by hypoxic exposure. Human umbilical vein endothelial cells (HUVECs) were cultured with endothelial cell basal medium supplemented with growth factors (EGM-2) in cell cultured dish. HUVECs were collected with SDS buffer after 5-hour incubation under hypoxic (3% O2) or normoxic (21% O2) condition, and the collected proteins were examined by SDS-PAGE and Western blotting. Time-lapse observation of migration of HUVECs was then performed using a microfluidic device with oxygen tension controllability. The device had a central gel channel flanked with media channels, and gas channels were placed next to the media channels being separated by polydimethylsiloxane (PDMS) wall. It was fabricated with PDMS embedding a polycarbonate film. The type I collagen gel (2.5 mg/mL) was placed in the gel channel, and the surface of the media channels was coated with Matrigel (2.0 mg/mL). HUVECs were seeded at a density of 2.5×10⁶/mL in the media channels and cultured by EGM-2 for three days to form a vascular endothelial cell monolayer covering the channel. In order to investigate a contribution of intracellular PAK, the cell culture medium was changed to EGM-2 supplemented with an inhibitor of PAK at 100 nM one day before the experiment. The device was placed in a stage incubator mounted on microscope. Phase-contrast images were captured every 10 minutes for five hours while controlling oxygen tension by supplying gas mixtures to the gas channels. The migration speed of cells was measured by particle image velocimetry (PIV) using the time-series phase-contrast images.

Phosphorylated level of PAK in HUVECs exposed to hypoxia was lower than that under normoxia. PIV analysis of time-lapse microscope images revealed that the hypoxic exposure increased the migration speed of HUVECs. However, the migration speed of HUVECs under supply of the PAK inhibitor decreased even though they were exposed to hypoxic condition. In addition, the HUVECs represented similar values, which were lower than that under normoxia without the PAK inhibitor, regardless the oxygen condition. These results indicate PAK contribute to the changes of cell migration under hypoxic exposure.

We presented the increased migration speed and decreased phosphorylation of PAK in HUVECs exposed to hypoxia for 5 h. However, inhibition of PAK decreased the migration speed, implying PAK contributes to changes of the cell migration.

Abstract Number: ICBME1130

**LEGO®-Like Modular Magnetic Digital Microfluidics with Programmable Liquid Path for Bioanalytical Assays**

Pojchanun Kanitthamniyom, Yi Zhang, Ahmad Adnan Bin Firdaus, Haider Ali Lokhand, Rohit Kumar
Nanyang Technological University of Singapore, Singapore

Magnetic digital microfluidics controls fluids in the form of droplets. Recently, 3D printing has been used in modular microfluidics for the fabrication of complicated structures. We combine the simplicity and high accuracy of the 3D printing with the pumpless and leakless fluidic manipulation of magnetic digital microfluidics to create a novel modular magnetic digital microfluidic building blocks platform for various bioanalytical assays.

The modularized magnetic digital microfluidics system comprises of three parts: motherboard, daughter modules, and board supporter, all of which are fabricated by 3D printing. All droplet operations are controlled automatically by a permanent magnet on an x-y axis translational stage below the glass coverslip coated with 1% Teflon AF. A LEGO®-like structure motherboard is designed with holes between studs for sample loading and observation. Four daughter modules are created for four different droplet operations, including the particle extraction module, droplet dispensing module, droplet mixing module, and droplet transferring module. Each module is coated with 1% Teflon solution and Polydopamine at designated places. These modules can be attached to different locations and arranged in various configurations on the motherboard in order to accomplish the desired fluidic operations for assorted bioanalytical assays.

Each daughter module has unique physical structures and surface coatings, all of which are designed for a specific function. We have demonstrated several types of droplet manipulation facilitated by the functional modules. The particle extraction module has a large contact area with Polydopamine coating at its tip, gives it the desired wetting property to immobilize droplet while splitting the magnetic particles from the droplet. The
Day 2 – 10 December 2019, Tuesday

Liquid dispensing module has a small wettable surface. As the droplet with magnetic particles passes through the dispensing module, a small amount of liquid is held back at the tip of the module as a means of passive liquid dispensing. It comprises of a few pillars that stretch and retract the droplet to induce mixing as the droplet passes through. The transfer module holds a glass coverslip coated with Polydopamine surface energy trap, which picks up droplets from one platform to another. We have also demonstrated convoluted droplet manipulations by programming the droplet path using various modules. For example, a number of particle extraction modules are arranged along a zigzag path for ELISA. Several particle extraction modules and mixing modules are arranged in parallel for multiplexed enzymatic assays.

Magnetic digital microfluidics often rely on micro-physical structures and/or surface modifications to assist the droplet manipulation. This work is the first demonstration of detachable modules with physical structures and chemical modifications for programmable droplet manipulations on the magnetic digital microfluidic platform. This innovation provides unprecedented ease for the design of magnetic digital microfluidic platforms and shows a great potential for applications in magnetic digital microfluidics-based point-of-care diagnostic applications.

Abstract Number: ICBME1238

Patient Specific Factors Governing the Success of Trans-Catheter Aortic Valves

Lakshmi Dasi, Hoda Hatoum, Scott Lilly
The Ohio State University, USA

Heart valve disease is a major component of heart disease in the western world and more so in the developing world. Although artificial heart valves have prolonged countless lives, critical challenges still remain due to issues surrounding durability, thromboembolic risks, operative risks, and high cost. The rapid adoption of trans-catheter valves has only magnified these issues which in order to be completely addressed require a truly multi-disciplinary and translational collaboration between engineering and medicine. In this invited talk, I will present our current efforts towards transforming the entire clinical pipeline and relevant guidelines from diagnosis, planning, delivery, and follow-up using patient specific factors. This will be illustrated through a series of experimental and computational studies aimed at revealing the complex interaction between trans-catheter aortic valves in patient-specific anatomies in the context of the development of adverse outcomes such as leaflet thrombosis, coronary obstruction and residual pressure gradients. Over the long term this research aims to bring precision medicine guidelines based planning and personalization of artificial heart valves replacement therapy.

Abstract Number: ICBME1412

Development of a Magnetically Levitated Extra-Corporeal Ventricular Assist Device in China

Po-Lin Hsu, I-Fan Yen, Tingting Wu, Sascha Gross-Hardt, Thomas Logan
magAssist Inc., China

In China, about 700,000 patients suffer from acute heart failure and many patients die in its worst form - cardiogenic shock. In light of the limited number of therapeutic options of mechanical circulatory support devices available in China, it has been our ambition to develop the newest generation ventricular assist device which meets the gold standard hemocompatibility to serve the clinical need.

The magAssist Pump system is composed of a single-use pump head, a maglev motor, and a console. Magnetic bearing was employed in the maglev motor to give more freedom to manipulate the flow path in the pump head cavity using computational fluid dynamics (CFD) for optimal hemocompatibility. The magnetic bearing was further optimized for higher stability; the driver and controller electronics were customized and embedded in the maglev motor to allow for an ultra-compact design with improved reliability. The user interface and the ergonomics of the console were carefully designed using clinical feedbacks to achieve superior portability and usability.

The CFD simulations demonstrate a comparable outcomes for the hydraulic performance and hemolysis estimation in various operating points between the magAssist Pump and the gold standard blood pump design. The prototypes with high precision manufacturing technology were engineered and assembled for comprehensive performance bench testings. Furthermore, the in vitro hemolysis experiments shown a satisfactory outcome compared to the predicate devices. Successful 7 and 14 days animal trials have proved the short-term reliability and safety in vivo.

The magAssist Pump demonstrated adequate hydraulic capability for extracorporeal circulatory support for cardiogenic shock patients and a superior hemocompatibility in terms of hemolysis level to currently available devices. More and longer in vivo experiments will be performed to guarantee the safety and reliability before the device enters clinical trials in China.

Abstract Number: ICBME1413

Electromechanical Modelling of the Left Ventricle to Investigate Mechanisms of Myocardial Infarct Extension

Chin Neng Leong, Leong Chin Neng, Socrates Dokos, Andri Andriyana, Liew Yih Miin, Chan Bee Ting, Yang Faridah Abdul Aziz, Chee Kok Han, Ganiga Srinivasasah Sridhar, Lim Einly
University of Malaya, Malaysia
Plane Wave Blood Vector Velocity Imaging
Yinfei Zheng
Zhejiang University, China

Objectives: Measuring the blood flow velocity accurately and precisely is of significant importance in the diagnosis and treatment of clinic. Plane wave (PW) blood vector velocity imaging, has been developed to measure the 2D or 3D flow vector at a high frame rate. However, this technique still has the following limitations: (1) The non-focus nature of PW brings a high-sidelobe-level point spread function (PSF), which introduces interferences between blood scatterers and degrades the accuracy of flow vector estimation. (2) The complicated emission sequence commonly used in PW will cause severe reverberation clutter and requires a high-throughput signal processing ultrasound system. (3) Clutter filtering will result in corrupted blood velocity vector estimates. To solve the above problems, we present the PW imaging technique combining single unsteered PW (SUPW) blood vector velocity imaging and the regularized least-squares (RLS) algorithm to improve the accuracy of velocity vector sensing.

Methods: Single unsteered plane wave blood vector velocity imaging: according to the theoretical investigation of the PSF induced by dual steered PW (DSPW) emission, an SUPW emission scheme is designed to reduce the influences of sidelobe level and reverberations on blood velocity estimation. Directional beamform is used to obtain the flow velocity components in different directions and the corresponding vector velocity is derived by RSL reconstruction. The estimation error of the proposed SUPW method was examined using simulations of a 9-mm-radius rotating cylindrical phantom with an angular speed of 20 rad/s. Also, in vivo experiment on carotid artery was performed.

Results: The median of root-mean-square errors (RMSEs) of the lateral velocity component estimates for the proposed SUPW method is 0.025 m/s, compared with 0.051 m/s for the DSPW scheme. The medians of RMSEs of the axial velocity component estimates are 0.005 and 0.008 m/s, for the proposed SUPW method and the DSPW scheme, respectively. In vivo experiments show that the proposed SUPW method can reveal the complex fluid field (e.g., vortex) in a health carotid artery bifurcation better than the DSPW scheme.

Conclusions: This PW technique combining single unsteered PW blood vector velocity imaging and the regularized least-squares algorithm can significantly reduce the velocity vector estimation error of the vortex and improve the accuracy of velocity vector sensing.

Left Ventricular Remodeling to Heart Failure in Response to Hemodynamic Stress: from Mechanisms to Interventional Therapies
Muralidhar Padala, Daniella Corporan, Daisuke Onohara
Emory University, United States

Introduction: Left ventricle (LV) dilatation after myocardial infarction increases wall stress (WS) which drives adverse LV remodeling toward heart failure. Reshaping the LV to reduce WS is promising strategy to treat patients with ischemic cardiomyopathy. Surgical ventricular restoration has been attempted successfully, however the procedural complexity and risks have impeded widespread adoption. Transcatheter solutions for ventricular reshaping (VR) are now in development, and their chronic impact on LV reverse remodeling and improving cardiac function are unknown. In this study, we investigated the impact of VR using a trans-ventricular reshaping device (TRD) in preclinical animal model.

Hypothesis: Reducing WS with TRD can inhibit adverse LV remodeling and can improve LV contractility.

Methods: Thirty-eight rats were induced with an MI by left coronary ligation. At 3 weeks post infarction, the TRD was implanted in 19 rats (MI+TRD) and the rest were considered sham animals (n=19, MI only). All the rats were followed with biweekly echo, and invasive hemodynamics were acquired at 6 and 12 weeks.

Results: TRD implantation was successful in all the rats in MI+TRD, with a 30.5% reduction in sphericity index . At 12 weeks post-MI, WS in MI+TRD were significantly lower than MI only (10.6±1.4 vs 27.4±3.1 x103dyn/cm2; p<0.0001). In systolic indices, ESPVR and pre-load adjusted LV dP/dt max were significantly higher in MI+TRD. Ventricular-arterial coupling (Ea/Ees) in MI+TRD were significantly lower compared to MI only (0.77±12 vs 1.25±0.12; p=0.0127), indicating improvement of the efficiency of cardiovascular system in MI+TRD. SW and pressure-volume area (PVA) in MI+TRD were significantly lower than MI only, indicating reduction of myocardial oxygen consumption.

Conclusion: Reducing WS with a trans-ventricular device can inhibit functional deterioration and reduce myocardial oxygen demand in this rodent model of ischemic cardiomyopathy."
Feeding Baby in Utero: An Imaging and Computational Modelling Study of How Uterine Artery Blood Flow Impacts Placental Function

Alys Clark, Sophie Couper, Ali Mirjalili, Andrew Melbourne, John Thompson, Dimitra Flouris, Rosalind Aughawane, Anna David, Joanna James, Peter Stone
University of Auckland, New Zealand

Objectives: Changes in blood flow to the uterus impact upon fetal health, as this maternal blood provides the fetus with its only source of nutrients in pregnancy (via the placenta). Supine sleep position late in pregnancy is associated with increased risk of stillbirth, partly due to a reduction in maternal cardiac output with compression of the inferior vena cava. We aimed to use magnetic resonance imaging (MRI), combined with computational modelling, to assess how acute changes in maternal blood flow to the uterus with changes in posture impact on materno-fetal oxygen exchange in the placenta.

Methods: MRI imaging was conducted in 11 healthy pregnant women between 34-38 weeks gestation in both left lateral decubitus and supine positions. Axial phase contrast imaging was used to quantify volumetric blood flow in the internal iliac arteries and umbilical vein. A novel technique combining T2 relaxometry and DWI-IVIM (DECIDE) was used to assess perfusion and oxygenation in maternal and fetal compartments of the placenta. To further interpret these imaging data, we use a computational model of the whole placenta, which predicts placental oxygenation by coupling a porous medium model of maternal blood flow to an advection-diffusion model of oxygen transport within placental tissue.

Results: There was a mean 19.0% (p=0.04) reduction in right internal iliac flow, when a mean 34.1% (p=0.0005) reduction in flow in the left internal iliac artery, and a small 1.3% (p=0.43) reduction in flow in the umbilical vein when the woman was supine compared with being in a left lateral position. Blood diffusivity, a measure of oxygen transfer in the placenta, and fetal oxygen saturation were both reduced slightly (not significant). Flux, the product of these two measures was reduced 11.4% in supine compared to left lateral (p=0.048). The computational model, parameterised to a normal placenta, confirms that a normal oxygen saturation can be obtained with observed decreases in volumetric flow to the placenta from the uterus. In addition, the model can be used to predict the potential impact of placental structural deficiencies on exchange when mother lies supine.

Conclusions: In normal late gestation pregnancy, reductions in internal iliac blood flow in the supine compared with the left lateral position are associated with reductions in oxygen flux to the placenta, but only small reductions in umbilical venous blood flow, placental blood diffusivity, and fetal oxygen saturation. Development of computational models of placental exchange function, alongside novel imaging, allows in depth interpretation of the mechanisms leading to inadequate oxygen delivery in some women when they lie supine. This may be particularly important in pregnancies complicated by placental mediated conditions, who may be particularly susceptible to risk of stillbirth with supine sleep position.

Analysis of the Placenta Biomechanical Characteristics for Detection of Intrauterine Growth Restriction

Choon Hwai Yap, Shier Nee Saw, Citra Nurfarah Zaini Mattar, Arijit Biswas
National University of Singapore, Singapore

Introductions: Intrauterine Growth Restriction (IUGR) is a pregnancy with insufficient blood flow through the placenta. It is highly prevalent (>3%) and is an important cause of fetal mortality and morbidity. Current detection for IUGR is poor and alternative strategies are needed. We show that biomechanics approaches, such as ultrasound strain elastography (USEL) can be a good detection modality, and that machine learning modelling using a large number of parameters can improve detection rate.

Methods: We performed USEL on post-delivery 89 (43 diseased and 46 normal) human placenta samples, using a proposed a new USEL protocol with the use of an external polymeric pad with known stiffness as the reference layer, and with motorized control of USEL palpation. For USEL validation, we performed mechanical testing on the same samples. Further, we extracted 16 clinical parameters from each of 347 patient’s data (202 diseased, 145 normal) for machine learning modelling, so as to enable 2nd trimester early prediction of low birth weight.

Results and Discussions: IUGR placenta were stiffer than normal placenta, however the difference was only significant only with low compression rate. Correspondingly, USEL testing was more accurate at low compression rates. However, high spatial variability
of stiffness required that USEL be performed over several locations in any one placenta and averaged. The viscoelastic properties of placenta required that USEL compression rate be controlled, such as with a motor. Motorized USEL significantly reduced measurement variability compared to freehand USEL. Machining learning model could improve early detection rate from 28% to 75%, and the best model was that using all 16 clinical parameters. Nuchal Fold was found to be the most important parameter, unexpectedly. This could be due to growth restricted fetuses having less subcutaneous fats.

Conclusion: With our demonstration of the importance of both biomechanics and machine learning in predicting IUGR, we believe that applying machining learning on a set of clinical and biomechanics parameters will be the most promising way to achieve optimal prediction of IUGR for management and treatment purposes.

Abstract Number: ICBME1159

Bioengineered Cell Based Nanostructured Strategies in Urogynecology: New Era in Prolapse

Shayanti Mukherjee, Saeedeh Darzi, Kallyanashis Paul, Fiona Cousins, Anna Rosamilla, Jerome Werkmeister, Caroline Gargett

Hudson Institute of Medical Research, Australia

Introduction: Pelvic organ prolapse (POP) is urogynecological disorder, caused by vaginal childbirth and affects 1 in 2 parous women aged 50+ years. Until recently, non-degradable meshes were often used as a surgical treatment option. However, serious complications from prolonged inflammation have led to their ban. At present there is no optimal therapy for POP. This study aims to investigate foreign body response, angiogenesis and extracellular matrix formation to a nano-topographically controlled mesh made of poly (L-lactic acid)-co-poly(ε-caprolactone) and gelatin incorporating therapeutic endometrial Mesenchymal Stem Cells (PLCL/G/eMSC) in a mouse model. We further more compared the differences between the treatment capacity of eMSCs delivered using degradable and non-degradable.

Methods: PLCL polymer and gelatin was electrospun to form uniform nanofibers and assessed for biophysical and biomechanical properties. SUSD2+ eMSC were purified from single cell suspensions obtained from endometrial biopsies by magnetic bead sorting and transfected with mCherry lentivirus for cell tracking. SEM was used to characterize eMSC incorporation into the nanofiber meshes in vitro and their degradation in NSG mouse skin wound repair model of vaginal repair. Macrophage response was assessed by evaluation total (F4/80+), M1 (F4/80+CCR7+) and M2 (F4/80+/CD206+) macrophages using confocal microscopy. Gene expression for foreign body response, angiogenesis and extracellular matrix genes were obtained using RNA isolation followed by quantitative PCR.

Results: Addition of G to PLCL increased fiber size 40% (P<0.05) and pore size 25% (P<0.05) rendering meshes hydrophilic without change in tensile properties. In vitro, eMSC rapidly adhered, penetrated, incorporated and proliferated (P<0.01) in PLCL/G mesh with a 2.5 fold greater coverage than PLCL alone (P<0.05). In vivo, mCherry+ eMSC survived 1 wk in PLCL and PLCL/G implanted mesh, but only a few were retained in PLCL/G and none in PLCL at 6 wk. eMSC prevented PLCL/G nanofiber degradaton 2 fold (P <0.0001) and increased cellular infiltration into the mesh 1.5 fold (P<0.05) at 6 wks. Our in vivo analysis of gene expression by fluidigm biomark highlights that role of eMSCs in controlling the immune response and tissue integration indicated by differences in gene expression of NOS2, Mrc, Angl, AngII, MMP-9, Col1a1, Col3a1. PLCL/G/eMSC scaffolds promoted macrophage switching from M1 to M2 phenotype to a greater extent than similarly seeded PLCL mesh and both meshes implanted without eMSC. There was also an influx of endogenous F4/80+ cells (possibly fibroblasts) and collagen matrix deposition into PLCL/G/eMSC implants.

Conclusions: This study shows that degradable nanofiber meshes, in particular PLCL/G boost cell based tissue regeneration without undesirable foreign body response as they enable eMSCs to be retained longer at the site of implantation. Such bioengineered nanostructured meshes have significant potential an application.

Abstract Number: ICBME1525

Microfluidic Precision Medicine – Processing the Minimal Representative Unit for Top Down Diagnostics and Bottom Up Treatment

Abraham Lee

University of California, Irvine, USA

Precision medicine is the paradigm to develop treatments for patients based on molecular-targets that are effective in vivo when administered. That is, one must not only be able to identify molecular and cellular targets that are the source of disease but also understand how these targets behave in the body based on physiological principles. Recent developments in microfluidics have contributed to burgeoning precision medicine fields such as liquid biopsy, immunotherapy, single cell analysis, genotyping and gene sequencing, and microphysiological systems. This is due to the fact that microfluidics bridges the scales of molecular, cellular, tissue, and can even recapitate organ and circulatory functions of the body. In liquid biopsy, microfluidics can analyze biological samples such as blood for the detection of biomolecules or cells that are indicative of disease or physiological state (top down diagnostics). A key bottleneck is to identify the critical subpopulation of cells, often at single cell resolution among billions of cells in circulation. On the other hand, the ability to recapitate the in vivo physiological system is critical to ensure that the therapy delivered is precise yet holistic. Our 3-D vascularized micro organ (VMO) system connects microfluidic channels to vascularized tissues, forming the basis of the “human body on-chip”. Applications for this platform include microphysiological systems for screening of drugs, studying vascular malformations, and understanding immune responses. Ultimately this on-chip microcirculation platform maintains ‘microfluidic homeostasis’ for studying bottom up treatment options.
Frontiers of Biorobotics and Bionics Science and Engineering

Paolo Dario  
*Sant'Anna School of Advanced Studies, Italy*

Biorobotics and bionics are new, deeply interconnected frontiers of biomedical engineering.

Robotics is a highly interdisciplinary domain that is rapidly growing and that, together with artificial intelligence, will have a dramatic impact on our society in the next decades. Biorobotics means bio-inspiration and bio-application. Bio-inspired and biomimetic robots can be used as physical models to better understand the behavior of living systems, whereas robots can be used, with increasing success, for medical applications, for example in surgery, rehabilitation, assistance to the disabled and frail elderly, for limb substitution, and more. In particular, the evolution of surgical robotics is a very interesting and inspiring story, and can be regarded as a paradigm of the challenges and accomplishments of Robotics in the last three decades. Considered, initially, as little less than science fiction and a field for visionaries, surgical robotics has evolved to reach full clinical acceptability and the status of a widely cited success story on how to create a highly profitable industry and a new market, virtually from scratch. Whereas teleoperated and autonomous surgical robots are continuing to find new applications and their room in clinical practice and industry, the field of endoluminal robotics is emerging from research to clinical application and industrial development.

The term “bionics” is increasingly used at international level to indicate the research area that integrates the most advanced bioengineering and robotics technologies with life sciences, such as medicine, biology and neuroscience, with the ultimate goal of inventing and deploying a new generation of artificial organs and limbs and biomimetic machines.

In recent years, deformable and smart materials have been proposed as possible constituents of biorobots and of bionic systems.

In this talk the history, definitions and evolution of biorobotics and bionics engineering will be illustrated, and numerous examples will be outlined of research lines and medical applications, including bio-inspired and biomimetic robots that are capable of reproducing both human and animal functions; systems able to mimic the natural senses; neural prostheses and neural interfaces; advanced prosthetic and orthotic devices for movement assistance and rehabilitation of disabled persons; systems for minimally invasive therapy and regenerative medicine; social robots and smart environments for assisted living, active ageing and wellbeing.

Finally, the research frontiers of biorobotics and bionics will be discussed.
Our computational model combines a 3-D thrombolysis agent concentration was characterized by using an indentation test. A spherical indentor was used, and the cyclic loading and unloading test was performed to get load-displacement curve of PDMS was controlled by varying mixing ratio of a curing agent. Viscoelastic property of the PDMS with different curing agents was characterized by using an indentation test. The results showed that the viscoelastic properties of PDMS can be tuned by adjusting the mixing ratio of the curing agent. The viscoelastic properties of PDMS were also found to be affected by the curing temperature and curing time.

Atherosclerotic arterial phantom was manufactured using PDMS (polydimethylsiloxane), and the viscoelastic properties of PDMS was controlled by varying mixing ratio of a curing agent. Viscoelastic property of the PDMS with different curing agent concentration was characterized by using an indentation test. A spherical indentor was used, and the cyclic loading and unloading test was performed to get load-displacement curve of PDMS was controlled by varying mixing ratio of a curing agent. Viscoelastic property of the PDMS with different curing agents was characterized by using an indentation test. The results showed that the viscoelastic properties of PDMS can be tuned by adjusting the mixing ratio of the curing agent. The viscoelastic properties of PDMS were also found to be affected by the curing temperature and curing time.

The rupture of atherosclerotic plaques causes acute coronary syndrome and stroke which are the leading cause of death in the developed countries. It has been known that plaque wall with large contents of smooth muscle cell (SMC) were stable and the SMC content affected the viscous nature of arterial wall. Therefore, estimation of viscoelastic characteristics of plaque wall would provide indirect measure of plaque rupture risk. The objective of this study is to clarify the effect of arterial wall viscoelasticity on wall motion by measuring the phase lag between pressure and wall displacement waveforms.

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curves. Pulsatile flow was generated using a mock circulation system with a pulsatile blood pump, and pressure and flow were measured. The arterial wall motion was measured using ultrasound crystals. The phase lag between pressure and wall displacement waveforms were computed, and pressure and wall displacement waveforms were analyzed using a fast Fourier transform.

Viscoelasticity of the PDMS with different mixture composition was estimated from the indentation force and displacement curve. As the curing agent concentration increased, elastic modulus decreased while energy dissipation, which was represented by the area in the hysteresis loop, was the largest at some mixing ratio. This result showed that the viscoelastic characteristics of silicone elastomer could be controlled by varying the mixture ratio. As the viscous nature of wall increased, the phase lag between pressure and wall displacement increased, and the arterial wall thickness of also affected the phase lag.

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Abstract Number: ICBME1046

Finite Element Simulation of the Mitral Heart Valve Closure

Kamran Hassani
Islamic Azad University, Science and Research Branch, Iran

Objectives: The mitral valve (MV) is one of the four heart valves located between the left atrium and left ventricle, and it regulates the flow between them. The pressures applied from the left atrium and ventricle on the leaflets can lead to a set of complex structural stresses and strains which are not plausibly to be determined experimentally. We have used a simplified 3D patient-specific finite element (FE) model of the mitral heart valve and papillary muscles to calculate the stresses and strains in the leaflets and muscles during the closing phase.

Methods: A 3D FE model of the heart mitral valve and papillary muscles were reconstructed according to the patient-specific data. The homogeneous-isotropic linear mechanical properties here were employed to address the mechanical properties of the MV leaflets and papillary muscles under the applied loads. The leaflets were then imported into Abaqus (Dassault Systèmes, Vélizy-Villacoublay, France) for assembly, materials, loading, and boundary conditions assignment. Extracting patient-specific geometry of the MV and its chordal structure is challenging and recent computational models therefore simplify the models used.

Results: The highest stresses and strains were located in the anterior leaflets with 1.79 MPa and 49.51%, respectively. The stresses and strain in the muscles where attached to the anterior leaflets were the highest with 7.09 MPa and 14.21%, respectively. The results have implications for the medical and biomechanical experts to understand the stresses and deformations in the mitral valve leaflets and papillary muscles during the closing of the leaflets of the heart valve.

Conclusions: The results have implications for providing a comprehensive information for the medical and biomechanical experts in regard of the stresses and deformations in the mitral valve leaflets and papillary muscles during the closing of the leaflets of the heart valve.
Objectives: The present study evaluated the efficacy of Kay repair in treating severe FTR in a novel ex vivo pulsatile system.

Methods: Porcine tricuspid valve (TV) (n=3) was extracted and incorporated into a patient-specific silicon RV emulating severe FTR, on which Kay repair was subsequently performed. TV area metrics and RV hemodynamic assessment by means of stereoscopic particle image velocimetry were quantified in both FTR and post-repair conditions.

Results: Bicuspidization led to significant increase in cardiac output although the overall increment due to this approach alone was generally small, possibly due to existence of residual TR and the large reduction in TV opening area. Kinetic energy and viscous loss levels were increased post-repair. Main vortex structures were generally maintained post-procedural, nevertheless the repair led to more irregular vortex cores and more isolated vorticity residuals. In general, there was enhanced swirling motion in larger RV domain. Although this might reduce mural-thrombus risk, the relatively more complex vortex phenomenon likely resulted in elevated viscous loss observed and may potentially impact long-term adaptation.

Conclusions: The results shed light on RV hemodynamic alteration under TV repair which allows better treatment design and planning. Further investigations are needed to evaluate other treatment approaches and to elucidate the link between vortex and energy parameters with clinical outcomes.

Abstract Number: ICBME1164

Determining the Efficacy of Drug Coated Balloon Therapy through In-Silico Modelling

Karthic Anbalakan, Martin Lindsay Buist, Hwa Liang Leo
National University of Singapore, Singapore

Often, de novo coronary atherosclerotic lesions are treated either using drug-eluting stents, or in more severe cases, coronary artery bypass graft surgery. Recently, there has been a greater interest in the use of drug-coated balloons in place of drug eluting stents. However, even though drug-coated balloons have proven non-inferior to drug eluting stents and superior to bare metal stents in treating restenosis, there is a lack of information about its use in de novo coronary lesions. Consequently, in this study, we have developed an in-silico model, using Chaste – Cancer, Heart and Soft Tissue Environment, to analyze the efficacy of drug-coated balloon therapy and to understand how the transient deformation during angioplasty, degree of calcification and morphology of atheroma influences the drug uptake and distribution in pathological models. We have demonstrated that transient deformation has minimal impact on drug uptake and distribution, while calcification impedes drug delivery. This was illustrated by a logarithmic increase in the percentage of drug transfer with decreasing levels of calcification. Moreover, larger occlusions were associated with a smaller percentage of drug transfer together with a significantly higher maximal von mises stress. Therefore, we conclude that drug-coated balloon therapy would be most efficacious in smaller non-calcified lesions and could potentially be a viable treatment modality in such de novo cases.

Abstract Number: ICBME1190

Understanding the Flow Patterns of Beating Embryonic Heart via Computational Fluid Dynamics Simulation

Yoke Yin Foo, Shuhao Shen, Huiping Shermaine Tay, Nurgul Imangali, Nanguang Chen, Christoph Winkler, Choon Hwai Yap
National University of Singapore, Singapore

Objectives: Recent studies proposed that dysregulated fluid-induced forces can adversely influence the early stage of heart development through mechano-transduction pathways, thereby resulting in congenital heart malformations. It is thus, essential to understand the fluid mechanical environment of the embryonic heart. The objective of this study is to perform an in-depth study of fluid mechanics in healthy 5 days-postfertilization (dpf) zebrafish embryonic ventricles via image-based computational fluid dynamics (CFD) simulation.

Methods: Three embryos from a transgenic line, Tg(phpCa3.1 attP2A,-0.8myli7: EGFP), with green fluorescence protein-tagged myocardium, were investigated. The embryonic hearts were imaged with a custom-built Line-Scanning Focal-Modulation Microscope (LSFMM), which could provide exceptional signal-to-noise ratio at 5 dpf. Automated cardiac motion estimation was then performed to track ventricular motion. It involved a 3D pairwise non-rigid image registration to extract the displacement fields across all time points, followed by fitting a global motion model of spatial B-spline of temporal Fouriers to the registration displacement fields. Dynamic-mesh image-based computational fluid dynamics (CFD) was executed in ANSYS with the use of cyclic Fourier functions.

Results: The flow profile of zebrafish hearts was highly laminar as the computed peak Reynolds number was lower than 0.1. The zebrafish hearts exhibited a wave-like motion, where systolic contraction and diastolic relaxation started from the inlet and propagated towards the outlet, a configuration that is shown to give flow energy efficiency. Nevertheless, pressure and velocity waves were not observed, thus ruling out impedance pumping mechanism. Due to its tube-like configuration, inflow velocities were higher near the inlet and smaller at the outlet, and vice-versa for outflow velocities. Consequently, wall shear stresses (WSS) waveforms at the near inlet region were consistently out of phase with those at the near outlet region. Large spatial variations of WSS was observed, peak WSS were 47.5-300 dyne/cm² at the narrower inflow and outflow tracts, but were only 4-11 dyne/cm² in the mid-ventricular section. Due to very low Reynolds number and the highly viscous environment, intraventricular pressure gradients were high (up to 0.22 mmHg), suggesting substantial energy losses of flow through the heart, suggesting substantial energy losses of flow through the heart.

Conclusions: We characterized the fine details of organ and fluid dynamics for 5 dpf zebrafish embryonic heart. Data serves as a benchmark for disease model to be compared to. The embryonic ventricle exhibited energy efficient wave-like contractile motion, substantial spatial variability in WSS and high energy losses.
**Abstract Number: ICBME1249**

**Construction of Predictive Model of Patency in Venous Graft Based on Image Feature of Anastomotic Wall Shear Stress under Coronary Artery Bypass Graft**

**Boyan Mao, Feng Yili, Liu Youjun**

*Beijing University of Technology, China*

**Objectives:** Coronary artery bypass grafting (CABG) is a common surgical procedure for the treatment of coronary heart disease. The primary problem currently exists is the risk of the graft failure after surgery. Venous graft is the most common vascular material in surgery, but the failure rate of venous graft in the early period of postoperation is 15-30%, and it will reach 50% after 10 years. It is of great significance how to predict the patency of the graft. The present common predictive model of patency is a clinically common parameter based on the waveform of the transit time flow meter (TTFM). The adverse hemodynamic environment at the anastomosis is a key factor that lead to the venous graft failure. Therefore, this study will try to construct a predictive model of patency in graft through the image of wall shear stress at the anastomosis.

**Methods:** A total of 61 venous grafts of 37 patients were selected in this study, and the intraoperative TTFM waveforms of each graft and the CTA review results in one year after surgery were collected, showing that 21 grafts failed and 40 were unobstructed. Constructed an ideal model of bypass graft, the hemodynamic environment of each graft was calculated by using a periodic waveform after TTFM stabilization as the inlet boundary condition. Average divided one cycle into 10 moments, and extracted the contour of wall shear stress at the anastomosis at each moment. For each image, extracted its color features and texture features. The features of the 10 images were sequentially arranged, and it was used as an image feature of a graft after dimensional reduction by the principal component analysis (PCA). The predictive models of patency based on support vector machine (SVM) were constructed based on the clinical features of TTFM and the image features after dimensional reduction, respectively, and the classification effect based on two groups of features was obtained by cross-validation.

**Results:** For predictive model based on TTFM clinical features, the average accuracy was 62.28%, and the mean sensitivity and mean specificity were 44% and 72.5%. For the predictive model based on the image feature at the anastomosis after dimensional reduction, the average accuracy was 70.52%, and the mean sensitivity and mean specificity were 58% and 77.5%.

**Conclusions:** This paper constructs a prediction model of patency in venous graft based on the image feature of wall shear stress at the anastomosis, and its accuracy, sensitivity and specificity are higher than the predictive model based on TTFM clinical features.

**Abstract Number: ICBME1332**

**A Numerical Study on the Aerodynamic Characteristics of Newborn with Severe Congenital Laryngomalacia**

**Juanya Shen, Youjin Li, Jinlong Liu, Xiaoqing Rui**

*Shanghai Children’s Medical Center, Shanghai Jiao Tong University School of Medicine, China*

**Objectives:** Laryngomalacia (LM) is a congenital softening of the tissues of the larynx above the vocal cords, accounting for approximately 60% in all congenital laryngeal disorders. The malformed and floppy tissue of supraglottic structures is a condition that causes inspiratory stridor due to a partially blocked airway. Failure to thrive, difficult breathing, apnea and cyanosis may occur in more severe cases. The aim of this study was to perform numerical simulations of airflow in a model of pediatric airway with LM to disclose the relationship between clinical symptoms and aerodynamic characteristics, which employed to evaluate airway sufficiency in a group of patients who underwent a supraglottoplasty.

**Methods:** The computed tomography (CT) images of an infant without LM were obtained for the reconstruction of three-dimensional (3D) airway model as control. Based on pre-and postoperative diagnostic endoscopy, the angle of epiglottis and supraglottic plane in control model was decreased by 90% to imitate the epiglottal collapse circumferentially on inspiration (i.e. Type II of LM), decreased by 20% to mimic its postoperative airway. We used computational fluid dynamics (CFD) to simulate airflow within three models on inspiration and to analyze the local aerodynamics. Comparisons of aerodynamic parameters, such as velocity, pressure, wall shear stress (WSS) and energy loss rate, were made among three models.

**Results:** The highest values of velocity and WSS and the lowest value of pressure (i.e. negative pressure) appeared in preoperative LM airway around the rim of epiglottis and arytenoid-epiglottic fold which resulted in epiglottic collapse. It led to gastroesophageal reflux and further aggravated the edema of posterior wall of supraglottic structure. Complex turbulence airflow can be seen in the downstream of epiglottis, which would result in higher energy loss rate and increase the workload of inspiration. After supraglottoplasty that the lateral edges of the epiglottis were trimmed, the values of velocity, WSS decreased obviously and value of pressure increased. The airflow in the downstream of epiglottis became smoother, which caused lower energy loss rate and would greatly alleviate obstruction during inspiration.

**Conclusions:** According to the above results, there are considerable differences in flow patterns on inspiration among three models. The characteristics of airflow dynamic are strongly related to clinical symptoms. Abnormal aerodynamic parameters should be caught serious attention by surgeons. Combining technologies of CFD and virtual reconstruction as a noninvasive way, the flow features and quantified aerodynamic parameters can be analyzed to reveal the reason why the clinical symptoms occur from the perspective of aerodynamics. It can be a potential tool for further surgical therapies.

**Abstract Number: ICBME1360**

**A Multi-Dimensional Approach to Investigate the Effects of the Physiological Properties on the Aortic Dissection**

**Hamed Keramati, Erik Birgersson, Hwa Liang Leo**

*National University of Singapore, Singapore*

Aortic dissection (AD) is one of the most catastrophic aortic diseases. AD is defined as a disruption in the inner wall of the aorta. Having complex physics there are many aspects which
are yet to be fully understood. In recent decades, numerical simulation has been used as a suitable method to understand the complex biomechanical properties of AD. However, by increasing the complexity of the problems, the three-dimensional (3D) methods get computationally costly. Our objective is to reduce the computational time of numerical simulation for the AD without compromising significant information required for the decision-making process to treat the patient. We hypothesized that a zero-dimensional (0D) model developed based on the fully 3D geometry provides significant information in a relatively short time. Benefitting from the simplicity of a 0D model, a sensitivity analysis can be performed more effectively. To meet the desired accuracy, we used a 3D simplified simulation to calculate these quantities in a complex geometry such as that of AD. The 0D model of a dissected aorta was derived from a series of 3D numerical experiments under controlled conditions to determine the quantities of interest. To minimize the errors of discretization in the 3D simulations, we used Richardson extrapolation to calculate the pressure drops in the true and the false lumens. COMSOL Multiphysics was used to conduct the finite element numerical simulations. The mesh was systematically refined, and the solution relative error was kept under 5%. Furthermore, we performed a sensitivity analysis and determined that most severe conditions for our case-study. The process was also tested on a patient-specific geometry to determine the most significant factor in the severity of the disease. According to the results, the resistances of the dissected aorta are not constant. The results showed that second-order polynomial functions of velocity are suitable fits for the resistances in both lumens. Using constant values for the compliances in the 0D model were shown not to be accurate. An acceptable agreement was achieved between the responses of the 0D and the fully 3D finite element fluid-structure interaction (FSI) simulation under physiological inlet velocity and outlet pressure conditions. According to the results, the movement of the intimal flap and the maximum aortic stress is correlated with the combination of the diameters of the entry and re-entry tears. We concluded that the combination of a large entry and a small re-entry tears can be the worst case. Our multi-dimensional approach reduces the computational time and enables us to determine the outcome of different scenarios for AD in a shorter time which is potentially useful for treatment optimization.

Abstract Number: ICBME1065

Development of Robust Amphiphilic Coating for Drug Coated Balloon

Han Wei Toh
National Heart Centre Singapore, Singapore

Background: Drug Coated Balloons (DCB) are one of the treatment options available to treat arterial diseases like atherosclerosis or in-stent restenosis (ISR). The usage of stent while safe, might give rise to acute complications like stent thrombosis or lead to potential long term issues such as stent fractures or ISR. Moreover, the use of stents in femoropopliteal segments provides patency rates of only 54-63% at 1 year and 28-55% at 2 years, which leads to the need for repeat revascularization. DCBs are able to provide a non-stent approach to treat peripheral artery diseases (PAD) which can address the shortcomings of present endovascular options. However, current DCB platforms lack a robust and safe coating that can improve drug transfer and reduce embolization. Hence, this project seeks to develop a novel, robust DCB excipient that would allow the device to achieve similar or better treatment efficacy while avoiding the pitfalls of current options.

Methods: A combination of polyethylene glycol (PEG) and an amphiphilic biomolecule (not revealed due to intellectual property reasons), compound ‘D’, was used in the DCB formulations. The drug choice for the DCB testing would be paclitaxel (PTX), at a dose of 2μg/mm2 of DCB area.

A few variations of D:PEG drug formulations were made to be evaluated against a hydrophilic and hydrophobic control, Urea/PTX and BTHC/PTX respectively. Methods of evaluation include maximal particulate determination for particle sizes and SEM imaging to understand coating morphology. Drug transfer to an ex vivo porcine artery after performing a simulated angioplasty treatment was determined using high performance liquid chromatography (HPLC).

Results: From the results obtained, increasing the ratio of PEG produces a smoother coating appearance which is observed as finer aggregates in the SEM analysis, this can potentially translate into a more homogenous drug delivery. When comparing particulate formation of DPEG/PTX drug coatings to the hydrophilic control Urea/PTX, less particulate matter was produced, which minimizes the unintended downstream effects of the drug upon DCB inflation at the lesion site. Increasing the PEG concentration also led to lesser particulate generation. The optimal DPEG/PTX formulation resulted in a drug transfer of 48% (out of total drug coated) to the porcine artery, and had the least drug loss due to tracking and residual. The use of an amphiphilic biomaterial led to a robust DCB coating with improved tissue transfer and minimized drug wastage.

Conclusion: The DPEG drug formulation shows good potential to be used in DCB application. The mass ratio of 1:1 for D:PEG produces the most desirable characteristics needed for DCBs among the drug formulations that were explored here, with a good balance between drug integrity (loss during tracking and particulate generation) and drug transfer. The novel formulation can be applied to other therapeutics such as sirolimus, which is used increasingly in DCB platforms.

Abstract Number: ICBME1431

Electromechanics of Gastrointestinal Smooth Muscle

Satish Kumar Panda, Martin Lindsay Buist
National University of Singapore, Singapore

Gastrointestinal (GI) motility is the result of highly coordinated contraction and relaxation patterns generated by smooth muscle cells (SMC) to mix and transport ingested food along the GI tract. The contraction patterns of the wall are controlled by the underlying electrical activity of the pacemaker cells and SMC. This electrical activity, known as slow waves, regulates motility in the GI tract, and any abnormalities in their generation or propagation can cause motility disorders. Thus, it is of paramount importance to investigate and understand the underlying root causes of these functional disorders to mediate and alleviate them with an evidence-based approach.
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Over the past few years, mathematical models have frequently been adopted to quantify the healthy and diseased states of GI tissues. This approach has provided a succinct description of the complex electromechanical interactions in smooth muscles without the considerable operational difficulties often incurred in experimental protocols. However, the existing approaches utilize simplified mechanics and electrophysiology models to describe the complex GI electromechanics which is not sufficient. Thus, this research study was undertaken to develop a fully coupled electromechanical model of the GI tract.

We coupled biophysical SMC electrophysiology and excitation-contraction models with a finite nonlinear hyper-viscoelastic model to construct a cellular-level electromechanical model to describe the transduction process of cellular electrical activity into mechanical deformation. The key input to this model is an electrical pulse which then estimates the resulting stress and deformation in the cell. The proposed model was used to recreate experimental observations performed on canine and porcine gastric tissue strips. In all cases, the simulation results were well matched with the experimental data (R² > 0.9). Finally, the model was upscaled for organ-level simulations. With this integrated model, it is possible to gain a better understanding of how cellular level events control organ level deformations. In the future, this modelling strategy will offer a multitude of opportunities to investigate GI motility in health and disease.

Abstract Number: ICBME1098

Assistive Soft Robotic Glove Stroke Rehabilitation Using EEG-Based Motor Imagery Brain-Computer Interface for Elderly Stroke Patients

Nicholas Cheng, Phua Kok Soon, Lai Hwa Sen, Kai Kei Cheng, Tang Ka Yin, Lim Jeong Hoon, Ang Kai Kei, Raye Yeow Chen Hua
National University of Singapore, Singapore

Objectives: Stroke is one of the leading causes of disability with 17 million new cases worldwide each year, and it greatly affects the quality of life of the survivors. Recovery of the motor functions after the onset of stroke is important in order to perform activities of daily living. The main mechanism underlying motor recovery involves enhancement of the primary motor cortex through neuroplasticity, leading to the formation of new neural pathways in the brain. Conventionally, neuroplasticity is brought about by active motor training and pharmacological interventions. However, the use of motor training is highly dependent on the residual motor performance of the stroke survivor and may exclude survivors with poor motor performance. Given that physical movements by stroke survivors are often not possible, alternate strategies are needed. Motor imagery, the mental rehearsal of physical movement tasks, represents such an alternative. Unlike active motor training, motor imagery is not dependent on residual motor performance and can be applied to a wider range of stroke survivors. Further studies have shown that in tandem with the practice of motor imagery, the provision of feedback such as visual and kinesthetic feedbacks can enhance the effect of neuroplasticity by engaging the different senses of the patient. In this work, we have integrated visual and kinesthetic feedbacks into the practice of motor imagery using a brain-computer interface to result in a novel stroke rehabilitation system.

Methods: The setup consists of an EEG acquisition system, a monitor screen projecting a rehabilitation game, and a soft robotic glove capable of assisting in the flexion and extension of the hand’s fingers. The use of our system involves the stroke patient performing motor imagery through playing a computer game projected on the monitor screen while donning on the soft robotic glove. The game depicts a virtual avatar in the midst of performing several activities of daily living involving the use of his/her affected hands. Triggering of the virtual avatar within the game in carrying out the task is achieved through performing motor imagery of the intended action. This simultaneously causes a visual event, in which the virtual avatar moves, and another mechanical event, in which the soft robotic glove actuates to move the fingers of the patient. These form the feedbacks to the patient, which enhances the effect of rehabilitation.

Results: Our system has been implemented in a preliminary randomized-controlled clinical trial involving chronic stroke survivors, and sustained improvements have been observed in the Fugl-Meyers Assessment (FMA) and Action Research Arm Test (ARAT) scores of the users of the system.

Conclusions: Our system of stroke rehabilitation had been shown to be effective and can be potentially introduced clinically as a rehabilitation scheme for stroke survivors.

Abstract Number: ICBME1176

Development of a Soft Wearable Robotic Device for Gait Assistance

Tiana Miller-Jackson, Raye Yeow Chen Hua, Rainier Natividad, Sun Yi
National University of Singapore, Singapore

Objectives: Mobility disability affects a large portion of the world population. For example, in the United States, it was reported that more than 1 out of 8 adults (approximately 12.6% of adults) suffered from mobility disability in 2016. Mobility disability stems from numerous causes, such as amputation, arthritis, birth defects, developmental disease, injury, Parkinson’s disease, or stroke and can even be indirectly caused by respiratory or visual impairments. Walking is a basic necessity of normal human life and is usually performed continually throughout the day. Therefore, a gait-assistive device should be able to be worn for extended hours to realize the most effective gait rehabilitation outcome. Although some gait assistive devices exist, they tend to be impractical for extended wear. The objective of this study is to design and build a soft robotic device for extended wear for lower limb gait assistance.

Methods: Firstly, a soft robotic variable stiffening beam was developed in order to transmit large forces without buckling. The stiffening method developed, tubular jamming, is a positive pressure variable stiffening method for soft robotic members. A corresponding fabrication technique was developed and
characterization tests were performed for the variable stiffness beam. Next a soft robotic actuator capable of large torque generation was developed. The design, titled torque-generating array (TGA) features a set of modular rotary actuators which are combined in an array to generate a large torque. Characterization tests were also performed for the TGA modules. Subsequently the two structures were combined into a soft wearable robotic gait assistive device and the device was assessed to determine its efficacy in providing human hip flexion and extension assistance.

Results: The variable stiffness beam was found to provide nearly three times the stiffness of a standard soft beam design and was found to increase up to 8.9 N/mm in stiffness between unpressurized and pressurized states. A single module of the torque-generating actuator was found to require only 85 kPa pressurization to produce a torque of 10N.m or more across a positional range of 0° - 50°. The soft wearable robotic gait device was found to be capable of generating sufficient torque for the assistance of human hip actuation.

Conclusion: The variable stiffening beam is effective because it is able to transmit forces necessary to actuate the human hip without buckling. The TGA structure is able to generate a sufficient torque to actuate the human hip. The combination of these two structures into a wearable device is a step toward realizing a fully soft wearable robotic exoskeleton to provide continuous gait support to those with gait disability.

Abstract Number: ICBME1137

Self-Wearing Glove with Bidirectional Actuators

Azmall Fraiszudeen, Cheng Zi Yi Nicholas, Low Jin Huat, Raye Yeow Chen Hua
National University of Singapore, Singapore

Objective: The rigidity of traditional exoskeletons, due to its components like linear actuators and rigid linkages, pose constraint on the human hand joints. This often leads to misalignment of the human exoskeleton on the patients’ limbs and increased setup time. As a result, the levels of comfort and safety of patients are reduced. In view of this, there is an apparent need for the development of wearable exoskeletons that may be conform to the deformities of the patient’s joints, allowing increased alignment of the patients’ limbs on the device and reduced setup time. In this work, soft self-wearing glove with bidirectional actuators are developed. This glove provides a novel method of wearing hand exoskeletons with better alignment and faster time of donning/doffing on the user’s body and limbs as compared to the conventional rigid and sleeve-like design.

Methods: The fabrication processes of the self-wearing glove are simple without the need of mould and inner air bladder. It consists of five self-wearing finger actuators and one palm actuator that open up and envelope around the fingers and palm of the user upon depressurization/pressurization. The glove is a fabric-based soft robot, made with TPU-coated fabric and with recoiling endoskeletons embedded in each of its component actuators. This is to generate the elastic force that keeps it in its default folded state, in order to lock around the user’s fingers and palm when worn. As this glove have a novel method for donning/doffing, it has the potential to function as assistive device for rehabilitation and ADLs. Hence five fabric based bidirectional bending and extension actuators are attached to each finger actuators of the glove to develop a self-wearing soft robotic hand exoskeleton.

Results: Characterization tests of the self-wearing glove with bidirectional actuators revealed its locking force (1.64 ± 0.10, 1.67 ± 0.10 and 1.65 ± 0.12 N) and bending angle (103.6°). The opening distance within parts of the actuator when unfolded upon inflation is also found to be 40 ± 1.1 cm, 41.8 ± 1.4 and 43.8 ± 2.0 cm at 70 kPa. In the future, fatigue testing to study the life cycle of the fabric-based self-wearing glove with bidirectional actuators will be conducted. Also, it is planned to characterize the performances of the glove with hand impaired patients, such as those with Rheumatoid Arthritis. This is to determine the optimal dimensions and the effectiveness of the self-wearing glove’s alignment when worn via such users. Also, it serves to evaluate the control strategies for effective hand assistance and rehabilitation.

Abstract Number: ICBME1341

Towards Full Fabric Robotic Exoskeletons for the Shoulder

Rainier Natividad, Raye Yeow Chen Hua
National University of Singapore, Singapore

Humans are highly reliant on the efficient function of their upper limb. The human hand must work in concert with the shoulder in order to properly execute complex motor tasks and neuromuscular disorders that impair the function of the shoulder consequently reduce quality of life. Robotic rehabilitation serves as an attractive treatment choice due to its promising results and its ability to alleviate the demands on therapists and clinicians. Nevertheless, current robotic architectures are not optimized for the human body but are more apt for industrial environments. A fully flexible robotic exoskeleton was conceptualized and tested. The exoskeleton is able to provide assistance throughout the shoulder’s entire workspace. Powering the exoskeleton is an antagonistic pair of fabric, modular, 3-D bending, pneumatic, robotic actuators. Each pair is responsible for the motion in one axis, allowing the exoskeleton to move in two distinct axes. A proof-of-concept actuator was first conceptualized and explored using a hybrid plastic-fabric construction. The proof-of-concept actuator is composed of a plurality of fabric inflatable modules, attached to flexible, plastic spine. The modules inflate when pressurized and generates spatial interference between adjacent modules. The actuator exhibits a linear pressure-torque relationship and behaves as a 2nd-order dynamic system. This concept was adapted into a full-fabric structure and was installed into the exoskeleton. The plastic spine was converted into a fully flexible fabric segment, and the modules were redesigned to unfold to minimize their geometric footprint. The full-fabric configuration enables full 3-D bending and which is what allows the exoskeleton to have an identical workspace to the human shoulder. The actuators were constructed using a combination of origami, thermal bonding and fused deposition modelling. The exoskeleton similarly exhibits a linear-pressure torque relationship, capable of generating a maximum, measured torque output of 15.54 N-m. A customized electromechanical pneumatic system was constructed in order to regulate the
pressure supplied to the exoskeleton and subsequently, its torque output. It has a minimum rise time of 2.121s. Healthy subjects were recruited in order to ascertain if the exoskeleton is capable of reducing the muscular effort required in performing upper arm movements. The results show that the exoskeleton is capable of assisting users in manipulating their arms throughout the entirety of their workspace. Moreover, the modular aspect of the actuator was leveraged in order to ensure proper sizing was achieved among various subjects.

Abstract Number: ICBME1262

Application of Novel Graphite Flex Sensors in Closed-Loop Angle Feedback on a Soft Robotic Glove for Stroke Rehabilitation

Aaron Goh, Yap Hong Kai, Gokula Krishnan Ramachandran, Raye Yeow Chen Hua
National University of Singapore, Singapore

Introduction: Stroke survivors require physiotherapy and rehabilitation programmes to restore their hand function so that they can carry out activities of daily living (ADLs) independently. Soft robotic gloves can reduce manpower costs through their designed assistance in rehabilitation, but their pressure-activated actuation mechanisms require closed-loop position feedback for finer motor coordination for the hands, thereby improving hand rehabilitation for patients suffering from stroke. We present a novel design of graphite-based flex sensors, which we implemented in a soft robotic glove to evaluate its performance in closed-loop metacarpophalangeal (MCP) joint angle feedback.

Materials and Methods: The graphite-based flex sensors are embedded into a sensor glove and characterised in terms of baseline stability and drift, over 20 continuous loading cycles per trial for 5 times. Curve-fitting using both linear and non-linear equations were done to determine the relationship between resistance and MCP joint angle, using Vicon MX motion capture system to obtain 3D coordinates and joint angles, and Arduino circuitry to obtain signal voltage samples. Pneumatic pressures are regulated using proportional-integral-derivative (PID) control, with a safety factor (SF) of 1.2. Two control algorithms were developed to make use of angular feedback to control set point pressures: 1) Intent Recognition Mode makes use of a single MCP angle threshold at 50° to activate a maximum output pressure was set at 100 kPa (83.33 kPa after SF), and 2) Fixed Interval Assist Mode makes use of different MCP joint angle values (30°, 45°, 60° and 90°) to derive corresponding set-point pressures set at 25, 50, 75 and 100 kPa (20.83, 41.67, 62.50, 83.33 kPa after SF).

Results: Non-linear equations consistently provided better fits as compared to the linear equations. However, linear MCP joint angle models are preferred as a calibration method, since non-linear equations are harder to implement in control algorithms in practice. PID control for Intent Recognition activates and deactivates at around 18% and 95% of each full flexion-extension exercise cycle progression, respectively. For Fixed Interval Assist Mode, thumb MCP joint angle feedback is less repeatable due to the difficulty in placement of the sensor at the thumb MCP joint, close proximity to other sensors and physiological crosstalk between the fingers. Conclusion: This work has presented a novel integration and implementation of graphite-based flex sensors with a soft robotic glove for stroke rehabilitation. The relationship between the signal voltage and the MCP joint angle varies greatly with anatomical differences between each individual, and with sensor placement. For practical reasons a linear mapping calibration algorithm for the graphite-based flex sensors was implemented. The effectiveness of the calibration algorithm is also demonstrated via the Intent Recognition and Fixed Angle Assist control algorithms.

Abstract Number: ICBME1410

Clinical Trials for Efficacy of Ankle Mobilization Using Soft Robotic Device for Immobile Stroke Patients

Fan-Zhe Low, Kai Kei Cheng, Hwa Sen Lai, Jeong Hoon Lim, Jeevesh Kapur, Raye Yeow Chen Hua
National University of Singapore, Singapore

Objectives: Immobility of the lower extremity due to medical conditions such as stroke can lead to medical complications such as Deep Vein Thrombosis or ankle contracture, and thereafter prolonged recovery process of the patients. In this two clinical trials that will be presented, we aimed to examine the effect of a novel soft robotic sock device, capable of providing assisted ankle exercise, in improving blood flow in the lower limbs of immobile patients to prevent complication of stroke such as Deep Vein Thrombosis and joint contracture.

Methods: In the first trial, stroke patients were recruited (n=17) to compare patients using the conventional intermittent pneumatic compression (IPC) device with our robotic sock device on separate days while looking at the immediate effect towards preventing of Deep Vein Thrombosis. The primary outcome was to compare the venous flow profile of the superficial femoral vein in terms of the time average mean velocity and volumetric flow. The secondary outcome was to identify the ankle joint range of motion with assistance of the device. In the second trial, stroke patients were recruited for an extended duration of 4 weeks (n=14), where patients were assigned to the control group which used the conventional intervention or to the robotic sock group (RS) which used the IPC device and robotic sock device on alternate days. The efficacy of the treatment was evaluated using compression duplex ultrasonography, modified Ashworth scale (MAS) of ankle, medical research council scale (MRC) of ankle and passive range of motion (PROM) of ankle.

Results: For the first trial, we noted improvements in the venous profile at the early phase of the device use, though its efficacy decreased with time, as compared to the IPC device where there was significant improvement in the venous profile. The ankle joint dorsiflexion-plantarflexion range of motion assisted by the device was 11.5±6.3°. For the second trial, 11 patients completed the trial, with 6 patients in the control group and 5 patients in the RS group. One thrombosis case was confirmed in each group. MAS increased by 0.3±1.0 levels and 1.4±1.3 levels in the control and RS group respectively. Ankle dorsiflexor MRC increased by 0.7±1.4 levels and 1.2±1.3 levels in the control and RS group respectively. Ankle plantarflexor MRC increased by 0.8±0.8 levels and 0.6±0.9 levels in the control and RS group respectively. Ankle dorsiflexion PROM improved significantly in our RS group with 3.4±5.5 degree as compared to a decrease in the control group with -2.5±2.3 degree (p<0.05).
Conclusions: Both clinical trials showed promising results in the application of the robotic sock device for early ankle mobilization for immobile patients, where the device was able to provide assisted venous blood flow in the early phase of device application. In the extended clinical trial, alternate-day application of RS and IPC showed equivalent effect when compared to solely applying conventional IPC therapy in DVT prevention. RS increased the range of ankle dorsiflexion significantly compared with IPC therapy, which suggested additional benefit in ankle joint contracture prevention.

Method: An optical fiber (125 micro-m diameter) was used as a sample fiber material. The sample fiber surfaces were irradiated with a horizontally polarized beam of an amplified ultrashort pulse laser (Light Conversion UAB) with 513 nm wavelength, 20 kHz repetition rate, 0.35 to 7.64 J/cm² fluence, and 170 fs pulse width. The beam was focused to a spot size of 10 mm. The scan line overlap was set to be 60%. The morphology of the surface structures was analyzed with an atomic force microscopy (AFM; SII Nano technology Inc.).

Results & Discussion: After the laser processing, regular protuberances were observed on the surfaces by AFM. With increasing the fluence, this surface structure became coarse. A LIPS of 934 nm pitch and 752 nm height was produced at 1.78 J/cm² fluence on the fiber surface. Then, any breakage did not observed for the sample fiber. A part of surface area were compared before and after the laser processing. The reaction area of the fiber could be enhanced 39.6% by forming LIPS using the femtosecond pulse laser processing. Conclusions: It was considered that the reaction area-enhanced fibers might be useful to increase the sensitivity of knitting based-biosensor.

Objectives: Thin-layered enzyme-linked immunosorbent assay (thin-layered ELISA) is a heterogeneous immunoassay with antibodies immobilized directly onto the surface of a microchannel. Miniaturization in microfluidic systems speeds up antibody-antigen reaction due to increased surface-to-volume ratio resulting in significant reduction of incubation time from hours to seconds, while smaller scales reduces the consumption of reagents.

Thin-layered ELISA is a third type of miniaturized immunoassay pioneered by our group after a beads-based microfluidic ELISA and an extended-nano ELISA. In the first type antibody-coated polystyrene beads were trapped in a microchannel, in the second type an antibody was immobilized on the surface of extended-nano channels and a specific protein was detected at single-molecule level. However, microbeads have the risk of adsorption and clogging, while single-molecule detection has no practical use yet. Therefore, to keep up with demand for actual use in the clinical site we have developed a thin-layered ELISA which provides high through input comparable with the beads-based ELISA and maintains the high efficiency capture level of the extended-nano ELISA.

In this work, we study the analytical performance of the thin-layered ELISA, apply it for C-reactive protein (CRP) detection, and compare with previously developed methods.

Methods: For antibody immobilization we used a glass substrate, activated by oxygen plasma with following vacuum deposition of a thin layer of 3-aminopropyltriethoxysilane (APTES). The excess of the linker was removed by VUV decomposition using a channel mask. A cover glass substrate was also activated by...
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oxygen plasma with Teflon pieces, then two substrates were aligned and bonded under the low temperature (110°C) for 3h. After bonding, the channels were treated by PEG to reduce non-specific adsorption and CRP-antibody was immobilized on the APTES area. For fluidic operations we used pressure-driven flow. For an enzymatic reaction TMB solution was introduced and the signal was detected by a photo-thermal detector DIC-TLM (wavelength = 660 nm) and sent to a PC.

Results: We optimized a secondary antibody concentration, time and flow rate for immobilization. The results are similar to the beads-base ELISA. The sensitivity is resembling the nano fluidic ELISA and approaching the sub ng/mL level. LOD and LOQ of 0.9 and 3.1 ng/mL, respectively, were verified for CRP measurements. Also the repeatability of this method was studied and CV of 4.7% was obtained. Sample injection volume was 0.1 µL with total sample consumption of about 100 µL. Total analytical time was 25 min per one assay.

Conclusions: We developed a fast and sensitive thin-layered ELISA with immobilized antibody directly on the microchannel surface, and succeeded in realizing all steps of immunoassay in microfluidic. This method can be applied for monitoring C-reactive protein as a biomarker for inflammation diagnosis using a small amount of blood samples.

Abstract Number: ICBME1387

Colorimetric Analysis of Hemoglobin on Laser Printed Microfluidic Paper-Based Analytical Devices (µPADs)

Shizhao James Ng, Michinao Hashimoto
Singapore University of Technology and Design, Singapore

Fabrication of microfluidic paper-based analytical devices (µPADs) has been demonstrated by different methods of micropatterning such as lithography, wax printing, inkjet printing and screen printing, albeit with the requirement for particular printers, in-house instruments and materials. To overcome these limitations, we developed a technique to fabricate µPADs with a widely available toner laser printer. The toner of ordinary laser printers consists of acrylate-based polymers, and we identified the conditions for the thermal reflow of the polymers present in the toner. The printed polymers in the toner penetrated the filter paper, and the rates of penetration and the spreading of the polymer through the filter paper were characterized. The ability of toner as a material to create hydrophobic barriers of the polymer was confirmed. Thermal reflow of the acrylate polymers required heating at 200°C for 60 min, resulting in pyrolysis of cellulose in the filter paper. Pyrolysis caused the formation of aldehydes acting as a reducing agent, which may potentially interfere with the assay on the developed µPAD; we developed a method to remove them from the substrate using a laboratory bleach. Using the fabricated devices, we successfully conducted colorimetric assays of bovine serum albumin (BSA) and glucose, and demonstrated the measurement of the concentration of hemoglobin using a branched channels of µPAD fabricated using a toner laser printer. The use of widely available toner printers will make prototyping of µPADs accessible in resource-limited environments.

Abstract Number: ICBME1195

MoS2-MWCNT Based Fluorometric Nanosensor for Exosome Detection and Quantification

Mahnoosh Tayebi, Mohammad Tavakkoli Yaraki, Hui Ying Yang, Ye Ai
Singapore University of Technology and Design, Singapore

Exosomes are nano-sized (50-150 nm) membrane-bound extracellular vesicles (EVs) that contain lipids, proteins, microRNAs and mRNAs originating from their parental cells. Exosomes are invaluable biomarkers in cancer diagnostic assessments due to their essential functions not only in cell-cell communication but in causing the tumor proliferation. Probing exosome compositions can be used as a powerful diagnosis and prognosis tool in many diseases such as cancer. It is therefore crucial to selectively identify exosomes based on their composition and quantify them based on an specific biomarker expression. Here, we have developed a fluorometric nanosensor by utilizing molybdenium disulfide/multiwall carbon nanotube (MoS2-MWCNT) as a fluorescence quenching material to measure the expression of exosomal protein biomarkers in exosomes derived from MCF-7 breast cancer cells. We propose this approach to provide a rapid and straightforward quantification method to detect expression of CD63 protein, as the most common biomarker in different sub-populations of exosomes, based on the retrieved fluorescence of the fluorophore which showed a good linear response range of 0-15 %/v/v. In addition, this nanosensing technique enables quantification of exosomes with different surface biomarker expressions and has revealed that exosomes secreted from MCF-7 breast cancer cells have a higher CD24 expression compared to CD63 and CD81.

Abstract Number: ICBME1072

Tumor Localization in Ultrasound-Guided Liver RFA on Swine

Yanling Chi, Weimin Huang, Jiaxin Zhou, Kyaw Kyar Toe, Chee Kong Chui, Stephen Chang
A*STAR, Singapore

Objectives: In US-guided radiofrequency ablation (RFA), multiple applications of RF are required for big liver tumors. Gas bubbles, or bleeding resulting from the first ablation may reduce visibility of tumors subsequently. Improving tumor localization during ablation benefit its efficacy. Image fusion of intra-intervention US with pre-intervention CT is a potential solution even though it is challenging due to respiration, pose position, and similarity measurement of US and CT. We proposed to use a learning-based registration of 3DCT with 2DUS to predict positions of tumors from visible vasculatures around them in the liver RFA. Learning-based methods have not been reported on registering US and CT/MR images of the liver in the state-of-the-arts [1-4] so far.

Methods: Our solution is a two-step registration, a fiducial point - based registration followed by a feature image - based
registration. The feature image is generated using a learning-based feature descriptor. The initial transformation obtained by aligning the corresponding fiducial points of CT and US images, three points interactively selected on vessel bifurcations. The US/CT transformation is then refined around the initial alignment by searching the maximal correlation of feature images. To train feature descriptor, density and local structures of vessels are input a supervised learning framework. The local structure is measured using Eigen values of 3D Hessian matrix and calculated at each voxel as $LS = |\lambda_2| - |\lambda_1|$, if $|\lambda_1| \leq |\lambda_2| \leq |\lambda_3|$, and $\lambda_2, \lambda_3 < 0$ otherwise where $\lambda_1, \lambda_2, \lambda_3$ are eigenvalues of Hessian matrix at that voxel, with absolute value in ascending order. LS predicts voxel’s probability to be vessels [5, 6]. Correlation coefficient (Corr) is used to measure similarities on feature images, and gradient descent method with Corr as objective function and six dimensions of freedom as input transformation parameters search maximum correlation automatically.

Results: The algorithm was tested in an animal trial at NUH. FRE was calculated when US and CT images were both acquired at inhale phase and the root-mean square (RMS) error of fiducial points after registration is 1.24mm. TRE was calculated in restoring a target liver tumor location during respiration. For ground truth, CT volumes were scanned at the inhale and exhale phases. A fix liver landmark was labelled on both volumes. Its coordinate change measured the tumor movement during respiration, and was viewed as ground truth. During experiment, a selected vessel bifurcation was scanned for a respiration cycle with US probe. The CT volume in inhale phase was registered with two US images in the end of inhale and exhale phase respectively. Two coordinates were calculated. Their difference estimated the tumor movement during respiration. The ground truth was -0.7, -11.4 and 4.1mm in X, Y, Z-axis while experimental estimation was 4.5, -5.5 and 2.2mm. Their root-mean square error, TRE, was 8.02mm.

Conclusions: A learning-based 2DUS/3DCT registration is proposed. Compared with the state-of-the-arts [1-4], the performance of our solution was in the middle if ranked in TRE, similar to that of a 3DUS/3DCT registration [5], 8.1mm, though ours is 2DUS.

Abstract Number: ICBME1124

A Data-Driven Algorithm for Interpretation of Surface Electromyograms During Functional Electrical Stimulation with Time Variant Parameters

Yuxuan Zhou, Mingjie Ji, Zhengyang Bi, Benhui Hu, Keping Wang, Xiaoying Lu, Zhigong Wang
Nanjing Medical University, China

Objectives: Recording electromyography (EMG) while functional electrical stimulation (FES) is a signal processing challenge due to the overlapping power spectra of EMG and FES artifact. The goal of this study is to design a novel approach for extracting volitional EMG contaminated by FES with time-variant amplitudes and frequencies.

Methods: Empirical mode decomposition (EMD) is an adaptive tool extremely suitable to analyze non-stationary noise stemming from FES. However, the initial large transient spike of FES artifact often causes serious mode mixing. Considering the initial spike is short and lacks of EMG information, a selective interpolation (SI) is adopted at first. Then the interpolated signal is decomposed into intrinsic mode function (IMF) by using complete ensemble EMD with adaptive noise (CEEMDAN) which can further alleviate mode mixing. Each IMF is window filtered based on a logistic regression (LR) classifier to identify IMFs contaminated by artifacts. Permutation entropy and number of zero crossing of a 150ms window are selected as classification features. To evaluate the performance of SICEEMDAN-LR algorithm, semi-simulated signal was generated using EMG and stimulation artifact with various artifact to pure EMG ratios. Three quantitative metrics were adopted to validate the performance on simulated data including a) signal to noise ratio (SNR) b) normalized root mean squared error (NRMSE) c) cross-correlation coefficient between root mean square (RMS) values of clean EMG and extracted EMG. To test real application performance, FES contaminated EMG were collected from flexor carpi radialis of 6 able bodied volunteers during 3 repetitions of voluntary wrist flexion under FES with ramping amplitudes/frequencies of bipolar and monopolar pulses. Correlation coefficients between extracted EMG and wrist torque were analyzed.

Results: Simulation results showed a higher SNR (>-0.63 dB), higher correlation (>0.72) and lower NRMSE (<1.08) than comb filter and recently reported EMD-Notch algorithm under artifact to EMG ratio ranging from 4 to 20. The EMG-Force correlation coefficients during real FES were 0.81±0.09 for monopolar pulses and 0.77±0.07 for bipolar pulses, which were very similar to the clean EMG-Force correlation (0.82±0.06). In addition, no significant differences (p>0.05) were found among repetitions.

Conclusions: All results show that SIEEMDAN-LR is capable of extracting EMG during FES with time-variant parameters. The selective interpolation strategy and windowed filtering based on LR can further isolate EMG contributed IMFs. This study provide a solution to interpret EMG during FES of simultaneously modulating amplitude and frequencies.

Abstract Number: ICBME1160

Automatic Detection of Malignant Cells from Cervical Cancer Cytodiagnosis Images

Toshiyuki Tanaka, Ayaka Iwai
Keio University, Japan

Objectives: Recently, the number of cervical cancer patients in Japan has been increasing year by year. In keeping with this trend, the consultation ratio of cervical cancer has also increased and moreover the number of specimen keeps to increase. On the other hand, the shortage of pathologists is one of the big problem and there is the issue of concern that false positive cases may increase. Therefore, there is a significant necessity to develop an automatic diagnosis supporting system for cervical cancer. Some systems for cervical cytodiagnosis are not prevalent in Japan, although they have been implemented by many researchers and companies. Because there are some restrictions such as dyeing solution and examinees and they are very expensive. In many previous studies selected analysis target images which include no overlapping cells. When only single cells are analyzed, its accuracy is high because area extraction and feature calculation of overlapping cells are difficult. There are a lot of overlapping cells in actual cytodiagnosis images and these studies cannot be applied.
to a screening support system in a medical field. Other studies mainly focused on an accurate nuclei extraction, not on detection of malignant cells and a distinction between negative images and positive ones. Those are also imperfection for screening tools.

Methods: In this study, the methods for detecting malignant cells are proposed to support cytopathologists’ screening without removing overlapping cells. First of all, the multi-focused images are reconstructed from 5-layer virtual slide images with wavelet transform for increasing accuracy of nuclei extraction because overlapping cells are thick and out of focus. We also propose the segmentation method for nuclear aggregates which cause false detection of nuclear enlargement. Watershed segmentation based H-minima method and ellipse fitting method are used. Moreover, a koilocyte detection method is proposed in addition to NC ratio and nuclear enlargement to detect malignancy.

Results: As a result, the sensitivity of nuclear extraction is 89% and positive predictive value was 94%. In segmentation accuracy of overlapping nuclei, 82% of nuclei are segmented and it leads to a decline of false nuclear enlargement detection. In feature calculation, when nuclei extraction is automated, sensitivity of malignant cells detection has achieved 90%. Although positive predictive value is 73% and lower than sensitivity, the result shows effectiveness of this study for screening support tool because malignancy detection accuracy of single cells is difficult to detect for human screening is high and the number of cells that cytopathologists have to observe have decreased.

Conclusions: This study deals with an automatic detection method of malignant cells from cervical cancer cytodiagnostics images. It is shown in laboratory analysis that our proposed method is valuable for the screening system and second opinion system for cervical cancer diagnosis. The performance of this system must be checked by some doctors in hospital in the next step.

Abstract Number: ICBME1234

Classification of B-Cell Acute Lymphoblastic Leukemia Microscopic Images Using Crow Search Algorithm

Bharanidharan N., Harikumar Rajaguru
Bannari Amman Institute of Technology, India

Background: B-Cell Acute Lymphoblastic Leukemia (ALL) is a type of blood cancer caused due to disproportionate production of leukocytes which substitutes the normal healthy cells. Blood smear microscopic imaging technology is used to detect the presence ALL and there will be a huge number of microscopic images per patient. Hence machine learning techniques are required to assist the physician to decide about the presence of cancer cells. Crow Search Algorithm (CSA) is generally used to crack numerical optimization, training neural networks and feature selection problems. We believe that this is the first work that uses CSA to classify medical images.

Objective: The objective of this research work is to use CSA for categorization of blood smear microscopic images into two classes: Leukemic B-lymphoblast cells (cancer cells) and normal B-lymphoid precursors (normal cells).

Methodology: Microscopic image dataset named C-NMC is collected from cancer imaging archives website and the microscop images of 30 ALL subjects and 30 normal subjects are considered in this analysis. The input image is divided into 25 regions and five statistical features namely mean, variance, skewness, kurtosis, and entropy are extracted for each region. In a numerical optimization problem, the position of crows is randomly initialized. But in a classification problem, the normalized 125 statistical features will be used to initialize the position of crows. The maximum number of iterations is used as a stopping criterion and the output of CSA is given to adaptive binary thresholding algorithm which decides the class of input microscopic image. In CSA, flight length of crow per iteration and awareness probability are the control parameters and they will have a significant impact on the classification accuracy.

Results & Conclusion: To understand the significant performance of CSA, popular bench-mark optimization techniques like Particle Swarm Optimization (PSO) and Harmony Search (HS) is used. With optimum values for control parameters, the CSA based classification is able to provide a good accuracy of 86.66% while 73.33% & 70% accuracy is achieved for PSO and HS based classification. In future, the classification accuracy of CSA can be further improved by using hybridization with appropriate meta-heuristic technique.

Abstract Number: ICBME1255

Continuous vs. Discrete Decoding of Movement Intentions - Which Is Better for Control?

Rosa So, Brian Premchand, Toe Kyaw Kyar, Camilo Libedinsky, Kai Keng Ang
Institute for Infocomm Research, Singapore

Two main modes of control are usually adopted for an implantable brain-machine interface control system – continuous control using kalman filter, and discrete control using classifiers. The advantage of kalman filter is having smooth trajectories of end actuators. However, oscillations in continuous control occur and ground truth movement intention is uncertain during brain control. Control using discrete decoding may result in sudden changes in trajectory, but can be compared to ground truth labels easily. Furthermore, methods such as reinforcement learning can be applied easily for discrete decoding. This study aims to compare the two modes of control using the same animal experimental setup to determine if the different modes of control affect the performance during a brain control task.

A platinum microelectrode array (100 channels, Blackrock) was implanted in the primary motor cortex of one adult male rhesus monkey. Neural signals were recorded while the monkey used a joystick to control a cursor in a center-out task. Each trial was considered a success if the cursor reaches one of eight targets within 8 s, and remained in the target for 2 s. Two modes of control were tested. For continuous control, the cursor was allowed to move in any direction and distance at each time step. For discrete control, the cursor moved to unit length in one of 8 directions during each time step. Wideband neural signals were recorded at 30 kHz. The raw signal first passed through a 300-3000 Hz band pass filter, and a threshold-based multiunit firing rate was calculated for each channel. Decoding of movement intention during brain control with dummy joystick was performed every 100ms, either using a kalman filter for continuous control, or an 8-class linear discriminator for discrete control.
During direct joystick control, there was no significant difference between continuous and discrete control modes for both time to target and trajectory length. However, during brain control with dummy joystick, continuous control resulted in significantly increased time to target, while discrete control resulted in significantly increased trajectory length. The success rate was comparable between joystick and brain control. Discrete 8-class decoding resulted in an average accuracy of 70.43% and average correlation coefficient of 0.825. In comparison, continuous decoding resulted in a correlation coefficient of 0.810.

Our results show that under brain control, differences between continuous and discrete control became more pronounced. Discrete control resulted in increased trajectory length, but shorter time to target compared to continuous control. Correlation between true joystick position and predicted positions is also higher for discrete decoding. Therefore, these results indicate that the animal is able to use both continuous control and discrete control to perform a brain control task, with discrete control outperforming continuous control in terms of time taken to reach target.

Results: FCs derived from the proposed indices can improve the classification accuracy of support vector machine (proposed vs mean-based method, 100% vs. 73%), naive Bayes classifier (100% vs. 61%), Random Forest classifier (100% vs. 60%), and k-nearest-neighbour classifier (89% vs. 53%).

Conclusions: We propose an index construction method to effectively extract key signals from brain regions, which can dramatically improve the accuracy in a classification task of AD vs. NC. The proposed method can be used to find potential fMRI biomarkers and facilitate the understanding to neuropsychiatric disorders.

Applicability of an Embryonic Vascular Growth Model in Pediatric Cardiovascular Surgeries

Kerem Pekkan
Koc University, Turkey

Embryonic arterial development is governed through highly dynamic microstructural changes due to pressure and wall shear stress changes. A strain-based vascular growth model is developed as a FeBio plugin to model a relatively large period during great vessel morphogenesis. The results are validated through immunohistochemistry and mechanosensitive gene expression measurements. The model also simulates perturbed loading cases including conotruncal banding and conotruncal banding - release models. Together with a simplified spring network model of elastin and collagen this model illustrates how vessels inner diameter and thickness changes in response to mechanical loading. The model also applied to neonatal patch reconstruction surgeries to predict the growth of native tissue in relation to the artificial patch. A number of key assumptions and predictive capability of this approach in a real patient-specific clinical setting will be discussed.

Left Atrial Structure and Strains in Heart Failure with Reduced and Preserved Ejection Fraction

Liang Zhong, Shuang Leng, Xiaodan Zhao, Rusan Tan
National Heart Centre Singapore, Duke-NUS Medical School, Singapore

Objective: Heart failure (HF) imposes a major global health care burden on society. Impaired pump function, which is often measured by a reduction in left ventricular (LV) ejection fraction (LVEF), is the most widely used clinical imaging biomarker of heart failure. Unfortunately, about 30%-50% of heart failure patients have preserved EF (i.e., HFrEF), making diagnosis of this class of patients difficult. Left atrial (LA) function alters differently in heart failure with reduced ejection fraction (HFrEF) and with preserved EF (HfEF). Accordingly, the aim of this study was to 1) assess the LA structure and function using cardiovascular magnetic
Objective: Leaflet thrombosis remains pronounced in the latest generation of the transcatheter aortic valves devices and specifically, post-ViV. In this study we presented realistic simulations of post-procedural hemodynamics that were combined with several near-wall stagnation models as measures for leaflet thrombosis. The current results can help guiding the clinicians in choosing the device with the lowest risk of leaflet thrombosis and valve mismatch. The proposed methods can also help optimizing future designs of transcatheter aortic valves with minimal thrombotic risks.

Conclusion: The considered approaches included both Lagrangian and Eulerian measures of near-wall stagnation and therefore, implemented by either particle tracking or concentration equations, respectively. The measures are based on residence times, exposure time to wall shear stress (WSS), and directly on the WSS field as a predictor of stagnation and separation points on the leaflet. The results were compared between the various approaches and between the ViV and BASILICA configurations.

Results: The different approaches implemented in this study to predict leaflet thrombosis indicate that there is a higher risk for leaflet thrombosis in the Edwards Sapien 3 device because of its intra-annular implantation. All models predicted similar locations for the potential thrombus formation in the belly region of the leaflets, as previously found in clinical cases. Additionally, the BASILICA technique is shown to decrease the thrombogenicity but in the price of weaker support and anchorage for the implanted device.

Abstract Number: ICBME1393

Numerical Hemodynamics Models for Leaflet Thrombosis Estimation Post Valve-In-Valve Implantation

Gil Marom, Romina Piltman Mayo, Halit Yaakobovich, Ariel Finkelstein, Shawn C. Shadden
Tel Aviv University, Israel

Objective: Reduced leaflet motion as a result of hypoattenuated leaflet thickening (HALT) is a severe complication in bioprosthetic aortic valves and leaflet thrombosis has been suggested as the reason for it. This complication is mostly revealed after transcatheter implantation in failed bioprosthetic valves (Valve-in-Valve; ViV). A recent technique known as BASILICA, which was originally proposed to prevent coronary artery obstruction, has also been suggested to decrease the risk of leaflet thrombosis. In this technique, the leaflets of the failed valve are lacerated to allow more physiologic blood-flow in the implant region. This work aims to estimate the risk of leaflet thrombosis post-ViV using several numerical approaches. These approaches, which are based on numerical models of the post-procedural hemodynamics, will be compared and the effect of the BASILICA technique on the risk of thrombosis will be evaluated.

Methods: Realistic ViV configurations were calculated by modeling deployments of the latest version of transcatheter aortic valve devices (Medtronic Evolut PRO, Edwards Sapien 3) in surgical Sorin Mitroflow, both intact and lacerated leaflets (BASILICA). The dry models were followed by computational fluid dynamics (CFD) simulations of blood flow in the deployed configurations. Several approaches were implemented to estimate the thrombogenic potential and to predict the locations with high risk of leaflet thrombosis. The considered approaches included both Lagrangian and Eulerian measures of near-wall stagnation and therefore, implemented by either particle tracking or concentration equations, respectively. The measures are based on residence times, exposure time to wall shear stress (WSS), and directly on the WSS field as a predictor of stagnation and separation points on the leaflet. The results were compared between the various approaches and between the ViV and BASILICA configurations.

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Abstract Number: ICBME1393

Hemodynamic Effects of Conduit on Systemic-to-Pulmonary Shunt: A Numerical Study Using Virtual Design

Jinlong Liu, Yi Qian, Liwei Hu, Zhirong Tong, Jinfen Liu, Qi Sun
Shanghai Children’s Medical Center, Shanghai Jiao Tong University School of Medicine, China

Objective: Different types of systemic-to-pulmonary arterial shunts are used as the palliative treatment for the first step procedure of congenital heart disease (CHD). Although the surgical techniques improved over the years, the implantation position of the conduit connected between the systemic circulation and the pulmonary artery is still one of the controversial issues. The aim of the present study is to investigate the hemodynamic features in four types of systemic-to-pulmonary arterial shunts in order to provide more flow information for surgical design.

Methods: A modified central shunt with a conduit of 4 mm in diameter was reconstructed based on the patient-specific medical images. According to the initial vascular structures, geometric models of Modified Blalock-Taussig (mB-T) shunt, Melbourne
shunt as well as central shunt with a relatively long U-shaped conduit were acquired to perform the virtual procedures by the technique of computer-aided design (CAD). And the method of computational fluid dynamics (CFD) was applied for hemodynamic analysis. Pulsatile simulations were done to capture the physiological information of blood flow.

Results: The local hemodynamic features in different models were demonstrated by pressure, streamlines, wall shear stress (WSS), blood flow distribution and energy loss. Relatively higher pressure drops and WSS were generated in the conduits, which may increase the risk of blood cell damage. The proportion of blood flow distribution of the shunt in modified central shunt with a short conduit was larger than that in the U-shaped central shunt, but both of them fell into the range between Melbourne shunt and modified B-T shunt. Turbulence in the long curved conduit of U-shaped central shunt pointed to high risk of thrombus formation.

Conclusion: The pulmonary flow distribution changed as the conduit position varied in all types of the shunts, but performed more balanced in the modified B-T shunt and modified central shunt with a short conduit than that in the U-shaped central shunt and Melbourne shunt. The numerical study is a useful approach for the investigation of local hemodynamics and the evaluation of the different types of systemic-to-pulmonary arterial shunts.

Abstract Number: ICBME1406

Mechanical Environment in the Left Atrial Ligated Whole Embryonic Heart at HH25 and Comparison to Growth at HH28

Sheldon Ho, Wei Xuan Chan, Nhan Phan-Thien, Choon Hwai Yap
National University of Singapore, Singapore

Objective: Past investigation found that fluid mechanical forces influenced cardiovascular development and abnormal flow conditions could lead to congenital heart malformations, which is clinically a leading cause of birth defect related deaths.

Methods: We utilized a previously established 4D high-frequency imaging technique on HH25 chick embryos (just before septation), tracked the cardiac motion with a novel motion estimation algorithm, which could enable wall strain calculations, and performed flow simulations to understand the hemodynamic. Studies were also performed on left atrial ligated (LAL) embryos, an animal model of the hypoplastic left heart syndrome, to understand how altered flow can lead to malformations.

Results: Studies on the normal embryonic heart demonstrated that the atrial appendages had outsized contributions towards atrial blood pumping. The appendages occupied only 15.7% of the atria’s volume, but accounted for 30% of the atrial stroke volume and 40% of ejection work done. They were also the most contractile region of atrium, with strain magnitudes comparable to the ventricle. These suggested that the embryonic atrial appendage may play the critical role of enhancing atrial blood pumping. However, the ventricle seemed to be self-sufficient in its blood pumping, as it could directly draw inflow from the veins during late ventricular diastole, without the aid of the atria, and it provided circulatory energy that was 1 order of magnitude higher than that of the atria. We thus suggest that the atrial pumping function was not essential for providing circulatory energy, but could be important for creating appropriate flow and wall shear stress (WSS) stimuli to ensure normal heart development. This was supported by literature evidence where removal of atrial contractility was found to be embryo-lethal, causing maldevelopment the cardiac cushions, heart valves and septum. Further, at regions of valvulogenesis and septal development, fluid WSS were elevated, which could be important stimuli for valve and septal development.

In the LAL heart, at 4.5 embryonic days, the cardiac anatomy was altered, such as a medial shift in atrioventricular junction and sharper ventricular apex. This causes the reduction of WSS at left ventricular wall and apex, and oscillatory flow and WSS in the left ventricle. At 5.5 embryonic days, the left ventricle was observed to be smaller, but interestingly, the contractility of the entire ventricle was elevated, which could be a compensatory mechanism.

Conclusions: The LAL embryonic heart is found to be capable of responding to changes in flow environment by remodelling of cardiac geometry, altering growth rate or improve contractility. Coupled with the elevation of mechanical stimuli at sites of septation and valvulogenesis, the results suggest that mechanical stimuli may play a role in ensuring proper development of embryonic heart.

Abstract Number: ICBME1534

Reflections on Muscle Contraction

Walter Herzog
University of Calgary, Canada

Muscle contraction has fascinated scientists since the time of Ancient Greece, and with Leonardo da Vinci and Alfonso Borelli, was a topic of scientific debate and investigation of human and animal movement in the Renaissance. In 1954 and 1957, Hugh Huxley and Andrew Huxley, independently, proposed the last revolution in muscle contraction mechanisms when they proposed the sliding filament and cross-bridge theories, respectively. In these theories, the contractile filaments actin and myosin are the only “active” force producing elements in skeletal muscles, while passive forces were associated with connective tissues. In the mid- and late 1970s, Maruyama and Wang discovered a third filamentous protein in sarcomeres, first called connectin now referred to as titin, that spans a half sarcomere from the M-band to the Z-line. In 2002, we discovered the so-called “passive” force enhancement property of muscle, which showed that passive force in an active muscle is greater than the passive force in a passive (non-activated) muscle. We then demonstrated that titin is a spring-like filament that becomes stiffer when a muscle is activated compared to when the muscle is passive. The molecular details of how titin achieves this increase in stiffness, and associated increase in force when an active muscle is stretched, remain largely unknown. However, there are at least two recent proposals that may explain the molecular mechanisms of stiffness regulation in titin that contribute to muscle force. The first of these mechanisms is associated with calcium binding...
to titin. Upon muscle activation, calcium is released from the sarcoplasmic reticulum, and we showed that calcium can and will bind to titin, and make specific segments of titin (for example, certain immunoglobulin domains) stiffer. Aside from calcium binding, phosphorylation of specific sites of titin has also been shown to change titin’s spring stiffness. The second mechanism implicated with changes in titin stiffness is the binding of titin’s proximal domains to the essentially rigid actin filament, thereby stiffening the proximal domain and just leaving the distal domains of titin to accommodate changes in muscle (sarcomere) length. There is some preliminary evidence from work on mechanically isolated sarcomeres and myofibrils that titin may indeed bind to actin upon muscle force production and stretch, thereby increasing its force contribution in actively compared to passively stretched muscles. If we accept the current evidence of a modular titin spring stiffness, then it becomes possible to explain many experimental observations in skeletal muscle contraction that have no explanation in the traditional cross-bridge theory. These include the residual force enhancement property, the elimination of the creep phenomena, the stabilization of sarcomeres on the descending limb of the force-length relationship, and the stabilization of myosin filaments in the centre of sarcomeres. In summary, a three filament sarcomere model including titin with the traditional actin and myosin complex, allows for explanation of many currently non-understood phenomena, while maintaining the explanations that have been made successfully by the cross-bridge theory for other mechanical properties of muscles, such as the static force-length relationship and the steady-state force-velocity relationship.

Results: We have applied the new method to CMAC data. Results showed that our incompressibility regularization successfully enforced incompressibility, where average divergence improved from 0.2885 to 0.0528 (from the initial cardiac motion estimation to after incompressibility regularization). Further, this regularization achieved lower tracking errors than current cardiac motion estimation techniques in the literature, and it could maintain diffeomorphism of the myocardial motion, resolving negative volume problems from the initial cardiac motion estimation. Conclusions: A novel add-on regularization framework to achieve the incompressibility constraint on cardiac motion estimation from noisy ultrasound images was proposed, and found to achieve high motion estimation accuracy, and successful enforcement of incompressibility and diffeomorphism. This cardiac motion estimation framework will be helpful for computing myocardial strains, and for finite element biomechanics modelling of the myocardium.

Abstract Number: ICBME1198

Cardiac Motion Estimation from Noisy Medical Images

Hadi Wiputra, Wei Xuan Chan, Sheldon Ho, Yoke Yin Foo, Choon Hwai Yap
National University of Singapore, Singapore

Objectives: Accurate tracking of cardiac tissues from clinical scans is an important task to aid the evaluation of organ function, detect disease, and boundary condition for image based computational fluid dynamics. Image registrations are commonly used in MRI images, but in noisy images such as ultrasound (US), its accuracy is limited [1]. Since pairwise image registration is typically performed on consecutive time points, accumulation of tracking errors over time points will lead to tracked objects drifting away. Also, smoothing of the noise also damped the cardiac motion and underestimated the stroke volume.

In this study, we proposed a novel method for cardiac motion tracking on US images, using a mathematical model for cyclic motion of myocardial points to avoid drift. Furthermore, by placing emphasis on time points when the heart was largest and smallest, we could preserve stroke volumes. Compared to techniques reported in a recent Cardiac Motion Analysis Challenge (CMAC) [1], our technique achieved better accuracy. We successfully applied the method to cardiac scans from multiple modalities, such as human fetal and adult cardiac US, chick embryo cardiac US, and zebrafish ventricle from confocal microscopy.

Methods: 3D Non-rigid pairwise image registration was performed with an open source module, Elastix [2]. In essence, we performed regularization of a set of pairwise image registration outside of the registration framework. A cyclic mathematical model we ascribed for image coordinates motion as spatially distributed B-splines of temporal Fouriers (BSF). Optimisation for the fit were performed using Levenberg-Marquardt algorithm with objective functions described in image pyramids. The initial descent were calculated by Fourier decomposition and multi-level B-spline fit [3] to the displacement fields from pairwise-registration. The optimization takes in a series of pairwise image registration displacements, which can be weighted heavily towards end diastole and systole volumes. These accounts for underestimation of stroke volume commonly found in tracking due to smoothing. The tracked cardiac wall could then be used for computational fluid dynamic simulations of cardiac ventricles in various animal models of various imaging modalities.
Results: CMAC provides 15 adult cardiac US data with 12 tagged landmarks provided from tagged MRI. The Euclidean (Eu) distance error between tracking and ground truth were measured. Our method obtained average Eu of 3.31mm, significantly lower than the other research groups (INRIA=3.76mm, MAVIS=3.72mm, UPF=3.63mm) with p-value less than 2%. The method were further applied to three other datasets: fetal US, zebrafish confocal microscope and chick embryo high frequency US, with average Eu of less than 3% of the width of the respective cardiac ventricles.

Conclusions: We had exploited the cyclic nature of cardiac systems to regularize a set of pairwise image registrations. Compared to the other participant of the CMAC challenge, our tracking error were reduced by ~10%. The proposed method is also able to emphasize end diastole and systole geometry in order to counter excessive smoothing. The proposed approach of having a regularization framework outside of registration can be thought as a greedy approach to optimization, which we shown to reduce errors in the datasets analyzed.

Abstract Number: ICBME1283

Numerical Analysis for the Influence of Heart Disease on the Blood Flow Field in Left Ventricle: Influence of Mitral Regurgitation

Tsuyoshi Takada, Suguru Miyauuchi, Toshiyuki Hayase
Tohoku University, Japan

The number of mortality due to heart failure accounts for more than one third of that of heart disease. Approximately one fourth of heart failure patients have valvular heart disease as the underlying disease. Valvular heart disease affects the blood flow field in a left ventricle (LV) due to obstruction of blood flow due to stenosis and backflow due to regurgitation. In our previous study, numerical analysis was performed for the blood flow in a LV with an aortic stenosis using the LV model constructed from magnetic resonance imaging (MRI) to clarify the influence of aortic stenosis. Mitral regurgitation (MR) is a type of heart valvular heart disease. The mitral valve (MV) opens during diastole of the LV to take in blood from the left atrium and closes during systole to prevent backflow. In MR, the closing function of the MV does not work sufficiently during systole resulting in the backflow from the LV to the left atrium. This backflow changes the blood flow in the LV from the healthy state and possibly causes local stagnation and thrombus formation. Therefore, clarification of the influence of MR on the blood flow field in a LV is important. In this study, numerical analysis was performed to clarify the influence of MR on the blood flow field in the LV, and hemodynamic parameters were compared between the LV model considering MR (MR model) and the healthy model (H model). In the computational method, the LV model was constructed from the MRI data of a left cardiac system, and papillary muscles and trabeculae were modeled as an internal structure in the model. The aortic valve part was modeled by a cone mimicking the actual opening of an aortic valve shape. The MV part was modeled by a cylinder for the H model and a crescent-shaped cylinder for the MR model. Measurement data of the left ventricular volume and the length between the MV and the apex was obtained for 20 time steps in one cardiac cycle and interpolated into 200 time steps. The deformation of the LV model was introduced in the calculation. The model shape at each time step was defined from two LV shapes just before the atrial contraction and at the time of minimum volume, and the corresponding LV volume and the length between the MV and apex. Computation was performed for seven cycles, and the time-averaged wall shear stress (TAWSS), oscillatory shear index (OSI) and relative residence time (RRT) were calculated using the results after fourth cycle at which the flow field becomes almost periodic. Differences in distribution of these parameters were clarified between H and MR models. In this study, numerical analysis was performed on two LV models with and without MR in order to clarify the influence of MR on the blood flow field in the LV. As a result of comparison for TAWSS, OSI and RRT between the models, the influence of MR on the blood flow stagnation in the LV was clarified.

Abstract Number: ICBME1324

Development of Blood Vessel Model Made of Polyvinyl Alcohol Hydrogel Embedded with Flexible Pressure Distribution Sensor for In Vitro Evaluation of Endovascular Devices

Takeshi Moriwaki, Keisuke Narumi, Kazuhiro Fujisaki, Kazuhiko Sasagawa
Hiroasaki University, Japan

In developing endovascular treatment devices, understanding their physical property is one of the most important points. Especially, excessive contact pressure between device and vessel wall closely affects inflammation and intimal thickening after surgery. We have been developing film-type sensor for pressure measurement, and applied to the biomechanics. In previous study, blood vessel model embedded with pressure distribution sensor was fabricated by using silicone gel, and contact pressure change at plaque vessel model and stress concentration by scoring balloon, a balloon with wedges, were measured. In this study, polyvinyl alcohol (PVA) hydrogel was used to fabricate a blood vessel model with almost the same elastic and friction properties as the native vessel. The physical characteristic change during long-term preservation of PVA hydrogel and usefulness of the vessel model were discussed.

PVA hydrogels were made from dimethyl sulfoxide solution and PVA powder. The gels were fabricated dissolution stirring of PVA powder and gelation at 253K (24 hour). Fabricated gels were preserved at distilled water (277K, about 3200 hour), and were measured for time-dependent change of size, mass and elastic modules. Pressure-detectable curvature blood vessel model was fabricated by PVA hydrogel and film-type sensors. The sensor with 16 measurement points was constructed by a couple of electrodes and conductive rubber. Bending shaft and bath shaped mold were fabricated by using 3D printer, two film sensors were placed inside and outside the bending shaft and then PVA solution was poured. The diameter and curvature radius of the bending shaft were 7 mm and 60 mm, respectively. The pressure distribution of longitudinal direction at inside and outside the bending vessel was observed under dilation of 7mm diameter balloon catheter.

The fabricated PVA hydrogels had high-transparency and their elastic modulus could be controlled by the PVA concentration of gel. The size and mass of PVA hydrogels increased till 200 hours and became almost constant. Conversely, the elastic modulus of that decreased till 200 hours and became almost constant. It is considerable that the replacement of dimethyl sulfoxide to water occurred in about 200 hours and the state became stable. At balloon dilation, high pressure areas were observed at the center of the balloon on the inner side and both ends on the outer side of the curvature vessel model. It is thought that the contact pressure
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was concentrated as the expanding balloon tried to straighten. The contact pressure increased with the balloon dilating pressure. Although the balloon pressure was 1000 kPa, the contact pressure at the high pressure areas were on the order of 10 kPa.

The long-term availability of the PVA model and the usefulness of the blood vessel model with pressure distribution sensor were confirmed. By fabricating a pressure-detectable model having actual shape and deformation characteristics, it can be expected to be useful for physical property tests of developed endovascular devices and training of endovascular surgery.

Abstract Number: ICBME1351

A Patient-Specific Hemodynamic Analysis of Modified Blalock-Taussig Shunt: with and Without Ligation of the Patent Ductus Arteriosus

Jiwen Xiong, Qi Sun, Zhirong Tong, Jinfen Liu, Jinlong Liu
Shanghai Children’s Medical Center, Shanghai Jiao Tong University School of Medicine, China

Objectives: The modified Blalock-Taussig shunt (MBTS) is widely used as palliative operation or the first stage surgery in neonates with hypoplastic pulmonary artery (PA) to transport blood from systemic circulation to pulmonary circulation. Patent ductus arteriosus (PDA) is a natural passage with similar function as MBTS, which should have been physically closed during one or two months after birth. Due to difficulties in pulmonary perfusion control and unpredictable flow features, whether to ligate the PDA when performing MBTS is controversial. Present study is aimed to analyze hemodynamic characteristics of MBTS with and without closure of the PDA based on computational fluid dynamics (CFD) and computer-aid design (CAD), for preoperative virtual surgery design and prediction of postoperative prognosis.

Methods: A patient with pulmonary atresia and PDA was included and informed consent was acquired. Patient-specific three-dimensional model (Model 1) was reconstructed based on computed tomography images. According to surgeon’s suggestion and spatial position of great vessels, CAD was applied to virtually interpose a 4 mm Gore-Tex conduit between innominate artery and right pulmonary artery (RPA), namely Model 2. The PDA of Model 2 was artificially removed to mimic the ligation of ductus arteriosus (Model 3). Inlet boundary conditions of three models were uniformly assumed according to pulsatile mass flow measured by echocardiography. Vascular resistance was considered in outlets. Local flow features and calculated hemodynamic parameters including the ratio of pulmonary perfusion to systemic perfusion (QP/QS), flow distribution, and wall shear stress (WSS) were analyzed.

Results: Compared with Model 1, QP/QS of Model 2 increased after MBTS was done, provided more pulmonary perfusion. In Model 2, velocity streamlines showed that ductal flow pushed shunt flow into right lung, and left pulmonary perfusion was mainly supplied by ductal flow. Complicated turbulence appeared especially in PA between MBTS and PDA. When only MBTS existed, less shunt flow distributed to LPA possibly caused insufficient left pulmonary perfusion. Shunt flow streams through vertical conduit and impacted upon PA wall, formed turbulence flow around anastomosis site of RPA. Both velocity and WSS through MBTS of Model 2 were lower than that of Model 3. The QP/QS of Model 2 was larger than that of Model 3. Inadequate pulmonary perfusion may occur in Model 3.

Conclusions: Co-existed MBTS and PDA provide more pulmonary perfusion, but controlling pulmonary blood flow to keep balanced flow distribution is crucial. Due to slow process of PDA physiological closure and cumulated effect of continuous flow through MBTS, it is requisite to take consideration of the interaction in hemodynamics between PDA and MBTS. CFD combined with CAD is a helpful tool to predict patient-specific hemodynamic changes postoperatively.

Abstract Number: ICBME1401

Hemodynamic Characteristics of the Pulmonary Artery in the Child with Pulmonary Hypertension Related to Congenital Heart Disease: A Numerical Study by Computational Fluid Dynamics

Liping Wang, Mingjie Zhang, Jinlong Liu, Zhuoming Xu
Shanghai Children’s Medical Center, Shanghai Jiao Tong University School of Medicine, China

Objectives: Pulmonary hypertension related to congenital heart disease (PH-CHD) is a devastating disease caused by hemodynamic disorder of the pulmonary vascular. Right heart catherization is a golden standard in the diagnosis of PH-CHD. However, it’s an invasive technique with radiation. In the present study, we aim to use the noninvasive and visualization technique of computational fluid dynamics (CFD) to assess the hemodynamic characteristics of pulmonary artery which will give clinician more comprehensive information for the diagnosis and improve PH-CHD therapy.

Methods: Five moderate-to-severe PH-CHD patients and five age matched controls were enrolled. Based on the CT imaging, the ten subject-specific three-dimensional PA models from the main PA (MPA) down to its second or third generation branches were reconstructed. Mesh generation of the computational domain was performed with mixed unstructured grids. Pulsatile velocity of the main PA obtained from transthoracic echocardiography was used as the inlet boundary condition. We assumed vascular resistance as the outlet boundary condition, and a rigid with no-slip boundary conditions for the vessel wall. Hemodynamic characteristics of PA, including flow pattern, wall shear stress (WSS) and energy loss (EL) were analyzed. In order to controlling intergroup variation caused by age, body surface area was used to normalize EL (ELnorm) and other quantitative indexes.

Results: Morphology analysis implied that the diameter of main PA (MPA), the diameter ratio of MPA/ aorta (DMPA/DAO) and MPA/(Left + Right PA) (DMPA/D(LPA+RPA)) in PH patients were significantly larger than control group. The simulated results showed that velocity of the MPA in the two groups were similar. However, the velocity at the PA branches was observed higher in PH-CHD patients. The inflow in PH-CHD patients predominantly increased. The WSS of PH-CHD patients decreased at the main PA and increased at the PA bifurcation. The ELnorm of the PA in PH patients was significantly higher when compared with control group (z = -2.619, p = 0.008). Statistical analysis showed ELnorm is positively correlated with DMPA, DMPA/DAO ratio and DMPA/D(LPA+RPA) ratio (rs = 0.626, p = 0.053; rs = 0.821, p = 0.004; rs = 0.748, p = 0.013). Conclusion: The morphology of PA and hemodynamics in patients with PH-CHD are different from non-PH subjects. Velocity, WSS and ELnorm are the potential biomechanical parameters for the evaluation of PH-CHD. The alteration of EL is closely related to the PA morphology. The analysis of these hemodynamic factors may reveal the potential
CE-IT Alarm Management Technology to Improve Alarm Fatigue and Precision Nursing Based on Physiological Monitor Signals

Kang-Ping Lin, Wen-Chien Chen, Mei-Feng Chen, Ming-Chih Yang, Mei-Chu Chen, Chih-Chieh Shih, Chao-Yuan Hsu, Ke-Hong Lin, Chien-Wen Lai
Chung-Yuan Christian University, Taiwan

Importance: When physician, nurse, and medical staff refers physiological monitors to monitor the patient's physiological information, the staff may have become desensitized to the alarms because of alarm fatigue, which is an important issue for improving medical care quality, and strengthening patient safety. The setting of the alert notification, which is too sensitive, causes many false alarms. As a result, the medical staff will be overwhelmed with excessive alarms, and also affect the patient's peace of mind.

Goal: For smart hospitals, the information technology development is an inevitable trend. More automatic devices and alarms also expand the scope of alarm risk events. By screening important information, nurses can obtain accurate catalogue of alarm types of physiological monitors from the ward and proper response. Based on the patient's safety, the goal to reduce excessive unnecessary alarms, to improve quality and precision of the medical care could be achieved.

Methods: A design has been implemented in Chang-Hua Christian Hospital, Taiwan, focused on the detection differences of vital signal characteristics of individual types of wards. There are three parts included in this implementation. The first part includes the collection of alarm data, analysis, and the analysis of the actual practice of the medical staff. The second part is a model for alert notification, and an analytical model for alert notification constructed in a smart care architecture model. The third part is based on the actual ward situation and alarm data to test and verify the local actual data under the established model analysis. This will cooperate with the big data of the clinical information of the hospital to obtain the physiological information of the medical device used in the real ward, and the physiological information when important alarms and non-essential alarms occur which have been defined by a committee. It is expected that by means of signal analysis and big data analysis, the best decision to judge alarm classification to improve of alarm fatigue in the hospital.

Results: Based on the ward alarm notification system set up in the ward of the Chang-Hua Christian Hospital, Taiwan, the design expects to establish a practical and feasible method, to reduce unnecessary alert notifications by automatically intelligent detection. Under the policy which can improve the medical care quality and patient safety, the non-essential alarms of the physiological monitors are effectively reduced.

Conclusions: With the design of CE-IT technology, through the effective integration of the process, the patient information is directly collected from the monitoring side with their physiological data, and transmitted to the central control station to reduce human errors. In addition to the shortening of the response time of the nursing cares, the information is also linked into the electronic medical record. According to the online validation results, after the integration of CE-IT technology, the number of non-essential alarms after intervention was reduced by 74% compared with that before intervention. Other indicators of medical care quality assessment have also been significantly improved.

Abstract Number: ICBME1474

Pilot Study -- Portable Evaporative Cooling System for Exercise-Induced Hyperthermia

Seng Sing Tan, Eng Koon Lim, Chin Tiong Ng
Nanyang Polytechnic, Singapore

Current first-line treatment for heat stroke patients consists of cold packs applied over crucial areas to bring down the body temperature quickly on site before arriving at the hospital for proper treatments. However, such on-site treatment is not able to cool the body fast enough. Most effective cooling systems available today are not portable for onsite treatment. The objective of this pilot study was to test a portable evaporative cooling system which could be deployed on site. Such a system allowed for continuous cooling even during transportation in the ambulance. It stimulated effective evaporative cooling through phase-change.

Integrated on a stretcher, atomizer nozzles were connected to a small bag of water supply together with a compressed air cylinder, to supply a continuous flow of dehumidified gas. Such a system could create massive cooling-mist flow over heat stroke patients without the need for external electrical power supply. This pilot study using swine to compare with the proposed system with EMCOOLS cooling pads. The results showed that a steady cooling rate of 0.150°C/min or lower was achievable, using the proposed portable system. Typical cooling pads could not achieve effective cooling rate beyond 12 minutes, which is not sufficient for treating an exertional heat stroke patient.

In conclusion, such a portable evaporative cooling system is able to provide a steady cooling rate to treat heat-stroke patients effectively onsite, as well as on the way to a local emergency department before proper treatments are made available at the hospital. With this approach, the system could be deployed in sporting event sites for immediate treatment for heat stroke patients and this could translate into quicker medical responses and saving more lives.
Development of a Hospitalized-Patient Monitoring System Using Medical Radar for Continuously and Remotely Monitors of Respiratory Rate

Guanghao Sun, Masakazu Okada, Yukiya Hakozaki, Tomoya Matsushima, Tetsuo Kirimoto, Takemi Matsui
The University of Electro-Communications, Japan

Objectives: The most common cause of hospital-acquired pneumonia is infection, which is associated with prolonged hospital stay and increased mortality in hospitalized elderly patients. Continuous and long-term monitoring of respiratory rate is vital for early detection of pneumonia and its severity. We evaluated the feasibility of a medical radar system in detecting the risk period of pneumonia from continuously monitored respiratory rates in bedridden hospitalized elderly patients.

Methods: A newly developed 24GHz medical radar system was attached under the mattress of a standard hospital bed for noncontact to perform 24-h monitoring of the patient’s respiratory rate by capturing the chest wall motion during breath. To predict the risk period of pneumonia, a nonlinear dynamics model, named return map, was implemented into the system to analyze the time series respiratory rates.

Results: The results indicate that continuously monitored respiratory rate is a significant predictor in identifying pneumonia; the dynamics of respiration features are more significant than changes in the other vital signs.

Conclusions: The proposed system introduces a new approach in investigating respiration dynamics measured by a noncontact medical radar sensor for early prediction of pneumonia.

Abstract Number: ICBME1208

Usefulness of Ozone Water for Preventing Infection in Home Care

Koichi Umimoto, Aki Kamada, Syunji Nagata, Junichiro Yanagida
Osaka Electro-communication University, Japan

Objectives: The prevention of opportunistic infection for the elderly is important in home care and the hygiene management for infection is required. The chemical disinfectants are used to prevent infection, however, the residual chemical components cause environmental pollution. When water is electrolyzed by direct current, ozone water with strong bactericidal ability are generated. The attraction of ozone water is to be produced easily and returns to the original water after use. In this study, we developed an apparatus producing ozone water for home care and investigated its property.

Methods: The device for making ozone water has a lead dioxide electrode for the anode. 1L of tap water in device was electrolyzed by direct current (DC 20V) and the ozone concentration on the anode side was measured. The ozone concentration was measured by 4-aminophantoin absorption photometry. To investigate the sustainability of ozone water, the water on the anode side was put into beaker and its ozone concentration was measured over times. The bactericidal activity of ozone water was measured with two kinds of bacteria (E.Coli and S.aureus). These bacteria were cultivated at 37°C for 24 hours, respectively. After cultivation, each one colony was incubated with ozone water and were cultivated for 48 hours. The colony of bacteria was counted and the bactericidal activity was judged.

Results: The ozone concentrations were 0.3 ppm at 10 minute and 1.0 ppm at 20 minute after start of electrolysis. The ozone concentration in fresh ozone water was 1.0 ppm, however, its concentration after 30 and 60 minutes were 0.3 ppm and 0 ppm, respectively. There were many colonies of E.coli(6.5×107 cfu /ml) and S. aureus(5.2×107 cfu /ml) as controls. While there were no colony of bacteria after added 1.0 ppm of ozone water.

Conclusion: This device could produce 1.0 ppm of ozone water simply, and the ozone water had not persistence and showed strong bactericidal activity. Our device is useful for producing ozone water as a disinfectant to employ in home care, when considering economic and environmental factors, since it returns to ordinary water after use.

Abstract Number: ICBME1128

A New Approach for the Design of AFOs

Paula Silva, Arlindo Silva
SUTD- MIT IDC, Singapore

The need for assistive devices is increasing due to increasing global population and its average age. Technology to develop better assistive devices is available but is not, at present, fully utilized in practice. On the one hand, practitioners do their best with the tools they have, and patients use the assistive device, often with discomfort/pain; if they do not see improvement in their condition after continuous use of the device, they simply abandon it. On the other hand, researchers typically focus on the device as a standalone, without much attention to the interface between device and patient.

One very commonly used assistive device is the Ankle-Foot Orthosis (AFO) that promotes locomotion and rehabilitation of individuals with gait pathologies. The current work uses a model of the AFO that considers the interface between the AFO and the patient’s lower limb. A two-dimensional computational multibody dynamics approach is adopted, to analyse an AFO and its interaction with the user throughout the gait cycle, using laboratory gait data. The net moments-of-force in the articulations of interest and the interface forces are calculated, allowing an assessment of the solution in terms of actuation needs of the AFO, biomechanical effort requirements from the patient and the overall comfort of the integrated solution.

The design parameters of the AFO are its mass and mass distribution, number of AFO-limb contact points and their location, and the mechanical properties of the AFO-limb contact (stiffness, damping, and friction coefficient). The response of the model to change in the design parameters is studied in terms of...
motorization, effort and comfort. Results indicate that: (a) the motorization is not sensitive to the design parameters; (b) the effort required changes due to mass and mass distribution of the AFO but is independent of the number and location of the contact points; and (c) comfort depends on the stiffness and friction coefficient of the interface, but not on its damping. Furthermore, and contrary to common belief, increasing the number of contact point does not lead to a decrease in the maximum contact forces.

The current design practice is focused exclusively on the determination of actuation needs. As a result of this study, a new design methodology for these devices is proposed. In this methodology, there are three decoupled AFO design steps: computation of the actuation needs; computation of the effort requirements; and assessment of comfort issues. This procedure simplifies the design of AFO devices and allows the application of other techniques which are not an element of current practice, namely determining effort requirements and assessing comfort issues.

Abstract Number: ICBME1230

A Practical Gait Feedback System for Wearable Drop Foot Correction Devices

Lin Meng, Uriel Martinez-Hernadez, Craig Childs, Arjan Buis
Tianjin University, China

Objectives: Patients with a drop foot suffers from limited ability to lift the foot during early swing, which would lead to a pathological gait with a high risk of tripping and falling. A drop foot assistance device can provide certain actuation for the drop foot correction. To maximise the efficiency of gait intervention, real-time gait feedback needs to be explored to augment proprioceptive feedback for closing the loop in a robotic controller. The study aimed to develop a robust gait feedback method using a minimal number of inertial sensors for both joint kinematics and gait phase detection during walking.

Methods: Two inertial measurement unit (IMU) sensors were used in this study. They were attached to the shank and foot respectively whilst linear acceleration and angular rate data were collected. We proposed a two-layer model. Gait stance and swing phases were detected in the high-level layer with a Bayesian formulation. In the low level, the ankle dorsi-/plantarflexion angle was calculated using a complementary filter and sensor-to-segment calibration procedure.

An experiment was set up to validate the real-time gait feedback model. A 12 camera Vicon motion capture system was used as reference. Ten participants participated. Each participant wore IMU sensors attached to the shank and foot and a marker set for gait analysis. Firstly, the participants were instructed to perform knee flexion/extension and ankle dorsi-/plantarflexion for the sensor-to-segment calibration with a repetition of 10 times. A static trial was collected with the participants standing in an anatomical position where the angle offsets were calculated. Lastly, the participants walked on the treadmill at three various speeds (0.5, 1.0, 1.5 m/s) for 1 minute. The gait measurement system generated the ankle angle and gait phase recognition results simultaneously while the marker trajectories were gathered.

Results: Results show that the high-level Bayesian algorithm reached an accuracy of over 94% for various speeds. The recognition method achieved the highest accuracy (97.85% for stance and 96.27% for swing) at the speed of 1 m/s. The result for the swing phase detection was more affected when the participant walked at the speed of 1.5 m/s. In the low-level layer, the proposed IMU-based algorithm achieved a root-mean-square error (RMSE) of less than 3.5 degrees.

Conclusions: The study proposed a novel gait measurement method for providing sensory feedback for the control of drop foot correction. A two-layer model was developed to recognise the stance and swing phases and measure the ankle angle simultaneously. The online performance of the method was investigated. The recognition of gait phases and ankle angle were compared to optical references when the participants walked on a treadmill with three different speeds. The results demonstrated that our method offered an efficient approach for applications in the adaptive control of drop foot assistance.

Abstract Number: ICBME1279

Prototype of Measurement System for Clothing Pressures in the Spinal Orthosis

Sakamoto Koji, Kodai Kitagawa, Yuji Katae, Naoki Chijiwa, Aki Kuwazono, Hitashi Arizono, Chikamune Wada
Kyusyu Institute of Technology, Japan

Objectives: The spinal orthosis is used in the rehabilitation after vertebral fractures. However, the spinal orthosis causes uncomfortable due to clothing pressures. Therefore, it is necessary to measure the clothing pressures quantitatively and to propose the new design and wearing method of the spinal orthosis. In this study, we developed a quantitative measurement system of clothing pressures by using multiple pressure sensors. In addition, we investigated the clothing pressures of the spinal orthosis in three wearing conditions, including wiping backside clean.

Method: In our system, sixteen pressure sensors were put on chest pad, back pad, axillary bar, abdominal girdle and axillary girdle of a spinal orthosis. One subject was asked to wear the system and asked to perform a motion in order to wipe backside clean with right or left hand. Also, three wearing conditions for spinal orthosis were prepared: normal wearing (NM), wearing with loose chest belt (LC), and loose chest belt and loose abdominal belt (LCA). The subject was asked to perform wiping motion 10 times for each condition, and the number of motions was 60, that is 20(right/ left hand)x3(wearing conditions). During wiping motion, sixteen pressure data were measured simultaneously with 100 sampling frequency and calculated average pressure for each motion. The significant differences in clothing pressures among wearing conditions and orthosis parts were evaluated using the Kruskal Wallis test and Bonferroni adjustments.

Results: The clothing pressures on the back pad were significantly highest among all parts. In addition, the clothing pressures of the chest pad and axillary bar tended to be higher than other parts. The clothing pressures in NM condition were significantly higher than those in other wearing conditions at many parts. The pressures on the back pad significantly decreased, when wearing condition was changed from NM to LC and LCA. The pressures on chest pads and axillary bar located near the chest belt tended to decrease in LC compared to LCA. Thus, these results showed that the proposed system was able to measure changes in clothing pressures for each orthosis part during wiping motion.
Conclusions: In this study, we developed a quantitative measurement system by using multiple pressure sensors in order to evaluate clothing pressure of a spinal orthosis. As experimental results, it was found that the proposed system could measure changes of clothing pressures, caused by motion and wearing conditions.

Abstract Number: ICBME1416

A Low-Cost Force Myography Sensor for Upper Limb Prosthesis Application

Alok Prakash, Shiru Sharma
Indian Institute of Technology, Banaras Hindu University, Varanasi, India, India

Objectives: Measurement of muscle contraction has extensive applications in the diagnosis of neuromuscular disorders, muscle fatigue study, and control of the prosthesis. Contraction can be either measured by monitoring the electrical or mechanical activity of the muscle. Surface electromyography (sEMG) is the predominant technique used for detecting the electrical activity of muscle under the skin. Currently, sEMG is widely utilized for controlling active prostheses and other human-machine interfaces (HMI) due to its intuitiveness. However, EMG measuring system suffers from many challenges such as requires use electrodes in direct electrical contact with skin, sophisticated conditioning circuitry and is sensitive to external electrical interference. Force Myography (FMG) is an alternative method which can measure the mechanical variations in muscle volume that occurs during contraction. This work proposes a sensitive, dual channel (FMG) sensor to detect muscle contraction applied for controlling hand prosthesis.

Methods: The sensor is designed using a pair of FSR elements mounted inside a 3D printed chassis which receives muscular contractile force through hemispherical elastomer couplers prepared from polydimethylsiloxane (PDMS) material. The sensor also includes a specific conditioning circuit (with appropriate power supply) for producing a voltage output proportional to the intensity of contraction. The static and dynamic characteristics of the sensor were determined and analyzed using the recorded data to show its effectiveness. A quantifiable comparison between the designed FMG sensor and traditional EMG sensor was performed by simultaneous measuring the FMG and EMG signals from eight subjects for their contraction of forearm muscles. Finally, the ability of the designed FMG sensor was further tested for controlling hand prosthesis implementing proportional control scheme.

Results: The sensor showed decent static characteristics over time. The frequency response of the sensor was obtained large enough to detect the rapidly varying FMG signals. The similarity test performed for the simultaneously acquired FMG and EMG signals from subjects showed a high correlation coefficient ($r > 0.87$) with $p$-value $< 0.0001$. The sensor was successfully tested on human subjects for controlling the operation of an intrinsically actuated 3D printed hand prosthesis utilizing the proportional control strategy. Conclusions: The designed sensor is simple, low-cost, and can provide smoother and faster operation of the prosthetic device as compared to a conventional EMG sensor. Such a sensor can effectively monitor the muscular contraction as detected by the EMG device without any effect of noise sources such as electromagnetic interference, motion artifacts, etc., and can be used as a good alternative to EMG sensor for controlling prosthesis or, other assistive devices.

Abstract Number: ICBME1454

Development of a Novel Rollator with an Active Driving Chest Pad to Achieve the Effectiveness of Walk Assistance

Jian Huang, Hiroaki Ashida, Ryosuke Abe, Noriho Koyachi, Takashi Harada
Kindai University, Japan

With the rapid increase in the elderly population suffering from diseases of the lower limbs, gait training at rehabilitation centers or walking independently at home as a part of their daily life is typically anticipated to prevent elderly people from becoming bedridden and having dementia. To support elderly people walking, many commercialized robots or devices have been developed in recent years. However, the effectiveness of the commercialized gait-trainers in walking assistance has not been thoroughly investigated. In our previous studies, a rollator with a chest pad equipped with a freely rotating mechanism was developed. The advantage of the developed rollator is that waist swaying is induced naturally in the user by the freely rotating mechanism. Walk measurements with the developed rollator were attempted in the previous studies to evaluate the effectiveness of walking assistance of the rollator. However, with using the previous rollator, it was difficult for the elderly who is difficult to move his lower limbs. According to the physical therapists, pulling the user’s leg caused by the waist swaying is beneficial for walking assistance. In this study, a novel rollator with an active motor driving chest pad was developed to enable the elderly people to easily take his first step. The features of the novel rollator are shown below.

(1) Compared to the previous rollator developed only fits the people with body heights under 170cm, the novel rollator developed in this study can be used for the persons with heights of up to 180cm.
(2) Two linear motors with excellent quietness were used for weight lift and gesture adjustment.
(3) A DC motor for driving the chest pad was selected for the user with a maximum body weight of 100Kg.
(4) Four load cells were layered in the chest pad to measure the pressing force produced by the user’s body weight.
(5) In order to achieve a compact data acquisition system mounted on the rollator, a compact and high processing power microcomputer of Arduino Due is introduced.

This study is an ongoing project. Performance evaluation of the developed rollator will be conducted in next stage. Walk measurements for elderly are planned in the final stage of our project.
Hematology analysis is the most requested clinical test due to the importance of peripheral blood cell biomarker for clinical routine. Today's automated hematology allow for low cost Complete Blood Count with Differential but the flow cytometry-based method barely changed in the past few decades limiting opportunities for new biomarkers and novel workflows. By developing a label-free quantitative phase imaging-based workflow we believe to be able to extend the biomarker portfolio and allow for novel workflows. We demonstrated that a complex differential of leukocytes, and even various forms of leukemia, can be automatically discriminated label-free.1 The high-throughput method (>1,000 cells/s) even allows discrimination of all cycle stages of Plasmodium falciparum including the clinically-relevant ring stage.2 Due to the label-free microfluidic workflow potentially any statistical power can be achieved because operator are not bound to a defined stained blood volume which leads to new workflow opportunities.

Abstract Number: ICBME1078

A Pump-Free Tricellular Blood-Brain Barrier On-a-Chip Model to Understand Barrier Property and Evaluate Drug Response

Yu Fang, Nivasini D/O Selva Kumar, Lynette C Foo, Ng Sum Huan, Gary, Satnam Singh, Walter Hunziker, Deepak Choudhury
SIMTech, Singapore

Objective: Disruptions of the blood-brain barrier (BBB) leads to various neurovascular diseases. Development of therapeutics targeting the BBB is difficult due to a lack of relevant in vitro models. We developed a 3-dimensional (3D) microfluidic BBB chip (BBBC) to study the cells interactions in the brain microvasculature and to test drug candidates of neurovascular diseases. We isolated primary brain microvascular endothelial cells (ECs), pericytes, and astrocytes from neonatal rats and co-cultured them in the BBBC. To mimic the 3D in vivo BBB structure, we used type I collagen hydrogel to pattern the microchannel via viscous finger patterning technique to create a matrix. EC, astrocytes, and pericytes are co-cultured in the collagen matrix.

Methods: We develop an in vitro BBB model by arranging endothelial monolayers in tube-like structures in a pump-free microfluidic platform. We validate the tightness of the constructed model by visualizing the delayed dye leakage across our BBB, the expression of endothelial junction proteins, Zonula Occluden-1 (ZO-1) along the cellular boundaries. We demonstrate the potential relevance of this model in studying inflammation, by measuring the effect of tumor necrosis factor alpha (TNF-α) on BBB. We aim to develop a functional drug testing model for brain microvascular tissues with robust chip-to-world connections and proper packaging, as an attractive product for the pharmaceutical industry.

Results: Immunofluorescence images of primary endothelial cells, pericytes, and astrocytes confirms the formation of BBB in the microfluidic chip. Measurement of specific gene expression...
in brain microvascular cells. Comparison of Trans Epithelial Electrical Resistance (TEER) measurements in transwell plates and measurement of TEER on the BBB chip (relative ohm values measured with the epithelial voltohmmeter) confirms formation of BBB in the chip. Constructed 3D BBB model shows reduced dextran dye leakage. The diffusion of FITC-dextran (M.W. 40 kDa) is significantly reduced through the BBB. In the absence of the BBB, the fluorescent dextran diffuses through the collagen gel easily.

Measurement of specific gene expression in brain microvascular cells shows that the BBB model response to neuroinflammation stimulus. Expression of tight junction protein occludin is reduced in models with tumour necrosis factor alpha (TNF-α). To model the treatment of brain disorders with compromised BBB integrity, a glucocorticoid drug: dexamethasone (dex) is used. The models with Dex treatment show restoration of occludin expression.

Conclusions: We report a microfluidic platform that mimics physiologically relevant BBB structure and flow condition in vivo, the model is suitable for in-vitro functional studies and screening of drug candidates targeting the BBB. This model supports 3D dynamic co-culture of ECs, pericytes and astrocytes, making it more physiologically relevant compared with 2D BBB models and static well-plates-based BBB models. By including 3 cell types, we studied cell-cell interaction and its effect on BBB functions. Compared with traditional pump-driven BBB-on-a-chip models, the medium flow on the platform is gravity-driven and controlled by capillary effect of a paper resistor.

Abstract Number: ICBME1359

Microscale-Based, Lamina-Plate Extracorporeal Blood Processing: A Platform for Advancing Personalized Medical Therapeutics

Matthew Coblyn, Jaturavit Pantakitcharoenkul, Jad Touma, Goran Jovanovic
Oregon State University, USA

The most well-known form of therapeutic processing of blood is hemodialysis for End-Stage Renal Disease treatment which conventionally utilizes a hollow-fiber filtration cartridge. Over decades, this form factor has remained relatively unchanged and, generally, extracorporeal blood processing therapies are sequestered to hemodialysis and blood oxygenation. There are a number of opportunities to treat diseases via this route such as treatment of thalassemia, gout, sepsis, and more. In this work, we propose a platform founded on microscale-based chemical processing and utilizing surface functionalized Lamina-Plates that can be leveraged to develop novel therapies and adapt current therapies into safer and more effective approaches in what is referred to as the i-Blood platform.

The fundamental hardware component of the i-Blood device is a Lamina-Plate. Micro- and mesoscale architectural features on the plate create flow geometries for blood and other fluids (gas or liquid) to flow through. At these size-scales, transport rates of solutes, dissolved gases, etc. can be intensified, along with heat transfer. These process advantages have been extensively studied in the microfluidic research field where numerous technologies have been developed for analytics, diagnostics, or lab-on-a-chip applications. The Lamina-Plate provides higher throughput than a single or few microchannels and still maintains a high surface area to volume ratio. This allows for the integration of the next key component which is surface functionalization or therapeutic functionalization of the device itself. This ranges from antifoiling block copolymer brush layers, to covalently tethered drug molecules, to encapsulated or immobilized proteins or cells in hydrogel layers. Lastly, the Lamina-Plates can be numbered-up into a laminae module that contains the necessary processing throughout for the application along with opportunities for further process integration via a combination of different Lamina-Plates.

In this talk, we will describe the fundamentals of the i-Blood platform and findings and lessons learned across various application development projects. This includes fluidic characterization of microscale multilayer systems, management of gas bubbles and other obstructions in microchannels and process design using Time Scale Analysis. Additionally, through collaborations with mechanical and industrial engineering researchers, we had opportunities to address challenges in manufacturing commercial devices, manufacturing cost analysis, and identifying Lamina-Plate fabrication defects and their impact on performance. Lastly, we will provide an overview of past and current applications and their approaches to functionalizing the Lamina-Plate surfaces. The i-Blood platform provides a new opportunity to augment a patient’s blood for highly specific treatments and the potential of this technology extends beyond our current application development, and with unforeseen therapies that others will pursue in the future.

Keywords: Microscale, Microchannel, Process Integration, Extracorporeal, Blood Processing.

Abstract Number: ICBME1501

Large-Scale Integrated Platform for Digital Mass Culture of Adherent Cells

Dae-Hyeong Kim
Seoul National University, Korea

A platform capable of culturing anchorage-dependent cells in large-scale with fast, efficient, and accurately controlled manner is extremely important in the industrial applications that require large amount of cells, such as personalized cell-therapy and in vitro toxicity testing in pharmaceutical and cosmetic industries. And cellular activities such as proliferation and differentiation during the cell culture, including large-scale cultures, have long been observed by microscopy and/or impedance sensing methods. However, microscopy allows observation of only localized area of the entire cell substrate, which is time-consuming and needs high manpower to monitor entire cells in the large-scale cell culture. The systems using the impedance sensor also have several limitations in multifunctionality, spatial mapping capability, and automatic feedback controllability. We herein present a large-scale integrated smart culture platform of anchorage-dependent cells. This novel platform technology can digitalize the mass cell manufacturing process to become simple, fast, and highly productive by allowing thorough monitoring of key indicators with high spatial resolution during the cell culture, individual control of cells at specific locations in 3D cell culture space, and in situ maintenance of the cell culture process including culture medium exchange and perfusion, and wireless connectivity of entire cell culture substrates to the central control system. Our platform is
developed by a series of integration methods incorporating arrays of ultrathin impedance, temperature, pH, potassium sensors and electrical and thermal stimulators transfer-printed onto the 3D-printed polyactic acid substrates. These porous and stackable smart sensor/actuator-integrated substrates, which are coated with graphene oxide nanosheets for enhanced cellular adhesion, can be assembled into 3D multilayer stacks for mass culture of various types of cells with high space efficiency. The sensors and stimulators in each stack are interconnected through the wireless system, transmitting signals to and being managed by a central control system wirelessly. With our system, a single person can control numerous cell culture platforms, automatically acquiring massive amount of data about the cultured cells, and delivering appropriate feedback stimulation and/or media circulation actions in real time to ensure that the cell culture environment is well maintained throughout the culturing process.

Abstract Number: ICBME1161

Computational Fluid Dynamics Modeling for Lateral Migration of Extracellular Vesicles in Spiral Inertial Microfluidics

Sheng Yuan Leong, Hui Min Tay, Han Wei Hou
Nanyang Technological University of Singapore, Singapore

Exosomes (~50-200 nm) and microvesicles (~100nm – 1 um) are extracellular vesicles (EVs) secreted from all types of cells in health and diseases. They contain proteins, lipids and nucleic acids, and serve as key mediators of intercellular communication in pathophysiological conditions including inflammation and tumor metastasis [1]. Our group has recently developed a novel spiral inertial focusing technique termed as High-resolution Dean Flow Fractionation (HiDFF) to directly isolate sub-micron microvesicles from whole blood [2]. The size-based separation technique is highly dependent on flow rate conditions and channel geometry which will directly impact the hydrodynamics forces experienced by the particles. In this work, we conducted numerical simulation to study the flow profile and Dean-induced migration of particles in HiDFF devices for optimal EVs separation.

Computational fluid dynamics (CFD) modelling using ANSYS FLUENT was conducted in a 2-inlet spiral microfluidic channel. Exosomes were assumed to behave like fluid particles, and the fluid streamlines were tracked from sample inlet throughout the channel to characterize Dean-induced lateral migration. Under the effect of Dean drag force, exosomes were initially pinched to the channel outer wall by shear flow at the inlet, and they slowly migrated towards the inner wall [3]. The simulated particle trajectory at different positions along the channel were in excellent agreement with the experimental data of 50 nm bead lateral migration. At higher flow rate or outlet hydraulic resistance, particle band became defocused which affected the EVs separation efficiency into the inner wall outlet. We also conducted CFD studies on stacked HiDFF devices (2-3 layers) and observed the importance of PDMS channel deformation and channel resistance to ensure uniform fluid distribution in each layer.

In conclusion, we have conducted CFD and experimental studies on single and multi-layered HiDFF devices to characterize the effects of flow rate and channel outlet hydraulic resistance for EVs separation. Our model successfully predicted the transient behavior of 50 nm bead migration without using the complicated particle tracking algorithm, thus significantly saving computational time and cost, and can be further developed to guide HiDFF channel design and optimization.

Word count: 339


Abstract Number: ICBME1103

Analysis of the Spheroid Morphological Characteristics Using Pseudo-Color Image Processing

Takeshi Shimoto, Chihiro Teshima, Kodai Kuzushima, Toshiki Watanabe, Xi-Ying Zhang, Atsushi Ishikawa, Hidehiko Higaki, Koichi Nakayama
Fukuoka Institute of Technology, Japan

Objectives: In tissue engineering, building cell constructs in vitro has been researched intensively in recent years. Our research group has established a technique to make a three-dimensional cell constructs using only cells. The cell constructs are made using spheroids consisting of only cells. The quality of the spheroids is important as it is necessary to provide reproducible spheroids. Therefore, it is necessary to morphologically evaluate spheroids non-invasively. The quality of spheroids was evaluated regarding area, diameter, and circularity. However, the concentration distribution of the spheroids had not previously been visualized. This study aimed to visualize the cell distribution inside spheroids using pseudo-color display processing.

Methods: We developed a spheroid morphology evaluation system to quantitatively evaluate the morphology of spheroids. To minimize the damage to the spheroids, a plate with 96 wells containing spheroids was set up to allow the spheroids to be photographed while the camera moved. The developed system installed a camera in the lower part and a light in the upper part. Firstly, the developed system automatically took photos the spheroids in each well. Secondly, these photos were converted from color photos to grayscale images and were used to analyze the morphology of the spheroids. The pseudo-color processing was applied to the grayscale image using the produced pseudo-color chart. The pseudo-color chart was divided into 10 values from the central part to the outer peripheral part of the spheroid with consideration to the characteristic of the spheroid's spherical shape. Finally, the pseudo-color images of the spheroids indicated the concentration distribution by visually showing parts of low...
density and high density. We observed the cultured spheroids using the developed spheroid morphology evaluation system every 24 hours after seeding cells for a five day duration.

Results: Spheroid pseudo-color images of the first day and the second day had low density at the center and the density of the outer periphery was high. The spheroid pseudo-color images of the third day showed high density of the cell. It was considered that the size of the spheroids decreased with aggregation inside the spheroid and increased in overall concentration. On the fourth day and fifth day, the cell density reduction inside spheroids could be confirmed. This may be due to the death of the cells in the spheroids. This method enabled visualization of the cell distribution of spheroids in detail.

Conclusions: By applying pseudo-color processing to the grayscale spheroid images, we succeeded in visually grasping cell distribution and shape. In the future, we will actually observe inside the spheroid and aim to further improve the accuracy by correlating with the specific conditions.

Abstract Number: ICBME1485

Two Photon Excited Fluorescence Microscopy Methods Are Sensitive to Early Phenotypic Changes in Calcific Aortic Valve Disease in Vitro and Ex Vivo

Kartik Balachandran, Ishita Tandon, Olivia Kolenz, Shelby Johns, Delaney Cross, Alan Woessner, Isaac Lopez, Timothy Muldoon, Kyle Quinn
University of Arkansas, USA

Objectives: There is a critical need to develop early diagnostic measures to aid mitigation and prevention strategies for calcific aortic valve disease (CAVD). Two-photon excited fluorescence (TPEF) microscopy has shown potential in providing label-free quantitative metrics that associate with CAVD markers - osteogenic differentiation, calcification and collagen remodeling.

Methods: TPEF imaging was used to obtain autofluorescence intensities at 755nm, 860nm, and 1020nm excitation with 460nmx40nm and 525nmx45nm emission wavelengths to assess TPEF 755-860 ratio (A860/525) / (A755/460) + (A860/525) and TPEF Collagen-Calcium Ratio ( [(A810/525) / (A810/460) + (A810/525)] via in vitroand ex vivostudies. Porcine valve interstitial cell cultures in Dulbecco’s Modified Eagle Medium, 50 U mL−1 penicillin, 50 U mL−1 streptomycin, and 10 mM HEPES under quiescent (supplemented with 2% fetal bovine serum (FBS), 10ng/ml FGF-2 and 50ng/ml insulin) or pro-osteogenic conditions (supplemented with 10% FBS, 10 mM β-glycerophosphate, 100 nM dexamethasone, and 50 µg/ml ascorbic acid) were imaged using two-photon microscopy and quantitative RT-PCR for osteopontin, osteocalcin, RUNX2 and αSMA. Early CAVD model was developed by feeding 20-week old C57BL/6J mice a control vs pro-calcific diet. Echocardiography was performed every 4 weeks and aortic valve transverse sections were obtained on weeks 4 and 5 with histology and immunohistochemistry.

Results: Porcine aortic valve interstitial cells were cultured in quiescent or osteogenic conditions for 28 days. TPEF 755-860 ratio (Fig. A) decreased by day 14 for osteogenic cultures (Fig. B) and correlated with osteocalcin, RUNX2, TGFβRI, and osteopontin gene expression for day 1-7. Mitochondrial clustering, quantified from A755/460 intensity maps correlated with RhoA for day 1-7. The pro-calcific mice showed lipid deposition and alizarin red S positive calcification at commissures by 16 weeks but did not show altered left ventricular function. TPEF 755-860 ratio (Fig. C) and TPEF Collagen-Calcium Ratio decreased at the commissures of pro-calcific mice at 16 weeks (Fig. D) coinciding with calcium deposition and RUNX2 expression.

Conclusions: The in vitroand ex vivostudies show that the TPEF autofluorescence markers identified the pathological changes and correlated with the early CAVD progression suggesting it is a promising tool to look at the structural, functional, and metabolic changes occurring during the CAVD progression.

Abstract Number: ICBME1308

Raman Signal Noise Removal Using Dual-Tree Complex Wavelet Transform

Taresh Savesh Sharan, Shiru Sharma
Indian Institute of Technology (BHU), India

Noise is inherent in any measurement and generally ignored due to high signal to noise ratio. In Raman spectroscopy, simply neglecting the noise will influence the further analysis and may impose incorrect information and classification of the sample. Use of highly sensitive and stable instrumentation along with measurement in optimal condition is recommended for reducing noise in the spectrum. But it is not always possible to obtain ideal condition for the measurement and thus noise is present in Raman spectrum. This leads to need for additional pre-processing step, denoising, before further analysis of spectrum. Random noise is only considered here.

Number of denoising methods has already been proposed among which Savitsky-Golay smoothing is most commonly used for the Raman signal. It dynamically fits polynomial to consecutive windows of signal to follow the shape of randomly varying signal. But if the selected window size is small, smoothing will be poor and if the selected window size is large, spectral resolution will be less and small spectral features will be distorted. Another option is Wavelet transform based denoising. Wavelet transform denoising methods decomposes the signal into two components: Approximations sub-band and Details sub-bands. In Raman spectrum, random noise are high frequency components, fluorescence are low frequency components and Raman peaks are generally mid-frequency components. These separate regimes of the noise, signal and background makes it more useful technique for Raman signal denoising. In this study,1st, 2nd and 3rd order Savitzky-Golay smoothing is compared against Dual-tree complex wavelet transform based denoising (DT-CWT). First, the proposed method is applied to test signals like Bump, Blocks and HeaviSine if noise is added to test signals and denoised using above stated methods, best values are obtained for DT-CWT (for Bump test signal, SNR are 12, 14.26 & 13.99 for SGolay 1st order, 2nd order, 3rd order and 15.68 for DT-CWT respectively and 19.63, 22.40, 21.17 and 25.99 respectively for SGolay 1st order, 2nd order, 3rd order and 15 dB added to it. SNR for DT-CWT is 23.53 while for SGolay1st order, 2nd order, 3rd order is 23.1, 20.7 and 22.11 respectively. For Raman signal too, DT-CWT gives better results than SGolay based smoothing. RMSE for all methods are also calculated and DT-CWT
values are better. This gives an idea that DT-CWT is best capable method among all above to denoise Raman signal too. Also, when noise of different level are added to Raman signal and denoised, it is observed for some value of noise, 3rd order is working better while for some other 1st and 2nd order. On the other hand, DT-CWT always gives better denoising. It can be concluded from above results that DT-CWT works better than other method for denoising test signals as well as biological sample Raman signal.

Abstract Number: ICBME1215

Respiratory Motion Simulation of Lung by Deformable Image Registration and Interpolation

Jing Zou, Lin Shi, Simon Chun Ho Yu
The Chinese University of Hong Kong, Hong Kong

For interventional therapy or radiotherapy of lung cancer, image-guided navigation system has greatly enhanced its accuracy and efficiency. However, in such navigation system, organ motion due to respiration is a major challenge for accurate tumor targeting. Currently, patients are asked to hold their breath, and repeated CT scans are taken to track the tumors. This approach is a compromised choice due to the radiation exposure and prolonged procedures. In addition, the breath-holding strategy is difficult to manage due to the poor tolerance of patients in severe conditions.

We proposed a patient-specific respiratory motion model to synchronize respiratory motion in the navigation system. The proposed motion model was built from the DIRlab 4D CT data[1]. Firstly, the end of inspiration image and the end of expiration image were down-sampled to reduce memory requirement and improve computational speed. Considering the major deformation in diaphragm may be larger than 20 mm[2] and the intensity variation as a result of air volume, the Symmetric Normalization (SyN) registration algorithm in ANTs[3] was applied to the register the end of inspiration image to the end of expiration image. During registration, a five-level image resolution strategy was adopted to improve accuracy and speed. After registration, intermediate deformation fields are generated by linearly interpolating the deformation field obtained before[4]. Next, these intermediate deformation fields are used to generate intermediate images through image warp. At last, lung border and tumor were segmented simply by threshold and morphological operations.

The dice coefficients of simulated CT images and real 4D CT images from Phase 1 to Phase 9 are 0.879, 0.929, 0.958, 0.952, 0.903, 0.923, 0.940, 0.953 and 0.968 respectively (average dice coefficient: 0.934). This approach can simulate good quality 4D CT images from Phase 1 to Phase 9 are 0.879, 0.929, 0.958, 0.952, 0.903, 0.923, 0.940, 0.953 and 0.968 respectively (average dice coefficient: 0.934). This approach can simulate good quality 4D CT images and the simulated respiratory motion model can be used to track tumor during operation without extra CT scans.

Reference:

Abstract Number: ICBME1287


Hirose Kudo, Suguru Miyauchi, Toshiyuki Hayase, Kosuke Inoue
Tohoku University, Japan

Atherosclerosis is related to a wide variety of circulatory diseases, and its onset and progression has a close relationship with hemodynamics. Therefore, hemodynamic information is crucial for elucidation of the mechanism and the development of a new diagnostic method for circulatory diseases. As a method to acquire hemodynamic information, Funamoto et al. proposed ultrasonic-measurement-integrated (UMI) simulation that feeds Doppler velocity measurement data back to blood flow analysis. Furthermore, Kato et al. developed two-dimensional UMI (2D-UMI) blood flow analysis system for clinical application. In 2D-UMI blood flow analysis system we cannot obtain the blood flow information outside the measured cross section. The 2D analysis results may be different from three-dimensional (3D) ones. In order to solve these problems, 3D analysis was required. 3D-UMI blood flow analysis system was developed in the previous study for mouse carotid arteries. In this system an arm type 6 degrees of freedom (6-DOF) measurement device was used for an ultrasonic probe position. The measurement range of this system was limited and it cannot be used for humans. The final target of this study is the development of a 3D-UMI blood flow analysis system for clinical use. In the previous work, we proposed a 3D-UMI blood flow analysis method and confirmed the effectiveness of the method for pseudo blood flow in a flow phantom by numerical analysis of the flow in a pipe using ultrasound measurement data. The purpose of this presentation was to verify the effectiveness of the system by performing 3D-UMI simulation for unsteady flow of pseudo blood in the flow phantom by using the geometry reconstructed from the ultrasonic measurement data. The subject of this presentation is unsteady flow of the pseudo blood (Model 046, CIRS, USA) in 50 mm region in a flow phantom (Model 524, ATS Laboratories, USA) with a diameter of 6 mm and a length of 220 mm. The velocity waveform was generated by PC-controlled piston simulating the blood flow in a carotid artery. Color Doppler measurement was performed on a plane inclined 20 degrees to the plane perpendicular to the pipe axis at axial positions moved continuously or positions with 5mm interval. A linear type probe (ML6-15-D, GE Healthcare Japan, Japan) and an ultrasonic measurement device (LOGIQ S8, GE Healthcare Japan, Japan) were used. A 6-DOF magnetic sensor (Patriot System (TX-4L), Polhemus, USA) was used to measure the positions of the ultrasonic probe. 3D shape of the flow phantom was reconstructed based on the color Doppler image data and the positional data of the probe. Inflow rate estimation was performed using fixed-point iterative method and feedback was applied on nine measurement cross sections. Accuracy of the present system was evaluated by comparison with those of the 2D-UMI simulation and Doppler velocity measurement. We verified the effectiveness of the system by performing 3D-UMI simulation for
Abstract Number: ICBME1311

fMRI-BOLD Response in Rat Brain Against Direct Motor Cortical Stimulation

Zonghao Xin, Yoshifumi Abe, Shuang Liu, Kenji F. Tanaka, Koichi Hosomi, Youichi Saitoh, Masaki Sekino
The University of Tokyo, Japan

Neuropathic pain (NP), often caused by lesions or dysfunction in the nervous system, has become a complicated and severe syndrome in modern medicine. From 1990s, motor cortex stimulation (MCS) has emerged to be a potential effective treatment for chronic neuropathic pain. Both mature non-invasive and invasive approaches based on MCS have been increasingly applied in the treatment of NP. Notwithstanding large amount of reports have demonstrated the pain relief effectiveness of MCS, the precise mechanisms underlying analgesia induced by MCS still remain unclear. The purpose our study is to investigate the blood-oxygen-level-dependent (BOLD) response of the brain during the MCS procedure.

The MCS was accomplished by an inserted bi-polar electrode made of tungsten and the target was the primary motor cortex (M1) region of the adult male Wistar rats. Functional magnetic resonance imaging (fMRI) scan was implemented simultaneously with the electrical stimulation of the motor cortex and the BOLD signals taken from fMRI were used as an index to reflect the response against MCS. Initially general linear model (GLM) based statistical parametric analysis was individually employed on fMRI data of each rat to investigate which part of the brain reveal a pattern of activation. Then group analysis was conducted to assess the variability of effects over all the rats in the group. Additionally, we carried out a group independent component analysis (ICA) on the fMRI data of all the rats for the comparison with our GLM based results.

We accumulated data from eight subjects in total and activation map of the whole brain was depicted individually. The group analysis result showed that bilateral primary motor cortex (M1), ipsilateral caudate-putamen (CPu) and ipsilateral primary somatosensory (S1) to the stimulation spot were activated after the onset of the MCS and the BOLD signal time courses were analyzed in these regions. Next, we performed region of interest (ROI) based small volume analysis in each animal to assess signal intensity changes in activation maps of these encephalic regions. Similar temporal characteristics were showed in all the regions that were observed to be activated. The ICA results further verified the conclusion obtained from previous analysis, however, we also found that two independent components (IC) from all twenty ICs suggested highly symmetrical signal changes in bilateral hippocampus regions. This possibly indicated the participation of hippocampus in our MCS procedure. We simultaneously investigated brain response against enlarged stimulation scope and results demonstrated reliable signal variation in ipsilateral thalamus region which was not observed in the first group analysis. To our knowledge, only a few studies have been conducted on direct cortical stimulation of the rodent brain to investigate its instant effect using fMRI; reproducible results in the CPu have not been previously found. We anticipate our results to be effective to the establishment of neural pathways involved in MCS.

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Time-Dependent Material Properties of Mouse Cervical Tissue During Pregnancy

Nicole Lee, Charles Jayyosi, Shanmugasundaram Nallasamy, Maia Mahendroo, Kristin Myers
Columbia University, USA

Objectives: The dramatic remodeling of soft tissues in the reproductive system are critical in a healthy pregnancy. The cervix, which acts as a barrier between the fetus and environment, must remodel sufficiently by term to allow for delivery [1]. Mouse cervixes undergo a dramatic softening from day 6 to 12 of a 19-day pregnancy and a gradual softening later in pregnancy. These changes have been attributed to collagen reorganization [2]. Decorin is a major proteoglycan in the cervix and plays a role in collagen synthesis and formation [3]. Decorin has a gestation time point dependent effect on the stiffness and strength of mouse cervical tissue as shown through load-to-failure tests [4]. Hydrated soft tissue typically presents a hyperviscoelastic behavior. A viscoelastic response is more likely observed in vivo as the cervix experiences repeated loads from the fetus or other external forces. This research aims to implement a viscoelastic protocol and identify decorin’s effect on time-dependent properties of mouse cervix.

Methods: Wild type (WT) and decorin knockout (DcnKO) mouse cervixes were collected at the non-pregnant (NP) time point. WT and decorin knockout with biglycan heterozygous (DB) were collected at day 18 (d18). Samples were prepared for whole-specimen ring tensile loading as previously described [5]. Samples swelled for 2 hours and then a preload of 0.001 N was applied. The loading protocol consists of 2 sections: 1) strain rate sensitivity cyclic load-unloads and 2) stress relaxation ramp-holds. Different loads were applied at each time point to ensure samples could sustain a majority of the test without breaking. Images were taken throughout to record deformation. Comparison is contained to each time point as different loads were applied.

Results: Strain rate sensitivity was not observed at either gestation point. At d18, the DB samples were stiffer than the WT. For NP, DcnKO and WT exhibited similar levels of relaxation, but a striking difference is the DcnKO broke sooner than WT, with only 1 of 4 DcnKO samples making it to the highest load level. There was no difference between the relaxation behavior of d18 DB and WT samples.

Conclusions: Decorin has a complex effect on viscoelastic behavior that manifests differently at each gestation point. Overall, NP DcnKO samples could not sustain the full loading regimen. The lack of difference between d18 was not surprising as there wasn’t a difference observed in collagen microstructure through imaging [4]. There are various mechanisms that can contribute to a tissue’s
viscoelasticity, such as unraveling and reforming of collagen crimps; how decorin’s viscoelastic effect manifests structurally needs to be explored. Further studies will include hormone-treated cervixes.

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**References**


**Abstract Number:** ICBME1085

**Biaxial Active and Passive Mechanical Properties of Fibulin-5 Deficient Mice Vagina**

**Gabrielle Clark**, Laurephile Desrosiers, Leise R. Knoepp, Kristin S. Miller

**Tulane University, USA**

**Objectives:** Pelvic organ prolapse (POP) is a global health problem characterized as the descent of the pelvic organs into the vaginal canal. Although the pathophysiology is not fully understood, decreased elastic fibers and smooth muscle composition are reported in vaginal specimens from women with POP. Further, mice with elastic fiber deficiency readily develop POP similar to humans. The objective of this study was to compare the biaxial contractile response and passive mechanical properties of the vagina from fibulin-5 deficient mice (fbln5 -/-) and controls. Additionally, to use elastase digestion to quantify the mechanical contribution from elastic fibers.

**Methods:** The vagina was secured in a pressure myograph system (n=3-7; 3-6 months of age; IACUC Approved). The outer diameter was optically tracked and the axial force was measured with a transducer. At the physiologic length and pressure, the organ was maximally contracted with KCl. Smooth muscle tone was removed and the organ was subjected to increasing pressures under the passive condition. After the organ was exposed to elastase (15U; 45 mins) and testing was repeated. Constitutive modeling was performed with the two-fiber family Holzapfel–Gasser–Ogden Model. Unpaired t-tests evaluated differences between genotype and paired t-tests evaluated changes due to treatment.

**Results:** The material parameters describing the stiffness of the ground matrix and diagonal collagen fibers were decreased (p<0.01) and increased (p<0.01), respectively, for the fbln5 -/- mice when compared to controls. Significant differences were not observed in the tangent moduli between genotype, however, elastase digestion resulted in a significant increase in the circumferential (p<0.02) and axial (p<0.01) tangent moduli for the controls. Statistically significant differences were not identified in contractility between genotype.

**Conclusion:** This study investigated the vaginal biaxial contractile response and passive mechanical properties from the fibulin-5 deficient mouse model. Although statistically significant differences were not observed in material stiffness, differences in the material parameters suggest that there are microstructural differences between genotype. Further studies on the fibulin-5 deficient mouse model may aid in better understanding the pathophysiology of POP. To that end, future work quantifying the extracellular matrix composition and organization is needed.

**Abstract Number:** ICBME1424

**The Fiber Architecture and Anisotropic Material Properties of the Human Uterus**

**Shuyang Fang**, James McLean, Christine Hendon, Joy Vink, Kristin Myers

**Columbia University, USA**

**Objectives:** The mechanical function of the uterus is crucial for protection of the fetus in a healthy pregnancy. Throughout gestation, the uterine wall remains in a passive state and accommodates the expanding amniotic sac by growing, unfolding, and stretching. Then—ideally at term (defined as 37 weeks)—the tissue becomes highly contractile to safely facilitate the final delivery. Early contractile activation of uterine tissue can lead to preterm labor and birth (PTB). In 2014, 10.6% of pregnancies ended in PTB; it is also the leading cause of death in children under five years of age [1]. Characterizing uterine smooth muscle fiber architecture and the anisotropic material properties are significant for understanding the mechanical failure of the uterus and the cause of PTB.

**Methods:** One nonpregnant (NP) and one pregnant (PG) term uterine tissue sample were collected from consenting hysterectomy patients. Immediately after hysterectomy, a specimen was collected from each of three anatomical locations: the anterior, the posterior, and the fundus. All specimens spanned the depth of the uterine wall and covered a square cross-sectional area with an edge length of 10-15 mm. All specimens were flash frozen using dry ice immediately after collection and stored in a −80°C freezer. Each specimen was sliced into 5-8 slices parallel to the uterine wall and imaged from both sides. Three-dimensional volumetric image-sets were obtained from using a commercial spectral domain optical coherence tomography (OCT) system, TELESTO (Thorlabs GmbH, Germany. Masson trichrome stained histology was applied to some of the specimen slices to reveal the tissue compositions and later on compare with the OCT results. Image processing was performed to remove background noises and binarize selected images to calculate the relative abundance of smooth muscle content through different uterine layers (endometrium, myometrium and perimetrium) and at different anatomical locations.

**Results:** Smooth muscle abundance appears to be uniform across different uterine layers and at different anatomical locations of NP human uterus, while PG uterus appears to have a higher level of abundance than NP uterus. NP uterine muscle fibers appear to run longitudinally near the uterine cavity at the anterior internal layer. At the anterior external layer of the uterine wall, NP and PG uterine muscle fibers both appear to have an interweaving fiber structure running parallel to the uterine wall, and PG uterine tissue appear to have more distinct artery structure.

**Conclusions:** In this study, a workflow of tissue collection, experiments and digital image processing techniques were
Role of Elastic Fibers in the Biaxial Passive and Active Properties of the Murine Vagina

Gabrielle Clark, Laurephile Desrosiers, Leise R. Knoepp, Kristin S. Miller
Tulane University, USA

Objectives: Pelvic organ prolapse (POP) is a global health problem characterized as the descent of the pelvic organs into the vaginal canal. Although the pathophysiology is not fully understood, decreased elastic fibers and smooth muscle composition are reported in vaginal specimens from women with POP. Further, mice with elastic fiber deficiency readily develop POP similar to humans. The objective of this study was to compare the biaxial contractile response and passive mechanical properties of the vagina from fibulin-5 deficient mice (fbln5 -/-) and controls. Additionally, to use elastase digestion to quantify the mechanical contribution from elastic fibers.

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Conclusions: This study investigated the vaginal biaxial contractile response and passive mechanical properties from the fibulin-5 deficient mouse model. Although statistically significant differences were not observed in material stiffness, differences in the material parameters suggest that there are microstructural differences between genotype. Further studies on the fibulin-5 deficient mouse model may aid in better understanding the pathophysiology of POP. To that end, future work quantifying the extracellular matrix composition and organization is needed.

Abstract Number: ICBME1315

Characterization of Biaxial Biomechanical Properties of Human Post-Menopausal Uterosacral Ligament – Importance of Collagen on Biomechanical Anisotropy

Elvis Danso, Jason D Schuster, Lyndsey Buckner-Baimonte, Laurephile Desrosiers, Leise R Knoepp, Kristin S Miller
Tulane University, USA

Objectives: Over 300,000 surgeries are performed annually in the United States to restore native anatomy and relieve symptoms due to pelvic organ prolapse (POP), resulting in direct annual costs of greater than 1 billion dollars [1,2,3]. The uterosacral ligament (USL) provides structural support to the female pelvic floor. Decreased structural or mechanical integrity of the USL may contribute to development of POP [4]. To the best of our knowledge, biaxial USL properties have not been quantified in women with POP. Therefore, the aim of this study was to determine the biaxial mechanical and microstructural properties of healthy and POP-affected post-menopausal USL tissues.

Methods: USL samples were obtained from post-menopausal women without POP (n=11), with Stage I/II POP (n=8), and Stage III/IV POP (n=6) (IRB Approved: 2017.016.A). Samples were cut into squares and speckle-coated for strain tracking. After 10 preconditioned cycles, samples were loaded biaxially at 0.2%/sec in both directions to different loading ratios of 1:0.5, 1:0.75, 1:1, 0.75:1 and 0.5:1. A Fung-type constitutive model [5] was used to describe the experimental data, and the anisotropy index was calculated [6]. Collagen, elastin, and smooth muscle cell area fractions were quantified from histological sections along both axes, stained with Picrosirius Red, Harts elastin, and Masson’s Trichrome, respectively, for evaluation at a magnification of 4X.

Results: Regarding the main in vivo loading direction, USL from Stage III/IV POP exhibited the largest extensibility and lowest tangential moduli for all the loading ratios. However, USL tissue from Stage I/II POP exhibited the lowest extensibility for the same loading direction. Regardless of the loading protocol, no significant differences were identified in the perpendicular loading direction in any groups. Apart from the parameter tissue from Stage I/II POP USL exhibited the largest values for all model parameters and the anisotropy index. In the main in vivo loading direction, collagen I in POP III/IV specimens (53.64±4.08) was significantly lower than in POP I/II (69.21±3.71) and non-POP (72.07±4.45) samples. Additionally, in the perpendicular loading direction, collagen I in the POP III/IV group (61.85±3.79) was also significantly lower than non-POP group (73.63±3.19). Further, in the perpendicular loading direction, collagen III was significantly higher for POP III/IV specimens (21.49±2.04) than their non-POP counterparts (12.97±2.19), although no significant differences in the main in vivo loading direction were noted. No significant differences in smooth muscle cell or elastin components were identified in either direction.

Conclusions: In the main in vivo direction, Stage III/IV POP USL were more extensible than Stage I/II POP or non-POP USLs. This may be due, in part, to changes in extracellular matrix with POP and POP progression. However, no significant differences in mechanical properties were observed in the perpendicular loading direction. It is possible that the properties in this direction are primarily dictated by non-collagenous extracellular matrix
and elastic fibers, neither of which were significantly different between any groups. Incorporating model parameters obtained in this study into existing finite element models may help to improve surgical planning/treatment options [7].

Abstract Number: ICBME1120

Investigations Into the Biomechanics of the Cervical Cerclage

Alexa Baumer, Megan C. Leftwich, Alexis Gimovsky, The George Washington University, USA

Premature cervical remodeling, or cervical insufficiency, is a condition during pregnancy in which the cervix softens and dilates before full term, causing a miscarriage. It is a common cause of second trimester pregnancy loss. Once diagnosed, the prevalent treatment is to perform a cervical cerclage (a purse string suture to close the cervix) and prescribe progesterone medication. Studies on the efficacy of this treatment plan are conflicting and mostly rely on statistical investigations. The importance of biomechanical factors such as cervical length, canal geometry and tissue softness are not as well documented.

To understand the effectiveness of the cerclage procedure from a biomechanics framework, we created a generalized model of a cervix using ultrasound images. Then, we 3D printed a mold for this model and fabricated synthetic cervixes using silicone. Because the properties of the cervix change dynamically throughout pregnancy, we relied on qualitative analysis by physicians of our synthetic, silicone tissues to mimic the feeling of softening, pregnant cervical tissue. These qualitative assessments were assigned quantitative values of tensile strength and compressibility through material testing. We varied parameters such as cervical canal geometry, cervical length, tissue softness, and suture material. Physicians at George Washington University Hospital stitched these synthetic cervices with a McDonald cerclage. Each synthetic cervix was placed into a capsule designed to contain the material while it is being compressed. Using a custom steel insert attached to a 5kN load cell, force was applied directly to the suture and measured as a function of time until failure (designated as when the cervical tissue begins to rip). We found that the harder cervices withstood the highest amount of force before ripping. With this protocol, we can analyze the importance of various biomechanical parameters on the integrity of the cerclage procedure.

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Abstract Number: ICBME1111

TAP vs DKC Stenting Technique: An Evaluation of Double Stenting Bifurcation Technique Thrombogenicity Using Metallic DES in an in Vitro Left Main Bifurcation Model

Jaryl Ng, Shengjie Lu, Hanwei Toh, Nicolas Foin, Hwa Liang Leo, Philip Wong, Hui Ying Ang
National Heart Centre Singapore, Singapore

Objectives: Bifurcation lesions remain one of the most challenging lesions in interventional cardiology. Percutaneous coronary intervention of bifurcation lesions may sometimes require the implantation of two stents to effectively restore physiological blood flow. For double stenting, there are multiple techniques, two of which are gaining popularity among cardiologists: the double kissing crush (DKC) and the T and small Protrusion technique (TAP). However, there is a lack of direct comparison between the two techniques. High shear gradients and flow recirculation are a known risk factor for platelets activation. Therefore, malapposed and floating struts may increase the chance of stent thrombosis. The objective of this in vitro benchtop study is to compare both techniques in silicone bifurcation models to assess the techniques in terms of thrombogenicity.

Methods: A metallic drug-eluting stent (Synergy™, Boston Scientific, MA, USA) was implanted in silicone left main bifurcation models using TAP (n=3) and DKC (n=3) techniques. These stented models were then perfused with porcine blood containing 10% anticoagulant with a peristaltic pump at a flow rate of 200ml/min for 4 minutes. Optical coherence tomography (OCT) was used to perform thrombus area measurement in frames of the bifurcation region. Frames were separated into three equidistant regions: proximal, middle and distal to analyze which region within the bifurcation was most thrombotic. Computational fluid dynamics (CFD) was done using 2D models generated based on the OCT images to compare regions of high shear rate, maximum shear rate and region of flow recirculation.

Results: Overall, there is no significant difference in thrombogenicity between the two techniques (TAP:0.11±0.07mm² vs DKC:0.16±0.23mm² p=0.74). Upon further analysis based on different regions of the bifurcation, there were no difference in the proximal region (TAP:0.04±0.06mm² vs DKC:0.01±0.02mm² p=0.46). However, TAP was more thrombogenic in the middle region (TAP:0.10±0.01mm² vs DKC:0.03±0.01mm² p=0.001) whereas DKC was more thrombogenic in the distal region (TAP:0.18±0.01mm² vs DKC:0.42±0.15mm² p=0.05). CFD analysis showed that DKC had a slightly larger region of flow recirculation (4.01mm² vs 3.91mm²) and slightly larger region of high shear rate (>1000s⁻¹) (1.70mm² vs 1.55mm²). However, DKC had a lower maximum shear rate compared to TAP (5670s⁻¹ vs 9404s⁻¹).

Conclusion: In terms of stent thrombogenicity, both double stenting techniques showed no overall significant difference. However, TAP showed more thrombus formed in the middle region of the bifurcation while DKC was more thrombogenic in the distal region of the bifurcation.

Abstract Number: ICBME1112

Effect of Thin-Strut BRS vs Metallic DES on Stent Expansion in a Lesion Model

Jaryl Ng, Shengjie Lu, Hanwei Toh, Nicolas Foin, Hwa Liang Leo, Philip Wong, Hui Ying Ang
National Heart Centre Singapore, Singapore

Objectives: First iterations of biodegradable scaffolds (BRS) required larger strut profiles to ensure sufficient radial strength to reduce stent recoil. However, this was reported to cause increased thrombogenicity of the stents. Newer generations of BRS have promised increased radial strength with reduced strut profiles (<100µm). However, the expansion capabilities and the
Virtual Operation of Chordae Transposition for Anterior Mitral Leaflet Prolapse

Hyunggun Kim, Soohwan Jeong, Woojae Hong
Sungkyunkwan University, Korea

Objectives: Mitral valve (MV) repair for anterior mitral leaflet prolapse is still technically challenging as the gold standard repair technique has not been found unlike that for the posterior mitral leaflet prolapse. Chordae transposition is employed in patients with anterior mitral leaflet prolapse due to elongation or rupture of the anterior chordae. We have previously developed novel computational methodologies to create a variety of pathologic MV types and performed virtual MV repair simulations to predict the features of post-repair MV function. In the present study, we present a new computational protocol to simulate virtual operation of chordae transposition for anterior leaflet prolapse. Physiologic and biomechanical improvement of a pathologic MV model suffering from anterior leaflet prolapse is evaluated after implementation of virtual chordae transposition repair.

Methods: A virtual normal MV model containing the saddle-shaped annulus, anterior leaflet with a single cusp, tri-scalloped posterior leaflet, and strut and marginal chordae tendineae connecting the two leaflets and papillary muscles was created. The pathologic MV having anterior leaflet prolapse was modeled by eliminating the marginal chordae in the A2 scallop. Virtual operation of posterior chordae transposition for the pathologic MV with A2 chordal rupture was designed strictly following the standard clinical guideline of the surgical procedure. First, virtual posterior leaflet resection of the P2 scallop was performed such that the marginal chordae in a pre-defined quadrangular segment of the P2 region were detached, the elements of the segmented P2 leaflet portion removed, and the excised edges of the remaining posterior leaflet merged to mimic virtual suturing. The next step is to displace and merge the detached P2 marginal chordae to the prolapsing anterior leaflet segment to complete the virtual chordae transposition procedure. Pre-repair and post-repair MV functions across a complete single cardiac cycle were simulated using our previously developed dynamic finite element analysis protocol under the physiologic transvalvular blood pressure condition. Both qualitative and quantitative evaluations of the morphologic and biomechanical characteristics of the normal, pre-repair, and post-repair MVs were performed.

Results: The Normal MV demonstrated well-distributed leaflet coaptation at the fully closed configuration indicating no mitral regurgitation and relatively uniform leaflet stress distribution. The pre-repair MV having A2 chordal rupture showed large anterior leaflet prolapse and malcoaptation in the A2 scallop with greatly increased local stress concentrations both in the leaflets and the intact neighboring anterior chordae. The post-repair MV revealed the transposed A2 chordae from the P2 scallop, markedly decreased anterior leaflet prolapse, fully restored leaflet coaptation, and reduced stress concentrations. This indicates that virtual operation of chordae transposition was successfully performed providing predicted features of post-repair MV function.

Conclusions: We have developed a novel computational protocol to perform virtual operation of chordae transposition for anterior mitral leaflet prolapse. Large anterior leaflet prolapse found in the pre-repair MV disappeared and leaflet coaptation was fully restored following virtual operation of chordae transposition. This computational simulation strategy to virtually perform complex MV repair techniques for anterior leaflet prolapse has the great potential to predict intervention outcomes and help pre-surgical planning for MV repair.

Abstract Number: ICBME1228

Development of a Covered Stent to Reduce Membrane Infolding

Gideon Kumar, Pei Ho, Hwa Liang Leo, Fangsen Cui
Institute of High Performance Computing, Singapore

Objectives: As part of our initiative to develop covered stents, we used a new coating method where the stent is coated in a semi-crimped profile and is then allowed to recoil along with the membrane. In this work we have compared our new coating method with the conventional dip-coating method to study the mechanical and hemodynamic performance of the covered stents.

Methods: We conducted structural analysis of the coated stents using finite element analysis (FEA) to evaluate the...
membrane deformation post deployment. We then explored the hemodynamic behavior of the stents using computational fluid dynamics (CFD) to evaluate the flow of blood through these stents post deployment. We also implanted the covered stents developed using the two methods in a pig model to study the flow patency.

Results: From the structural analysis it was found that the membrane in the covered stent coated using the conventional dip-coating method undergoes infolding which could be minimized in the stent coated using our new method. From the CFD studies it was inferred that the covered stent coated using the dip coating stent was susceptible to thrombogenesis. From our angiogram flow patency test, it was inferred that by using the stent coated using our new technique, stenosis can be brought down by 24% which is in accordance to our prediction as shown by the CFD studies.

Conclusions: This study compares our new coating method with the conventional dip coating method used to fabricate covered stents. Through our FEA, CFD and angiogram studies, we found that the membrane in the covered stent fabricated using the conventional dip coating method undergoes infolding which could be minimized when covered stents are fabricated using our new technique. This is because in our new coating technique where the stent is in a semi-crimped profile and coated, the membrane is stretched upon recoil which helps in minimizing membrane infolding. This infolding is also the reason why our CFD results showed high chances of thrombogenesis and in-stent stenosis in the covered stent fabricated using the conventional dip coating technique.

Methods: With the system described above 201 healthy subjects of different age were measured in normal level gait at a sampling rate of 60 Hertz while walking on a treadmill at four different speeds (2, 3, 4, 5 km/h) and in upright standing position. The complete data sets recorded and preprocessed were compiled in a master data archive. After processing the data set to 3 remaining gait cycles per subject, the data archive contains a total of 17.8 million position data. In a first step towards a practically meaningful analysis and easy-to-visualize presentation of the information contained in the large data content of the measurements, we initially focused on the analysis and description of selected characteristic parameters of motion in the transversal plane only.

Results: Calculating standardized gait cycles by suitable statistical procedures the evaluation and visualization of every single selected gait parameter or of several parameters simultaneously is possible. It could be shown, for example, that the time lag between “initial contact” of the right foot and the associated contralateral pelvic rotation maximum has a significant impact on the movement behavior of the vertebral bodies of the lumbar spine. Many further and in part unexpected results of this kind could be evaluated and functionally interpreted as yet.

Conclusions: Modern motion analysis systems generate, due to technical progress, an ever increasing enormous number of measuring data of a different kind. A number of practically meaningful parameters can be evaluated by the standard data processing procedures available. Very interesting results can already be achieved in this manner. A systematic analysis simultaneously including all data generated by modern motion analysis systems necessitates new dedicated data processing approaches like pattern recognition by deep learning artificial intelligence. Trained with the data obtained from comprehensive measurements of healthy people and patients with well-defined diseases, the development of automated motion analysis and pattern recognition suitable for clinical diagnostics seems to be possible by such a system. We try to contribute with our work towards the achievement of this goal.

Analysis of Human Body Motion: towards Comprehensive Pattern Recognition Techniques in the Processing of Measuring Data

Ulrich Betz, Juergen Konradi, Janine Huthwelker, Claudia Wolf, Friedrich Bodem, Philipp Drees
University Medical Center of the Johannes Gutenberg University Mainz, Germany, Germany

Objectives: Motion analysis of the pelvic and the leg region using a wide range of measuring methods has been developed to an established tool in research and clinical practice in the past. Recent technical advances allow a dedicated 3-dimensional movement analysis of the spine, too. The DIERS formetric 4D system employed in our laboratory facilitates for this purpose dynamic body surface topography in gait. In addition to foot pressure distribution and the movement of a number of leg markers, a large set of motion parameters can be determined in space and time. With a data processing interface established in cooperation with the manufacturer a total of 102 specific spinal motion parameters can be exported for a further analysis by a dedicated software. The thus configured system is currently used to collect data from a large number of healthy subjects in order to establish comprehensive findings about the spinal motion characteristics in normal gait.

Methods: From the structural analysis it was found that the membrane in the covered stent coated using the conventional dip-coating method undergoes infolding which could be minimized in the stent coated using our new method. From the CFD studies it was inferred that the covered stent coated using the dip coating stent was susceptible to thrombogenesis. From our angiogram flow patency test, it was inferred that by using the stent coated using our new technique, stenosis can be brought down by 24% which is in accordance to our prediction as shown by the CFD studies.

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silicone. Based on the clinical report that the threshold of calcification thickness which could be fractured using lesion preparation devices was approximately 450 μm, the mechanical strength of the calcification was adjusted so that non-compliant balloon (NCB) (NC Emerge, Boston Scientific) with 3.0-mm diameter and 10-mm length could fracture the calcification with a thickness of 400 μm and could not fracture the 450-μm thick calcification. We investigated that potential capability of other kinds of balloons for fracturing the 450-μm thickness calcification. The cutting balloon (CB) (Wolverine, Boston Scientific) with 3.0-mm diameter and 12-mm length, the scoring balloon (Scoreflex, OrbusNeich) with 3.0-mm diameter and 15-mm length and the non-slip element balloon (NSEB) (NSE Alpha, Aesculap) with 3.0-mm diameter and 13-mm length were compared. The CB equips with blades made of stainless steel, the SB with wires made of Nitinol, and the NSEB with non-slip elements made of nylon. Balloon inflation pressure for fracturing the calcification using each device was compared.

Results: The 400-mm thick calcification models could be fractured at 19 ± 1.1 atm (n=6) and the 450-mm thick calcification models could not be fractured by using the NCB. Thus, the calcification model whose fracturability threshold of the thickness is 450 μm was successfully developed. The CB could fracture the 450-mm thick calcification models at lower inflation pressure of 13.0 ± 1.2 atm (n=6) than the SB at 16.5 ± 1.22 atm (n=6) (p < 0.001) and the NSEB at 19.2 ± 1.72 atm (n=6) (p < 0.001). The calcification fracture occurred at the locations where the blade or wire came into contact with the calcification and the stress concentration area. These data indicated that the CB could fracture calcification safely at the lowest pressure and the CB blade is the most stress-concentrating element compared to wires and non-slip elements.

Conclusions: It was elucidated that the CB is effective for fracturing completely tubular calcification with lower inflation pressure as compared with the NCB, SB and NSEB. It was also suggested that the fracture position of the calcification was associated with the portion of stress concentration.

Flow Inside Large Cerebral Aneurysm Models After the Deployment of “Flow Diverter” Stent: Influence of the Location of Aneurysms at the Internal Carotid Artery

Koichi Hoshino, Yuki Matsushashi, Yoshinori Honobe, Zhuran Rai, Koh Shinoda, Mitsuo Ummez, Satoshi Tateshima, Kiyotaka Iwasaki
Waseda University, Japan

Background: Flow Diverter (FD) is a medical device covering the neck part (the entrance into the aneurysm) of an unruptured large cerebral aneurysm (15mm £ diameter) with a dense stent, to induce stagnation of blood flow, form thrombus inside the aneurysm, and prevent rupture. There are some cases in which complete thrombus formation cannot be achieved despite the deployment of the FD. However, the reasons are not well understood yet.

Objective: We aimed to reveal the influence of the aneurysm location along the curved internal carotid artery on the flow patterns inside the cerebral aneurysm after deployment of the FD.

Methods: Cerebral aneurysm models with an aneurysm diameter of 15mm and a 9mm-long neck were developed. Three silicone transparent models in which the aneurysm is located at the distal, middle, and proximal sites of the curve between C1 and C2 of the internal carotid artery were fabricated (distal-site, middle-site, and proximal-site aneurysm models). A circulation system which can duplicate the maximum flow of 450mL/min, the average flow of 275mL/min, and the arterial pressure of 120/80 (100) mmHg was developed. The FD was deployed in each three models. Particle image velocimetry was employed to investigate the flow inside the aneurysm before and after the FD deployment. To examine the morphologies of the FD deployed at the aneurysm sites, a microscope and a micro CT were used.

Results: By the FD deployment, the average flow velocity at the peak flow moment in the aneurysm decreased from 0.249m/s to 0.021m/s in the distal-site aneurysm model. The flow decreased from 0.137m/s to 0.050m/s, and from 0.104m/s to 0.015m/s, respectively, in the middle-site and proximal-site aneurysm models. Before the FD deployment, anti-clockwise flows entering from the aneurysm from the distal site and exiting from the proximal site were observed in the three models. The inflow into the aneurysm was observed at the proximal site of the neck in the distal-site aneurysm model. The inflows were observed at both the middle and distal sites in the middle-site aneurysm model, and at the distal site in the proximal-site aneurysm model. After the FD placement in the distal-site aneurysm model, the flow direction inside the aneurysm changed and clockwise flow was observed. In addition, the inflow into the aneurysm was observed at the proximal site of the neck. In the middle-site aneurysm model, a flow perpendicular to the FD mesh was observed. In the proximal-site aneurysm model, the flow direction inside the aneurysm and the inflow site into the aneurysm did not change. The analysis of the mesh density of the FD using the micro-CT showed no relationship between the mesh density distribution of the FD at the neck site.

Conclusion: Our study indicated that the flow into the aneurysm after the FD deployment is strongly influenced by the location in which the aneurysm is present in the internal carotid artery. The inflow was not associated with the mesh-density distribution of the FD at the neck site.

What Evaluation Is Appropriate for Regulatory Use of Pediatric Medical Devices?

Sara Takahashi, Kiyotaka Iwasaki, Yusuke Oribe, Haruki Shirato, Mami Ho, Mitsuo Ummez
Waseda University, Japan

Objectives: Japan Pharmaceuticals and Medical Devices Agency (PMDA) is in charge of the pre-marketing review process for the safety and effectiveness of of high-risk medical devices. The evaluation with clinical data is usually required for “brand-new device” in the pre-marketing phase. About 450 brand-new medical devices were approved by Japanese Ministry of Health and Welfare between 2007 and 2017, however, the number of “brand-new medical devices” approved for pediatric patients is less than 10. Then, it takes longer time for the development of pediatric medical device (PMD) as compared with those for adults in Japan. Although the various regulatory processes have been conducted for resolving the delay of development of PMDs, the problem has not been cleared yet. One of the burdensome issues
is a difficulty to establish a methodology to evaluate an efficacy and safety of PMDs. In this study, we investigated what evaluation for regulatory use was conducted towards an approval of PMDs and discussed the appropriate evaluation methods for early developments of PMDs.

Methods: We investigated submitted pre-marketing data of the brand-new PMDs which were approved between 2007 and 2017, using the review reports and materials of these brand-new PMDs which were published on the PMDA website. Moreover, we studied what approval conditions were imposed in the post-marketing phase.

Results: We investigated the review results of six approved PMDs. We found that pre-clinical data and clinical data was submitted for the review of all six pediatric medical devices. For two of these devices, a clinical evaluation report which was composed of results from published academic research papers was submitted instead of a clinical trial. Furthermore, approval conditions for a marketing authorization holder were imposed on all devices. In addition to post-marketing surveillance, the approval conditions regarding education for users, cooperation with academic societies and requirements for medical institutions were included.

Conclusions: In this study, it was exhibited that the evaluation was performed not only by a usage of clinical trial data, but also by utilization of existing clinical data and the review was adopted based on what should be evaluated for each device in regulatory application. Moreover, instead of a large clinical trial in pre-marketing phase, strict control in post-marketing phase was conducted to ensure a safety. A large clinical trial for PMD is not realistic because of a few patients and low profits. Therefore, we consider it becomes more significant for improvement of pre-clinical trial, the effective use of pre-marketing clinical data and strict control in post-marketing phase under a close cooperation among industry, academic society and regulatory become more significant.

Session 3.13: Surgical & Therapeutic Devices
Date 11 December 2019, Wednesday
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Abstract Number: ICBME1334

Design and Development of Multi-Directional Needle Stabilizer System for Image-Guided Biopsy Procedures

Karupppasamy Subburaj, Jie Wei Fung, Benjamin R. L Goh, Md. Hamizan H. Mannauwir, Yue Xiang Teo, Le Roy Chong, Karupppasamy Subburaj
Singapore University of Technology and Design, Singapore

Image-guided needle biopsies are an integral part of the medical diagnostic process, performed by the clinician with the guidance of various imaging modalities to insert a specialised needle into the patient, manipulating its trajectory and depth to reach the target lesion allowing successful retrieval of tissue samples. These precise manipulations usually require dexterity and multiple imaging attempts by skilled clinicians, but could potentially lead to multiple insertions, patient discomfort and high radiation dosages. The current state of the art non-robotic devices in the market have targeted to achieve needle stability through the use of skin adhesion. However, significant drawbacks of skin adhesion-based systems are the assumptions of no relative skin movement and use of gravity. These assumptions could result in the entire device being dislodged or misaligned due to the needle’s weight, high subcutaneous fat in obese patients, and the target lesion area at a steep angle relative to the patient position. With regards to robotic devices, although they provide a higher degree of stability as well as a form of automation and guidance, these are not available for routine clinical use and could disrupt workflow in hospitals. Thus there is a need for a device that assists with biopsy procedures by providing a means of stabilising the biopsy needle, holding it in place and allowing for precise adjustments during initial penetration phase.

The proposed device utilises the patient’s weight to provide the much-needed device stability by attaching the base of the device to the CT-scanner bed via friction pads on which the patient lies. The device consists of three main sub-mechanisms: (1) rails along the side of the bed, mounted with the base, providing longitudinal (sagittal plane) movement, (2) the arc providing 180 degrees angular movement (axial plane), and (3) the universal needle holder assembly providing rotational movement at 3 degrees of freedom as well as the option for precise adjustment of the needle. The clip has been designed to support needles of varying sizes and weights. Specific sub-systems can be locked and unlocked in place using easily noticeable and accessible tightening knobs. Gripping of the needle is clinician-controlled via a springless clip which, when not being manipulated, remains in a closed position until actuation is required. These unique design features ensure that the needle is stable and maintain its depth and orientation when the images are being acquired.

The device was fabricated and tested to verify it meets the technical, functional, usability, and safety requirements. The device produced no artefacts in CT images, achieve less than 0.5mm difference in location at a depth of 30cm in different positions spread across 180 degrees from left to right side of the patient, set-up time of less than 2 mins, weighs less than 2 kg, and free of any vibration after releasing the needle. Preliminary experimental results suggest that, as compared to existing solutions, this device establishes itself as a more inexpensive alternative from robotic stabilizers while still providing more stability than non-robotic, patient mounted device.

Abstract Number: ICBME1335

RETRAB: A Novel Abduction and Traction Device for Reduction of Shoulder Dislocation

Karupppasamy Subburaj, Wen Ting Leong, Kayva Nair, Shaun Phua, Siang Hiong Goh, Shu Woan Lee, Karupppasamy Subburaj
Singapore University of Technology and Design, Singapore

Shoulder dislocation is the most common dislocation, representing 50% of all major joint dislocations with anterior shoulder dislocations making up 97% of all shoulder dislocations. Typically, reduction of shoulder dislocation is performed at Accident and Emergency settings, beginning with an X-ray to confirm the type of dislocation, followed by a closed reduction technique, requiring a practising physician and two nurses to assist. The most commonly used closed reduction technique is Modified Milch Method where the patient lies supine then the physician (1) straightens the dislocated arm, towards the feet with palm
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facing anteriorly, (2) pulls the arm distally, and (3) slowly abducts the arm on the coronal plane towards the head while maintaining the distal pulling force till the reduction force is felt. This process is physically demanding, qualitative of the amount of the force applied, and keep physicians away from time-sensitive emergencies. Thus, there is a need for a device to safely and efficaciously reduce anteriorly dislocated shoulders caused by falls or contact sports, in order to reduce skilled personnel time, physical exhaustion and improve procedural consistency.

The proposed device, RETRAB, is a novel assistive mechanical system that performs abduction and traction to reduce an anteriorly dislocated shoulder. Deriving its functions from the Modified Milch Method, the device consists of three major subsystems: (1) an abduction, (2) a traction, and (3) a force-sensing system. The abduction mechanism consists of a wheeled standing structure to support the patient’s arm and enable a full 180-degree abduction of the hand about the humerus, while its adjustable height ensures alignment with the body in the supine position. This abduction system is attached to a backplate which patients lie on to anchor the device, and ambidextrously designed straps minimise movement of the patient during the process. The traction mechanism has adjustable straps to vary traction force applied, a wrist guard to distribute the force applied to the patient and springs to provide an allowance for slight distal movements of the hand during abduction and prevents sudden changes in force applied. This design feature achieves relaxation of the shoulder muscles throughout the abduction to enable the humeral head to enter the glenoid cavity smoothly. The force sensing system consists of microcontroller, force-sensor, and visual and audio feedback to notify clinicians if the applied traction force is within the acceptable range.

RETRAB was fabricated and tested on dummies and healthy volunteers to verify the technical, functional, usability, and safety requirements. Preliminary results suggest that RETRAB was able to perform abduction and provide a traction force of 5 - 18 kgf with feedback to the clinician about the amount of force applied. Based on clinicians’ feedback, the device proved to be easy to use, adaptable, portable and disinfecable. Overall, only single untrained personnel was required to operate the device with minimal setup and teardown time, on subjects of various sizes the system was able to produce consistent and reproducible motion and force to reduce the involvement of skilled personnel and physical exhaustion.

Abstract Number: ICBME1337

Design and Development of a Hand-Held Automated Guidewire Threading Device for Endovascular Interventions

Karuppasamy Subburaj, Janice Hui Lin Tan, Clement You Jie Chen, Nur Farizah Binte Muhammad Segar, Jia Sheng Tay, Karuppasamy Subburaj
Singapore University of Technology and Design, Singapore

Endovascular interventions are now becoming more prevalent worldwide due to its less invasive nature resulting in lower morbidity and mortality rates. Each operation involves the passage of multiple endovascular interventional devices over various guidewires to the desired clinical site before instituting any treatment. Depending on the nature of the operation, the length and diameter of the guidewire vary anywhere between 0.5–3 m and 0.014-0.038 inches respectively. An experienced surgeon takes around 10 seconds to thread a guidewire or device, with a significant amount of time and energy spent on inserting and removing devices through threading during complicated
Extracorporeal Treatment of Hyperuricemia via Enzymatic Functionalized Microchannel Plate Platforms: Experiment and Modeling

Jaturavit Pantakitcharoenkul, Matthew Coblyn, Jad Touma, Goran Jovanovic
Oregon State University, USA

Hyperuricemia is the condition of excessive presence of plasma uric acid ≥ 6 mg/dL plasma. Conventional clinical/hospital urate-lowering treatment includes the administration of non-steroid anti-inflammatory drugs (NSAIDs) or xanthine oxidase inhibitor. In patients with refractory gout symptoms and tumor lysis syndrome, recombinant uricase is chosen to reduce the fatality risk of prolonged elevation of plasma uric acid level by converting uric acid into allantoin, a water-soluble compound. Numerous shortcomings exist in these conventional treatments. Significant side effects include allopurinol hypersensitivity syndrome in patients receiving xanthine oxidase inhibitor, and anaphylaxis in patients prescribed recombinant uricase.

In this work, we have designed and developed a portable device to assist in increasing the efficiency of inserting and threading a guidewire through another endovascular device. Our design constraints were adaptable to work with guidewires and endovascular devices of varying dimensions, sterilizable, automated, portable, intuitive, splash-proof, and disposable. The proposed device has two critical mechanisms to achieve the primary functions of (i) aligning and inserting guidewire through endovascular devices and (ii) threading of guidewire through endovascular devices. The device takes advantage of centrifugal forces generated by two fast-spinning wheels and friction between them to grip and feed the guidewire through endovascular devices like catheters and in-turn increase the safety as avoiding threading of the wires while glide the guidewire instead of forcing it in. An alignment track guides the guidewire into the endovascular devices. A v-shaped design element featuring both Luer-lock threading and a clamp-like slot at the front end of the alignment track adapts to both guidewires and catheters used during the procedure. The trigger button’s position at the handle grip of the device enables easy access. Rocker switch at the back of the device enables the user to activate the correct state (reel-in or reel-out) during a procedure.

The device was fabricated and tested to verify it meets the technical, functional, usability, and safety requirements. The device was able to accommodate a range of guidewires used in endovascular interventions, as mentioned above. The device was able to achieve the speed of 4 times than manual threading, 1/3rd of the typical time required to insert the guidewire into a catheter, no issues in using both dry and wet guidewires, and learn and use the device in 5 mins of training. Preliminary experimental results suggest that, as compared to existing solutions, this device reduced the repetitive and menial labour, which is the threading of guidewires through endovascular devices such as catheters. The intuitive design of the device also allows for easy use by medical professionals.

Abstract Number: ICBME1077

Design and Development of Safety Systems to Reduce Guidewire Retention in Central Venous Catheterization Procedure

Karupparasamy Subburaj, Wan Yun Lu, Janelle Pei Jie Ong, Vanessa Yu Jun Poh, Rajkumar Chandran, Seok Hwee Koo, Jerry Kian Teck Lim
Singapore University of Technology and Design, Singapore

A mathematical model and corresponding numerical simulation of mass transport and enzymatic kinetics accommodated for both methods of immobilization on the Bio-Lamina-Plate, were developed as a tool to facilitate in vitro experiments. The computational model of both Bio-Lamina-Plates depicted a significant reduction in plasma urate concentration and a well-regulated hydrogen peroxide level. The results of numerical simulation support remarkably well the trends observed in our experimental data.

This project aspires to provide a higher quality of life for hyperuricemia patients, reduction in mortality rate, reduced cost of treatment, and enhanced therapeutic effects.

Abstract Number: ICBME1339
One of the most dreaded complications pertaining to the usage of guidewires in Central Venous Catheterization (CVC) procedure is the retention of the guidewire, considered as a never event, which can lead to arrhythmias, cardiac perforations, thrombosis, infections and even death.

There are two main forms of factors associated with existing clinical solutions that contributes to retention of the guidewire: (1) human errors: heavy reliance on human factors to follow the defined preventive steps in the work-flow, including supervisor/buddy system, checklist of devices/tools, length-markings on the guidewire, and tools to maintain grip of the guidewire to prevent its retention. The existing checking procedure for guidewire removal requires high awareness and experience of clinicians. However, negligence can occur during the procedure due to complications, inexperience, urgency or other situational factors. (2) systematic errors: physicians do not have a clear view of the guidewire due to the opacity of the catheter body, making it difficult to track the guidewire advancement when within the catheter body.

Also, if physicians do not hold on to the distal end of the guidewire before the tip of the catheter enters the skin incision, the guidewire might get pushed along into the vein when an additional force exerted to advance the catheter through the skin. Thus, there is a need for a way to ensure that the guidewire exits the distal lumen of the catheter, with the minimal human factor, in order to prevent guidewire retention.

The proposed system consists of a two-element mechanical attachment to prevent guidewire retention in Central Venous Catheterization procedure by achieving a combination of reminder, prevention, and fail-safe as one integrated solution. The solution was devised to be seamlessly integrated into the existing Seldinger Technique used in CVCs, each element targeting one major cause of guidewire retention. The first element (the clamp) targets the issue of negligence by preventing access to the suture wings on the catheter and restricting procedural advancement until it detects the removal of the guidewire, thereby acting as a fail-safe mechanism. The second element (the catch) targets the issue of guidewire slippage with catheter advancement, by securing the guidewire after it extends into the distal lumen-port, preventing backflow of guidewire into veins. It is also effective in serving as a visual reminder for the physicians to anchor the guidewire and allowing for easy removal of it.

The device was fabricated and tested in the lab on the instruments in the ARROW CS-15703-E Catheterization Set to verify the technical, functional, usability, and safety requirements. The device integrates well into the current CVC work-flow as the technical, functional, usability, and safety requirements. The intuitive design of these elements in the device allows for easy use with minimal training. Adaptation to different catheterization sets and mass production at a low cost is easily possible due to the simple design and mechanics of the product.
microfluidic technology, our aim is to demonstrate long-term ex-vivo culture of human testis and epididymis tissues and to access their lumen to, respectively, study spermatogenesis, and probe the BTB.

Methods: Human testis and epididymis tissues were obtained from gender dysphoria patients and cultured in polydimethylsiloxane (PDMS) microfluidic platforms, produced by soft-lithography from 3D-printed molds. Testis tissues were loaded in a culture chamber (6mm x 800µm x 200µm) by applying mild suction from an outlet reservoir. Medium was perfused in a channel surrounding the chamber and connected to it via smaller microchannels (250µm x 125µm x 50µm, interval 250µm), to avoid shear stress on the tissues. Cell viability was assessed with a live-dead assay and live-microscopy imaging, and tissue integrity and functioning using immunostaining. In parallel, flow in the device and notably across the microchannels was modeled using COMSOL Multiphysics and experimentally evaluated using a fluorescent analogue of glucose. Epididymis tissues were clamped on a 3D-printed holder, which was next inserted in a PDMS device. Microchannel barrier was also employed for shear stress-free perfusion of fresh medium. Fluidic access to the tissue lumen was created using a glass micropipette secured in the 3D-printed holder.

Results: Computed shear stress produced on testis tissues were lower than 0.023 Dyn/cm², which is significantly below the 0.1 Dyn/cm² limit for non-endothelial cells. Nutrients successfully diffused across the entire tissues, as evaluated using small fluorescent nutrient analogs. Human testis tissues were cultured in our devices for up to 11 days, showing good viability and maintenance of their integrity and structure. Epididymis tissues could be viably cultured for several days, with both fluidic and electrical access to the lumen, allowing the injection of fluorescent dyes and electrical characterization of the BTB (Trans-Epithelial Electrical Resistance measurements).

References

Abstract Number: ICBME1344

Vascular Endothelial Responses to Fluid Flow under Hypoxic Condition

Naoyuki Takahashi, Yugo Tabata, Satomi Hirose, Kiyoe Funamoto, Daisuke Yoshino, Kenichi Funamoto
Tokuhu University, Japan

Oxygen tension in vivo microenvironment is lower than that in the air (21% O2). The hypoxic condition affects cell behaviors, such as viability, differentiation, proliferation, migration, and so on. Blood vessel is an essential organ for maintenance of homeostasis, which supplies oxygen and nutrition to tissues and collects wastes from them. For maintenance of vascular function and formation of vascular diversity, vascular endothelial cells, which line the inside of blood vessel, response not only to mechanical and chemical stimuli but also to hypoxic stress. We have developed microfluidic devices to reproduce in vivo hypoxic microenvironment. The device has a central gel channel which is flanked by a Y-shaped media channel, and two gas channels next to the media channels on the both sides. In our former cellular experiments using the microfluidic devices, a vascular endothelial cell monolayer exposed to hypoxic stress showed an increased permeability and an enhanced collective migration, resulting from loosening cellular junction by VE-Cadherin. However, we had not considered an effects of fluid flow because the experimental method becomes complicated. Therefore, changes of permeability and migration of vascular endothelial cells under hypoxic exposure with physiological shear flow is still not clear. This study reveals behaviors of vascular endothelial cells under exposure to hypoxia as well as shear stress. First, we investigated a method to apply physiological shear flow to the cells in a microfluidic device with controlling oxygen tension around the cells. Oxygen tension distribution and flow field in a microfluidic device were computed by three-dimensional simulation, searching an optimal method to simultaneously control those factors. In addition, actual oxygen tensions generated in the device were measured using oxygen-sensing beads. The computational and experimental results revealed that it was difficult to simultaneously control oxygen tension and shear stress in the media channel only by supplying gas mixture to the gas channel since media flew away before equilibrium of oxygen. Consequently, it was necessary to precondition oxygen tension in the media in case of generating media flow. Next, cellular experiments were performed with the settings obtained by the computations and validation experiments. Human umbilical vein endothelial cells were cultured in the media channel of the microfluidic device to form a vascular endothelial monolayer. The migrational behavior of the cells under either or both hypoxic and flow exposures were observed by time-lapse imaging. The morphological changes of cells were evaluated based on immunofluorescent staining, especially focusing on cell-cell junction. During six-hour exposure to either or both hypoxic stress and shear stress, cells elongated toward the flow direction, while no change was observed by oxygen conditions under no flow condition. The tendency of elongation toward the flow direction was more significant under hypoxic condition than normoxic condition.

Abstract Number: ICBME1231

Detachable Acoustophoretic System for Fluorescence-Activated Sorting at Single Droplet Level

Peixian Li, Zhichao Ma, Yining Zhou, David J. Collins, Zhenfeng Wang, Ye Ai
Singapore University of Technology and Design, Singapore

In recent years, rapid progress in the development of single-cell sequencing has provided numerous important insights for understanding the functionality and variation within cell types. Droplet-based microfluidics system is a very powerful and effective tool to isolate and analysis at single cell level. However, the existing droplet generation is a random process that captures cells at a single cell encapsulation rate of only 10%. To achieve high throughput analysis requirements, we present an eminently accurate and efficiently detachable, bench-top scale fluorescence-activated droplet sorting (FADS) system which uses highly focused travelling surface acoustic wave (HTSAW) with a beam width ~50 µm to sort droplets. The proposed detachable acoustic FADS system integrates droplet generation and acoustic sorting chip into one device with the ability to uniformly produce droplets and accurately sort single-cell droplets with purity higher than 90% at ~1 kHz. Meanwhile, the detachable system also prevents samples from cross-contamination and keeps the expensive
focused interdigitated transducer (FIDT) reusable. Furthermore, the presented FADS is able to sort submicrometer sized particles, it overcomes the limitation of the existing fluorescence-activated cell sorting systems.

Abstract Number: ICBME1059

Microengineered Artery-on-a-Chip for Study of Diabetic Vasculopathy

Chengxun Su, Hui Min Tay, Rinkoo Dalan, Han Wei Hou
Nanyang Technological University of Singapore, Singapore

Objectives: Endothelial dysfunction and aberrant endothelial cell (EC)-smooth muscle cell (SMC) interaction in the artery are major contributors to the development of macrovascular complications in Type 2 Diabetes Mellitus (T2DM). However, routine measurements of cardiovascular risk factors and inflammatory markers are suboptimal for monitoring the pathogenesis or vascular health of this complex disorder. Therefore, there exists an unmet clinical need to develop novel tools and strategies to study vascular health in T2DM. Organ-on-chips are biomimetic miniaturized platforms containing living human cells that reconstitute organ-level functions at physiological microenvironment. In this project, we aim to develop a novel micro-engineered in vitro human artery model that recapitulates various aspects of the native vascular microenvironment including the 1) presence of pathophysiological flow/shear perfusion conditions, 2) EC and SMC co-culture in an extracellular matrix (ECM)-patterned vessel structure, and 3) blood cell-EC interaction to study vascular inflammation. Furthermore, the artery-on-a-chip will be developed into an in vitro diabetic vascular model to elucidate the pathogenesis and drug response of macrovascular complications.

Methods: A pillar-free capillary burst valve-based method was used for patterning of ECM in the device. For polydimethylsiloxane (PDMS) device fabrication, a multiple-step photo lithography and soft lithography were performed. The device was then seeded with EC and SMC and grown to confluency to create the artery model. Multi-parametric analysis including EC barrier function (fluorescent labelled dextran), EC-SMC crosstalk (cell morphology, phenotype-specific markers), and blood cell-EC interaction in whole blood perfusion were performed. For study of diabetic vasculopathy, a diabetic vascular microenvironment was created using high glucose and inflammatory cytokines (TNFα, IL-6).

Results: A three-layer PDMS device was successfully fabricated to pattern multiple lanes of hydrogel. Arterial wall was reconstituted by co-culturing of EC and SMC in the device, as shown by formation of a 3-dimensional EC lumen with good barrier integrity, contractile-like SMC phenotype, and an additional ECM layer in between mimicking the basement membrane. We further demonstrated that the developed artery model can be used to study various vascular physiology including vessel inflammation, barrier permeability, shear stress-dependent response, leukocyte transmigration and monocyte adhesion.

Conclusions: We have developed a novel microengineered artery-on-a-chip to replicate pathophysiological aspects of human blood vessel. The development of a 3D EC-SMC diabetic vascular model is on-going, and can be further multiplexed for high throughput applications such as drug screening.


Abstract Number: ICBME1519

Robotic Intervention Utilizing Bioengineering Based Therapeutic Methods

Ichiro Sakuma
University of Tokyo, Japan

Minimally invasive therapy such as endoscopic surgery and catheter based intervention are being spread in many surgical intervention fields. The application of minimally invasive procedure requires new technologies for dexterity enhancement and sensing augmentation. Various technologies of Computer Aided Surgery (CAS) such as surgical navigation and robotics are key technologies. It is expected that robotic technology will provide the following functions: (1) Precise manipulation of biological tissues and surgical instruments in narrow and confined surgical field. (2) Precise and accurate localization of therapeutic devices using various pre and intra-operative medical information. Fusion of medical robotics, biomedical instrumentation, bioscience is required for realizing these functions. Information technologies such as signal processing, image processing, and pattern recognition are also important for extraction of clinically significant information. Other technologies that can be integrated with surgical robotic system include high intensity therapeutic ultrasound (HITU)[1, 2], physical stimuli responsive drug delivery system[3, 4], and a laser coagulation system[2, 5]. We have developed a simple suturing device manipulated by a robot for coronary artery anastomosis in bypass surgery[6]. In situ diagnostic capability provided by various biomedical measurement technologies such as fluorescence spectroscopy are also important[7].

Another important issue in surgical robotic system research is reduction of complexity of the system. Recent progress of computer vision enables us to realize surgical navigation system without conventional three dimensional position tracking system. For example, we have proposed tracking method where teeth are used as landmarks and three dimensional position and posture are obtained by conventional camera based image processing[8]. Integration of surgical robotics and various bioengineering based methods will contribute to developing novel therapeutic systems.

Abstract Number: ICBME1494

Augmented Reality for Orthopaedic Surgery

Jaesung Hong
Daegu Gyeongbuk Institute of Science and Technology, Korea

Augmented reality (AR) is used in many fields including medicine, education, manufacturing, and entertainment. With advances in optics, computer systems, and surgical instruments, AR application
to medicine is being vigorously researched. Particularly, as surgery using laparoscopy, endoscopy, or catheterized intervention have increased, AR takes an important role in many medical applications.

AR denotes a technique to combine a real world and virtual objects which are artificially generated digital content by a computer. As another aspect of AR is a registration between the real world and virtual objects, it aims to estimate three-dimensional (3D) position and orientation of virtual objects related to the real world. Therefore, AR can allow the user to see 3D virtual objects superimposed upon the real world. With the help of AR, a surgeon can see hidden organs inside a body and improve the perception of treatment procedure by interacting with the real world. After a brief description of three components of the medical AR, its applications in orthopedic area will be presented.

Abstract Number: ICBME1503

Medical Robot Link Architecture Connected to Smart Cyber Operating Theater (SCOT)

Ken Masamune
Tokyo Women's Medical University, Japan

Surgical robotics is one of the key technologies in the next medical generation, and their role is becoming more sophisticated manner with the advancement of information technologies. Thus, fast development is a key to create new systems. We focus on the methodology of developing the master-slave system like da Vinci, with open platform middleware named "MRLink". MRLink includes RI (Robot integrator) module, SI (Sensor integrator) module and MRLink application class, based on ORiN middleware architecture for robotics system. Using this system architecture, it becomes easier to combine any kinds of input robot/UIs and any kinds of output robot/displays. The connection with Smart Cyber Operating Theater (SCOT) is also discussed.

Abstract Number: ICBME1516

Transluminal Robotics with Delicate Continuum and Context Awareness

Hongliang Ren
National University of Singapore, Singapore

Representing a major paradigm shift from open surgery, minimally invasive surgery (MIS) assisted by transluminal robots and sensing is emerging by accessing the surgical targets via either keyholes or natural orifices. It is challenging to get delicate and safe manipulations due to the constraints imposed by the mode of robotic access, confined workspace, complicated surgical environments and the limited available sensing technologies, particularly in terms of endoluminal curvilinear targeting and guidance. Addressing the above transluminal challenges and aiming at human-centered intelligent robots, this talk will share our recent bio robotic researches in continuum mechanisms, delicate sensing, collaborative human-robot interactions, mostly in the context of surgical applications. The compliant somatosensitive robotics with embodied intelligence allows us to bypass critical important intracranial or intracorporeal structures, to conform its shape to be compliant with curvy passages and have direct access to the target sites under situation-aware navigation, thus significantly reducing invasiveness and trauma of surgery.

Abstract Number: ICBME1515

Robot-Assisted Interventions under Intra-Operative MRI-Based Guidance

Ka-Wai Kwok
University of Hong Kong, Hong Kong

Advanced surgical robotics has attracted significant research interest in support by image guidance, even magnetic resonance imaging (MRI) for effective navigation of surgical instruments. In situ effective guidance of access routes to the target anatomy, rendered based on imaging data, can enable a distinct awareness of the position of robotic instrument tip relative to the target anatomy in various types of minimally invasive interventions. Therefore, such MRI-guided robots will rely on real-time processing the co-registration of surgical plan with the imaging data captured during the intervention, as well as real-time localization of the instrument relative to the anatomy of surgical interest. This talk will overview recent advances in image-guided robotics which potentially resolve surgical challenges of providing a safe, precise and effective surgical manipulation by imposing visual feedback on robotic instruments in soft tissue surgeries.

Abstract Number: ICBME1216

Biomimetic Wrinkled MXene Pressure Sensors towards Collision-Aware Robots

Catherine Cai, Chen Po-Yen, Ren Hong-liang
National University of Singapore, Singapore

The use of surgical robots in the field of minimally invasive neurosurgical procedures can offer several benefits and advantages. However, the lack of force sensing hinders and limits their use in such procedures. Equipping surgical robots with pressure sensors can enhance robot-environment interaction by enabling collision awareness and enhance human-robot interactions by providing surgeons the necessary force feedback for safe tissue manipulation. With the emergence of soft robotics in biomedical applications, the attached pressure sensors are required to be flexible and stretchable in order to comply with the mechanically dynamic robotic movements and deformations. Inspired by the multi-dimensional wrinkles of Shar-Pei dog’s skin, we have fabricated a flexible and stretchable piezoresistive pressure sensor consisting of MXene electrodes with biomimetic topographies.

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Venue | EA-06-05

Abstract Number: ICBME1529

Development of 3D Cell Constructs with Perfusable Vascular Networks Generated from iPSC-Derived Endothelial Cells

Yu-Suke Torisawa
Kyoto University, Japan

Vascular networks are essential to maintain cellular viability and function; however, current 3D culture models lack vascular...
systems. Engineering perfusable vascular networks that can deliver reagents and blood cells to 3D cell constructs could be a powerful platform to recapitulate cellular microenvironments and to monitor cellular functions. We developed a microfluidic method to form 3D vascularized cell aggregates to model cellular interactions through blood vessels. When a tumor-like cancer spheroid containing human umbilical vein endothelial cells (HUVECs) and fibroblasts was cultured in our microfluidic device, a perfusable vascular network was formed through the cancer spheroid. We confirmed that peripheral blood mononuclear cells can be perfused inside the cancer spheroid through the vascular network. Thus, we used this system to model the interaction between cancer cells and immune cells. To study the interaction between cytotoxic T cells and cancer cells through blood vessels, allo-reaction between endothelial cells and T cells by mismatching of their HLA will be problematic. Therefore, we engineered 3D vascular networks using human induced pluripotent stem cell-derived endothelial cells (iPSC-ECs). CD8+ T cells exhibited higher cytotoxic activity toward HUVECs than autologous iPSC-ECs and HLA knockout iPSC-ECs, demonstrating that our vascularized 3D culture model can be used to monitor functions of T cells. We then developed a vascularized tumor-on-a-chip system using HLA knockout iPSC-ECs as well as hepatocellular carcinoma (JHH-7) cells and fibroblasts. After the formation of a vascular network connected to a cancer spheroid, T cells were injected into the vascular network and monitored behavior of T cells for up to 24 hours. This model successfully captured T cell migration and infiltration into cancer spheroids through vascular networks. Generation of in vivo-like vascularized 3D cell constructs using HLA knockout (universal) iPSC-ECs would provide a novel platform to develop models for cancer immunotherapy as well as organoids-on-chips.

Abstract Number: ICBME1429

**Patient-Specific Stem Cell-Based Blood Brain Barrier-on-Chip Platform Enables Predictive Personalized Medicine Applications**

Gad Vatine  
*Ben Gurion University of the Negev, Israel*

The blood brain barrier (BBB) is a multicellular neurovascular unit (NVU) in which pericytes, astrocytes, and neurons directly interact with brain microvascular endothelial cells (BMECs). In turn, BMECs form a specialized transporter barrier created by tight junctions and polarized efflux pumps. This fine-tuned cellular architecture permits the blood-to-central nervous system (CNS) passage of crucial nutrients and metabolic molecules while prohibiting the entry of deleterious factors and most drugs. Several neurological disorders involve BBB dysfunction, creating the need to understand BBB physiology and transport mechanisms in both health and disease. Marked differences in BBB substrate specificity and transporter activity across species limit the relevance of animal models. Therefore, a human-specific BBB model is crucial to study human diseases and for the discovery of new CNS permeable drugs.

Combining iPSC and organ-on-chip technologies we developed a novel platform in which isogenic iPSC-derived iBMECs, astrocytes and neurons mimic human BBB functionality. iBMECs form a bioengineered vessel-like structure on the Organ-Chip and human astrocytes, pericytes and neurons form direct cell-to-cell interactions that mimic functionality at the level of an organ. The BBB-Chip exhibits physiologically relevant transendothelial electrical resistance and faithfully predicts BBB permeability of molecules. Whole human blood perfusion through the ‘blood vessel’ introduces another physiological interphase and demonstrates that iBMECs can protect spontaneously active neurons from cytotoxicity. Finally, genetic neurological disease modeling in the context of a functional organ reveals substrate transport variability across individual BBB, demonstrating the feasibility of this approach for predictive personalized medicine applications.

Abstract Number: ICBME1493

**Organs-on-a-Chip: A New Tool for the Study of Human Physiology**

Ben M. Maoz  
*Tel Aviv University, Israel*

Micro-engineered cell culture models, termed Organs-on-Chips, have emerged as a new tool to recapitulate human physiology and drug responses. Multiple studies and research programs have shown that Organs-on-Chips can capture the multicellular architectures, vascular-parenchymal tissue interfaces, chemical gradients, mechanical cues, and vascular perfusion of the body. Accordingly, these models can reproduce tissue and organ functionality and mimic human disease states to an extent thus far unattainable with conventional 2D or 3D culture systems. Here we exploit the micro-engineering technology in a novel system-level approach to decompose the integrated functions of the neurovascular unit into individual cellular compartments, while retaining their paracellular metabolic coupling. Using individual, fluidicallyconnected chip units, we have created a system that models influx and efflux functions of the brain vasculature and the metabolic interaction with the brain parenchyma. Results of proteomic and metabolic assays indicate that this system mimics the effect of intravascular administration of the psychoactive drug methamphetamine observed in vivo. Moreover, this model reveals a previously unknown role of the brain endothelium in neural cell metabolism: In addition to its well-established functions in metabolic transport, the brain endothelium secretes metabolites that are directly utilized by neurons. This discovery would have been impossible to achieve using conventional in vitro or in vivo measurements.

Abstract Number: ICBME1524

**Drug Delivery Devices and Organ Chip Devices for Ophthalmologic Applications**

Hirokazu Kaji  
*Tohoku University, Japan*

Approximately 80% of all sensory input is received via the eyes, so suffering from chronic retinal diseases that lead to blindness causes a significant decrease in the quality of life (QOL). And because retinal diseases are most common among the elderly, developing treatments and pathological analyses for retinal diseases has become an urgent issue in super-aging countries such as Japan.

Although intravitreal injection can directly deliver drugs to the posterior segment of the eye, it is invasive and associated with serious side effects. The design of drug delivery systems (DDS) targeting the posterior segment of the eye in a less invasive
manner has still been challenging because of various anatomical and physiological barriers. Transscleral delivery has emerged as a more attractive method for treating retinal disorders because it can deliver a drug locally and is less invasive. Here, a transscleral drug delivery system that is implantable in the episclera and allows for controlled release of various molecular weight drugs will be presented [1]. Although evaluation of drug candidates against retinal diseases has been done on animal models, serious concerns arise regarding the ethics and costs in addition to the limitations of translating data from animal models to clinical settings. Pathophysiology of neovascularization in diabetic retinopathy (DR) and age-related macular degeneration (AMD) is complicated due to various factors involved, which include but are not limited to aging, oxygen concentration, energy metabolism, pressure, blood flow, and genetics. For more reliable outcomes, it is essential to understand the pathological mechanisms of eye diseases. Here, microfluidic co-cultures of ocular tissues to investigate choroidal angiogenesis will be also presented [2,3].

References

Abstract Number: ICBME1530

Intestine-Chip: A Human iPSC-Derived Microfluidic Chip Model for Studying Inflammatory Bowel Disease

Michael J. Workman
Cedars-Sinai Medical Center, USA

Background: Inflammatory bowel disease (IBD) is a complex polygenic disorder characterized by chronic inflammation of the gastrointestinal mucosa. This is believed to be caused by a dysregulated immune response in genetically susceptible individuals. While evidence suggests that the intestinal epithelium is involved, its precise role in IBD has remained elusive due a lack of suitable in vitro models. A major advance occurred with the development of human intestinal organoids (HIOs), whereby organoids from control individuals or IBD patients could be derived from induced pluripotent stem cells (iPSCs) or biopsy samples. However, in the context of IBD, this technology is challenging to use. HIOs are variable in size and shape and exhibit a closed luminal structure embedded in extracellular matrix. Studies involving luminal fluid flow or measurements of intestinal permeability in response to cytokine treatment are hampered in this model. Methods: We have overcome such limitations by developing a novel Intestine-Chip. Initially, iPSCs are differentiated towards intestinal tissue, dissociated to a single cell suspension, and sorted based on expression of Epithelial Cell Adhesion Molecule (EpCAM). EpCAM-positive intestinal epithelial cells are then seeded into microengineered poly(dimethylsiloxane) chips, which are composed of two channels separated by a flexible porous membrane. The system allows for application of continuous media flow, access to basal and luminal compartments, and generation of in vivo relevant mechanical forces critical for cell function. Results: Over the course of 7 days of continuous media flow, we observed the spontaneous formation of polarized villus-like structures, similar to those found in the human intestine. Upon closer examination we confirmed the presence of all major intestinal epithelial cell types, including Paneth cells, goblet cells, enteroendocrine cells, and enterocytes.

Administration of interferon gamma (IFNγ), a cytokine known to be upregulated in IBD, resulted in phosphorylation of STAT1 and upregulation of genes similar to what is seen in intestinal biopsies from patients with IBD. Additionally, coadministration of tumor necrosis factor alpha (TNFαs) with INFγ significantly increased intestinal permeability without affecting cell viability. Conclusions: We have developed a system whereby iPSC-derived intestinal epithelium can be incorporated into a chip microenvironment and changes in gene expression and permeability can be measured. Given we have previously generated intestinal tissue from iPSCs derived from lymphoblastoid cell lines (LCLs), we can now obtain genotyped LCLs from the nearly 20,000 patient samples stored in the MIRIAD Biobank at Cedars Sinai to generate intestinal epithelium containing genetic variants associated with IBD. This technology will allow us to assess how these variants influence the differentiation.

Abstract Number: ICBME1508

Bariatric Surgeries as a Discovery Platform for Metabolic Diseases and Basic Biology

Danny Ben-Zvi
The Hebrew University of Jerusalem, Israel

Bariatric, or weight-loss surgeries are common surgeries performed on morbidly obese patients that usually lead to substantial weight reduction. The various surgeries we designed to induce malabsorption or restrict food intake by altering the gastrointestinal (GI) tract anatomy. However, clinical experience has shown that the surgeries improve the condition of some diseases such as type 2 diabetes and fatty liver diseases also independent of weight-loss. My group uses data from human and mouse models to study those weight-loss independent effects of surgery in order to achieve the positive effects of surgery without having to undergone the procedure. I will present data showing how the surgery affects gastric homeostasis, glucose control, resolution of fatty liver disease and progression of neurodegenerative disorders, some of the molecular mechanisms underlying these processes, and how the field can benefit from integrated organ-on-chip systems.
Day 4 – 12 December 2019, Thursday

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Abstract Number: ICBME1535

**AI and Data-Driven Support for Prevention, Intervention, and Cure in Healthcare**

**Beng Chin Ooi**  
*National University of Singapore, Singapore*

While AI and data-driven approaches are still evolving, they are likely to surpass current medical practices in the healthcare domain soon. The potential advantages are not only faster and more accurate analysis, but also the democratization of healthcare services. Notwithstanding, there are some common challenges when applying existing approaches onto the healthcare domain, due to the noise and bias of electronic health records (EHR), complex and heterogeneous feature relations, access control and data privacy and etc. In this talk, I shall discuss our design and implementation strategies: solve common challenges, instill domain knowledge, automate knowledge extraction, and enable system-based global optimization. I discuss our rationale on building a general analytics stack instead of solving individual problems, and explain how these challenges are being addressed. Several detailed technologies from both system and algorithm perspectives in our healthcare data management and analytics framework are also described. I shall also discuss our new translational project on reducing 3H (hyperglycemia, hypertension, hyperlipidemia) problems.

**Results:** As a result, we successfully obtained the standard conditions of our mechanical circulatory simulator to be 100 mmHg of mean aortic pressure, 3.0 L/min of mean aortic flow rate, 100 mmHg of mean coronary arterial pressure, 160 mL/min of mean left coronary flow and 80 mL/min of right coronary flow. Thus, the reproduction of systemic and coronary hemodynamic waveforms was achieved.

**Conclusions:** We successfully reproduced both coronary and systemic hemodynamics by using a newly developed pulsatile circulatory simulator.

Abstract Number: ICBME1169

**Fabrication of Dissecting Aortic Aneurysm Model and Visualization of Flow in False Lumen Before and After Placing the Stent Graft**

**Kazuma Nakamura, Junya Kozaki, Kota Shukuzawa, Yusuke Tsuboko,**  
*Mito Umezu, Kiyotaka Iwasaki*  
*Waseda University, Japan*

**Objectives:** When medial membrane of the aortic wall is torn and the aortic dissection occurs, it becomes divided into two chamber lumen structures. It consists of the false lumen of the newly formed wall lumen dissociating from the true lumen which is the original arterial lumen. Stent grafts (below: SG) are using for aortic dissection seals the blood flow by sealing the tear that carries the true lumen and the false lumen. Blood flow in the false lumen could be stagnate and turn into thrombus as intended for preventing further ruptures. However, in some cases, aortic dissection could cause multiple tears. If all the tear are sealed, it also cuts off the blood flow to important branch blood vessels. Therefore we can only seal the main tear which located near Ventricle. (below: entry) However, in some cases blood flow in false lumen turned into thrombus successfully and others were not. By elucidate the mechanism of Thrombosis, it will help to set up a clinical guidelines for SG treatment. In this study, we aimed to visualize the flow in the false lumen before and after SG implantation, and examine the influence before/after SG implantation to the blood flow in false lumen.

**Methods:** Dissecting aortic aneurysm model made of silicone, with two chamber lumen structures of true lumen and false lumen. It has entry and tears which are called re-entry on the descending aorta. A pulsatile circulation simulator creates an average flow rate of 5.0L/min and an aortic pressure of 140/70 mmHg for simulating the living body of aortic dissection patient. The liquid filled with fluorescent particles, a laser was applied, and the movement of the particles was traced by a camera and use the measurement method to calculate the flow velocity. Visualization of flow before and after SG placement was performed using these. The distance between model`s tears was set to 200, 250, 300 mm.

**Results:** We successfully reproduced both coronary and systemic hemodynamics by using a newly developed pulsatile circulatory simulator.

Abstract Number: ICBME1149

**Development of a Mechanical Simulator of the Systemic and Coronary Circulation for Hemodynamic Evaluation of Transcatheter Aortic Valve Replacement**

**Yusuke Tsuboko, Ryunosuke Ai, Rumi Maebara, Xuetong Xu,**  
*Kiyotaka Iwasaki*  
*Waseda University, Japan*

**Objectives:** Transcatheter aortic valve replacement (TAVR) is a less invasive therapy and the number of operations is increasing. TAVR has become an important alternative to surgical aortic valve replacement in aortic valve stenosis patients with intermediate- or high-surgical risk. Although TAVI has technically matured, the occurrence and clinical significance of thrombus formation after TAVR remain unclear. Hydrodynamic considerations are necessary to reveal the mechanism of subclinical leaflet thrombosis after TAVR. In this study, we focused on the flow field in the vicinity of the aortic root including coronary ostia, and newly developed the pulsatile circulatory simulator which was capable of reproducing the coronary and systemic hemodynamics.

**Methods:** The pulsatile circulatory simulator consists of a...
Results: Before the implantation of the SG, in the entry, flow from the true lumen to the false lumen was confirmed in the re-entry from the false lumen to the true lumen at the early systole phase. However, at the late systole phase, flow from the false lumen to the true lumen in the entry and flow from the true lumen to the false lumen in the re-entry was confirmed. After SG implantation, the flow of entry was blocked, and we had observed a flow blow up from the true lumen to the false lumen. Comparing the distance between tears, the longer the distance between tears, the easier it becomes thrombus. Because the part where the flow velocity stagnated is large. The area where the flow velocity stagnates is called the low flow velocity area. If the distance between tears is 200, 250, 300, the ratio of the area to the whole false lumen is 67, 78, 82%.

Conclusion: Our research elucidated visualizing the flow in the false lumen before and after implantation SG and relationship between tear distance and thrombus.

Abstract Number: ICBME1168

Experimental Investigation of the Influence of Stent Design on Jailed Struts and Stent Malapposition Using a Left Main Coronary Artery Model

Kaito Matsubara, Yutaka Hikichi, Kouta Sugiyama, Ryouta Ito, Xiaodong Zhu, Yusuke Tsuboko, Yuki Matsuhashi, Mitsuo Umezu, Kiyotaka Iwasaki
Waseda University, Japan

Background and Aims: Presence of stent struts over the flow tract of the left circumflex artery (LCx) ostium and incomplete stent apposition of left main trunk (LMT) at left main bifurcation is a concern for future thrombus formation, neointimal formation, and late narrowing. The aim of this study is to investigate the influence of stent designs and stent expansion capacity which are different in diameter on incomplete stent apposition (ISA) areas at the flow tract of LCx ostium, and on stent malapposition of LMT after a single stenting plus kissing balloon inflation (KBI) using a left main coronary bifurcated artery model.

Method and results: A left main coronary bifurcation model with the diameters of 4.3 mm at LMT artery, 3.3 mm at left anterior descending artery (LAD) and 3.0 mm at LCx ostium was fabricated using silicone. The diameters of these arteries meet Murray’s law. We used the mean left main bifurcation angle data from 209 de novo patients who underwent 64 multi-slice computed tomography. The angles between LMT and LAD, and between LMT and LCx were 141° and 122°, respectively. A 80% stenosis was equipped along the flow tract of LCx ostium, and incomplete stent apposition (ISA) areas at the flow tract of LCx ostium, and on stent malapposition of LMT after a single stenting plus kissing balloon inflation (KBI) using a left main coronary bifurcated artery model.

Conclusion: Our data indicated that the choice of stent with larger stent capacity of stent cell can reduce the protrusion of stent struts and stent malapposition, which may become a potential source of thrombus formation. Link design of stents is a primal factor which is inducing the incomplete stent apposition. Further study is needed to find better technique or design a bifurcation-specific stent in the left main bifurcation.

Abstract Number: ICBME1468

Application of Class-E Amplifier to Transcutaneous Energy Transmission System for a Totally Implantable Artificial Heart -Comparison of Resonance Circuit and Rectifier Mode-

Masatoshi Sonda, Takahiko Yamamoto, Kohji Koshiji
Tokyo University of Science, Japan

The Transcutaneous Energy Transmission Systems (TETS) can non-invasively transmit power to a totally implantable artificial heart. One of the most important problem is the improvement of power transfer efficiency. We aimed to improve the power transfer efficiency by applying a class E amplifier and reducing the switching loss. Moreover, the insertion mode of the capacitor for resonance (series resonance or parallel resonance) and the rectification mode are also important. We compared the power transfer efficiency and the frequency characteristics by the resonance circuit and the rectification mode by simulation and measurement. In the measurement, the maximum efficiency was 69.1% at series resonance, and the maximum efficiency was 60.9% at parallel resonance.

Abstract Number: ICBME1448

Blood Flow Interactions in Aorta - Pulmonary Artery System

Takahisa Yamamoto
National Institute of Technology, Gifu College, Japan

Hypoplastic left heart syndrome is one of the congenital heart disease. The disease is characterized by hypoplasia of left atrium, mitral valve and aortic arch. In such the patient, blood flow balance is kept by patent ductus arteriosus closing instead of the Norwood procedure and the Bidirectional Glenn procedure. This surgery makes less burden on the patients compared with the conventional procedures. However, some clinical reports have reported that PDA stenting...
Day 4 – 12 December 2019, Thursday


Kazunori Uemura, Toru Kawada, Takuya Nishikawa, Masaru Sugimachi
National Cerebral and Cardiovascular Center, Japan

Objective: Occlusive cuff inflation in ambulatory blood pressure (BP) monitoring disturbs the daily life of the user, and affects efficacy of monitoring. To overcome this limitation, we have developed a novel minimally-occlusive cuff method for stress-free measurement of BP. This study aimed to experimentally evaluate the reliability of this method, and improve the precision of this method by implementing a machine learning algorithm.

Methods: In this method, a thin-plate-type ultrasound probe (Size:5.6mm-thickness×28mm×26mm; weight: 10g; equipped with a linear array transducer with a total of 64 piezoelectric elements transmitting/receiving 6 MHz ultrasound pulse) placed between the cuff and the skin, and is used to measure the ultrasonic dimension of the artery. The cuff pressure (Pc), arterial dimension at systole (Ds) and diastole (Dd), systolic BP (SBP) and diastolic BP (DBP) during cuff inflation are theoretically related by the following equations,

\[ SBP - Pc = P_0 \exp[\alpha D_s] \]

\[ DBP - Pc = P_0 \exp[\alpha D_d] \]

where P0 and \( \alpha \) are constants, and \( \alpha \) indicates arterial stiffness. Since multiple sets of the two equations may be defined over multiple cardiac beats while monitoring \( P_c, D_s \) and \( D_d \) during mild cuff inflation (\( P_c < 50 \) mmHg), it is possible to estimate SBP (SBPe) and DBP (DBPe) as solutions to the equations. We evaluated this method in 6 anesthetized dogs by attaching the cuff with the probe to the right thigh to get SBPe and DBPe, which were one-time calibrated in each animal against reference SBP and DBP.

Results: DBPe correlated tightly with DBP with a coefficient of determination (R2) of 0.85 ± 0.08, and predicted DBP with mean ± SD of error of 3.9 ± 7.9 mmHg after one-time calibration. PAT correlated poorly with DBP (R2 = 0.49 ± 0.17), and predicted DBP less accurately than this method. SBPe correlated well with SBP (R2 = 0.78 ± 0.08). However, even after one-time calibration, difference between SBPe and SBP was 2.6 ± 18.9 mmHg, which was not acceptable. To improve the precision in SBP prediction, we used supervised machine learning approach with use of a support vector regressor algorithm (Python, Scikit-learn), which regressed feature variables (SBPe, DBPe, Ds, Dd heart rate, and PAT) against the teacher signal (reference SBP). Support vector regressor algorithm, once trained, predicted SBP with acceptable accuracy with error of 0.7 ± 6.9 mmHg.

Conclusions: This method reliably tracks BP changes without occlusive cuff inflation. Once calibrated, this method measures DBP accurately. With the aid of machine learning, precision in SBP measurement was greatly improved to an acceptable level. This method with the machine learning approach has a potential for stress-free BP measurement in ambulatory BP monitoring.

Development of a Novel Implantable Bladder Pressure Sensor
Chih-Wei Peng, Yu-Ting Li, Ling-Yu Yang
Taipei Medical University, Taiwan

Objectives: The lower urinary tract (LUT) comprises the urinary bladder and the urethral outlet for the storage and periodic elimination of urine. However, various physiologic and anatomical deficits could cause the disorders of LUT functions, such as incontinence and urine obstruction. Those LUT disorders could cause overactive bladder, vesicoureteral reflux and even death by complications. Many of these bladder disorders can be prevented and predicted by monitoring the abnormal bladder pressure. Thus, the bladder pressure measurement provides critical information for evaluating the state of bladder conditions in patients suffered from LUT disorders. The aim of this study was to implement a fully implantable wireless bio-microsystem that can provide bladder pressure measurement for evaluating the real-time state of bladder conditions in patients.

Methods: The implantable microsystem was implemented with a pressure sensing module and a wireless module, which was fabricated with small components and built on printed circuit board (PCB). The pressure signal was wirelessly transmitted to a graphical user interface (GUI) written in LabVIEW and stored in PC for evaluating the real-time pressure signal.

Results: The wireless mini-implantable pressure module was fabricated with small components and built on PCB. The size of the microsystem was 1.7 cm (L) x 0.8 cm (W) x 1 cm (H) and a total weight of about 3 grams. The performance of its wirelessly transmission pressure data to host unit was verified.

Conclusions: In the present study, a mini-implantable wireless microsystem was successfully designed and implemented for monitoring pressure in a hermetical container which filled with saline solution. The pressure sensing device can correctly transmit real-time measured pressure data to host unit. The implantable device should be small enough for in vivo study by placing the device into bladder cavity via urethra, which makes it feasible for the future long-term verification of our device in in-vivo experiments.
Correlating Electromechanical Patterns with Hand Gestures Based on Cytoadhesion-Inspired Hybrid Electrodes

Pingjiang Cai, Xiaodong Chen
Nanyang Technological University of Singapore, Singapore

Hand gesture recognition based on muscle activity monitoring has been implemented in robust human-machine interactions, bionic prosthetics, and the prognosis of neuromuscular disorders. Muscle activities involve the myoelectrical trigger of motor neurons at the neuromuscular junctions and the mechanical actuation of muscle fibers. Monitoring the functionality of either single event has been fulfilled with various electromyogram electrodes or skin-mountable strain sensors. However, the patterns of myoelectrical triggers and mechanical shortening of myofibers can be different spatiotemporally, intrinsically arising from the excitation-contraction coupling process. Hence, the fidelity of interpreting muscle activities by retrieving either single event is disputed. There is an unmet demand on establishing the electromechanical coupling of the myoelectrical triggers and mechanical responses in muscle for the high-fidelity hand gesture recognition.

To address this, we developed the hybrid Coup-On to spatiotemporally couple the surface electromyogram (sEMG) signals and the mechanical strain of local skin. By resembling the transmembrane architecture of cytoadhesions, the Coup-On utilized discrete “adhesion plaques” to mechanically and electrically integrate the microcracked metallic nanopills for strain sensing at a gauge factor of ~34, and the ionic gel with low contact impedance for sEMG collection at a high signal-to-noise ratio of ~32.2 dB. By establishing the electromechanical patterns of forearm muscle contraction, the Coup-On was able to distinguish loose and tight fist clenching, as well as the flexion of different fingers. In addition, the Coup-On was able to orthogonally recognize the hand gesture dynamics (e.g., magnitude and speed), which could be transferred to robotic hands for recapitulating human grip gestures with varying dynamics. In short, we have demonstrated that the correlation of electromechanical patterns of muscle contraction with hand gestures, allowing a higher predictive power and improved fidelity of reflecting hand gesture dynamics. Undoubtedly, such dynamic coupling of electromechanical patterns in muscle contraction would not only leverage the controllability of prosthetic limbs and other cyber-human systems but also advance the prognosis of neuromuscular disorders.

Abstract Number: ICBME1312

Highly Stretchable and Tissue-Adhesive Near-Field-Communication (NFC) Patch Devices

Kento Yamagishi, Wenshen Zhou, Terry Ching, Shaoying Huang, Michinaka Hashimoto
Singapore University of Technology and Design, Singapore

We demonstrated direct ink writing (DIW)-based fabrication of highly stretchable and tissue-adhesive wireless patch devices that can be operated via near-field-communication (NFC) with an operating frequency of 13.56 MHz. A variety of wireless powered devices have been demonstrated for light emission, biosensing, and actuation in skin-contact and/or implantable medical applications, but currently demonstrated devices often involves bulk metal wires that may cause a mechanical mismatch between biological tissues and devices. To overcome this limitation, we used elastomeric materials and liquid metals to develop fully flexible and stretchable wireless-powered biodevices. We fabricated stretchable microfluidic sheet devices by DIW 3D printing of silicone-based elastomeric materials to pattern channel walls (minimum line and space: 300 mm) on a commercially available polyurethane-based skin-adhesive tape (18 μm thick) and Ecoflex microsheets (7.4 μm thick). We covered the printed channel walls with another freestanding Ecoflex microsheets to form closed microfluidic channels. Galinstan was perfused through the microchannels to create fully stretchable conductive lines that showed over 400% of elongation with a small change of resistance (< 10 times of initial value). We fabricated free-standing antenna coils on the substrate embedded with LEDs and IC chips; the fabricated devices were wirelessly controlled for light emission and IC chip-based operations. We exposed the developed flexible patch to harsh operating conditions (e.g., during sport with sweating, in water, under tensile stress) and confirmed the stability of the NFC-based operation over time. In particular, the resonant frequency of the flexible antenna sheet devices remained the same under mechanical deformation (at least 60% strain). Such highly stretchable and tissue-adhesive patch capable of operation under NFC should open an avenue for various applications such as skin-contact biomonitoring, implantable and wireless light-based medicine and stably adhesive tags of soft robotics with dynamic motions.

Abstract Number: ICBME1200

An Update Algorithm for On-Line Monitoring Cardiac Output System Based on Pulse Wave Contour

Qiwen Yu, Chen Jing, Fu Wei, Liu Wenxin, Xu Linxin
Zhejiang University, China

Background: Hemodynamic parameter monitoring plays an indispensable role during the clinical operation time. At present, there are many methods for measuring cardiac output (CO), such as the transpulmonary thermodilution technique (TPTD), which is used as the gold standard for measuring CO. However, this method put high demands on the doctors’ operation and is susceptible to the patients’ temperature. Compared to TPTD, pulse wave profile analysis methods has the advantages of small wound and simple operation, but it is only based on large amounts of data to calibrate the physiological status of patients, it’s imprecise for individual patient. In addition, the sampling rate of the pulse wave in the current measurement method is too low, which may miss some pathological signals in pulse wave. Therefore, we designed a sampling filter signal acquisition circuit with high frequency, combined with the self-designed upper computer software, and adopted machine learning method to calibrate the hemodynamic parameter.

Methods: Stroke volume (SV, CO=SV*heart rate) were calculated by the area under the pulse wave contour, which was based on the positive correlation between arterial blood pressure and SV; Pulse wave velocity (PWV) was calculated from the data of two different sensors to obtain the vascular compliance of a single patient. Moreover, the mean arterial pressure (MAP) and the slope of ascending branch of pulse wave were analyzed according to the waveform. Then, the SV could be calibrated with physiological parameters such as patient age, height, weight and gender. In our system, the signal acquisition circuit board was connected with the front-end pulse pressure sensor, and the sampling rate was...
increased to 1KHz to restore the original waveform of pulse wave. In addition, signal data was transmitted via Bluetooth wireless for real-time data processing and saving. We have enrolled 16 patients and acquired more than 18 hours of data containing events, such as anesthesia induction and postural changes, which may cause hemodynamic change.

Results: We chose the FloTrac/Vigileo system (Edwards Lifesciences, Irvine, CA, USA) as the reference device, \( r \) between the two systems for SV is 0.8. This indicates a good correlation of SV measurement with the reference system. The Bland-Altman plot analysis was used to evaluate the consistency of SV data measured by our system with those recorded by FloTrac/Vigileo system. The results consistently indicated that our method is nearly equal to the FloTrac/Vigileo system (the mean difference and 95% limits of agreement are between -0.96 ± 14.52 in SV).

Conclusions: We have developed a novel CO monitoring system while using innovative algorithm. The system exhibited comparable performances on CO detection comparing to the FloTrac/Vigileo during surgery.

Abstract Number: ICBME1281

Relationship Between Lipid Accumulation and Electrical Characteristics of 3T3-L1 Cells under Three-Dimensional Culture Condition

Daiki Zemmyo, Miyata Shogo
Keio University, Japan

Adipocyte has been concerned with many diseases such as obesity and metabolic syndrome. To understand the cause of these diseases, it has been considered that evaluation and efficacy screening for in vitro adipocyte culture is required. Staining method using Oil Red O is generally used for evaluating lipid accumulation, however it is impossible to perform quantitative and real-time monitoring. ECIS (Electrical cell-substrate impedance sensing system) is one of methods to enable quantitative and real-time evaluation of cell proliferation, cell death, cell adhesion, or others. Although some studies about the evaluation of lipid accumulation in adipocytes using ECIS method have been reported, there are no studies that examined detailed relationships between lipid accumulation and electrical characteristics. Furthermore, the evaluation under three-dimensional culture condition has not been performed.

In this study, the relationship between the amount of lipid accumulation and the change in electrical characteristics was evaluated during in vitro three-dimensional culture. Cell culture device that can simultaneously measure the electrical characteristics of cell-seeded hydrogel was developed. Briefly, two platinum wires were placed in parallel in the gel to enable to measure the electrical characteristics of cells in the gel. To evaluate lipid accumulation in adipocytes under three-dimensional culture condition, preadipocytes 3T3-L1 cells were seeded in collagen gel, and differentiated into adipocytes, then cultured further to cause lipid accumulation. Specifically, in addition to no-cell group, two kinds of culture medium were used for 3T3-L1 cells-seeded collagen gel to evaluate the effect of glucose concentration high-glucose and low-glucose on lipid accumulation. To monitor the lipid droplets accumulated inside adipocytes, the complex impedance at high frequency (1 MHz) was measured. The electrical impedance was monitored every 48 hours.

As a result, lipid droplets were accumulated in adipocytes cultured in the three-dimensional collagen gel, and the amount of lipid accumulation was larger in high-glucose group than that of low-glucose group. It was revealed that preadipocyte could be differentiated into adipocyte and matured in our device. In addition, the change in the impedance during lipid accumulation process was larger in high-glucose group than that of low-glucose group. From the regression analysis, there was the correlation between the amount of lipid accumulation and the change in impedance at 1 MHz. Therefore, it was suggested that the amount of lipid droplets affect the electrical characteristics of 3T3-L1 cells cultured in collagen gel.

In conclusion, it was shown that the amount of lipid droplet accumulation in 3T3-L1 cells cultured under three-dimensional condition could be evaluated using electrical impedance. Moreover, it was suggested that it could be applied as a new evaluation system for the lipid accumulation.

Abstract Number: ICBME1478

Spatially Selective Pelvic Nerve Neuromodulation for Functional Mapping of Visceral Nerves

Marlena Raczkowska, Nitish V. Thakor
National University of Singapore, Singapore

Introduction And Objectives: Current neuromodulation therapies, such as pelvic nerve stimulation in underactive bladder management lack fiber- and molecular-specificity as they involve electrical stimulation of the entire nerve bundle. This results in random recruitment of both: sensory afferent and motor efferent pathways, which might result in bladder-sphincter dyssynergia. To better understand the contributions of different fiber subtypes in the pelvic nerve, we propose a new tool to map function of the different branches of a pelvic nerve. We found that direct stimulation of a single branch of the pelvic nerve evoked different functional response. Our results suggest pelvic nerve branch specificity, thereby opening an avenue for potential selective, fiber-specific neuromodulation of the pelvic nerve. Split ring electrode, developed in our lab demonstrated that selective muscle stimulation can be achieved by varying the stimulation configuration of the four active electrodes on the nerve to produce different muscle activation patterns. Translating this approach to a mixed visceral nerve could help mapping and selecting the nerve branch that stimulation will evoke maximum stimulation efficiency with minimum stimulation current and undesirable effects.

Methods: All procedures were performed in accordance with protocols approved by the Institutional Animal Care and Use Committee of the National University of Singapore. Female Sprague-Dawley rats were used in this study. A pair of platinum-iridium hook wires (778000, A-M Systems, WA, USA) were implanted onto the distal pelvic nerve unilaterally and used as a control experiment, in which the whole nerve was stimulated, using constant current isolated stimulator (2100, AM-Systems). Next, the nerve was teased into three branches, and the stimulation was repeated for each branch.

Results: Selective branch stimulation evoked different void outcomes (branch 1: 206-461 µl, branch 2: 216-256 µl; branch 3: 146-351 µl). Interestingly, the similar voiding response (450 µl) might be elicited by stimulation of only one nerve branch. Graded
stimulation of separate branches showed that stimulation threshold for eliciting voiding is divers and, in this animal, equal to 25 µA, 50 µA and 200µA. Moreover, two of the single branches evoked voiding response at lower current than the control entire nerve stimulation (25 µA and 50 µA vs. 100 µA).

Conclusions: Our results suggest that separate nerve branches have different functions in conduction of bladder signals, that should be explored further with subsequent external urethral sphincter EMG and pelvic nerve ENG recording. The branch-specific activation of the sensory afferent and motor efferent pathways in the pelvic nerve might help in minimizing the bladder sphincter dyssynergia. Employing selective stimulation in future bioelectronic will allow for precise targeting of visceral nerve to achieve desired outcome and elimination of undesired side-effects of neuromodulation. Another advantage of such precise stimulation is minimizing the stimulation amplitude, needed to elicit the anticipated outcome.

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Abstract Number: ICBME1520

Climbing-Inspired Twining Electrodes and Buckled-Based 3D Bioelectrodes for Peripheral Neurmodulation

Xue Feng
Tsinghua University, China

Peripheral neurmodulation has been widely used throughout clinical practices and basic neuroscience research. However, the mechanical and geometrical mismatches at current electrode-nerve interfaces, and complicated surgical implantation often induce irreversible neural damage, such as the axonal degradation. Here, compatible with traditional 2D planar processing, we propose two kinds of novel 3D bioelectrodes based on flexible shape memory substrate, which has permanent shape reconfigurability (from 2D to 3D), distinct elastic modulus controllability (from ~100 MPa to ~300 kPa) and shape memory recoverability at body temperature (~37°C). Inspired by the climbing process of twining plants, we developed a twining electrode capable of naturally self-climbing onto nerves driven by 37°C normal saline from a the temporarily flattened 2D state, and forming 3D flexible neural interfaces with minimal restraints on the deforming nerves. To further solve the dilemma between the mechanical mismatch at the neural interface and the conformability, we propose a buckling-based 3D bioelectrode with “pressure-limited” property. That is, certain pressure can be applied on the interface between buckled bioelectrodes and soft tissue, forming a flexible 3D bio-interface, such that the interfacial impedance can be lowered while limiting the pressure below a critical value that the soft tissue can withstand. In vivo animal experiments including the right vagus nerve stimulation for controlling the heart rate and the action potential recording of the sciatic nerve demonstrate the potential practicability.

Abstract Number: ICBME1070

NeuroWiz – a Software System to Acquire, Preprocess and Visualize Wide-Band Neural Data

Chuanchu Wang, Rosa Qi Yue So, Ng Soon Huat, Toey Kyaw Kyar, Brian Premchand
Institute for Infocomm Research, Singapore

Objectives: NeuroWiz is a software system to obtain neural signal from micro electrode array implanted in brain for real time processing and visualization. It is an essential tool in Brain Machine Interface application systems.

Methods: Using Universal Serial Radio Protocol (USRP) interface to read raw data from USRP B210 board, we developed algorithms and exploited technologies to process huge amount of raw data, consisting 100 channels at 30k hertz. These algorithms include raw data parsing with error checking and correction, common average reference (CAR) and band-pass filtering, threshold calculation for individual channel and spike detection for all channels. We utilized advanced modern CPU multiple core technologies to adapt our algorithms for parallel processing via simultaneous multi task running to overcome the possible CPU processing speed limits, to make it possible to run the system on moderate PC. GUI is designed in multiple views to display detail raw data, filtered data, spike train data for multiple channels, and spike waveform and detail spine train for a specific selected channel. System provides controls for viewer to manipulate the display windows, such as zooming in and zooming out of brainwaves, changing display page, saving to data file, simultaneous reading of Joystick data, etc. A replay function is implemented to simulate real-time data input with recorded data file, for system debugging or to assist the analyzer to preview and study recorded data files. In order to save data, a SSD hard disk is preferred for system to write data on it, to make sure the system runs smoothly.

Results: The final system is tested on a moderate modern laptop PC with USB 3.0 port connecting USRP B210 board and ADC hardware, feed with simulation data created in the form of audio file playing on PC/headphone outputting from audio jack. It is already used in the experiment lab to collect neural data from monkey, and will be used on locked-in human patients.

Conclusions: Algorithms developed for offline neural data analysis need to be modified for real time system processing. The technics and algorithms developed in this system achieved our design goal, and can be employed to use in similar system developments in this field.

Abstract Number: ICBME1127

An Electroencephalography-Based Brain-Computer Interface System with Immersive Virtual Reality Using Android Mobile Device for Affective Computing Studies

Zheng Yang Chin, Chuanchu Wang, Zhuo Zhang, Kai Keng Ang
Institute for Infocomm Research, Agency for Science Technology and Research, Singapore

Affective Computing is the study and the development of systems to recognise human emotions, possibly from scalp brain signals or electroencephalogram (EEG). In such a study, while EEG is recorded, emotional responses of the subjects are induced by displaying audiovisual stimuli, usually on a computer monitor. Virtual Reality (VR)
has been proposed as a more immersive medium to study emotional responses, diagnose or treat medical conditions such as social anxiety or post-traumatic stress disorder. In recent years, advances in computer graphics technology have enabled the display of immersive VR content even on consumer mobile phones, making this technology more accessible to everyday consumers. Incorporating feedback from the subject through subjective questionnaires and physiological signals such as EEG obtained during the VR experience could help improve the design of such VR content.

Hence, this paper presents an EEG-based Brain-Computer Interface (BCI) system that can record EEG and present audiovisual stimuli using a commercially available Android handheld placed in a VR headset. This system also works with commercially available dry EEG headbands and medical grade gel EEG headsets. The software architecture of EEG-based BCI VR system comprises the BCI and the VR components. The former component handles the data acquisition from various different EEG devices to interface with wireless Bluetooth dry EEG headbands such as Muse2 or to interface with wired gel-based full EEG headset such as Neuroscan NuAmps. The system can be deployed as single Unity3D application on Android mobile devices using Bluetooth-enabled EEG amplifier, or be deployed in combination with a desktop computer connected to the wired EEG amplifier to send data via TCP/IP to the Unity3D application. The latter component presents the VR audiovisual stimuli, logs event and records subjective feedback during the experiment. It can display a variety of normal, VR180 or VR360 video clips to induce emotional responses in the subject.

This system facilitates experiments using existing EEG headsets and using immersive VR to induce emotional responses for affective computing studies. A prior study which examined the display of IAPS pictures on the computer monitor and performed classification of high/low valence and arousal ratings yielded an inter-subject accuracy of about 60% on 16 subjects. Hence future plans for this system include planning data collection experiment to address questions such as whether it would be more immersive than a computer monitor in the prior study or what the degree of simulator sickness would be.

Abstract Number: ICBME1210

LANDSCAPE: An MRI-Based Project for Computational Neuromodulation

Hanna Lu, Li Zhang, Sandra Sau Man Chan, Linda Chiu Wa Lam
The Chinese University of Hong Kong, Hong Kong

Objectives: Non-invasive brain stimulation (NIBS), including transcranial electrical stimulation (TES) and transcranial magnetic stimulation (TMS), encompass a broad array of treatments that target a variety of brain regions to achieve desired outcomes in psychiatric disorders. However, given the documented data on overall treatment effects, considerable discrepancies in the efficacy of NIBS have been found across the populations with different age range. It should be noted that TMS and TES use coils or electrodes placed on the scalp to deliver a magnetic or electrical current through the scalp to the cortex where the power levels are attenuated with the distance. Scalp to cortex distance (SCD), as a key parameter, has been shown to potentially impact on the focality and strength of electric fields induced by NIBS. Collectively, there remains a dearth of data on how age-related SCD differs between different cortical regions. Therefore, this study aimed to examine the region-specific SCD in individuals with young age, middle age and old age.

Methods: In 2018, we launched an MRI-based project named as “Localized Analysis of Normalized Distance from Scalp to Cortex and Personalized Evaluation” (LANDSCAPE) to systematically investigate the region-specific SCD. We analyzed the SCD of left dorsolateral prefrontal cortex (DLPFC) and primary motor cortex (M1) in 643 cognitively normal adults from the Cambridge Centre for Ageing and Neuroscience (Cam-CAN). Based on the 3D reconstruction of the brain in Brainsight neuronavigation system, the identifications of left M1 and DLPFC were conducted individually. We localized the left M1 using the Montreal Neurological Institute (MNI) coordinates as \([x=42, y=16, z=68]\), and left DLPFC using the MNI coordinates as \([x=46, y=45, z=38]\). To better mimic the realistic brain stimulation, the corresponding locations on scalp are conducted in Brainsight neuronavigation system with pointing back the cursor to the scalp and adjusted with the orientation of the coil from the midline at 45 degrees. Each target location and the angle with coil were checked visually and individually. And the accuracy of the two targets was further verified in the planes of axial, coronal and sagittal. The SCD was directly measured in the Brainsight system as the distance from scalp to cortex. Computational head model was developed to simulate the impact of SCD on the electric field.

Results: Gender ratio and global brain volume among four groups were similar. We found age-related increased SCD in the left DLPFC \((p < 0.001)\), but not M1 \((p = 0.134)\). The electric field induced by stimulation was consequently decreased with the increased SCD across normal aging individuals.

Conclusions: Impetus for measuring SCD has largely focused on understanding and optimizing the key parameter in NIBS across a variety of brain disorders. By using a localized and normalized measurement, we presented that age have differential impacts on the SCDs of left DLPFC and M1. The findings suggest that it is important to be aware of region-specific distance measures when conducting neuromodulation in individuals with old age, such as life-life depression.

Abstract Number: ICBME1241

Short-Term Neuromuscular Electrical Stimulation Increased Corticomuscular Coherence of the Healthy

Rui Xu, Yaoyao Wang, Dong Ming
Tianjin University, China

Objectives: Neuromuscular Electrical Stimulation (NMES) is a technique that can generate contractions of paralyzed or paretic muscles by applying electrical current on these muscles. Confidential evidence has shown that NMES can increase the maximal voluntary contraction and neural activation assessed by the twitch interpolation technique. Poststroke rehabilitation with NMES has been found to effectively prevent muscle atrophy, improve muscle strength and coordination. Some studies found an increased corticomuscular coherence (CMC) after a long-term NMES. The accurate CMC during NMES is also necessary as it provides direct information on the effect of NMES, and reflects transient neural plasticity. However, it is difficult to obtain pure EMG, as the stimulation current contaminates EMG severely. Therefore, the EEG and EMG should be collected after NMES. The
aim of this work is to explore the immediate effect of a short-term NMES and analyzed functional connection via CMC before and after NMES.

**Methods:** We recruited 13 healthy participants and designed an experiment with short-term NMES. The experiment consisted of one long voluntary session (300 seconds) and three stimulated plus short voluntary sessions (100 seconds + 100 seconds). There was a rest for 5 to 10 minutes between two sessions. There were 30 trials in the long voluntary session, and 10 trials in each short voluntary session. Each voluntary trial started with 2-second wrist flexing, followed by 5-second wrist flexion holding and 1-second relaxing, and ended up with 3-second resting. The EEG and sEMG were collected during the voluntary sessions and processed (EEG: re-referenced and 5-45 Hz filtered; sEMG: 20-250 Hz filtered). The mean and area of the significant CMC before and after NMES were calculated and compared statistically.

**Results:** Not all the participants showed significant CMC during the tasks, which is a common case for CMC studies. For the spatial information, NMES had different influence on C1, C3 and C5 of coherence, with a significant CMC increase occurring at C3. For C3 EEG-sEMG coherence, the maximal value was increased from 0.0042 to 0.0175 (p=0.0020) and the area of CMC was changed from 0.0064 to 0.0247 (p=0.0098) after NMES.

**Conclusion:** Short-term NMES can still reinforce corticomuscular functional connection. This study verified the immediate strengthen of corticomuscular changes after NMES, which was expected to be the basis of long-term neural plasticity induced by NMES. This result will help understand NMES-induced corticomuscular connection, and predict the body change during NMES. Based on transient neural plasticity, the immediate change after NMES lays a basis of long-term neural rehabilitation.

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**Abstract Number:** ICBME1154

**Skeletal Bone Age Assessment in Radiographs Based on Convolutional Neural Networks**

**Junhua Zhang, Junhua Zhang, Mei Liye**

*Yunnan University, China*

Skeletal bone age assessment is a common clinical practice to investigate endocrinology, genetic and growth disorders in children. However, clinical procedures are time-consuming, labor intensive and often subject to inter-observer variability. To address these problems, several automated approaches have been proposed. However, few methods have been proven able to generalize to different races, age ranges and genders. The most advanced methods can only reach an average deviation of about 0.8 years.

In this paper, we design a system for assessing skeletal bone age automatically. Recently, very deep convolutional networks have achieved tremendous success in image recognition. Among them the Inception architecture that has shown excellent performance at relatively low computational. We improve Inception v4 network and Inception Resnet v2 networks, respectively, for bone age assessment. We fine-tune the Inception v4 network and Inception Resnet v2 network structures by removing global pooling layer, and using the mean square error as the loss function. The networks are specifically trained to place more attention to those bone age related regions in the X-ray images. The assessment of the correctness and the accuracy of the inception-based methods was carried out on the Digital Hand Atlas Database System, a public and comprehensive X-ray dataset. The dataset contains 1391 X-ray left -hand scans of children of age up to 18 years old, divided by gender and race. Data augmentation was performed by flipping each input image vertically. Images in the database were keeping aspect ratio, and normalized to have zero mean and unitary standard deviation. For all methods under investigation, we evaluated the performance over the whole Digital Hand Atlas Database using 5-fold stratified cross-validation. It requires that the ratio between each compromised category is the same as the ratio in the entire dataset, thus ensuring the training set is as uniform as possible. For each fold, we use the mean absolute error (MAE) to evaluate the performance of our method.

We train and test two kinds of convolutional neural networks through lots of experiments and parameter adjustment, Inception v4 network and Inception Resnet v2 network, reaching an average MAE across all races, genders and age ranges of 0.46 and 0.39. The result shows that the MAEs of the proposed models are about 0.4 years old respectively, which is the state-of-art performance.

Furthermore, the skeletal bone age assessment work test on a public dataset and for all age ranges, races and genders, thus representing an exhaustive baseline for future research in the field. Through the improvement and application of Inception series network, we have alleviated the problem of gradient disappearance and effective feature extraction of deep network for bone age recognition, thus reducing the average discrepancy from 0.8 years to 0.4 years.

**Abstract Number:** ICBME1309

**Actionable Machine Learning Using Electronic Health Records**

**Ming Lun Ong, Anthony Li, Mehul Motani**

*National University of Singapore, Singapore*

State-of-the art machine learning (ML) methods show immense promise for medical applications, as recent breakthroughs in prediction models offer significant improvements in chronic disease prediction. However, the black-box nature of these models poses a significant obstacle in healthcare: it is difficult for a clinical end-user to trace the decision-making process, or identify key factors contributing to a model’s prediction. A compelling framework that integrates explanations for actionable insights is lacking. We propose a method to bridge the explainability gap through two stages. Firstly, we explain the variance of feature importance across clinically possible physiological variables; subsequently, we identify actions to take on these features to minimise the incidence of disease, as classified by ML models.

Electronic health records (EHRs) contain a cornucopia of salient patient information. State-of-the-art machine learning (ML) methods are promising for extracting information from EHRs: natural-language processing (NLP) models can parse textual information in clinical notes, and recurrent neural networks (RNNs) are effective for longitudinal time-series data. As
reliability is imperative in healthcare, clinicians need to be convinced that black-box ML models can be trusted before they can be deployed in practice. Explainable Machine Learning (ex-ML), a class of methods to interpret and understand ML model behaviour, partially addresses the problem: feature attribution methods, SHAP and LIME, identify the significance of features in a model’s prediction by assigning an importance value to each feature. However, such explanations may be insufficient if clinicians cannot act upon them. Also, actionability is critical to know which actions to take to alleviate a medical condition.

Our work outlines a solution to translate explanations into actionable insights. The Clinical Explainability step addresses a few concerns. Conventional ex-ML methods are static and do not consider changes in feature values. Additionally, different machine learning models produce different explanations, and individual explanations may not necessarily aggregate on a population-wide level. We vary features across the possible physiological range of values and track the change in explanations. This section concludes with a population-level understanding of key features. Subsequently, we present a framework for Clinical Actionability. Taking input from doctors on the actionability of a clinical feature, we develop actionable recommendations, consist of a treatment order which doctors can follow to reduce a patient’s likelihood of disease. We also create a dataset-wide ranking of critical features to act on, that reduce disease likelihood across the population-level. In conclusion, we develop a method more relevant to medical practitioners, thus allowing more trust in ML-enabled healthcare systems.

Abstract Number: ICBME1115

Machine Learning Improves Early Prediction of Low Birth Weight and Reveals Unexpected Predictor

Shier Nee Saw, Arijit Biswas, Citra Nur Farah Zaini Mattar, Hwee Kuan Lee, Choon Hwai Yap
Agency for Science Technology and Research (A*STAR), Singapore

Introduction: Newborns with low birth weight have increased neonatal morbidity and mortality and have been shown to have a significant association with chronic disease in later life [1]. Current detection tools for small babies are imperfect and poor [2]. In this study, we aim to babies with low birth weight during the second trimester, using machine learning models and compare their performances with clinicians’ diagnosis.

Methods: A retrospective cohort of 347 ultrasound scanned data was collected. A total of 16 features, which included patient demographic data and ultrasound parameters scanned from 21-25 gestational week, were used as inputs to develop the models. Three supervised machine learning models, random forest (RF), support vector machine (SVM) and multilayer perceptron (MLP) models were adopted to predict small-for-gestational-age (SGA) and severe SGA infants with birth weights below the 10th and 3rd centile, respectively [3]. Performances of the models were evaluated and compared with clinicians’ diagnosis in term accuracy, sensitivity, and specificity.

Results: Compared to clinicians’ diagnosis, machine learning models achieved significant improvement in predicting both the SGA and severe SGA infants, achieving a sensitivity of 69% and 75% respectively, as compared to clinicians’ diagnosis with a sensitivity of 38% for predicting SGA and 28% for severe SGA. The RF model revealed that nuchal fold thickness had the highest importance score among all the 16 features in predicting SGA cases, suggesting that nuchal fold thickness played the an important role for predicting SGA infants. Statistical analysis corroborated with machine learning model results, showing that SGA and severe SGA had significantly thinner nuchal fold (Healthy: 4.77 ± 0.65 mm, SGA: 4.36 ± 0.76 mm, severe SGA: 4.29 ± 0.80 mm, p-value < 1e-5), which could explain the high importance score of nuchal fold thickness. Furthermore, the performance metrics of the RF model dropped when nuchal fold thickness was removed as input feature from the model, again showing the importance of nuchal fold thickness in predicting SGA.

Conclusion: Machine learning models improved the prediction of SGA and severe SGA infants in the second trimester and revealed that nuchal fold thickness might be an important predictor for SGA. Early prediction of SGA allows closer clinical and ultrasound monitoring and provides an opportunity to discover the underlying mechanism for the disease.

References

Abstract Number: ICBME1397

Deep Learning Based Prediction of Colorectal Cancer Recurrence and Survival

Danliang Ho, Fun Loon Leong, Dawn QingQing Chong, Iain Bee Huat Tan, Pavitra Krishnaswamy, Mehul Motani
National University of Singapore, Singapore

Colorectal cancer is among the top three most commonly occurring cancers worldwide, and around 30-40% of patients treated by curative intent surgery will experience cancer recurrence. Proactive prognostication would enable clinicians to better plan treatment modality and intensity, and follow-up frequency to reduce recurrence. Previous studies for cancer prognostication employ traditional epidemiological or bio-statistical methods (e.g., linear Cox proportional hazards models). Recent studies have explored data-driven methods employing machine learning or deep learning techniques for prognostic tasks in the setting of breast cancer and acute myeloid leukaemia. However, there is limited investigation of such methods for colorectal cancer prognostication applications.

Here, we study the application of machine learning models to predict cancer recurrence in a cohort of 904 post-resection colorectal cancer patients. For this prediction task, we employ heterogeneous structured and temporal clinical features including demographic and diagnostic information, tumour stage and location details, biochemistry and molecular typing results, as well as surgical details and treatment parameters. We characterize the performance of multiple machine learning classifiers including logistic regression, gradient boosting and multi-layer perceptron on structured data. We also do the same for Long Short-Term Memory (LSTM) networks on a combination of structured and temporal data, and demonstrate its feasibility for accurate prediction. Our results have implications for
management of colorectal cancer patients in the post-resection setting. For example, our model can be used to identify patients with high risk of recurrence and subsequently monitor and treat them more aggressively.

Abstract Number: **ICBME1385**

**Unsupervised Deep Learning for Automated Fundus Image Quality Assessment in Retinopathy of Prematurity**

Huijuan Yang, Aaron S. Coyer, Khalil Ouardini, Susan Ostmo, J. Peter Campbell, Chuan Sheng Foo, Michael F. Chiang, Pavitra Krishnaswamy

*Institute for Infocomm Research, Singapore*

Accurate diagnosis of ophthalmic diseases requires good quality fundus images. Reliable automated assessment of diagnostic quality at point-of-acquisition would be particularly relevant to telemedicine and screening scenarios. Conventional image quality assessment methods employ handcrafted features derived from generic and structural quality parameters, but these require significant feature selection and engineering. Recent works have proposed deep convolutional neural networks (CNNs) for more automated feature extraction and quality assessment. However, these methods require large datasets containing samples with variations in image clarity and the associated quality annotations. This is often infeasible in practice because (a) routine clinical databases may only store images with good clarity for diagnosis, and (b) obtaining detailed quality annotations on a variety of acquisition devices and settings is resource-intensive.

To overcome these challenges, we propose a novel unsupervised deep learning approach for image quality assessment. Specifically, we formulate the problem of detecting images that do not have sufficient clarity for diagnostic assessment as a novelty detection problem. We extract features using a CNN that is pre-trained on ImageNet, and then feed the learned representations into a tree-based anomaly detection method. This allows us to perform model training on a dataset of good quality fundus images, and seamlessly detect any deviations in quality that might present at the point of acquisition.

We demonstrate the method on a large Retinopathy of Prematurity (ROP) dataset comprising posterior pole fundus images from across eight institutions. We use 4,956 good quality images for model training and validation, and evaluate the results on a held-out test set of 1,317 fundus images. Three independent experts graded each image in the test set for diagnostic quality, and we use consensus labels for evaluation. About 94% of the images in the test set are of acceptable quality while the rest are anomalies with unacceptable quality. Our approach achieves a 5-fold cross-validation performance in terms of Area under Receiver Operating Characteristic (AUROC) of 71.6%, and outperforms several unsupervised baselines. Our method is potentially applicable as a precursor check in automated image analysis pipelines and in clinical settings across a range of modalities.

Abstract Number: **ICBME1146**

**Choroid Segmentation in Optical Coherence Tomography Images Using Deep Learning**

Ruchir Srivastava, Ee Ping Ong, Beng-Hai Lee

*Institute for Infocomm Research, Singapore*

**Objective:** Automated analysis of the choroid is important to assess diseases such as age-related macular degeneration, serous chorioretinopathy and choroidal melanoma, which accompany choroidal changes. Automatic segmentation of the choroid is essential for such analysis. Existing works on automatic choroid segmentation focus on detecting the choroidal boundaries (Bruch’s membrane or BM at the top and choroidoscleral junction or CSJ below the choroid) by utilizing the edge-related information. This approach fails to utilize the unique texture of the choroid. The objectives of this work are two-fold: 1) To segment the choroid in optical coherence tomography images by utilizing the texture in the choroid. 2) To experimentally assess the effect of removing the retinal layers before choroid segmentation.

**Methods:** The proposed method uses a deep learning architecture called U-Net which performs a region-based segmentation of the choroid instead of segmenting boundaries of the choroid as in the related works. U-Net takes patches extracted from optical coherence tomography (OCT) images as input. Before extracting these patches, the BM is detected so as to remove the retinal layers. Data augmentation is performed to increase the amount of training data. From the test images, patches are extracted and fed to the trained U-Net for choroid segmentation. U-Net outputs a binary segmentation map with choroid pixels as 1 and others 0.

**Results:** The proposed method was evaluated on a dataset consisting of macula-centered OCT scans corresponding to 20 eyes from 20 healthy subjects. The scans were captured using Topcon’s Atlantis swept source OCT machine. Each scan consisted of 64 images each of size 512 × 992 pixels resulting in a total of 1280 images. BM and CSJ boundaries were manually marked by a grader to provide the ground truth. For evaluation, a 4 fold cross validation was performed and intersection over union (IoU) was used as the metric. For the proposed method, a mean IoU of 0.85 was obtained after cross validation. If the segmentation was performed without removing the retinal layers, the IoU was 0.81. We also compared the proposed method with a graph-based method which detects boundaries of the choroid and the IoU for this method was 0.51.

**Conclusions:** The proposed method shows promising results as compared to the related work which indicates that utilizing the texture in the choroid can be useful especially in cases where choroidal boundaries may not be clear. This is especially useful in diseased cases where the boundaries are irregular and utilizing the choroidal texture may prove to be more accurate. In order to perform the proposed segmentation, results of the additional experiments show that removing the retinal layers will improve the choroid segmentation accuracy as compared to not removing them. The proposed method can help in automatic analysis of choroidal changes which is crucial in assessing many ocular diseases. At the same time, the results are still preliminary and will be further improved as a part of the future work.
The results revealed the stress and strain of the ONH in glaucoma. There is still a lack of knowledge on biomechanics in glaucoma, and there is still a lack of knowledge on the stress and strain of the ONH in glaucoma. To do that, our well-established patient-specific fluid-structure interaction (FSI) model of the eye was employed and the IOP of 5 kPa (37.50 mmHg) was applied to the interior surface of the sclera, where the vitreous body is in interaction with the eye components.

**Results and Conclusions:**

The results revealed the stress and strain of the ONH in glaucoma. The highest stress and strain of 217.60 kPa and 15.07%, respectively, were observed in the anterior of the eye globe, where the lens, ciliary body, iris, aqueous body, and cornea are located. These results have implications not only for an understanding of the stresses and strains of the eye globe in glaucoma but also for providing comprehensive information for the ophthalmologists and biomechanical experts to clarify the impact of a high IOP on the stress and strain of the ONH.

**Objectives:**

Alteration of the intraocular pressure (IOP) has been shown to be implicated in the development of glaucomatous optic neuropathy, particularly at the level of the lamina cribrosa. The stresses and strains at the head of the optic nerve, where it attaches to the sclera, play a crucial role in the development of glaucoma in the eye. Although so far several studies have been conducted to investigate the optic nerve head (ONH) biomechanics in glaucoma, there is still a lack of knowledge on the magnitudes of the stresses and strains at the ONH site in the presence of all the components of the eye.

**Methods:**

This study, therefore, aimed to investigate the IOP-related stress and strain within the load-bearing connective tissues of the ONH in glaucoma. To do that, our well-established patient-specific fluid-structure interaction (FSI) model of the eye was employed and the IOP of 5 kPa (37.50 mmHg) was applied to the interior surface of the sclera, where the vitreous body is in interaction with the eye components.

**Results and Conclusions:**

The results revealed the stress and strain of 31.97 kPa and 0.37%, respectively, at the ONH. The highest stress and strain of 217.60 kPa and 15.07%, respectively, were observed in the anterior of the eye globe, where the lens, ciliary body, iris, aqueous body, and cornea are located. These results have implications not only for an understanding of the stresses and strains of the eye globe in glaucoma but also for providing comprehensive information for the ophthalmologists and biomechanical experts to clarify the impact of a high IOP on the stress and strain of the ONH.
Results: Results showed strong correlation within group subjects (0.88) and reasonable correlation to new subjects (0.71). The root mean square error was about 8.58% and 17.50% of the peak recorded value. And increasing gesture repetition frequency can affect the model estimation performance in both the two levels of generalization. In general, model generalization within subjects was good and model generalization to new subjects was suffered over subjects and gesture repetition frequency. A possible explanation for this might be that new subjects have different foot gestures and patterns. The dataset was still not adequate to train the model to predict the patterns of new subjects. Although the model generalization to new subjects was not satisfying yet, some of the good predictions revealed the possibility of generalization to new subjects.

Conclusions: This study presents a whole weight-bearing estimation method based on local force measurement and BP neural network model. The results of this study indicate that neural network has certain ability to approximate the relationship between the local forces and the whole weight-bearing. Further studies aim to establish a larger-scale data set with diverse subjects to improve the model generalization. This method can be a valuable alternative for the monitoring of weight-bearing in weight-bearing training as its wearability.

Abstract Number: ICBME1400

A Trial of Quantification of Mastication by Acceleration

Konishi Yuto, Atsushi Iwashita, Kayoko Otsuka, Masahiro Tanaka

Butsuryo of College Osaka, Japan

In the aging society, not only the average length of life but also the healthy life-span is important. A meal affects healthy life-span deeply. In addition, the meal is very important ADL movement and contributes to QOL. In order to eat a meal alone, it is important to be able to perform mastication. However, various devices are often used for a measurement of the chewing mastication. Therefore the measurement of the mastication is not easy. This aim of the study is to measure mastication easily. In this study, we measured mastication with an accelerometer fixed to the lower jaw. This accelerometer is used for an active mass meter. The subject masticate the chewing start food “process lead” (Otsuka Pharmaceutical Factory Co., Ltd.). We measured the period between food intake and swallowing. There were two subjects, one healthy elderly person and one person with dysphagia. We calculated the Index which integrated a measured acceleration signal. Therefore the measurement of the mastication by the acceleration is useful.

Abstract Number: ICBME1246

TSC1mKO Kyphosis Mice Model – Can Muscle Loss Induce Intervertebral Disc Degeneration?

Wing Moon Raymond Lam, Zhuo Wen Hai, Tsai Shih Yin, Elisa Marie Crombie, Cool Simon, Tan Tuan Chun, Liu Jing, Hey Hwee Weng Dennis, Wong Hee Kit
National Univeristy of Singapore, Singapore

‘Sarcopenia’ involves a progressive age-related loss of muscle mass and associated muscle weakness. During aging, muscle weakening by autophagy reduce extension force of lumbar which can accelerate disc degeneration. TSC1mKO mouse is a muscle loss model which develops kyphosis in late stages of their life cycle which has some similarity to an elderly with sarcopenia. We hypothesize that TSC1mKO mice develop intervertebral disc degeneration due to muscle loss induced overload in some vertebra level. The aim of study is to prove muscle loss can induce intervertebral disc degeneration in TSC1mKO mouse model.

Seventeen female mice were divided into four groups Group 1 9 months old TSC1mKO (n=4) Group 2 Age matched control (n=3). Group 3 12 months old TSC1mKO (n=5), Group 4 Age matched control (n=5) Lumbar vertebra was scanned by microCT for Cobb angle, vertebra length, disc height measurement and bone histomorphometry study. After microCT imaging, specimens were fixed by paraformaldehyde, degree of intervertebral disc degeneration was evaluated by Fast staining method.

At 9 months old, Cobb Angle of TSC1mKO (58.66 ±11.11°) was higher than age matched control (41.83 ±15.34°, p =0.075). The result matched with previous study. At 12 months old, Cobb Angle of TSC1mKO (65.00 ±10.97°) was significantly higher than age matched control (38.33 ±20.25°, p=0.025). Intervertebral disc height of TSC1mKO mouse was lower than age matched control. There was no significant difference of vertebra length between both all groups. At 12 months, intervertebral disc height of TSC1mKO mouse was significantly lower than control counterpart in L2-3 (181±24 vs 250±55mm, p=0.017), L3-4 (167±38 vs 237±25mm, p=0.004), L4-5(176±24 vs 231±36mm, p=0.011). From histomorphometry analysis, TSC1mKO mouse had higher bone volume/tissue volume, trabecular thickness and lower trabecular separation in L4-6 region than control group. From fast staining histology, L4-5 and L5-6 IVD of TSC1mKO mouse had lower glycosaminoglycans content and ossification of endplate of observed in anterior side. Degree of degeneration worsen in aged 12 months TSC1mKO mice.

This study demonstrates that muscle loss can induce intervertebral disc degeneration and disc height loss in TSC1mKO mouse model. These results are consistent with the elderly patient with muscle weakness and intervertebral disc degeneration.

Abstract Number: ICBME1402

Mechanical Characterizations of Metallic Scaffolds Fabricated by Selective Laser Melting Processes for Bone Tissue Engineering

Xue Wang, Liping Zhao, Heow Pueh Lee
National University of Singapore, Singapore

Bone tissue engineering has emerged as a promising solution for bone repair and regeneration after orthopedic surgeries. As popularly used implants in the tissue engineering, metallic scaffolds are required to mimic the microstructure and mechanical properties of trabecular bone which is highly porous with a low modulus, to reduce the potential stress shielding effect which would result to degraded and loosened tissue around the scaffolds. However, conventional fabrication methods show unavoidable limitations in producing controllable...
microstructure and handling the complex structures of the scaffolds. One advanced manufacturing technique which overcomes these limitations is selective laser melting (SLM) process, a well-known additive manufacturing technique for processing metallic material. It has been extensively reported in the literature as a good candidate for fabricating the bone scaffolds with controllable porosity and microstructure [1].

The objective of the present paper is to characterize numerically and experimentally the microstructure as well as the mechanical properties of highly porous metallic scaffolds fabricated by the SLM process. A numerical framework based on the actual microscopic details of the scaffolds is presented to estimate the mechanical properties and subsequently the numerical estimations are benchmarked with the experimental data. The numerical results obtained using the actual microstructure are closer to the mechanical properties characterized by the experiments, compared to the simulation results obtained using the designed dimension for the scaffolds, which are frequently adopted in the existing simulation works. The proposed model could benefit the scaffold development process by providing estimated mechanical properties without destructive testing cost.

Keywords: Bone scaffolds, mechanical behavior, selective laser melting, numerical modeling, experiment characterizations.

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References

Abstract Number: ICBME1081

Analysis of Fatigue Behavior in Forearm Muscle Based on Evaluation of Muscular Endurance Characteristics Using Force Myography

Tatsuya Igarashi, Kazuhiro Fujisaki, Kazuhiko Sasagawa, Takeshi Moriwaki
Hirosaki University, Japan

Estimations of muscle fatigue are important for evaluating the performance of motions and the anticipation of injury during works and sports. Recently, force myography (FMG) has been developed and studied for measurements of muscle activity as a wearable system of motion analysis. FMG detects the volumetric changes of the musculotendinous complex by force sensors such as tactile sensors placed on skin. FMG measurements are less affected by electrical noise and contact error between sensor and skin caused by sweating because the measurements focus on the displacement of skin resulted from the muscle contraction.

In our previous study, an FMG device consisting of thin pressure sensors was developed and used to measure the muscle activities under a situation to keep a certain magnitude of force for several tens of minutes. Muscle fatigue characteristics were detected as the changes of muscle activities during the measurement. The aim of this study is to explore whether FMG can evaluate the characteristics of muscle activities in fatigue including the effect of rest for recovery. The relationship between muscular endurance and length of rest period in lifting motion was investigated using forearm FMG signals.

An FMG measuring device consisting of 16 thin pressure sensors was used. This device was wrapped at proximal part of forearm and fixed by non-expandable band. The experiment was conducted in the following manner, (1) lift a weight placed in front of the body by using four fingers of dominant hand except thumb without elbow bending, (2) hold the weight at the height with a bit from the ground, (3) keep the posture until the weight slipped out of hand caused by decrease in grip strength, (4) take a rest with the fingers keeping the same posture. After the rest period, the motion from (1) to (4) was repeated several times. FMG signals were recorded whole the period including the lifting, holding and rest states.

In this study, the total sum of the sensor signals at a moment is regarded as a representative value (FMG value), and the length of holding time was used to evaluate the muscle activity performance. FMG value increased during the period of holding weight, and decreased with the time passed during the rest period. When the rest time was short, the value did not return to the initial state measured before lifting. There was a correlation between the magnitude of FMG value measured immediately before the lifting and the length of the holding time. It is empirically known that the swelling is occurred in the state of muscle fatigue. The swelling of forearm is detected as increasing of the FMG value. It is thought that the differences of the values measured in rest periods correlate with the physical change in muscle fatigue.

This study has shown that muscle fatigue properties and muscle recovery properties could be evaluated by monitoring the changes in FMG values. FMG is useful as a wearable sensing technique to prevent the accidents caused by fatigue.

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Abstract Number: ICBME1427

Cancer-Specific Metabolic Profiles of Circulating Tumor Cells on Live Single-Cell Mass Spectrometry

Kazufumi Honda
National Cancer Center Research Institute, Japan

Proteomic, metabolomic, and genomic techniques have had innovative impacts on clinical diagnosis in cancer research. With the discovery of targets for early detection, molecular therapy, and personalized medicine, we have undertaken comprehensive protein, metabolite, and gene expression profiling of various cancer tissues, as well as sera/plasma and circulating tumor cells (CTCs), from patients with cancer.

We report untargeted molecular profiling of single CTCs obtained from gastric cancer (GC) and colorectal cancer (CRC) patients, using live single-cell mass spectrometry integrated
with microfluidic-based cell enrichment techniques (LFMCTs). Using this approach, we revealed differences in the metabolomic profiles among CTCs originating from different cancer groups.

In addition, CTCs and circulating tumor DNA (ctDNA) are gaining attention as methods for real-time monitoring in cancer patients. We optimized a method for analyzing genetic alterations using next-generation sequencing (NGS) of extracted ctDNA and CTCs enriched using LFMCT as a first-phase examination of 30 patients with head and neck cancer, esophageal cancer, GC, and CRC. We also identified time-dependent genetic alterations that appeared during anti-EGFR therapy in CTCs and ctDNA from CRC patients. The results of NGS analyses indicated that alterations in the genomic profiles of liquid biopsy specimens could be expanded by using a combination of assays with CTCs and ctDNA.

Abstract Number: ICBME1256

Evaluation of Combinatorial Therapies Using a Preclinical Microfluidic Model

Bee Luan Khoo
City University of Hong Kong, Hong Kong

The emergence of drug-resistant cancer phenotype is a challenge for anti-cancer therapy. Cancer stem cells are identified as one of the ways by which chemoresistance develops. Using a preclinical micowell-based microfluidic model, we investigated the effects of an anti-inflammatory and anti-cancer combinatorial treatment with cancer cell lines and patient-derived circulating tumour cell clusters. The model had been previously demonstrated to predict patient overall prognosis. We demonstrated that anti-inflammatory combinatorial treatment for 72 h could generate higher killing efficacy and enhanced apoptosis than single anti-cancer drug treatment. Seven days of treatment significantly reduced the proportion of cancer stem cells and colony-forming ability. The response of patients varied due to clinical heterogeneity, with 62.5% and 64.7% of samples demonstrating higher killing efficacy or reduction in cancer stem cell (CSC) proportions after combinatorial treatment, respectively. These results highlight the importance of using patient-derived models for drug discovery. With the simple but unique microfluidic model, we seek to evaluate methods for the reduction of CSCs generated post-treatment by stressful stimuli. Our study will promote a better understanding of anti-inflammatory treatments for cancer and reduce the risk of relapse in patients.

Abstract Number: ICBME1490

Centrifugal Microfluidic Technology for Circulating Tumor Cells

Minseok S. Kim, Seung Joon Lee, Hyojung Kang, Soo Kyung Park, Yebin Son, Hyeongju Woo, Sohae Yang, Taehoon H. Kim, Jong Man, Joseph Sunoo
Daegu Gyeongbuk Institute of Science and Technology, Korea

Metastasis, the spread of cancer from a primary tumor to a distant site, is largely responsible for cancer’s lethality. Research into circulating tumor cells (CTCs) has suggested an important role for these cells in metastatic spread, inspiring hope of new and more effective ways to diagnose and treat aggressive disease. Detection of these exceedingly rare cells within the circulation may provide important clues regarding cancer prognosis and progression, potentially advancing, too, the assessment of anticancer drug treatment and optimization of individualized therapy. In developing CTC technology, the critical requirements are high recovery rates and high purity. Current CTC isolation technology, however, has more focused on the negative depletion approach to maximize the enumeration of heterogeneous CTCs. Moreover, full automation is one of the most important requirements for practical utility of CTC diagnosis. In this talk, I would like to introduce several methods to isolate the CTCs and analyze their own advantages and limitations. In addition, a novel rare cell isolation system, a centrifugal microfluidic technology, is demonstrated to satisfy full automation for circulating tumor cell isolation from blood. The disc-based device could process under 10 mL of blood sample at a time and the purity of the finally isolated fraction was enough to work direct sequencing for mutation analysis. The systems represent a potentially significant advance towards ensuring highly efficient isolation of these sparsely populated target cells in microfluidic study contributing, therefore, to the sensitive and robust clinical validation of studies towards precision and personalized medicine.

Abstract Number: ICBME1430

Single Cell-Based Diagnosis of Liquid Biopsies with Extremely Low Cellularity Using DEPArray Technology

Tong Seng Lim, Wei Jian Tan, Mona Meng Wang, Paola Ricciardi-Castagnoli, Anita Chan Sook Yee
Menarini Biomarkers Singapore, Singapore

Liquid biopsies are routinely used for medical diagnosis. The ability to select, sort and recover rare target pathogenic cells from liquid biopsies with low cellularity poses unique challenges that impede diagnostic accuracy. Heterogeneous cell populations with non-target immunoreactive cells in pausicellular liquid biopsies complicate conventional bulk-cell analysis, and could lead to disease misdiagnosis.

DEPArray™ is one of the best automated platforms that can sort and recover rare target cells with high resolution and purity required for sensitive downstream genomic and expression analysis (Carter et al., Nature Med, 2016; Hodgkinson C.L. et al., Nature Med, 2013). Here, we adopted a state-of-the-art multimodal strategy including real-time imaging-based, single-cell sorting DEPArray™ with downstream genomic and molecular assays for disease diagnosis and prediction of clinical outcome.

We provided proof-of-concept that DEPArray™ technology enables automated isolation and recovery of rare target cells from liquid biopsies including ocular vitreous fluids for single cell analysis. Using immunoglobulin clonality assay, chromosomal translocation, genetic mutation and copy number aberration analysis, we determined genomic and molecular characterizations of malignant cells at single cell resolution. The digital sorting DEPArray technology provided novel tool for single-cell based precision diagnosis of liquid biopsies with extremely low cellularity.
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POSTERS
Convolutional Neural Networks for Absence Seizure Detection with Frontal EEG Electrodes

Dajiang He, Zhang Zhuo, Mustafa Talha Avcu, Derrick Wei Shih Chan
Institute for Infocomm Research, A*STAR, Singapore

In order to develop light-weight EEG based systems for home-based long term seizure monitoring, algorithms depending on least number of EEG channels, preferably located at frontal area of the head, are highly desired. Furthermore, an end-to-end solution without EEG feature extraction would enable computational efficient online processing. We have developed a Convolutional Neural Network (CNN) based approach, called SeizNet [1], for absence seizure detection using only 2 frontal EEG channels. This study aims to evaluate the general performance of CNN based approaches for EEG-based seizure detection. We implement two more CNN nets which were reported by other groups earlier: SeizureNet [2] and pyramidal 1D-CNN (P-1D-CNN) model [3], and benchmark the 3 CNN nets against a support vector machine (SVM) classifier.

EEG data of 29 pediatric patients diagnosed with typical absence seizures are used in this study. IRB was located from the institutional review board of KK Women’s and Children’s Hospital, Singapore. We conducted leave-one-out cross-validation for all subjects. Performance of the methods are assessed with three parameters: sensitivity is defined as proportion of seizures that are correctly detected; false alarm rate is number of false positive, i.e., identification of seizure in the absence of seizure per hour (fp/h); latency is the mean delay between electrographic onset and detector recognition of seizure activity.

The experiment results show all 3 CNN models outperform the baseline SVM classifier (sensitivity 86.6% and false alarm rate 1.98). Among the 3 CNN models, P-1D-CNN achieved the best sensitivity 96.7%, but its false alarm rate is almost 2 per hour. SeizureNet’s false alarm rate is 0.30, however its sensitivity is only 90.8%. SeizNet attains an accuracy of 93.3% and false alarm rate of 0.60 per hour. In terms of balanced sensitivity and false alarm rate, seizNet is the most preferable one among the three nets we explored. A few features make SeizNet different from existing deep learning models for seizure detection. Firstly, additional dropout layers and batch normalization are added to every convolution layer to avoid model overfitting. Secondly, dropout is used in not only after fully connected layer, but various parts of the model. Finally, number of filters at each convolution layer is multiplied by two, so that it has less number of filters at lower levels but more filters at the higher levels.

Reference

An IoT Medicine Dispenser with an Alarm to Prevent Medication Nonadherence

Takanori Murai, Yasushi Yamauchi
Toyo University, Japan

Objectives: One issue concerning older adults with multiple illnesses is the high rate of medication nonadherence, with large amounts of unused medicine often found in the homes of these patients. In Japan, the most frequently reported reason for nonadherence (about 70%) is that the patients simply forget to take them. Another reason is that older adults may become confused over which medicines to take.

There are three essential approaches to addressing the issue of unused medicine. First, keeping a medication log; second, sharing medicine-taking information with one’s pharmacist; and third, employing an alarm system to monitor and notify patients and others of deviations from medication schedules.

The objective of this study is to develop a medication dispenser whose medication administration schedules can be programmed and tracked online, and that records patient medication-taking in graphical displays and has an alarm function when adherence falls out of scheduled ranges.

Methods: Small compartment boxes and proximity sensors are used to measure remaining quantities of medicine. Stacks of small boxes are designated for morning, noon, evening, and bedtime, and each has seven trays, one for each day of the week. At each medication time, the patient takes out an entire tray, thereby lowering the height of the stack. A proximity sensor attached to the back side of the cabinet lid measures the distance between the lid and the stack in order to calculate the amount of medication remaining. Opening or closing of the lid is detected by a tact switch, and each time the lid closes the remaining amount of medicine is measured by the proximity sensor and sent via Wi-Fi through the Internet, where the IFTTT (If This Then That) web service processes and records the data in a spreadsheet using Google Sheets. Then, the medication adherence and usage information is circulated via email.

To set up a cloud-based medication adherence alarm system, messages need to be controlled and sent from the cloud. For this function, we used the IoT cloud service Blynk.

Once medication times are set up using IFTTT, the Blynk server connects at designated times and controls an Arduino microcontroller in the cabinet, which delivers announcements from a speaker saying “It is time to take your medicine.” The announcement information is sent via the Internet and processed using IFTTT to generate an email notification to smartphones connected to the service.

Results and conclusion: Once medication times were set using IFTTT, we confirmed that the announcements and the
smartphone notifications were delivered at the designated times. These operations confirmed that the administration nonadherence alarm functions worked as intended.

Removing medicine from the dispenser triggered calculation of the remaining medicine, which was automatically recorded in a Google Sheets spreadsheet. We confirmed that notification of medication administration adherence was delivered, thus verifying that the medication administration history was being recorded and shared.

Thus we verified that our IoT medicine dispenser worked as intended. In future, we perform a usability evaluation of the system.

Abstract Number: ICBME1105

Design Concept for an Automated Lower Extremity Dressing Aid for Monoplegic and Elderly People

Aaron Raymond See, Allain Jessel Macas, Vu Trung Hieu, Yu-Yang Hsu, Zheng-Kai Wang
Southern Taiwan University of Science and Technology, Taiwan

Lower extremity dressing aid has been a useful piece of assistive device for the elderly people and people who suffer from monoplegia. However, some of the commercially available devices take too much time and even require the patient to ask help from others to operate the device which defeats the purpose to provide a sense of independence for the users. Other devices may also demand the patient to bend and exert more effort than necessary. To address these problems, we examined existing assistive devices and gym equipment, and designed an innovative structure for the assistive device to include a moving garment hanger. In this design concept, the hanger will be controlled using electromechanical parts by means of push buttons to trigger the rotation of a single motor. It has been successfully simulated using SolidWorks for the mechanical parts and Proteus 8 Professional for the electrical mechanism. The electrical part includes the motor driver which takes input from the push buttons and gives output to the motor for rotation. The motor is connected to the pulley which moves the belt vertically along with the garment hanger. This easy control will be beneficial for the user as it automates the whole movement of the lower garment in either upward or downward direction for dressing and undressing. There will be no need for the user to bend over in order to put on the lower garment. Furthermore, the garment hanger is made to be adjustable to accommodate different waist sizes. It is also designed to be portable for convenience and efficiency. The simulation showed a feasible automated lower extremity dressing aid for monoplegic and elderly people that will address their dressing problems brought by frailty or disability.

Abstract Number: ICBME1357

A Development of Deep Learning Framework for Forward Walking Biomechanics Due to Different Speed Factor

Chow Khuen Chan, Nizar Muhammad Hanif Ahmad, Kheng Yee Goh, Khin Wee Lai, Raye Yeow Chen Hua
University of Malaya, Malaysia

The study of human motion allows us to understand the work expenditure of the human body. The human motion technology has advanced rapidly in the past decades, which promotes the 3D-gait analysis system that can conveniently use to investigate movement deviations and abnormalities. Nevertheless, 3D-gait analysis is not applied widely in the clinical evaluation by the clinical practitioners despite the sensitivity and accuracy of the system. The tedious and complicated process of analyzing the movement data increases the workload of the users. Furthermore, the statistical investigation in assessing the movement performance is laborious and could prone to inconsistency in a certain extent, which causes the time taken for detection of movement deviation and abnormality is lengthy. Thence, this study intends to develop and investigate a deep learning framework in reducing the complexity of the movement data and shortening the time for data processing. In this study, a deep learning framework was developed to automatically classify the gait patterns of different walking speeds. 13 healthy subjects (age: 22.8 ± 1.5years; height: 1.70±0.08m; weight: 62.4±9.1 kg) without any muscular, neurological, cardiovascular, metabolic and inflammatory diseases were recruited. A motion-capture system consisting of eight high-speed cameras and two forceplate sensors. Fifteen reflective markers were placed at the bony landmarks of the participants based on the plug-
We used 60 CT images of patients with lung cancer to train AI. The classification model is based on convolutional neural networks, using other modern deep-learning approaches, such as batch normalization, dropout and residual blocks. Evaluation is done using two types of ECG signal segmentation for different parameters of the neural network: static segmentation (fixed number of samples fed into the network centred around the R-peak) and dynamic segmentation (each heartbeat starts from the R-peak) and dynamic segmentation (each heartbeat starts from the R-peak). According to the AAMI standards, we have investigated the intra-patient and the patient-specific paradigms. The development and the evaluation of the classification model was performed on a publicly available ECG database – the MIT-BIH Arrhythmia Database, and additionally, on data from a specific single-lead wireless ECG sensor – Savvy ECG.

Results: The scores obtained are higher for the intra-patient paradigm, with an accuracy of 0.99, but the patient specific paradigm is more valuable because it reflects a real-life classification scenario. For both paradigms, the sensitivity and the positive predictive value are not as good as the other metrics. Nevertheless, for the patient specific models we observe improvement with the dynamic segmentation: the sensitivity and the positive predictive value for the two most important classes (S and V) are higher than with static segmentation of the ECG data. In the other metrics, there is no such significant difference between the two types of segmentation, but still the dynamic one performs better. The most significant result obtained is patient-specific models that reach an accuracy of 0.947 with dynamic ECG segmentation.

Heartbeat Classification in Single-Lead ECG Using Convolutional Neural Networks

Alessandra Rashkovska Koceva, Aleksandra Rashkovska Koceva
Jozef Stefan Institute, Slovenia

Objectives: For an expert cardiologist, any irregularity in the cardiac rhythm or in the form of an ECG can be easily detected as an indication for arrhythmia. However, this is a big challenge for a computer system. The need for automatic recognition of arrhythmias comes from the development of many portable ECG measuring devices, the purpose of which is to function as a part of health monitoring platforms. These systems, due to their wide availability, will generate a lot of data that will need suitable algorithms for processing it. The Association for the Advancement of Medical Instrumentation (AAMI) gives recommendations for using certain databases and ways of evaluating the results of algorithms for classification of arrhythmias. The final results of an ECG arrhythmia classification algorithm highly depend on the choice of the evaluation paradigm, and furthermore, the choice in dividing the ECG signal into separate heartbeats, i.e., the type of segmentation. The aim of this study is to investigate which type of segmentation gives better classification results under two evaluation paradigms.

Methods: The classification model is based on convolutional neural networks, using other modern deep-learning approaches, such as batch normalization, dropout and residual blocks. Evaluation is done using two types of ECG signal segmentation for different parameters of the neural network: static segmentation (fixed number of samples fed into the network centred around the R-peak) and dynamic segmentation (each heartbeat starts from the R-peak and ends 200 ms before the R-peak and ends 200 ms before the next R-peak). According to the AAMI standards, we have investigated the intra-patient and the patient-specific paradigms. The development and the evaluation of the classification model was performed on a publicly available ECG database – the MIT-BIH Arrhythmia Database, and additionally, on data from a specific single-lead wireless ECG sensor – Savvy ECG.

Results: The scores obtained are higher for the intra-patient paradigm, with an accuracy of 0.99, but the patient specific paradigm is more valuable because it reflects a real-life classification scenario. For both paradigms, the sensitivity and the positive predictive value are not as good as the other metrics. Nevertheless, for the patient specific models we observe improvement with the dynamic segmentation: the sensitivity and the positive predictive value for the two most important classes (S and V) are higher than with static segmentation of the ECG data. In the other metrics, there is no such significant difference between the two types of segmentation, but still the dynamic one performs better. The most significant result obtained is patient-specific models that reach an accuracy of 0.947 with dynamic ECG segmentation.
Conclusions: The study has shown that the dynamic segmentation of ECG is better solution in the classification models described in this work. This is important finding since so far in the literature, some sort of static segmentation is encouraged. The most important part of this work is the development of patient-specific models. Therefore, we can conclude that dynamic segmentation is better for models for classification of patient-specific arrhythmias.

Abstract Number: ICBME1384

Lpaqr-Net: Lightweight Pyramid Attention Quick Refinement Network for Automatic Whole-Spine Vertebrae Segmentation from Lateral Radiographs of Patients with Adolescent Idiopathic Scoliosis

Liping Zhang, Lin Shi, Jack Chun Yiu Cheng, Winnie Chiu Wing Chu, Simon Chun Ho Yu
Chinese University of Hong Kong (CUHK), Hong Kong

Sagittal plane deformity of the spine is a common condition occurring in a variety of diseases and has a critical impact on the treatment and evaluation of spinal disorders. Vertebral segmentation of the whole spine in lateral radiographs is a prerequisite for accurate quantitative analysis of spinal deformity. As compared to manual vertebrae segmentation that is labor-intensive and subject to inter- and intra-observer variations, automatic vertebrae segmentation is a fast and reliable tool for radiologists who might benefit from the corresponding workload reduction. However, the automatic segmentation of the whole-spine structure from lateral radiographs is a very challenging task due to the difficulty in locating the thoracic vertebrae, especially for those overlapped with the ribcage and upper arms.

Previous attempts in vertebrae segmentation from lateral radiographs generally focused on cervical or lumbar vertebrae. However, the automatic whole-spine vertebrae segmentation from lateral radiographs remains an open problem in medical image computing community.

In this paper, we propose a novel lightweight pyramid attention quick refinement network (LPAQR-Net) to learn more efficient, condensed, and discriminative feature representations for the accurate automatic whole-spine vertebrae segmentation from lateral radiographs. Specifically, the proposed LPAQR-Net is modified from the U-Net but with fewer parameters to reduce the memory footprints and inference time. Moreover, the LPAQR-Net explores attention mechanisms to facilitate the feature refinement and captures weighted multi-scale contextual information to alleviates the thoracic vertebrae locating problems. Additionally, we employ the deep supervision techniques and the multi-class training strategy for network optimization. The LPAQR-Net takes a whole-spine lateral radiograph and predicts the corresponding segmentation that includes six cervical vertebrae (C2 to C7), twelve thoracic vertebrae (T1 to T12), five lumbar vertebrae (L1 to L5), and the sacrum.

A dataset consisting of 332 patients with Adolescent Idiopathic Scoliosis (184 for training, 48 for validation and 100 for testing) from the EOS X-ray imaging system is constructed to evaluate the effectiveness of the LPAQR-Net in whole-spine vertebrae segmentation from lateral radiographs. Compared to the U-Net and DenseUNet, the LPAQR-Net not only achieves the best results across various metrics (Dice coefficient: 93.07%, Jaccard coefficient: 87.13%, sensitivity:92.40%) but also has fewer network parameters (2,98M) and requires fewer memory footprints (771 MiB) for inference.

In summary, we present a novel LPAQR-Net for the accurate automatic whole-spine vertebrae segmentation from lateral radiographs. Compared to the U-Net and DenseUNet, the LPAQR-Net is highly parameter-efficient and requires fewer memory footprints for inference while achieving promising results in whole-spine vertebrae segmentation from lateral radiographs.

Abstract Number: ICBME1386

Application of Deep Learning in Medical Image Segmentation for Brain Stroke Detection

Alok Tiwari, Shiru Sharma
IIT-BHU VARANASI, UP, INDIA, India

Abstract: Stroke is the third largest cause of death in the world. Due to lack of awareness and less patient to doctor ratio it has become severe. So prior detection of this disease is necessary. With the advancement of computational equipment like GPU and with the availability of larger data-sets which are to be used for training complex neural networks; it has become possible to detect the brain tumor or any other disease automatically with the help of pre-trained network models. An MRI image is obtained by scanning the brain area with the help of MRI machine, which can be affected with several types of noises especially motion artifact because of relative motion of patient with respect to the MRI Machine. So a preprocessing step is necessary to remove the artifacts. Here we are going to use the Deep Learning for brain MRI segmentation. Deep learning refers neural network with more than 2 layers which can learn complex features inside an image. During the literature survey it has been found that CNN based image segmentation have achieved more than 90% accuracy in many cases as it utilizes the convolution operation between the image and kernel(filter) at its first step and then pooling, and the same task is repeated into various hidden layers depending upon the computational hardware capability and the size of data-set. CNN utilizes various filters which are used to detect specific features from the image. A general CNN architecture includes cascaded layers of convolution and pooling layers. Convolution layer performs convolution operation between image and filter matrix and pooling layer is used to reduce the number of parameters, to improve computational complexity by progressively reducing the spatial size of the network. Any particular layer includes various neurons which fire up depending upon the input, and in order to fire them, there is a special function called an activation function which is usually RELU and sigmoid function. Final hidden layer output is given to a fully connected layer where a sigmoidal function is applied to it.

Keywords: Deep learning, CNN, GPU, MRI etc.
Abstract Number: ICBME1392

An Evaluation on Effectiveness of Deep Learning in Detecting Small Object Within a Large Image

Nurul Nazirah Hassan, Fatihama Sahadattaly, Wai Ming Kong, Keng Wah Choo
Nanyang Polytechnic, Singapore

Objectives: Multiple Deep Learning (DL) algorithms have been developed recently and are shown to be achieving very high accuracy in object detection. However, challenges have been reported in detecting small objects within a large image (e.g. >2000 by 2000 in resolution). Various methods have been proposed using different detection algorithms in order to detect small objects. However, these approaches require high computational resources and are not suitable for edge computing devices used for practical applications such as pedestrian traffic light detection.

Method: We explored two different methods of detection to evaluate which method is best at detecting small objects. The first method is a two-step procedure with the first step being image processing and the second step, a RCNN based detection using Edge Boxes algorithm for the extraction of region proposals. The second method is solely Faster RCNN Detection that processes the entire image for training. A total of 4000 streets images of Singapore with pedestrian traffic lights were used as training data. The dimensions of the images range from 1200 by 900 to 4000 by 3000. The small object to be detected is the green or red man within pedestrian traffic lights. We evaluated these methods based on training time required, detection time, precision and recall, as well as suitability for deployment in edge computing devices.

Result: From the experimentation, the RCNN detection with image pre-processing method has a faster training and detection time. The precision and recall of the method are considerably higher. Therefore, we concluded that the RCNN Detection with image Pre-processing is most suitable for the detection of small objects. It ensures high precision and is able to perform in real-time. Furthermore, the complexity of the algorithm does not overload edge computing devices such as smart phones or surface tablets.

Conclusion: Our research shows that deep learning algorithm such as RCNN is useful for practical applications such as pedestrian traffic lights signal detection. The high precision of RCNN detection and the simplicity of the algorithm ensures that it can be efficiently used in edge computing devices to serve practical usage.

Abstract Number: ICBME1457

Cancer Extraction and Prediction Mutation from Colon Cancer Histopathology Images Using Image Processing and Deep Learning

Kenichiro Hashimoto, Toshiyuki Tanaka
keio University, Japan

The number of patients with colon cancer is increasing in Japan. Diagnostic process of colon cancer has three method. First, specimens collected from patients are stained by hematoxylin and eosin. Second, pathologist diagnose and classify cancer type to normal tissue and adenoma and cancer. Third, specimens
Electromyography Signal Assessment of Muscular Pain through Measurement of Electromyography Signal

Jing Niu, Jun Ren Low
Nanyang Polytechnic, Singapore

Accurate pain assessment is crucial for making the correct diagnosis and determine the most appropriate treatment plan for patients with pain. The current gold standard for pain assessment is by patient self-reporting. The presence, frequency, location and many other parameters of pain are assessed based on self-report of patient. However, this method is not adequate for infants, toddler and individuals with major cognitive or communicative impairments. Although many researchers have been working on development of a physiology-based pain assessment, thus far none has been proven to be valid and reliable. The objective of this research is the proof of concept of the proposed non-invasive, physiology-based method which utilizes Electromyography (EMG) signal for muscular pain assessment. The method could enable accurate and easy assessment of the presence, frequency and location of muscular pain. A platform for pain assessment through acquisition and analysis of EMG signal obtained with re-usable dry electrodes has been developed. EMG signal is acquired using two dry contact EMG electrodes. Participants were recruited for data collection using the developed platform. The results showed a clear difference between the painful and non-painful stimuli. This study presents the possibility of developing an accurate, and easy to use measurement device for pain assessment.

Abstract Number: ICBME1301


Arata Yamamoto
Tokyo City University, Japan

Wireless power transmission has been already put to practical use as charge methods of consumer electronics such as mobile phones, and now, is also considered in the medical field. For example, The Resonance Coupling Wireless Power Transmission is proposed as the method to supply electricity to the implantable medical devices. With this system, it is possible to transfer power efficiently by matching resonance frequency between transmitter circuit and receiver circuit. Nevertheless, there are still some difficulties in applying that technology to the implantable medical devices. One of the problems is that the electrical characteristic of a receiver coil may unpredictably change after implanting it in the body. Up to now, however, few reports about the characteristic of implanted receiver coils have been presented. In this study, we researched the effects of internal environment on the spiral coils implanted in the rat body, and tried to reproduce the similar effects in vitro using physiological saline and agar phantoms to know what are the dominant causes of those effects. Small thin spiral coils of 40 turns were made with 0.2mm enameled copper wire. The effective inductance (Leff) and the effective loss (Reff) of coils were measured in the air and in the Rat abdominal cavity just after implantation. The implant surgeries were carried out under deep anesthesia complying with the guidelines for animal experimentation of Tokyo City University. In the body, both Leff and Reff increased in proportion to the driving frequency in the range of 100-5.5MHz. The increase in Leff should be due to the increase in stray capacity generated between wires of coil (Cself) because the self-resonance occurred at the low frequency of about 4MHz. We found that the similar phenomenon was observed in physiological saline. Therefore, the electrolytes in solution is considered to be the cause of large Cself. However, the large increase in Reff observed in the body was not occurred in saline. The similar increase of effective resistance was reproduced in the agar phantom and the degree of loss was increased as the concentration of agar was risen. This result suggests that, in the body, the Reff increase may be caused by some organic substances that can be the barrier to ion mobility. To define the dominant parameters that affect those electrical characteristics, some equivalent circuit models were examined to exactly represent the frequency characteristics of Leff and Reff. As a result, the effects of internal environment could be explained using a simple parallel resistor-capacitor model. Our findings may be useful for designing the system of resonance coupling wireless power transmission for implantable medical devices.

Abstract Number: ICBME1248
Abstract Number: ICBME1245

Effect of Photofrin-Mediated Photodynamic Treatment on Chemo-Resistant Leukemia Cells Over-Expressing P-Glycoprotein

Yuichi Miyamoto, Tomoki Sakuma, Ayato Sekiguchi
Saitama Medical University, Japan

Photodynamic therapy (PDT) is a treatment for malignant tumors employing the interaction of a photosensitizer with light of the appropriate wavelength in the presence of molecular oxygen. This treatment modality has been considered as a possible approach for the mechanism of multidrug resistance (MDR) in spite of its therapeutic potential towards chemo-resistance tumor cells is still unclear. MDR mediated by drug efflux ATP-binding cassette transporters. P-glycoprotein (P-gp) is well-characterized transporters associated with chemoresistant mechanisms of various drugs. In the present study, we conducted a comparative examination of the cytotoxic effects Photofrin-mediated PDT on human chronic myelocytic leukemia K562 and its doxorubicin-resistant subclone K562/adr cells.

K562 and K562/adr cells were seeded into a 96-well flat-bottom culture plate at a cell density of 10x10^4 cells/well. The medium in each well was replaced with 10 µg/mL Photofrin-containing PBS(-) and incubated for 15 minutes. The cells were then washed with fresh medium and irradiated in the medium using a continuous wave laser at a wavelength of around 640 nm. The laser irradiation was carried out with an average fluence rate of 10 mW/cm^2 at light dose of 0.5, 1.0 and 3.0 J/cm^2. The cytotoxic effects of the PDT were estimated by XTT viability assay. The relative amount of P-gp expression between K562 and K562/adr cells was determined by fluorescence antibody technique (CD243 (P-glycoprotein)-PE) using a flow cytometry.

The viability value of the K562/adr cells without the PDT was three-fold more than that of the K562 cells. Both viability values were found to decrease with the increasing light dose. The value of the K562 and K562/adr cells viability normalized by each control (without PDT) at 3.0 J/cm^2 was 42.1% and 27.0% respectively. The relative expression rate of P-gp of the K562/adr cells was 1.5 times higher than that of the K562 cells. These findings suggested that the Photofrin-mediated PDT is effective for chemo-resistant cells over-expressing P-gp.

Abstract Number: ICBME1100

Efficient Cnn-Based Wound-Bed Segmentation for Mobile Applications

Ee Ong, Christina Ka Yin Tang, Beng-Hai Lee
Institute for Infocomm Research, A*STAR, Singapore

Objective: The objective of this work is to develop an iOS mobile application that enables automatic, fast, and accurate wound-bed segmentation.

Method: We propose a deep learning convolutional neural networks (CNN)-based architecture for wound-bed segmentation. Our network consists of an encoder block and a decoder block. Here, we used 5 down-sampling layers and 5 up-sampling layers (note that U-Net uses similar strategy but only 4 down-sampling layers and 4 up-sampling layers). The up-sampled feature maps are concatenated with encoder feature maps skipped from corresponding resolution levels on the contracting path at every resolution level to form a ladder-like structure. We designed our network by applying a stack of depthwise separable convolutions. This is different from U-Net where conventional standard convolutional filters are utilized. Each ‘depthwise separable convolution’ block consists of depthwise convolution, batch normalization, rectified linear unit (ReLU) activation, pointwise convolution, batch normalization and rectified linear unit (ReLU) activation. The ‘depthwise separable convolution with strides 2x2’ block in encoder part of the network consists of depthwise separable convolution operations performed with strides of 2x2, thus effectively down-sampling the layers by 2 in both directions. In this regard, we do not employ pooling explicitly in our CNN-based segmentation model (in contrast to max poolings being used in both FCN and U-Net). The up-sampling block in decoder part of the network consists of transposed 2D convolutions with strides of 2x2. We added a dropout layer after every ‘depthwise separable conv’ block. Our network has 2 parameters, ‘alpha’ and ‘alpha_up’, to control the number of filters used and hence provides a trade-off between speed and accuracy.

Results: Our proposed method was evaluated on a dataset of 583 chronic wound images collected from local hospitals and the ground truth was manually annotated by nurses. Our model is trained using a single NVIDIA Titan X GPU. When alpha = 1.0 is used, our proposed model gives better results in terms of both pixel accuracy and mean intersection-over-union (IOU) (0.941 and 0.869 respectively) compared to that of the U-Net model (0.915 and 0.813 respectively). In addition, the training time of our network is only about 40.2% of that needed to train a U-Net. Also, our network has much smaller number of parameters and tensorflow model file size (about 18.1%) that of U-Net. We have successfully converted our trained model to Apple CoreML model to run on an iPad. Our experiments show that we could achieve real-time wound-bed segmentation because of the small foot-print of our model.

Conclusions: We propose a fast and efficient CNN-based segmentation network that has much smaller number of parameters than U-Net, and requiring much less computational time to train than U-Net as well. We have shown that our proposed model achieves better performance in terms of both pixel accuracy and IOU segmentation evaluation metrics compared to that of the U-Net. Finally, we demonstrated that our model could be deployed to run in real-time on portable iOS devices such as an iPad.

Abstract Number: ICBME1109

Vital Sign Acquisition Using Doppler Radar under Random Body Movements Rejected by Pca Algorithm

Yuki Iwata, Koichiro Ishibashi, Guanghao Sun
The University of Electro-Communications, Japan

Background and Objective: Vital sign measurement using a continuous wave (CW) -Doppler radar technique is widely applied where non-contact detection and privacy protection is required, such as infection screening in quarantine stations and sleep monitoring system in home healthcare. However, CW-Doppler
raster measures velocity of chest surface movement consisting of cardiac and breathing signals with random body movement noise. Therefore, extracting cardiopulmonary information from the superimposed signal is a remaining challenge. Our objective is to remove the signal caused by the movement of the body and breathing, moreover, extract the heartbeat signal from the superimposed signal without relying on simultaneous measurements with other sensors.

Method: We proposed a novel adaptive algorithm based on a matched filter using a principal component analysis (PCA) to estimate the heartbeat signal measured under the breathing and random body movements. The proposed algorithm consists of four processes. Initially, we divide the measurement data at regular intervals and format a signal matrix. In this step, the interval is set to 2 sec in order to include 1-2 beats. Next, the signal matrix is decomposed using a PCA obtained by eigenvalue decomposition of its covariance matrix. Then, we compose template signals called a feature vector using lesser significance (i.e. low eigenvalues) eigenvectors. Finally, the matched filter can be realized by convolving the measurement data with the template signal. These processes are based on the fact that perturbation of the chest surface caused by the cardiac movement is much smaller than the movement of the body and breathing.

Results: The proposed algorithm was experimentally evaluated on 18 actual measurement data obtained by 6 healthy subjects. In the experiments, the chest perturbation was recorded while subjects keep their nature breathing for 3×10 minutes using CW-Doppler radar, and the ECG signal was recorded simultaneously as a grand truth. As a result, the average error of heartbeat per minute of 2.34 bpm and the average root mean square error of R-R intervals of 0.186 sec was obtained.

Conclusion: The proposed adaptive algorithm based on PCA showed good performance on extracting heartbeat signal from the CW-Doppler radar for vital sign measurement.

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Abstract Number: ICBME1133

Analysis of the Influence that the Different Format of the Sound Source Gives in the Brain of Listener

Rikiya Aida, Kazushige Magatani
Tokai University, Japan

Recently, music media recorded in many types of audio formats are commercially available. The recording characteristics differ depending on the difference in these formats, it is said that the difference can hardly be distinguished when a person listens to music. However, some person can find differences between these formats, and for these persons, we thought that differences in audio format give differences in perception of the human brain. In order to find these differences in perception of the human brain, we are recording and analyzing EEG when human listen to sound sources recorded in different formats.

In this study, we use CD format (44.1 kHz sampling, 16bit quantization) as a standard sound source, high-resolution format (96 kHz sampling, 24bit quantization) that is considered to have better sound quality than CD, and MP3 as typical compression sound. The subject listened to the same music recorded in these three types of format for about 3 minutes, and the 16 channels of EEG during this time were recorded with an EEG recorder. The electrode arrangement used for EEG recording was in accordance with the international 10-20 method.

In the experiment, all subjects wore headphones that can reproduce up to 40 kHz. After performing calibration so that the volumes reproduced by the sound sources of the three types of formats coincide, the subjects listened to the same music in the order of MP3, CD, and high-resolution without notifying the order of format. The hearing of all subjects participating in the experiment was normal.

The EEG for each format was extracted for about 20 seconds from the point of 40 seconds after the music was started, and wavelet transform was performed. Also, the extracted 20 seconds data was divided into five segments of 4 seconds each, and each segment was subjected to Fourier transform to calculate a power spectrum for each segment. By comparing the two types of data, the fluctuation of the subject’s EEG for the sound source recorded in each format was analyzed. It is possible to analyze the frequency fluctuation of the EEG with high time resolution by the wavelet transformed data. And it is also possible to evaluate the global EEG fluctuation from the power spectrum of five segments.

From the experimental results, the following was clarified.

In the case of the high resolution sound source, the power of subject’s EEG greatly fluctuates in the band of 8 to 12 Hz as compared with the sound source of the other format.

In case of MP3 with a bit rate of 256 kbps, a difference with the CD sound source is hardly detected, but in case of MP3 with a bit rate of 128 kbps, a pattern of EEG different from CD is detected. From these results, we think that a person detects a difference in music format to some extent. We would like to increase the number of experimental data and study in more detail in the future.

Abstract Number: ICBME1157

Quantitative Evaluation of Skin Micro-Relief in Different Age Groups by Image Analysis

Yue Wu, Toshiyuki Tanaka
Keio University, Japan

Objectives: Skin is the biggest organ in the human body and has a lot of functions such as protection from Ultraviolet light. Although the skin is smooth, the surface is not even, especially with age increases. Skin micro-relief is a pattern of network consisting of furrows, polygonal forms, and pores. Skin micro-relief takes an important role in both skin detection and skin condition evaluation. Skin micro-relief has been researched using various methods and devices. Usually skin micro-relief related parameters are as follows. (1) Skin surface, such as skin roughness, (2) pores, (3) skin furrows, (4) skin closed polygons. However, the most essential parameter of skin micro-relief and the relationship among these parameters are still unknown. This study aims to evaluate skin condition using skin micro-relief...
images quantitatively and comprehensively. We establish an image analysis method to extract the skin micro-relief related parameters, assess the most essential parameter among them and calculate the relationship. Also we apply the method in researching age-related change.

Methods: Skin images are obtained by the microscope, with a camera, white LED lamps and UV-LED lamps. 150 healthy Japanese females aged 3-60 years are enrolled in the research. Skin micro-relief images in cheek are obtained. These images are preprocessed before feature extraction. There are nine parameters included, which are skin roughness, skin anisotropy, number of pores, area of pores, skin furrows length, width, depth, number of polygons and area of polygons. ISO (International Organization for Standardization) areal topography is used to evaluate skin roughness. 2D Fourier transform is used to evaluate skin anisotropy. Pores are extracted by scanning the image with a specific circle. Then the number and mean area of pores are counted. Skin furrows are extracted using the short straight line matching method, and length can be counted. After the thinning operation, the width can be calculated. Depth is calculated according to color difference. Skin closed polygons are extracted by watershed segmentation and area of them is counted. The number of polygons is counted by labeling. After these parameters are extracted, we applied PCA (Principal Component Analysis) to explore the most essential parameter and propose a new comprehensive parameter SMR (Skin Micro-Relief) to evaluate skin condition according to these parameters. Continually we investigate the variation in SMR with age and searched the difference among age groups.

Results: The skin surface micro-relief can be conveniently quantified with the parameter SMR. The value of SMR increases with age. Conclusions: The parameter SMR proposed to analyze skin micro-relief is an effect and comprehensive tool to characterize the skin condition. The method in combination with other skin indexes like skin color, skin sebum may be applied to the quantified evaluation of skin aging.

Abstract Number: ICBME1211

Classification of Dementia MRI Images Using Hybrid Meta-Heuristic Optimization Techniques Based on Harmony Search Algorithm

Bharanidharan N, Harikumar Rajaguru
Bannari Amman Institute of Technology, India

Background: Magnetic Resonance Imaging (MRI) is the popular modality used to diagnose dementia and there is a huge necessity for an automated MRI classification algorithm to assist the clinician during diagnosis. Harmony search based hybrid optimization techniques are widely reported for solving numerical optimization and feature extraction problems. To the best of our knowledge, there are no reports in the literature regarding the usage of harmony search based hybrid optimization techniques to classify medical images.

Objectives: The main objective of this research work is to categorize the brain MRI images as demented and non-demented using harmony search based hybrid meta-heuristic optimization algorithms. With appropriate modifications on original algorithms, the classification performance of four meta-heuristic techniques namely Particle Swarm Optimization (PSO), Artificial Bee Colony (ABC), Ant Colony Optimization (ACO), Harmony Search (HS) is tested individually. Then the performance of HS-PSO, HS-ABC, and HS-ACO are analyzed.

Methodology: For this analysis, 65 non-demented and 52 demented subjects collected from Open Access Series of Imaging Studies (OASIS) are used. The input image is divided into 16 regions and five statistical features namely mean, variance, skewness, kurtosis, and entropy are extracted for each region and these 80 (16 regions *5 features) normalized statistical features are used to initialize the solutions. After reaching the maximum number of iterations, an adaptive binary thresholding algorithm is used to categorize the input as demented or non-demented. During iterations, the solutions of HS will always lie between the upper limit and lower limit while the solutions vary without any bounds in PSO, ABC, and ACO. This feature of HS makes it suitable for hybridization. The direct intensity values are used to initialize the harmony memory of HS in hybrid algorithms. The solutions of PSO or ABC or ACO are initialized with 80 normalized statistical features extracted from the output matrix of the HS algorithm.

Results: With optimum control parameters, the PSO provides the classification accuracy of 65.81% while the accuracy of ABC is 60.68%, ACO is 56.41% and HS is 61.53%. As a hybrid classifier, HS-PSO provides the highest accuracy of 83.76% while the accuracy of HS-ABC is 70.94% and HS-ACO is 66.67%.

Conclusion: The classification performance of individual meta-heuristic classifiers is largely improved by the usage of hybridization with Harmony Search. In future, the performance can be further improved by using various parameters like age, sex, total intracranial volume, etc.

Abstract Number: ICBME1340

Artifacts Rejection Based on the Identification of the Optimal Independent Components in an Electroencephalogram During a Cognitive Task

Kazu Kato, Takato Suzuki, Hiroyuki Kadokura
Tohoku Gakuin University, Japan

We have been developing an artifact removal method for the eye blink and movement in electroencephalograph (EEG) recordings. We proposed an identification technique of the optimal independent components (ICs) for noises that integrates independent component analysis and K-means, a type of machine learning [1]. We evaluated the performance of the method only for artificial EEG noises superimposed on eye-blink through an eye-movement template on a resting EEG. We conducted a study to evaluate the performance on the proposed method using real EEG data during a cognitive task, an implicit association task (IAT) [2] as it is known to allow for the detection of implicit biases in individual subjects. In this task, images or characters are presented visually, and thus many artifacts associated with eye blink and movement contaminate the EEG. The task constituted of seven blocks i.e. block-1-7. A 28-channel EEG was measured for block 3 consisted of 20 stimulus presentations, block 4 of 40, block 6 of 20, and block 7 of 40, respectively. The proposed method was applied for the
raw data. The first ICs of the selected 19 principle components of the analysis preventing overlearning of the ICA were identified for block 3, as well as the first IC for block 4 and for block 6, and the second IC for block 7, and these components were rejected. Then, Event-related potentials (ERPs) were obtained to evaluate the performance of the proposed method. ERPs were performed by averaging epochs (120 epochs at maximum), with the exception of those that included artifacts exceeding 50 mV using one subject. The proposed method showed that 30 epochs were eliminated from a total of 120 epochs, whereas 61 epochs using a conventional method without the rejection of independent components associated with the artifacts. The results showed that the proposed method performed well, and that its performance was acceptable and it can be used for visually cognitive tasks such as IAT as well as in artificial EEG.


Abstract Number: ICBME1363

Frequency Domain Near-Infrared Diffuse Optical Tomography Using Square-Wave Driving Light Sources

Yan Yang Hsu
National Central University, Taiwan

Objectives: This study aims to develop a novel measurement scheme for frequency domain near-infrared (NIR) diffuse optical tomography (DOT) in the application of breast tumor detection. The unique part is supplying square-wave driving NIR light sources to obtain amplitude and phase delay data for the reconstruction of tissue optical-coefficient images. Compared with the sine-wave powered ones, the former enables to gain more optical information at the same detecting time, improving the crosstalk between absorbing (ma) and scattering (m’s) coefficient; also strengthen the contrast between normal and tumor tissues. In clinical, it can play a role of assistance for mammography, declining the rate of false diagnosis.

Methods: A frequency of 29 MHz square-wave power supply is applied to excite 785 and 830 nm NIR laser diodes that generate the light to penetrate phantoms. In the path of penetration, the absorbing and scattering matters in phantom suppress light intensity and delay phase. The optical information is collected by photomultiplier tube and converted into electrical signals that are acquired by NI data acquisition card for subsequent calculation. The amplitude decreases delta A and phase delays delta B for the first three harmonics, i.e. 29, 87 and 145 MHz, of square wave can be captured through comparing with their reference signals. Eventually, the corresponding optical-property images could be reconstructed using an in-house-coded image reconstruction scheme based on the diffusion equation solved using the finite element method including forward and inverse algorithms. In the study, two phantoms were designed including cylindrical background with elliptic tumors and breast-shape one with round tumors. According to the published studies, tumor tissues possess a two- to four-times of absorbing contrast to the normal one, meanwhile a one- to two-times of scattering contrast. Thus, each shape of the phantoms was further divided into two sets, of which the tumor contrasts compared with the background imply [ma, m’s] = [4, 2] and [2, 1].

Results: After the measurement and image reconstruction using sinusoid and square-wave driving power, the latter one obviously improves the crosstalk between ma and m’s; besides, the computed contrasts between tumor and background has visible tendency of enhancement.

Conclusions: Using square-wave power supply to drive laser diodes, more optical information can be gained simultaneously compared to the sinusoid one. This dramatically decreases data acquisition time. Besides, it’s clear that the crosstalk between ma and m’s can be improved for the contrast between background and tumor. By this way, we achieve to better distinguish tumor from normal tissue of breast, and expect to get precise locations of tumors. In the study, the measurement responses of individual components that affect the signal to noise ratios are addressed.

Abstract Number: ICBME1370

A Doorknob Mounted Active ECG Electrode System for Personal Identification

Kosuke Sasaki, Yamamoto Arata, Tatsuta Masahiro, Kyoso Masaki
Tokyo City University, Japan

The spread of Internet connection has made the world to a highly advanced information society. In this society, protecting personal information is getting important. Password has been used for protecting personal information. But brute force attack and peeping can unlock the password key. Recently, as a solution for the problems, biometrics authentication attracts attention. For example, fingerprint authentication, iris authentication, face authentication are developed. But they have vulnerability such like copied fingerprint and facial photograph.

In this research, biometric authentication using ECG is focused on. ECG is difficult to be copied because it doesn’t leave trace. Especially, high frequency electrocardiogram (HFECG) has individual difference. However, ECG is usually measured with electrodes placed on the skin. This method is not suitable for practical ECG authentication system.

In this research, capacitive electrode was used to obtain ECG under unrestricted manner. Our final goal is measuring ECG from door knob and floor, and unlock the door with biometric authentication by HFECG.

In this report, three electrodes were prepared to measure ECG, and measuring ECG from door knob and floor with capacitive electrodes was tried. The first electrode was copper foil electrode which was installed on doorknob grip. This electrode was applied gold plating to avoid oxidation. This is a contact type electrode. The size of electrode was 35mm x 35mm. The other two were capacitive electrodes which were
made of copper substrate covered with PVC film. Electrode for different electrode was 40mm x 60mm. The other for indifferent electrode was 200mm x 300mm. These two electrodes were improved with additional circuits. The back side of different electrode was connected to a voltage follower circuit to reduce output impedance. The indifferent electrode was connected to differential amplifier circuit including driven right leg (DRL) circuit to remove noise made of common-mode noise. Capacitive electrodes were contacted to subject’s feet and subjects held door knob on right hand. As the comparative measurement, Ag/AgCl electrodes were attached same points. ECG were measured for five men in their twenties for two times. ECGs were measured without prepared circuits. Next, ECG were measured using them. Measured ECG were filtered 0.5Hz ~ 300Hz, and amplified to 46dB. ECG were evaluated by frequency analysis, and PSD were obtained. Integral values of each PSD were calculated. Integrated PSD of ECG measured using Ag/AgCl electrodes subtracted integral values of integrated PSD of ECG measured using circuit and integrated PSD of ECG measured without them. Noise improvement were evaluated by subtracted values. Subtracted value calculated from ECG using circuits were lower than subtracted calculated from ECG without them. And it was shown that measuring ECG from door knob and floor was possible.

Abstract Number: ICBME1373

Four-Dimensional Flow MRI Assessment of Valvular Flow Characteristics: Systolic Flow Patterns, Direction and Velocity of Supra-Valvular Jet in Experimental Bicuspid Aortic Valve Models

Kaoru Hattori, Jumpei Takada, Ryoh Kumazawa, Gohki Nishimura, Ryoh Moriwaki, Natsuki Nakama, Eita Kawasaki, Michinobu Nagao, Yasuhiro Goto, Hiroshi Niinami, Kiyotaka Iwasaki
Tokyo women’s medical university, Japan

Objectives: Time-resolved 3-dimensional phase contrast magnetic resonance (4D flow MRI) is a non-invasive and visually appealing tool for assessing blood flow characteristics. The aim of this study was to investigate, in-vitro, influences of 2 cusp angles of bicuspid aortic valve (BAV) on hemodynamics in the aorta using 4D flow MRI. Methods: Tricuspid aortic valve (TAV) and 2 types of bicuspid aortic valve (BAV) with different cusp angles of 180°~180° (symmetric BAV) and 240°~120° (asymmetric BAV) were prepared using porcine aorta and bovine pericardium. A MRI compatible pulsatile flow circulation system was developed. The pulsatile flow circulation system consisted of 3D-shaped aortic arch model, - a ventricle model, an aortic compliance model, a resistive unit, and a pre-load chamber connected to the ventricle model. Systolic flow pattern, direction and velocity of supra-valvular jet in the aortic part of the flow circulation system were assessed using 4D flow MRI. Results: The 4D flow MRI analysis showed the presence of a nested helical flow in the aortic arch, which was remarkable in the proximal part of the aortic arch model and almost normalized in the distal part of it, in the BAV models. The MRI analysis also demonstrated an eccentric supra-valvular jet toward anterior direction especially in the asymmetric BAV model. The velocity of the supra-valvular jet was 0.88, 1.71 and 1.48 m/sec in the TAV, the symmetric BAV and the asymmetric BAV models. Conclusion: This study indicated that the direction and velocity of supra-valvular jet might be influenced by 2 cusp angles of the BAVs.

Our experimental model consisted of a MRI compatible pulsatile flow circulation system and tissue-based aortic valve models was useful for assessing valve-related flow characteristics using 4D flow MRI.

Abstract Number: ICBME1377

Scanning through Using Flexible Channels for Prone Diffuse Optical Imaging System

Min-Chun Pan, Hao-Che Chang, Yen-Yang Hsu, Pei-Ting Liu, Ya-Fen Hsu
National Central University, Taiwan

Objectives: Our previous scanning module for a prone diffuse optical imaging (DOI) system using three zones with two light sources in each zone enables the acquisition of 6-source and 30-detection data during the optical information collection phase. The numbers of zones and light sources in each zone can be determined and adjusted up to need. It is frequently observed while a woman prostrates herself the cross section of breast is not always circular, but even elliptic. This may result in the effects of geometrical mismatch if one reconstructs diffuse optical images employing prone-type optical data obtained through fixed move-in-move-out channels. In the study, the flexible source-detector channels in the scanning module of imaging system were designed; further, the breast contour estimation was achieved by using optical displacement sensors without applying other structural imaging modalities.

Methods: A prone DOI system has been updated through implementing flexible optical channels. As an elastic tolerance with 20 mm was designated, the modified scanning platform thus enables to measure a maximum major axis 170 mm and a minimum minor axis 60 mm if the imaging task is performed on the subject with an elliptical contour. Twelve optical displacement sensors are mounted to measure the local moving distance when the optical channels reach the test subject and still translate inwards. To examine the estimation of a non-circular contour an inclined cylindrical phantom (80 mm diameter) with a leaning angle of 20° and 40°, respectively was employed. Numerical simulation to demonstrate the effects of geometrical mismatch was performed. Two elliptical phantom models with two inclinations along major and minor axis, respectively, were synthesized. Two situations are compared, one mimics fixed move-in-move-out optical channels and the other flexible optical channels. Besides, the measurement was performed on a 80 mm cylindrical phantom as well as the phantom with a 15° inclined angle to illustrate and compare the reconstructed images resulting from using fixed and flexible optical channels.

Results: The noncontact displacement measurement precisely indicates the positions of detection fibers, and thus the contour of test phantoms can be estimated. It is expected during clinical trial those optical fibers leaning on breast for optical data collection can estimate breast contour without using other structural imaging modalities. The reconstructed images using optical data from flexible channels clearly prevent the effects of geometrical mismatch so as not to distort the inclinations.

Conclusions: The benefits brought by this scanning scheme using non-fixed architecture with flexible channels are several folds.
Preprocessing to Handle Data Analysis Issue for Clinical and Tele-Rehabilitation

Min-Chun Pan, Sheng-Nan Li, Hao-Ting Chen
National Central University, Taiwan

Objective: Besides conventional subjective evaluation by physical and occupation therapists, in clinical rehabilitation inertial sensing data have been extensively acquired for objective evaluation. It is essential to assure and validate the collected data meaningful for subsequent analysis as well as in all engineering disciplines; but, a systematic approach is lacked to this purpose. Medical personnel in clinical environments usually possess no engineering background to handle measured sensing data, and to determine whether the acquired sensor signals are available and meaningful for subsequent analysis. Thus, in hospitals and tele-rehabilitation the inertial sensing system with a module to automatically screen and discard polluted useless data is an unmet need. This study aims to develop a signal preprocessing and screening system to determine the availability of inertial sensing data that are often acquired in rehab engineering tasks.

Method: This implemented screening system supplies three functions including (i) data cleaning and combination, (ii) data selection and conversion, and (iii) data mining. It was first justified by the collected wireless IMUs data from healthy subjects; further, the measured rehab task data in the clinical setting for walking and shoulder flexion IMU data were processed to examine its validity.

Results: The results show it enables to rapidly screen a large number of rehab data, and to provide users judgment on the validity of acquired data. Conclusions: Meaningless data to be processed in a big-data analysis for any data driven issues may disturb the convergence of the task, permits no conclusion and even misleads the classification and judgement. This study accomplished a data screening system to exclude and discard polluted and meaningless inertial sensing signals. The system was validated through using clinical data for both lower-limb IMU signals from degenerative arthritis patients and shoulder flexion IMU signals from hemiplegia patients. The results are promising and it is expected to aid medical personnel for data acquiring; especially, this screening function can be considered as a data preprocessing module for tele-rehab devices.

Abstract Number: ICBME1388

Faster RCNN Method for Detection of the Common Carotid Artery Transverse Section in B-Mode Ultrasound Images

Pankaj Jain, Neeraj Sharma
Indian Institute of Technology (BHU), Varanasi, India

Objective: Common carotid artery contains information regarding the patient’s cardiac health. Cardiologists get major information related to the patient’s cardiac health through its’ carotid artery stiffness, its’ lumen diameter (LD) and its’ carotid intima-media thickness (cIMT). Thus the primary concern of the radiologists is to locate the artery in B-mode ultrasound image correctly. Manual methods of localisation of the artery are time-consuming and may lead to error, while the automated approach may provide the localisation of the artery at real time. After localisation of the artery at real time, the arterial parameters may be determined at real time as well. With the modern deep learning technique, convolutional features replaced custom built features. The depth of the neural network refines the convolutional features, which is dependent on the CPU speed. The advent of modern graphics processing has aided in the enhancement of CPU operations.

Method: With the advancement in the technique, more fast and accurate methods are in demand. With the advent of modern graphics processing units, high-performance computing (HPC) methods have been developed. Deep neural networks based on deep learning techniques are an example of such high-performance computing methods. Deep neural networks are built up with interconnection of convolutional layers, activation layers, batch normalisation, fully connected layers, pooling layers, with the appropriate depth of the layers. This paper describes a novel method for the localisation of the common carotid artery (CCA) transverse section known as fast region based convolutional neural network (FRCNN). This automated method is designed using the stack of the convolutional layers, fully connected layers, and pooling layers. These organised layers are used twice for the prediction of the transverse section of the CCA, once for the generation of the proposal of the region and secondly for the classification of the region. B-mode ultrasound images of the transverse section of the CCA are exposed to the above network. Based on the training and validation data split three modes of partition protocols is used here K=2, 5, 10. Also for achieving the very fine-features from the feature map, training has been extended for 200, and 2000 epochs.

Results: We obtained a bounding box around the cross-section of the carotid artery with the score of prediction. We achieved validation accuracy of 95% after 2000 epochs for K=10 partition protocol (training 90%, testing 10%). Mean validation accuracy for K=10 partition protocol is 89.36%, which matches very close to testing accuracy of 87.99%.

Conclusion: This is an automated method involving modern deep learning technique and demonstrating accurate localisation results in carotid artery transverse section.

Abstract Number: ICBME1394

Performance Evaluation of High Frequency ECG Personal Identification under Uneven Heart Rate Condition

Satoshi Kawaguchi, Masaki Kyoso
Tokyo City University, Japan

We have propose ECG personal identification technique. It realizes safe, unaware identification applicable for daily health care. Especially, we have focused on high frequency component
in ECG (HFECG). It was already shown that HFECG gave excellent identification performance in the previous study. However, effects of heart rate (HR) change to performance has not been evaluated well. In this report, effect of HFECG measured under exercise load to the identification system was evaluated. Two kind of measurement under resting state and ergometer load were done for each collaborator. Measured ECG was filtered with the frequency band width between 40Hz and 150Hz to extract high frequency component. Beat by beat HFECGs were extracted and sorted by HR. HFECG wave samples were recognized by using three layered artificial neural network (ANN). ANN was trained with HFECG wave samples in resting state. HFECG wave samples at various HR were applied to the trained ANN. The performance was evaluated with recognition rate. Dependency between heart rate change and performance is evaluated. The ratio between instantaneous HR and HR in resting state was used for HR change index. HFECGs from five adult collaborators was evaluated. The result shows that HR change index exceeding a certain level gives largely degraded performance.

Abstract Number: ICBME1434

Dynamic Sleep Stage Transition in Sleep Apnea Patients with Parkinson’S Disease

Kohzoh Yoshino, Saki Inomoto, Saki Morita, Akinori Iyama, Saburo Sakoda
Kwansei Gakuin University, Japan

Parkinson’s disease (PD) is caused by the degeneration of dopamine neurons in the midbrain. About half of all PD patients have sleep apnea syndrome (SAS). Sympathetic cardiac overdrive is observed in SAS patients, whereas degeneration of the sympathetic nervous system is observed in PD. As such, there may be differences in the sleep pathophysiology between SAS patients with PD (PD+SAS) and SAS patients without PD. Since non-motor impairment precedes motor impairment in not few number of PD patients, the early detection of PD in SAS patients may be partly possible by detecting abnormalities in non-motor impairment. We focused on the sleep stage transition pattern in this study. The aim of this study was to clarify the differences in the dynamic sleep transition pattern between SAS patients with and without PD. Twenty-two patients with SAS and 19 patients with PD+SAS underwent overnight polysomnography (PSG) at Toneyama National Hospital. The time series of sleep stages were scored from the PSG data by a sleep technician. The experiment and the data analysis were approved by the research ethics committee of the National Hospital Organization Toneyama National Hospital and by the medical research ethics committee at Kwansei Gakuin University, respectively. The normalized transition probabilities of sleep stages were calculated. Moreover, the duration time distribution of each sleep stage was calculated. No significant differences were found in the static sleep stage indices (e.g., sleep efficiency) between the two patient groups, but several dynamic sleep stage transition indices showed significant differences. Significant differences were observed between the PD+SAS and SAS without PD patient groups in the normalized relative transition probability from the REM sleep stage to the waking stage, and that from the REM sleep stage to the NREM1 sleep stage. Since sleep apnea events likely occur during the REM sleep stage, this result implies that the arousal response to the sleep apnea event is not sensitive in the PD+SAS patients compared with the SAS patients without PD, probably because of the dysfunction of their sympathetic nervous system. Moreover, significant differences were noted between the two patient groups in the duration time distribution of the waking and NREM1 sleep stages. Thus, PD+SAS patients tend to have difficulty in returning to sleep compared with SAS patients without PD.
The condition of the skin has a great influence on human impression, so there is an interest in skin care to improve the condition of the skin. However, since skin conditions vary widely, it is important to choose the skin care that suits you. In order to select appropriate skin care, it is necessary to understand your skin condition correctly. Therefore, there is a growing demand for skin diagnostic systems.

According to previous researches in Japan, it is believed that people feel that the skin with no stickiness, transparent, and moisture is beautiful. They are deeply related to the amount of melanin, hemoglobin and specular reflection, and it was found that beautiful skin had both low levels of melanin and hemoglobin, and high specular reflection by moisture. Considering that texture, which is a structure on the skin surface, greatly affects specular reflection, we decided measuring and evaluating “color,” “texture,” and “moisture and sebum” that greatly affect the beauty of the skin. The purpose is to make a comprehensive assessment of skin condition from these elements.

First of all, the specular reflection of the well-textured skin leads to the beauty of the skin. We focused on the periodicity of the concavo-convex structure and proposed a method to evaluate the texture by processing the skin image using the two-dimensional Fourier transform.

Pigments that affect skin beauty include melanin and hemoglobin. Melanin is a pigment that affects the blackness, and hemoglobin makes up the redness. According to previous researches, skin with less melanin and hemoglobin feels beautiful, so on the image, it is thought that skin color is bright and skin with less redness feels beautiful.

Individual typology angle (ITA) was used as a method to evaluate the brightness of the skin. Since ITA is an index derived from white skin, we confirmed whether it could be applied to Asian skin. We asked for ITA of skin images and we marked images we felt dark and bright, we were able to obtain a correlation with the value of ITA.

Then the hue angle was used to assess skin redness. The hue angle is a method of expressing the degree of color by an angle. The skin color is considered to be located between 0° "representing red and 90° representing yellow. According to our experiments, there is a correlation between visual evaluation and hue angle, and as expected all hue angle values were between 0° to 90°, so the hue angle was used to evaluate skin redness.

Skin beauty can be evaluated from the “texture”, “color” and “moisture and sebum". In this study, we proposed a method using Fourier transform as an evaluation method of texture. Currently, we are devising a method using ITA and hue angle to evaluate skin color. In the future, we will propose a method for evaluating moisture and sebum, and finally aim to propose a method for comprehensively evaluating the skin based on these three factors.

In brain tumor surgery, when surgeon decide tumor resection region, they need to grasp the brain structure such as brain sulcus and blood vessel that around the tumor, and tumor area that is different according to patient exactly. Therefore, the expert surgeon estimates the brain structure from various pre-operative and intra-operative information and the visual information of the limited operating field based on own knowledge and experience. But it is difficult to the young surgeon that grasp the brain structure and tumor position intuitively. In this method, matching the feature quantities that extracted from pre-operative and intra-operative MR Images to microscope images to enable the surgeon to grasp the brain structure and tumor position intuitively. In this method, matching the feature quantities that extracted from pre-operative and intra-operative MR Images and microscope images, and overlay the feature quantities on the microscope images. For the feature quantities from MR Images, extracting the information of blood vessel, brain sulcus and tumor for the blood vessel information, using the pre-operative MR Images because it is higher resolution than intra-operative MR images and considered possible to extract thin blood vessels. Extracting blood vessel information using Vascular Modeling Toolkit, and integrate the blood vessel information extracted from pre-operative MR Images into intra-operative MR Images using the non-rigid registration in order to corresponds the brain shift during operation. For the brain sulcus information, using the intra-operative MR Images, do the brain sulcus identification processing using the brain image analysis software Brain VISA. For the tumor information, using the T2-weighted MR Images because tumor region is shown with high brightness value, and segment the tumor region. After extracting each feature quantity, extract the region that included by craniotomy region from each feature quantity using information of craniotomy region from intra-operative MR Images. For the feature quantities from microscope images, extracting the blood vessel and brain sulcus information. For the blood vessel information, extract the blood vessel information by color gamut specification of blood vessel region on microscope image. For the brain sulcus information, marking the brain sulcus on the microscope image manually. The Information extracted from MR Images and microscope images is used as feature quantities, and matching these feature quantities by calculating the plane projection transformation matrix. Intuitive grasping of brain structure is enabled by projecting matched information on microscope images. By the proposed method, the accuracy by extracting blood vessel information from microscope images was 94.3%, the integration error of blood vessel information was 2.3mm on average, the integration error of brain sulcus information was...
Heart rate variability (HRV) reflects the state of the autonomic nervous system's activity. Thus, its patterns can be used to assess psychological moods in daily life. Few studies have investigated the relation between psychological mood and HRV patterns in daily life in the long term. Yoshino et al. proposed a method for assessing psychological tension using HRV that is optimized to individuals based on psychophysiological signals measured over a two-month period of daily life. However, this method has shortcomings: (i) it can only apply to the resting or low-level body activity state, and (ii) mood data are measured using a paper-and-pencil questionnaire, which might induce fake compliance. One way to solve the former problem (i) is to use body acceleration signals to remove the influence of body activity from the HRV indices. To avoid the latter problem (ii), ecological momentary assessment (EMA) method has been developed to register subjective mood states in daily life using a smartphone or wearable device. This study aimed to clarify the correlation between psychological mood measured by an EMA smartphone system and HRV indices, including moderate- or high-level activity state, and mood data are measured using an acceleration measurement device (myBeat, Union Tool, Japan) for 35 days in daily life, including in their sleep but excluding time spent bathing or showering. The participants registered their current 11 types of psychological mood level using the smartphone EMA system (Healthcare IoT Consortium, Japan) in response to alarm messages (nine times per day). Principal component analysis was applied to the mood data after the removal of body acceleration correction. Normal healthy males (N = 3; age, 22-30 years) participated in the experiment after providing their informed written consent. The experiment was approved by the medical research ethics committee at Kwansei Gakuin University. The participants wore an ambulatory instantaneous heart rate (RR-interval) and body acceleration measurement device (myBeat, Union Tool, Japan) for 35 days in daily life, including in their sleep but excluding time spent bathing or showering. The participants registered their current 11 types of psychological mood level using the smartphone EMA system (Healthcare IoT Consortium, Japan) in response to alarm messages (nine times per day). Principal component analysis was applied to the mood data after the values were normalized. The linear regression line between the mean body acceleration level and heart rate was obtained from each participant, and the residuals of the heart rate from the regression line were calculated to remove the influence of body activity from the variation of the heart rate. The first principal component of the mood data was interpreted as positive mood, and the second principal component was interpreted as vigor. The normalized residuals of the heart rate showed a significant positive correlation with both the first and the second principal component scores of the mood data (r = 0.14 and 0.17, respectively). This result implies that heart rate has a significant positive correlation with positive mood and vigor not only in the resting or low-level body activity state, but in the moderate or high-level body activity state as well.

Abstract Number: ICBME1456

Correlation Between Heart Rate Variability Patterns and Mood in Long-Term Daily Life

Ryota Maegaito, Kohzoh Yoshino
Kwansei Gakuin University, Japan

Pathological diagnosis is integral for decision-making in cancer treatment. In the first process, pathologists observe the lesion condition and specify tissue parts for microscopic diagnosis, all of which constitutes the gross pathology. Recently, image diagnosis became more popular for telepathology and data storage; however, the gross images conventionally obtained are not of sufficient quality to support diagnosis. For getting true color images of gross tissues and highlighting cancer area in the tissue, we propose a method of multispectral imaging to support gross pathological diagnosis.

We propose two methods to highlight the region where cancer is present. One method is simply based on overlapping specific wavelength's absorbance areas. In several trials, we used 450-nm wavelength for experiments. The second method is based on using principal component analysis in 7-band spectral imaging; it uses the first component as a basic factor that is not concerned with lesions and treats other components to highlight the cancer area on a special wavelength. We have evaluated multispectral imaging as compared to RGB imaging with respect to their efficacy of predicting cancer area using a special wavelength for highlighting.

For the experimental investigations, we developed a multispectral camera with seven LED illuminance wavelengths, i.e. 450 nm, 465 nm, 505 nm, 525 nm, 575 nm, 605 nm, and 630 nm, with 4k definition and obtained tissue images with the multispectral camera. We also obtained a regular RGB image as a control image. We prepared a fixed tissue that included skin carcinoma. To obtain correct spectral data, three normal tissue points and three cancer tissue points each were selected and measured by a precise spectrum using spectrometer. After getting seven bands of a multi-spectrum image, we reconstructed a spectral absorption image. Furthermore, we used a regular RGB image for comparison.

The reconstructed image from multispectral images showed a more precise coloring than the RGB image; this was observed quantitatively on the basis of difference recorded with a spectrometer value. In the case of the first proposal to highlight cancer area, the image from multispectral imaging had more detailed texture than the RGB image. In the case of the second proposal, the main absorption wavelength was around 525 nm, which was attributed to blood vessel-covered area by a pathologist.

These results show that multispectral imaging applied for gross pathological tissue image shows good performance to depict natural conditions, and thus, this method to emphasize color at a special wavelength absorption might provide a good prediction of the cancer area. Furthermore, it indicates the possibility to support pathological gross diagnosis of tissues with cancer. To get more precise parameters on highlighting cancer by applying spectrum analysis, we must obtain more samples in future studies.
Automatic Extraction of Atypia Keratinocytes from Oral Cancer Cytodiagnosis Images

Shohei Yokoi, Toshiyuki Tanaka
Keio University, Japan

In recent years, the feasibility of early detection of oral cancer by cytology was recognized. The diagnostic criteria were reviewed in 2015 in Japan and the examination for oral cancer in general dental clinics has been expanded. However, laboratory technologists and pathologists in charge of pathological diagnosis work have not mastered oral cancer cytology skills for early detection. Therefore, we propose a computer-based diagnostic support tool with the aim of connecting to a more reliable diagnosis of early detection.

We performed some processing on the cell images provided by the doctor and extracted the region of keratinized surface cells from the images. These cells are effective for early detection of oral cancer.

We used the generalized Laplacian of Gaussian (gLoG) filters for nuclear seed detection. The filters are widely used as a method suitable for detecting circular and elliptical objects. In this research, in order to speed up the processing, we created the filters which are the sum average of circular and elliptic filters in each direction (θ = 0, π/4, π/2, 3π/4). These gLoG filters are used to perform convolutional integration on the images and detected the nuclear seeds from the local maximum points in the output images.

In the previous research, we extracted the region where the brightness value (0 ~ 255) of G component is 120 or less in the RGB image and detected the nucleus by using the gLoG filters. However, in this research, in the area extraction by brightness value, the value was divided into several ranges (for example, 0 ~ 40, 40 ~ 80 and 80 ~ 120), and then the nucleus was detected gradually.

In this work, in order to evaluate the detection of nucleus, three indicators were adopted: sensitivity, positive predictive value, and F-measure. As a result of our evaluation, we succeeded in improving F-measure over the previous work. Among them, we obtained the best results when the division interval of the brightness value is 30.

In this work, we proposed a new method of dividing the brightness value of cell images into several ranges when detecting the nucleus of keratinized surface cells of the oral cavity. We examined by this method and found that F-measure, which is an indicator of nuclear detection, is the highest when the division interval of brightness value is 30, and it is greatly improved compared to the previous work. In the future, we will develop new nuclear detection methods to further improve F-measure.

On-Spot Detection of Antibiotics in Milk

Narjes Allahrabbı, Dieter Trau
National University of Singapore, Singapore

Objective: There is an increasing demand for on-spot detection of various analytes in environmental screening such as testing food quality and biomedical applications such as point-of-care diagnostics. As an example, a rapid and low-cost solution for antibiotics screening will greatly help in the safe and secure supply of animal products such as milk. The proposed method utilizes a novel portable handheld fluorometer (called as Fluoropette) and a disposable measurement test tube or tip which requires sample volume as minimum as 30 μl. The low-cost Fluoropette transmits the analysis results to a smartphone via Bluetooth, which can be transmitted over the internet for prompt action. Conventional Fluoroluminunoassay (FIA) methods use samples of at least few milliliter volumes and utilizes bulky instruments such as microplate reader for performing detection. The proposed method involves competitive immunoassay for the detection of beta lactam family of antibiotics in milk (the most abundantly-found antibiotics in milk) using immobilized reagent/analyte on magnetic particles (MPs). The signal will be inversely correlated to antibiotic concentration.

Methods: Two experiments were designed which employed ampicillin-loaded MP (MP-Amp) and monoclonal antibody (Genetex, USA)-loaded MP (MP-mAb). Ampicillin/mAb was immobilized on Carboxyl-functionalized MPs (Bangs Lab, USA) through carbodiimide crosslinking. Subsequently, they were blocked using 5% glycine in diluent buffer (0.05% Tween 20 in 1X PBS). Ampicillin-iFluor488 (Amp-iF) conjugate was prepared and purified using 1kDa dialyzer.

For the experiments involving MP-Amp, 100 μl of diluted MP-Amp was added to each well followed by addition of 5 μl of biotinylated polyclonal antibody (Biorbyt, UK)(pAb-B) of 0.5mg/ml and 100 μl of solution containing a beta lactam (Ampicillin, Amoxicillin, Penicillin G or Cephalixin) with specific concentration (0 to 0.11 μM) that was prepared in diluent buffer and incubated for 1 hr at 37º C. Finally, 5 μl of a solution of Streptavidin conjugated Fluorescein isothiocyanate (S-FITC) of 0.5 mg/ml was added and the signal was measured after 30 min reaction.

For the experiments involving MP-mAb, 10 μl of MP-mAb was added to each well followed by addition of 100 μl of Amp-iF and 100 μl of Ampicillin solution prepared in diluent buffer/milk and incubated for 1 hr at 37º C and the signal was measured then.

Results: The maximum allowable level of beta lactam antibiotics is 0.016 to 0.03 μM according to Agri-Food and Veterinary Authority of Singapore. Our data shows that MP-mAb provides a higher dynamic range for detection of Ampicillin as compared to MP-Amp. Besides, Fluoropette shows competency in detecting the signal in the dynamic range as the one detected by the microplate reader. Immunodetection was carried in milk samples using MP-Amp. The MP-Amp successfully detected Ampicillin in milk.
Conclusion: A novel handheld Fluoropette was developed and showed successful application for on-spot detection of antibiotics. As a future improvement, the in-house antibody can be produced to ensure the performance and product sustainability. Besides, a specifically-designed tip that incorporates MPs can be prototyped to perform a single-step assay. As a prospective application, Fluoropette can be employed for biomedical tests such as point-of-care diagnostics with minimal training requirements.

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Abstract Number: ICBME1079

The Impact of Static Distraction in Disc Regeneration – a Pilot Longitudinal Study Using Magnetic Resonance Imaging (MRI) in Rabbit Model

Wing Moon Raymond Lam, Tan Kim Cheng, Ren Xiafei, Kishore Kumar Bhakoo, Ramruttun Amit Kumarsing, Liu Ling, Hey Hwee Weng Dennis, Wong Hee Kit
National Univeristy of Singapore, Singapore

Low back pain is a disabling condition that imposes an enormous socioeconomic burden. However, decompression and surgery can only provide symptom relief at the expense of accelerating degeneration of adjacent spinal levels. Intervertebral disc (IVD) regeneration strategies are ideal goals aiming to provide a better solution. While regeneration occurs with tensile loading of degenerated IVDs, no long-term longitudinal data exists to show the possibility of sustained impact of tensile loading under physiological conditions. The aim of this study is to develop an MRI-compatible rabbit IVD distraction model to enable longitudinal monitoring of nutrient supply and regeneration process of degenerated discs.

Distractor design was modified from previous study with two zirconia k-wire inserted into vertebral body, 4 zirconia holding rod, PEEK block holding frame and urethane washer replace stainless steel spring.

Rabbits were divided into two groups. 1) IVD stabbing, no treatment 2) IVD stabbing, distractor implant on 6 weeks post-stabbing, treated by 120N tensile force.

Under C-arm guidance, L4-5 IVD was identified by k-wire, a bone marrow aspiration needle was inserted into the disc space. At 6 weeks post stabbing, baseline IVD degeneration was assessed by T2 weighted MRI. The nutrient flow was assessed by difference of pre and post-contrast T1 MRI.

Under general anesthesia, surgery was performed through a dorsal approach to the lumbar spine. Blunt dissection of muscle was performed to exposed L4-5 vertebra. Under C-arm guidance, hole was created by stainless k-wire in L4, L5 vertebra. K-wire was replaced with zirconia k-wire and connected to zirconia rod holder and other distractor components. Rabbit disc health was evaluated by MRI at 7, 11- and 15-weeks post distractor implant. Rabbit was euthanized after the last MRI scan. The L4/5 IVD was

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harvested, processed according to fast staining protocol.

Degeneration of stabbed L4-5 IVD, represented by a loss of signal under T2-weighted MRI at 6 weeks after post-stabbing. From 7-15 weeks post-stabbing, further loss of signal under T2 weight MRI was observed in no treatment group but slowdown in treated group. From T2 STIR and post contrast MRI, disc distraction can arrest the progression of disc degeneration. From fast staining images, decrease of disc height and loss of proteoglycan was less severe in treated stabbed disc compared to untreated counterpart.

The development of MRI compatible distractor will allow a longitudinal study of the degenerated disc regeneration process under tensile distraction.

Abstract Number: ICBME1193

Development of Intravenous Injection Rate Monitoring System Using External Environmental Compensation Algorithm

Kyu Jin Cho, Shin Seung Hwan, Kim Do Hyung, Nam Yun Chan, Lee Bo Kyung, Shin Tae Min
Yonsei University Korea

It is important to maintain a constant injection rate when intravenous therapy is applied. Inconsistent infusion rate reduces the effectiveness of intravenous therapy and cause side effects to the body. Widely used infusion regulators couldn’t be quantitative during therapy and infusion pumps are expensive and difficult to apply to all patients because of the cost. To maintain a constant infusion rates, the intravenous injection rate monitoring system based on the optical sensor was developed. However, the system is vulnerable in external light interference and motion. In this paper, to solve these problems, algorithm for detecting infusion drops was developed by applying external interference compensation.

In this study, the systems are divided into three parts - sensor parts, control parts and display parts. Attiny816 (Microchip Technology, USA) is used as microprocessor and the sensor part is consist of IR diode (QEB363) and IR phototransistor (QSB363). Also, an analog amplifier stage was applied for TR signal amplification. To compensate for external light interference, the light emitting parts of the sensor are periodically switched on and off, and all signals from the light source are collected. Since the sensor unit is attached to the IV chamber, when the IV chamber moves or tilts, the signal pattern of the sensor unit is not constant. Signal integral was used to find the drop signal with a non-constant pattern. First, integrate the signal above a certain threshold to find the energy. And if the integral value is larger than the set energy value, it is considered that the drop is floating. The drop detection is performed by determining the time when the drop of the drop is significantly reduced.

An experiment was implemented to detect infusion drop in the case of an external light interference and moving environment. The number of drops is detected when external light interference and moving artifact were given was compared. As a result, errors in the external environment were better corrected and the accuracy was over 90%.

In this study, we developed a system to monitor the infusion drop rate using optical sensors and applied algorithms to compensate for external environmental errors. The application of algorithms was able to compensate for errors in external light interference and fluid retention movements. However, in the case of external light compensation, a limit was made that only the error of external light below a certain amount could be corrected exposure to strong light energy, such as direct sunlight, was not properly compensated. In further study, the improvements of these points by further study may lead to the development of a more fluid administration monitoring system for external environmental interference.”
Abstract Number: ICBME1034

Design and Fabrication of a Hierarchical Scaffold to Improve the Efficiency of Bone Scaffold for Cell Condensation

Greeshma Ratheesh, Mengchao Shi, Yin Xiao, Cedryck Vaquette
Queensland University of Technology, Australia

The lack of proper architectural design in an engineered scaffold hinders the cell migration and condensation which is the key to the new tissue formation. One critical parameters that allow sufficient nutrient transfer and cell migration in an engineered construct is the pore size. Though there were many attempts to improve the design of the scaffold, the importance and the relation between the pore sizes of the scaffold in cell condensation still remains unanswered. In this project we fabricated a unique hierarchical scaffold by combining two additive manufacturing techniques namely melt electrospinning writing (MEW) and fused deposition modeling (FDM). The fabricated scaffold was physically and biologically characterised using various methods. The scaffold possess controllable external macropores and internal micropores with interconnected channels that helps in cell condensation, osteogenic differentiation and bone formation. The strategy of 3D printing by integrating different additive manufacturing techniques can be extended to custom-designed structures to reconstruct the defects.

Abstract Number: ICBME1101

Is Highly Cross-Linked UHMWPE Hip Liner With/Without Vitamin E Compromising the Impingement Fatigue and Wear?

Tsung-Wei Chang, Yun-Chuan Chang, Fang-Yuan Ho, Jiann-Jong Liau
United Orthopedic Corporation, Taiwan

Objectives: Instability following primary THA is the most common indication for revision arthroplasty. Generally, an elevated lip liner placed with the lip positioned in the direction of maximum risk for instability can confer protection against dislocation. But impingement appears when the postoperative range of motion exceeds the technical limits of the implant and leads to increased acetabular liner damage and wear, and in severe cases, rim fracture and osteolysis. Although irradiated highly cross-linked UHMWPE (XPE) has dramatically improved wear performance, re-melting polyethylene can reduce mechanical properties, generate residual free radicals which are the precursors to delamination with oxidative embrittlement. Vitamin E (α-tocopherol) provides oxidative degradation by donating a hydrogen atom to free radicals and maintaining fatigue strength for XPE. The concern of thinner poly liners is the risk of rim fracture following impingement. This study investigated the performance of E-XPE and XPE hip liners under a critical challenge of impingement testing.

Methods: U-Motion II acetabulum system (United Orthopedic Corporation, Taiwan) was prepared for impingement testing. The combination was chosen under the worst scenario, which is 20° elevated lip design with the thinnest liner (ID 32 mm, OD 48 mm). The material of E-XPE liner is irradiated polyethylene with the pre-added 0.1% vitamin E; the XPE liner is irradiated polyethylene followed by re-melting. Both E-XPE and XPE liner were EO-sterilized. According to ASTM F2003, the E-XPE and XPE liners were aged for two weeks in sealed chambers (70°C and 5.03 bar O2 environment) prior to the test and were presoaked at 37°C. A constant joint reaction force of 600 N was applied to the metal back and the angular displacement pattern for impingement testing was adapted from ASTM F2582. The hip simulating impingement test was performed for 1.0 million cycles at a frequency of 1.5 Hz under physiological condition. For each group, three samples were used to determine the impingement wear and three additional samples were used as a reference without impingement in order to provide a comparison. The wear of each liner was determined according to ISO 14242-2.

Results: After 1.0 Mc, the average cumulative wear rate based on a linear regression analysis of the weight loss values for E-XPE and XPE was found to be 0.16 mg/Mc and 0.20 mg/Mc. Although the impingement loading results in deformation of cup liner, no local fracture was observed in any of the specimens and the function of crown tab locking mechanism remains integrated. Additionally, the wear rate of E-XPE liner was apparently lower than that of XPE liner in impingement and control couplings, respectively.

Conclusions: The accelerated aging to simulate severe oxidation has been described as a severe impingement and wear challenge. Both U-Motion II E-XPE and XPE cup liners with the thinnest elevated lip design successfully passed the impingement testing. By eliminating the concerns about the compromised mechanical strength, it highlights the benefits of using vitamin-E blended highly cross-linked UHMWPE as a bearing material in THA, such as maintaining the impingement fatigue strength and lowering the impingement wear.

Abstract Number: ICBME1111

Microfabrication of 3D Printed Devices for Directed Differentiation of Cardiomyocyte from Stem Cells

Rupambika Das, Javier Gomez Fernandez
Singapore University of Technology and Design, Singapore

Embryonic stem cells (ESCs) as a source has the potential to differentiate into various cell lineages opening up new dimension to study regenerative medicine. But for the differentiation to be in a very homogenous, precise and in a uniform pattern the cells are necessary to be directed by mechanical constraints. The mechanical micro-confinement can be provided by adopting additive manufacturing as a tool to direct stem cell development. The three-dimensional aggregate of the embryo formed in vitro is called an Embryoid Body (EB) which mimics a developing embryo in a viviparous organism. Forming these EBs with minimum dispersion is a crucial factor for cardiomyocyte development. But till date the technologies available have been lacking to deliver EB’s which are consist enough to differentiate homogeneously. Hence, using additive manufacturing unlocks the new vision of creating EB’s of as low as 40µm to as big as 500µm in contrast to the other available technologies. Additive manufacturing provides a cutting edge because it facilitates in producing pristine EBs with accurate diameters, controllable cell
Objective: Photoacoustic (PA) imaging has attracted interest for its capacity to capture functional spectral information with high spatial resolution in biological tissues. Current commercialized PA imaging systems in the market are variously limited by bulky size or user interface flexibility. Here, we present a new HAndheld dual-modality Real-time ultrasound/Photoacoustic imaging system (HARP), which consists of a detachable fiber-bundle-based illumination system integrated with an array-based ultrasound transducer and data acquisition platform. In HARP, different design concepts for PA probes can be adapted for different imaging applications by switching transducers and corresponding jackets to fix the fiber pads and transducer in a single setting. An intuitive user interface provided by HARP is based on a completely programmable MATLAB-based platform. Methods: In vitro and in vivo experiments were performed to validate the performance of the developed HARP. Blue and red ink in tubes were imaged at 750 and 850 nm to mimic vascular imaging. For in vivo experiments, we imaged relative blood oxygenation in hypoxic pancreatic tumor blood vessels. Epidermal growth factor (EGF) conjugated to CF750 PA contrast agent was also used for targeted tumor imaging in mouse pancreatic tumors. Results: In vitro imaging of blue and red ink demonstrated that we can image deoxyhemoglobin at 750 nm and oxyhemoglobin at 850 nm, where their absorbances are the greatest. In vivo imaging of pancreatic tumor blood vessels demonstrated that HARP can be used to detect hypoxic environment in the tumor. EGF-CF750 imaging demonstrated that Pan02 orthotopic mouse pancreatic tumors can be imaged using EGF receptor targeting. Conclusion: Collectively, this design concept for a customizable ultrasound/photoacoustic imaging system is intended to meet the diverse needs of medical researchers performing both pre-clinical and clinical photoacoustic studies.
Abstract Number: ICBME1364

Investigation of the Influence of the Commissure Orientation on Hydrodynamic Performances of the Bicuspid Aortic Valve

Jumpei Takada, Ryo Kumazawa, Kaoru Hattori, Gohki Nishimura, Ryo Moriwaki, Mitsuo Umezou, Kiyotaka Iwasaki
Waseda University, Japan

Background: The normal aortic valve was consisted by three cusps, while the bicuspid aortic valve was consisted by two leaflets. This disease was observed in about 1% of people, and caused aortic regurgitation and aortic stenosis1). As a surgical plasty, there was a method to control the commissure orientation of the bicuspid aortic valve leaflets by applying a suture to the commissure. However, the relationship between the commissure adjustment angle and the hydrodynamic performance of the bicuspid aortic valve was not clear because a) the commissure orientation differed on the patients and the number of patients was small, b) long term results had not been accumulated. There was a need for a basis for plasty.

Aims: The aim of this study was to investigate influence of the commissure orientation on hydrodynamic performances of the bicuspid aortic valve.

Method: A pulsatile circulatory system consisted of an elastic left ventricular model, the bicuspid aortic valve model made from porcine aorta and bovine pericardium, an elastic aortic arch model, a resistive unit, and pre-load tank. Then, we evaluated three different types of the bicuspid aortic valve models; a)120angle-240angle, b)140angle-220angle, c)180angle-180angle under the same pulsatile condition which aortic pressure were adjusted to 120/80(100) mmHg each n=6). An elastic left ventricular model was driven at 70 bpm using a pneumatic driver.

Result: Aortic forward flow and static back flow of the three bicuspid aortic valve models were successfully obtained from the pulsatile circulatory system. Aortic forward flow decreased when the commissure orientation was 180angle-180angle(120angle-240angle:4.9 L/min, 140angle-220angle: 4.7 L/min, 180angle-180angle: 4.5 L/min). And static back flow increased when the commissure orientation was 120angle-240angle(120angle-240angle:0.47 L/min, 140angle-220angle: 0.37 L/min, 180angle-180angle: 0.36 L/min).

Discussion: We considered that aortic forward flow and static back flow were affected by the orifice area and coaptation length. Therefore, we used finite element analysis to investigate the orifice area and coaptation length. The structure of the bicuspid aortic valve was taken from biaxial tensile test of porcine aortic valve leaflet2). As a result of finite element analysis, orifice area decreased when the commissure orientation was 180angle-180angle(120angle-240angle:23.22 cm2, 140angle-220angle: 23.44 cm2, 180angle-180angle: 17.44 cm2). And, coaptation length decreased when the commissure orientation was 120angle-240angle(120angle-240angle:5.9 mm, 140angle-220angle: 6.2 mm, 180angle-180angle: 8.0 mm).

Conclusion: When the commissure orientation was 180angle-180angle, aortic forward flow decreased due to the orifice area decreased. And, when the commissure orientation was 120angle-240angle, static back flow increased due to the coaptation length decreased. These data contribute to development of effective plasty for bicuspid aortic valve disease.

Reference
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Abstract Number: ICBME1462

Detailed Analysis of Thrombi Growth Direction at Gaps Between Tubes and Connectors

Yuki Matsuhashi, Kiyotaka Iwasaki, Mitsuo Umezou
Waseda University, Japan

Objectives: The dispersion of thrombus that forms at the gaps in interfaces between medical devices can cause severe complications. In the present study, we used a non-invasive method of visualizing thrombi with a previously-developed optical coherence tomography device to analyze the direction of thrombus-growth quantitatively in the area where a connector was attached to a tube. Methods: We manufactured connectors based on those used in continuous hemofiltration circuits. Specifically, they were made from polyurethane with an internal diameter of 6 mm, external diameter of 7 mm, a taper of 30°, and a gap of 100 μm at its tip. The inlet of this connector was attached to a polyvinyl chloride tube with an internal diameter of 6 mm, and their interface was used as the subject of analysis. The circuit was comprised of a roller pump, a compliant tubing, a polyvinyl chloride tubing, and a resistive unit. The volume of the circuit was 50 ml. The circuit was filled with whole human blood, which was promptly circulated using a roller pump with an average flow rate of 100 mL/min. Thrombi were extracted from the OCT images using a real-time thrombi visualization method. The present study was performed with the approval of the ethics committee of Waseda University. To analyze the direction of thrombi growth quantitatively, their length was measured at the inlet and outlet of the connector. Results: The results demonstrated that lengthening of the thrombi occurred in both the downstream and upstream directions from the connector-tube interface. At the connector inlet area, there was a growth of 0.28 ± 0.13 mm in the upstream direction at 10 min of circulation. This growth continued with further circulation until 60 minutes, when the length was 1.10 ± 0.40 mm. In the downstream direction, the growth at 10 min of circulation was 0.51 ± 0.20 mm. At 60 min of circulation, the length reached 1.42 ± 0.67 mm. At the outlet area, there was a growth of 0.07 ± 0.10 mm in the upstream direction at 10 min of circulation. This growth continued to 1.14 ± 0.97 mm until 60 minutes. The growth in the downstream direction at 10 min of circulation was 0.55 ± 0.18 mm, gradually increasing to 1.68 ± 0.87 mm until 50 min of circulation. At 60 min of circulation, the length had reduced to 1.47 ± 0.97 mm. At the connector outlet, localized
flow paths became larger, and seemed to have been reduced by the influence of the flow reattachment point. Conclusions: In the present study, we quantitatively analyzed the growth of thrombi by measuring the length of thrombi formed at the area where a connector was attached to a tube. Thrombus-growth was affected by the direction of blood flow and the orientation of the tip of the connector.

Abstract Number: ICBME1097

The Influence of Potential Fallers on the Comparison in Lower Extremity Muscle Strength Between Fallers and Non-Fallers

Jun Hyeong Cho, Seo Jeong Woo, Lee Jin Soo, Kim Jung Gil, Choi Jin Seung, Tack Gye Rae
Konkuk University, Korea

Objectives: A decrease in musculoskeletal function is known to increase the incidence of falls in older adults. In most studies, the classification of fallers and non-fallers is based on past experience of falls. However, this approach has a limitation in that if a fall occurs after the classification, those who already classified as non-faller might have a characteristics of the faller. This will affect the characteristics of the non-faller. Therefore, we quantitatively measured the muscles&rsquo; forces that affect the fall in the healthy elderly, and examined how the strength of the potential faller (the subject experiencing a fall after the experiment) affects the fall research.

Methods: Fifty-five healthy, community-dwelling senior individuals participated in this study (age: 77.24; 6.06years, weight: 60.75; 10.22kg, height: 155.47; 8.84cm). Based on the experiment days, the fall experience of the past one year was investigated. One year after the experiment, the fall experience of the past one year was examined too. A hand-held dynamometer (CITEC, CIT technics BV, The Netherlands) was used to measure the maximal voluntary contraction (MVC) of each muscle. The measurements were repeated three times in compliance with the user manual. The average of the measured maximum values was normalized by the subject’s height and weight. All experiments were measured by one person to eliminate errors caused by changes in the measurers. The measurement points were a total of 9 muscle groups (Grip Force, Three Point Grip, Hip Abductors, Hip Flexors, Knee Extensors, Knee Flexors, Foot Dorsi flexors, Foot Planter flexors, Hallux Plantar flexors). The independent t test was used to compare the traditional methods based on past experience of fall (Comparison 1), and the comparison of the traditional methods except the potential fallers (Comparison 2).

Results: Comparison 1 shows that the fall group showed less muscle strength in all areas except foot planter flexors compared to non-faller group, of which knee flexors showed significant differences. In comparison 2, the faller group showed less muscle strength in all areas except foot planter flexors and hallux plantar flexors compared to non-faller group, of which three point grip, hip abductors and knee flexors showed significant differences.

Conclusions: By eliminating potential fallers, the number of variables with significant differences was increased from one to three. Hip abductor muscles are muscles that maintain posture when walking, meaning weakness of muscles is likely to lead to falls. Since physical decline due to aging does not occur, potential fallers have physical characteristics of the fallers at the time of the experiment and appear to influence data analysis when included in the non-faller group.

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Abstract Number: ICBME1060

Flow Analysis of the Mitral Valve Double Orifice After MitraClip

Shelley Gooden, Hoda Hatoum, Konstantinos Boudoulas, Lakshmi Prasad Dasi
The Ohio State University, United States

Mitral regurgitation (MR) is the most common valvular disorder that occurs when leaflets of the mitral valve (MV) do not properly close during systole. The only device currently approved for MR treatment is Abbott’s MitraClip NT. MitraClip treats MR by clipping the two MV leaflets together to reduce MR, creating a double orifice. High-fidelity flow analysis (involving particle image velocimetry) beyond basic hemodynamic measurements have only been done in silico. In this study, a fresh porcine valve is tested in a left heart simulator with and without the MitraClip. The valve is tested in a pulse duplicator under simulated physiological conditions of 120/80 mmHg systemic blood pressure with a peak systolic ventricular pressure of 140 mmHg, cardiac output of 3.0 L/min, and heart rate of 60 bpm. Flow through the MV is collected at 100 Hz for 60 cycles. MR flow is calculated for each case and is defined as the ratio between regurgitant volume and forward volume. High-resolution time-resolved particle image velocimetry is currently in progress to visualize and quantify flow velocity field through the double orifice. Measurements will also include phase locked measurements to evaluate turbulence characteristics downstream of the valve. Results show that the pressure gradient increased from 8.6 to 15.6 mmHg after MitraClip. We anticipate that this study will for the first time illustrate and quantify the tremendous alteration with MitraClip, where velocity is increased from the reduction in effective orifice area. Elevation in Reynolds shear stresses (RSS) are expected in the order of 50-60Pa compared to the state where no clip is used. Studies are currently ongoing to evaluate the impact of multiple MitraClips on the flow characteristics downstream of the MV.

Abstract Number: ICBME1074

Numerical Analysis for the Velocity Distribution of the Outflow of a Left Ventricle: Effect of the Blood Flow on an Aortic Valve

Shuta Kosaka, Suguru Miyauchi, Toshiyuki Hayase
Tohoku University, Japan

A left ventricle (LV) has a mitral valve between a left atrium and a LV, and an aortic valve (AV) between an aorta and a LV. A mitral valve consists of two parts, anterior and posterior cusps, and an AV generally consists of three parts, left, right and posterior
cups. However, it has not been clarified why each valve has such a shape, which is a physiologically interesting problem. In our previous numerical study, the velocity distribution of the outflow of the LV model that was not affected by the shape of the AV was analyzed by attaching the circular opening AV shape model to the LV model. We confirmed that the shape of the fluid velocity vectors in the systole on the internal cross section of the LV parallel to the opening area of the AV formed a triangle shape which mostly matched to the actual opening AV shape and its orientation. This result suggests the physiological meaning of the valve cusps shape that actual AV shape and position are determined so as not to disturb the blood flow from a LV. It is assumed that the blood flow from a LV does not collide with an AV, leading to prevention of the hemolysis in an AV and suppression of the load on an AV, but nothing has been known so far. The purpose of this study was to clarify the effect of the blood flow near a LV outlet on an AV. We performed unsteady numerical blood flow analysis for the LV model with the opening AV model of the actual position or that of the virtual position. We clarified the blood flow velocity fields near the AV models and the shear stress on the AV model surfaces, and the effect of the blood flow near a LV outlet on an AV by comparing the results of the two LV models. The LV model for the blood flow analysis was created by extracting the LV shape from the MRI images and attaching papillary muscles and trabeculae carneaes as internal structures. The mitral valve part was modeled by a cylinder, and the AV part by cones mimicking the actual opening AV shape. The deformation of the LV model due to pulsation and twisting motion was reproduced by incorporating the method of our previous numerical study. We performed the numerical analysis of the blood flow for the two LV models with the actual AV position and the virtual AV position rotated in 180 degrees from the actual AV position, and clarified the blood flow velocity fields near the AV models and the shear stress on the AV model surfaces. The results of the two LV models were compared showing the difference of the blood flow near the LV outlet between these models. From the results of this study, the physiological meaning of valve cusps shape was clarified in terms of the effect of the blood flow on an AV.

Abstract Number: ICBME1145

Can Finite Element Analysis Replace Wear Testing?

Tsung-Wei Chang, Yun-Chuan Chang, Fang-Yuan Ho, Jiann-Jong Liau
United Orthopedic Corporation, Taiwan

Objectives: Ultra-high molecular weight polyethylene (UHMWPE) is a common and a successful bearing material in Total Knee Arthroplasty (TKA). However, the application of UHMWPE is limited by long-term outcome in patients due to recurrent wear problems of tibial inserts. In addition to permanent deformation and complete destruction of the component, the released wear particles have been connected to the onset of bone osteolysis. Although the wear simulators are often used to evaluate the wear properties of knee implants prior to clinical use, such studies are often time-consuming and costly. Therefore, a computational model becomes an attractive alternative to study the wear behavior of tibial inserts. The objective of this study is to develop a computational model for simulation of the wear testing and to compare predicted kinematics. Methods: In wear simulator testing, U2 Knee, PS type (UOC, Taiwan) TKA system was prepared to assess the wear performance. The wear test was performed for 5.0 million simulated gait cycles at a frequency of 1 Hz under physiological conditions based on ISO-14243-3. Weight loss was determined gravimetrically at 0.5 million cycles, 1 million cycles and at least every 1 million cycles thereafter throughout the test. In finite element simulation, the force-controlled inputs provided an evaluation of the overall numerical method by simultaneously predicting both kinematics and wear. The femoral component and tibial baseplate were modeled as a rigid body to save computational time. The coefficient of friction between the tibia and femur was 0.04. The numerical wear simulation followed Archard’s Law to calculate surface wear of the UHMWEPE insert: H= KPS where H is wear depth, K is an experimentally determined wear factor, P is contact pressure, and S is sliding distance. The wear factor was 2.64E-07mm3/Nm employed in this study which referred TKA system was prepared to assess the wear performance. The results of the two LV models were compared showing the difference of the blood flow near the LV outlet between these models. From the results of this study, the physiological meaning of valve cusps shape was clarified in terms of the effect of the blood flow on an AV.

Abstract Number: ICBME1243

Endothelial Cell Peeling Due to Fluid Mechanical Effect of Red Blood Cell Suspension in Parallel Flow Load Experiment

Kosuke Inoue, Suguru Miyachi, Toshiyuki Hayase, Miria Suzuki
Tohoku University, Japan

Endothelial Cells (ECs) coating the inner wall of blood vessels with mono layer play vital roles in maintaining homeostasis of the circulatory system by exerting various functions such as regulation of blood coagulation system, production/release of substances such as various kinds of growth factors and cytokines, and immune response. ECs respond to shear stress from blood flow, hydrostatic pressure due to blood pressure, and radial stretching due to deformation of blood vessels, and have the property of changing morphology, arrangement and function. Damage to ECs is known to lead to atherosclerosis. As far as we know, cell culture medium is commonly used as the working fluid in flow load experiments of ECs, and the effect of red blood cells (RBCs) in blood has not been considered. On
the blood vessel surface it is known that there exists a plasma layer with a few μm height where red blood cells do not exist. However, RBC may interact with the blood vessel surface in flows near blood vessel bifurcations, etc. In this study, we aimed to clarify the effect of RBCs in a working fluid on ECs’ damage in a flow load experiment using a parallel plate flow chamber as a fundamental study to examine the fluid mechanical effect of RBCs on EC damage. The ECs used in the experiment were cultured in an acrylic sample container until they became confluent, and then two types of cells were prepared: aligned ECs obtained by flow load after a normal culture and unaligned ECs by a normal culture. We prepared two working fluids: plain medium and RBC suspension with hematocrit of 40%. RBC suspension consisted of plain medium and goat’s RBCs. In the flow load experiment, the flow velocity in the chamber was gradually increased and peeling of ECs were observed by a phase-contrast microscope. The endurance strength of ECs was evaluated by the rate of ECs peeled off against the flow load. WSS applied to the ECs was evaluated from the pressure loss in a flow chamber. Experimental results were compared between the aligned ECs and unaligned ECs, and the plain cell medium and RBC suspension. When the Reynolds number was different due to different apparent viscosity and the same channel height, the endurance strength of ECs evaluated by WSS was decreased in the case of turbulent flow for the plain medium as compared with the case of laminar flow for the RBC suspension. When the Reynolds number was the same by changing the channel height, the endurance strength of ECs was the same between the RBC suspension and the plain medium. The endurance strength of unaligned ECs was found to be higher than that for aligned ECs in all experimental conditions.

Results: The novel knee biomechanical testing system is an in vitro knee bionical loading and biomechanical parameters recording system. The system is composed of pneumatic hardware and PC-controlled software, providing a quick and convenient loading strategy. Different from previous weights loading system, servo control is achieved by pneumatic system and the system can quickly adjust ankle flexion according to different experiment protocol. By mechanical design, the system can transfer the up-down movement of electric lifter to flexion of knee joint, and the Third Encoder can record the flexion angle. Moreover, the system provides multiple parameters recording system. The system is consisted of data collecting hardware and Human–computer interaction software. The six-dimensional force sensor can record the end reaction force of femur. The pressure paper can be used to detect the portion and mount of force in joint. Microscope can be used to detect the position of patella. The Forth Encoder can measure the external and internal rotation of tibia. Meanwhile, the First Encoder and Second Encoder can measure the lateral and medial stability of tibia. The micro-movement sensor can measure the strain of anterior cruciate ligament. All the aforementioned data can be utilized to judge the function of in vitro knee.

Conclusions: The knee biomechanical testing platform invented by our group is quite novel compared with previous studies and can provide credible data for surgical option, and is helpful for the invention of new surgical option and technique.

Abstract Number: ICBME1254

A Novel Knee Biomechanical Testing System

Junjie Xu, Liren Wang, Yuhao Kang, Jia Jiang, Jinzhong Zhao
Shanghai Sixth People’s Hospital, China

Objectives: Sport industry is developing rapidly accompanied with a higher quality of material life and the strengthened awareness of the importance of fitness. However, this change is followed by an increasing rate of injury that has become the burden on people’s life quality and social economy. The utilization of knee biomechanical testing system can illuminate the mechanism of knee movement, provide guidance for surgical option. Based on previous reported biomechanical testing system, we invented a novel biomechanical testing system which can apply bionical force loading, as well as recording various biomechanical characteristics.

Methods: Our newly invented knee biomechanical testing system is mainly composed of seven units, frame unit, femur position adjusting unit, femur reaction force and ligament strain recording and force loading unit, flexion driving unit, tibia position following unit, tibia position internal and external recording unit and patella position recording unit. The knee biomechanical testing system can record common postoperative, such as anterior cruciate ligament reconstruction and total knee replacement, biomechanical parameters which can be used to compare different surgical option.

Study on the Effects of Aeration and Lyophilization on Sterile Residues and Sterile Secondary Products of Decellularized Tissue After Sterilization

Shinya Imai, Jiang Hongxiao, Masahumi Ito, Akira Yasaka, Umezu Mitsuo, Kiyotaka Iwasaki
Waseda University, Japan

Purpose: In the present anterior cruciate ligament (ACL) reconstruction, the autologous tendon is used as the main reconstruction material. However, there are several problems such as highly invasive surgical treatment and shortage of material when re-rupture occurred.

In order to solve these problems, our laboratory is developing new reconstruction materials applying decellularization technology, which could suppress the immune response and to be self-organized after xenogeneic tissue has been implanted.

Sterilization is essential for implantation, and our laboratory developed ethylene oxide gas (EOG) sterilization technology that can maintain strength and viscoelasticity of tissue in 2017. The result of large animal experiment confirmed the usefulness of the decellularized tissue. For the safety of clinical application, it is important to further study the reduction of residual substances after EOG sterilization.

Methods: In this experiment, gas chromatography mass spectrometry (GCMS) was performed to quantify the sterile residue contained in decellularized bovine tendon after EOG sterilization. We compared the sterilization residue using the
aeration at 24, 36 and 48 hours and the lyophilization on days 1, 2 and 7 (each n = 4). The sterilization residues to be measured were main component ethylene oxide (EO), and sterilization secondary products ethylene chlorohydrin (ECH) and ethylene glycol (EG). Thereafter, ovine ACL reconstruction was performed using decellularized bovine tendons with modified aeration and lyophilization conditions (n = 2). The ovine was sacrificed at 13 weeks after surgery, and the knee joint was removed and performed hematoxylin-eosin (HE) staining on the cells. In the tissue parenchyma, the number of cells contained per 1 Mm² of measurement areas of 400 µm² was calculated (n = 2).

**Results:** There was no significant difference in EO with increasing aeration time (p <0.05, Tukey test). ECH and EG were significantly reduced in the 36 and 48 hours groups compare to the 24 hours group (p <0.01, Tukey test).

In addition, no significant difference was found in EO even if the lyophilization time was increased (p <0.05, Tukey test). ECH and EG were significantly reduced in the 2 and 7 days groups compare to the 1 day group (p <0.01, Tukey test).

Then, the group of aeration 48 hours and the group of lyophilization 2 days were compared. For EO and ECH, the residual amount of aeration method is significantly low (p <0.05, Tukey test). Therefore, longer aeration can reduce the residue after EOG sterilization more efficiently.

By compared the number of cells in the reconstructed tissue at 13 weeks after ACL reconstruction. It was revealed that after change of condition, the average cell number was higher, and more cells were engrafted.

**Conclusion:** The aeration condition and the lyophilization condition were examined by quantifying the sterile residue contained in the decellularized tissue, and it was revealed that extending the aeration time can reduce the post-sterilization residue more efficiently. In addition, by anterior cruciate ligament reconstruction using ovine, it was suggested that there were more cells in the reconstructed tissue after changes in aeration and lyophilization conditions, and that early remodeling was occurred.

**Abstract Number:** ICBME1348

**Fundamental Study of MR-Measurement-Integrated Simulation of Heart-Aorta-System: Effect of Feedback Points Distribution in Analysis of Ascending Aorta**

**Yuki Hori,** Suguru Miyauchi, Toshiyuki Hayase, Kosuke Inoue, Alain Lalande, Jean-Joseph Christophe

**Tohoku University, Japan**

Hemodynamics is closely related to progress of cardiovascular diseases. Medical imaging such as magnetic resonance imaging (MRI) and computational fluid dynamics (CFD) provide the blood flow information. Although MRI can obtain non-invasive information of blood vessel shape and blood flow velocity, the accuracy of MRI data is relatively low. Therefore, it is difficult to obtain accurate hemodynamic parameters from MRI data. On the other hand, numerical simulation provides detailed information of blood flow, but it is difficult to give accurate boundary conditions such as inflow rate and blood vessel deformation. In the previous study, the numerical experiment of blood flow analysis in a cerebral aneurysm by magnetic-resonance- measurement-integrated simulation (MR-MI simulation) was performed. In MR-MI simulation, it was suggested that accurate blood flow dynamics that is difficult to obtain with the measurement or numerical simulation alone can be obtained by feeding back the MR measurement data to the numerical simulation. An aorta is a common site for cardiovascular diseases, but it was difficult to obtain accurate hemodynamic parameters in the aorta. MR-MI simulations of blood flow in a descending aorta was performed in our group showing the validity of the method. Ascending aorta has a feature that bicuspid valve tends to cause an aneurysm and high risk in treatment of an aneurysm. In the previous report, MR-MI simulation and ordinary simulation in an ascending aorta were performed and the effectiveness of MR-MI simulation was shown by comparing the velocity error with that of MR measurement result. However, the influence of the density of feedback points on analysis result is unknown. The purpose of this presentation is to clarify the influence of density and distribution of the feedback points in MR-MI simulation on hemodynamic parameters. The aortic blood vessel model was created based on the MRI data of a 38-year-old female patient with expanded Valsalva sinus by correcting the enlarged part. For this model, a region of interest (ROI) was set in the ascending aorta. Unsteady flow analysis was performed using commercially available thermal fluid analysis software (FLUENT 19.0, ANSYS, USA). The inflow rate was modified so as to minimize the mean axial velocity error between MRI data and analysis result in ROI. MR-MI simulation was performed in three cases: 1) feedback was given to all calculation points in ROI, 2) the feedback was applied to the computational points within some specified distance from the MRI measurement points, and 3) feedback was not applied to the points within some distance from the wall. The results were compared with those of ordinary simulation and MRI data. As a result, the influence of the density of feedback points on the analysis result was clarified. It was suggested that blood flow dynamics and hemodynamic parameters close to those of the real flow can be obtained when the feedback is applied to calculation points except for those near the wall.

**Abstract Number:** ICBME1106

**Development of Multi-Monitoring System Based on WPF for Estimation of Limb Motor Grade in Patients with Neurological Diseases**

**Bo Kyung Lee,** Yeo Eun Choi, Seung Hwan Shin, Yun Chan Nam, Sang Hoon Nam, Tae Min Shin

**Yonsei University, Korea**

Neurological disease patients should periodically be checked the condition of muscle strength through motor grade evaluation to prevent muscle paralysis. Currently, a motor grade evaluation is used with the Medical Research Council (MRC) Scale to identify the condition of patients. The motor grade evaluation is a method in which a medical staff applies light stimuli to a patient such as pinching the fingertips weakly and then evaluates the patient’s reaction subjectively to obtain an MRC rating. Because this is
Based on the subjective judgments of the medical staff, different levels of stimuli rating may appear for each medical staff, which creates problems where assessments of patients are not unified.

In the previous study, a monitoring program that wirelessly communicates with one ‘Motor Grade Band’ has been developed, so that the arm or leg lifting angle can be monitored by a 6-axis motion sensor-based Motor Grade Band. In this paper, a WPF-based multi-motor grade monitoring program has been developed, which monitors the angle of each Motor Grade Band by attaching to each limb of the patient.

This system is divided into two parts. One is a ‘Main Device Module’ with limb attachment type and the other is a user interface WPF-based ‘PC Application’ to communicate with four Main Device Modules. The Main Device Modules, which is called as Motor Grade Band above, processes the data received from the 6-axis motion sensor by applying the angle estimation algorithm and transmits it to the PC Application using BLE communication. The PC Application shows each data received from the band in real time and stores it in the database so that the data can be observed even after the communication is finished.

To evaluate the developed system, the ‘System accuracy evaluation experiment’ and ‘Communication stability evaluation experiment’ were implemented. The system accuracy evaluation experiment was designed to measure the angles of 15° and 30° between the shoulder transverse and sagittal directions. The communication stability evaluation experiment is designed to send 10,000 numerical data sets to each module at intervals of 100 ms and to check the received data. Each experiment was taken 10 times.

In the case of the system accuracy evaluation experiment, the error rate was about 0.25%. In the case of the communication stability evaluation experiment, the receiving rate is 100%, which means the reception is well performed without the data loss.

In previous studies, UWP-based monitoring systems were developed which could be linked to one Motor Grade Band. In this paper, WPF-based multi-monitoring system has been developed which can measure patient’s every limb. Through this system, it is believed that objectivity of motor grade evaluation experiment was increased by combining directionality of patient movements. The communication stability evaluation experiment is designed to measure the angles of 15° and 30° axis gets closer. It can be applied to the system which can be used as a diagnostic tool to compare the bending angle of the rehabilitation patient with the normal bending angle and to help the athlete to improve the performance of the athlete. However, at a small range of angles, the resolution of the data is relatively low and the error is likely to occur. To overcome this problem, we will perform further experiments to obtain more quantified data by increasing the resolution of the data through more detailed experiments of each parameter set in the experiment.

Abstract Number: ICBME1218

Development of Wristband-Type Wearable CPR Feedback System

JiHee Yu, Do Hyung Kim, Yun Chan Nam, Bo Kyung Lee, Kyu Jin Cho, Tae Min Shin
Yonsei University, Korea

Introduction

Cardiopulmonary resuscitation (CPR) is a series of lifesaving actions that is provided for thousands of patients with cardiac arrest a year. According to the American Heart Association (AHA) guidelines, chest compression (CC) depth should be 50 to 60 mm and it is reasonable to perform chest compressions at a rate of

Abstract Number: ICBME1172

A Study on Human Joint Angle Measurement Using Infrared-Based Optical Sensor

Geon Ho Kang, Geon Ho Kang, Jae-Hoon Jun
Konkuk University, Korea

Objectives: As modern society develops, patients are increasing day by day due to accidents such as traffic accidents or industrial accidents. Research on rehabilitation for social rehabilitation of these patients is actively carried out. Especially, by analyzing the joint angle, it is possible to evaluate the rehabilitation state of the patient or the recovery after treatment. However, the angular measurement has different reference points to be measured for each measurement tool. Although there are existing equipments for measuring joint angles, it is difficult to perform motion analysis and angle measurement at the same time due to cost, expertise and fixed rotation axis. Therefore, there is a need for equipment to secure these shortcomings. The purpose of this study is to precisely measure and evaluate joint angular displacement considering user convenience and economical efficiency. To this end, we propose a new model that can be applied to bending angle measurement system using optical sensor.

Methods: The joint angle can be calculated by analyzing the optical sensor with the previously proven electronic goniometer. The electronic goniometer used as the reference point and the rotary axis of the goniometer are fixed at the same time, and the infrared sensor is designed so that the output value can be obtained simultaneously according to the change of the angle. The analog data of the goniometer obtained by varying the reference goniometer from 0° to 155° and the signals are is A/D converted using DAQ board and collected by Labview 8.0. In order to design a system with a linear characteristic, the height between the reflector and the sensor is set to 1–6 cm from the axis of the electronic goniometer. The distance of the sensor from the center axis of the electronic goniometer was changed to 17-21 cm.

Results and Conclusions: As the distance of the attached sensor from the same height is closer to the axis of rotation, the range of measurable angle is increased. As the height of the sensor increases at the same attachment distance, the inclination of the measurement value and the measurement angle range become larger. In other words, the range of the measurable angle increases as the sensor height increases and the center axis gets closer. It can be applied to the system which can be used as a diagnostic tool to compare the bending angle of the rehabilitation patient with the normal bending angle and to help the athlete to improve the performance of the athlete. However, at a small range of angles, the resolution of the data is relatively low and the error is likely to occur. To overcome this problem, we will perform further experiments to obtain more quantified data by increasing the resolution of the data through more detailed experiments of each parameter set in the experiment.

Abstract Number: ICBME1172

A Study on Human Joint Angle Measurement Using Infrared-Based Optical Sensor

Geon Ho Kang, Geon Ho Kang, Jae-Hoon Jun
Konkuk University, Korea

Objectives: As modern society develops, patients are increasing day by day due to accidents such as traffic accidents or industrial accidents. Research on rehabilitation for social rehabilitation of these patients is actively carried out. Especially, by analyzing the joint angle, it is possible to evaluate the rehabilitation state of the patient or the recovery after treatment. However, the angular measurement has different reference points to be measured for each measurement tool. Although there are existing equipments for measuring joint angles, it is difficult to perform motion analysis and angle measurement at the same time due to cost, expertise and fixed rotation axis. Therefore, there is a need for equipment to secure these shortcomings. The purpose of this study is to precisely measure and evaluate joint angular displacement considering user convenience and economical efficiency. To this end, we propose a new model that can be applied to bending angle measurement system using optical sensor.

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Abstract Number: ICBME1218
100/min to 120/min. High quality CPR has a positive impact on the survival of cardiac arrest patients and CPR feedback system can improve the quality of CPR. Therefore, in this paper, wristband-type wearable CPR feedback system that can calculate and show the CC depth and rate has been developed so that CPR can be performed in an accurate position.

**Method:** Developed wristband-type wearable CPR module for basic research can measure the CC depth only when the module and floor are perpendicular to each other. However, this system has disadvantages that it may cause errors depending on posture and environment and cannot be used when performing two-finger chest compression technique for infant. Also, the direction in which the wristband-type CPR module is worn has a big effect on its accuracy. Therefore, quaternion is used to obtain accurate CC depth and rate in various situations.

In this paper, MPU6050, 6-axis motion sensor, is used to obtain acceleration and quaternion values. In previous system, accurate CC depth can be obtained only when the axis does not change. However, when using the quaternion rotation transformation by rotating the acceleration axis to the reference axis, the axis of acceleration is always converted to have the same reference axis. So more accurate acceleration can be obtained even if the axis changes during the CPR.

The tilted angle of the module is calculated by quaternion. The pressure depth is obtained by integrating the acceleration twice through the trapezoidal integral. In integration, the trapezoidal integral is used to minimize the integration error. In addition, the CC rate is calculated from the peak-to-peak interval.

To evaluate the accuracy of the tilted angle of the module, electronic goniometer is used. Laser displacement sensor is used to measure the CC depth. And CPR mannequin is used to compare CC rate.

**Result & Conclusion:** This study proposed a wristband-type wearable CPR feedback system complemented by disadvantages of basic research. It can be estimated more accurate CC depth than before. It can also be able to measure when the floor is not horizontal and when performing two-finger chest compression technique. In the future, end-tidal carbon dioxide, which can be used to evaluate the quality of CPR and indicate the patient’s condition, will be measured and provided as a graph.

**Abstract Number:** ICBME1135

**Development of Embedded System for Control of Hyperbaric Oxygen Chamber for Animal Experiment**

**SangHoon Nam, JiHee Yu, Yeo Eun Choi, YunChan Nam, TeaMin Shin**

*Yonsei University, Korea*

Hyperbaric oxygen therapy is a treatment that allows patients to inhale 100 percent oxygen in 2.4 to 2.8 atmospheric pressure, as much as 5 atmospheric pressure. 100% oxygen inhalation in high-pressure environments is a treatment method in which more oxygen is dissolved in the blood and transported to tissues and organs. So, it often used to treat decompression sickness, carbon monoxide poisoning, high-altitude medical problem, and diabetes mellitus. But there has been no case globally yet that the mechanism for hyperbaric oxygen therapy has been revealed. It is necessary to experiment on animals before treatment is performed on humans to identify the mechanism of hyperbaric oxygen therapy. Therefore, in this study, the hyperbaric oxygen chamber for animal experiment with various gas ratios and pressure control was developed using Mess Flow Controller (MFC).

The hyperbaric oxygen chamber for animal testing developed in this study can be tested with a mixture of oxygen, nitrogen, carbon dioxide and atmospheric gases at the desired rate through the MFC. Inside the chamber, oxygen sensors, carbon dioxide sensors, pressure sensors, and flow sensors are attached, and the gas ratio of the mixed gas is estimated through these sensors. The proportional-integral-derivative (PID) control method was used to control the proportional control valves of three input parts and one outlet, and the solenoid valves were additionally attached for safe control. In addition, the operator can control the entire part of the chamber through the 7-inch LCD attached to the front face of the chamber and monitor the conditions inside the chamber in real time.

In this study, many patients receive hyperbaric oxygen therapy, but no experimental hyperbaric oxygen therapy is being carried out to identify the mechanism. To solve this problem, a hyperbaric oxygen chamber for animal experiment is needed, and to operate it, this paper developed an embedded system. Data from temperature and oxygen, carbon dioxide, pressure and flow sensors are collected by the microcontroller. The data collected is shown to the operator via LCD. Through this paper, it is believed that it will be able to provide an animal experiment environment to shed light on the mechanics of hyperbaric oxygen therapy, and it seems that we can expect the development of the hyperbaric oxygen therapy system.

**Abstract Number:** ICBME1140

**Estimation Method for Step Length of Caregiver by Machine Learning Technique Using Combination of Insole Pressure Sensor and Inertial Measurement Unit**

**Kodai Kitagawa, Takayuki Nagasaki, Sota Nakano, Mitsumasa Hida, Shogo Okamatsu, Chikamune Wada**

*Kyushu Institute of Technology, Japan*

**Objectives:** Recently, caregivers experience lower back pain due to their frequent care activities. Previous studies showed that the lumbar load was reduced by adjusting the trunk posture and foot placement during assistive motion. For example, a previous research showed that as the anteroposterior distance and lateral widths between both feet of the caregiver increased, compressive/shear stress of the L4–L5 joint during assistive motion decreased. Therefore, it is considered that a monitoring and feedback system for trunk posture and foot placement is important to prevent lower back pain. Previous monitoring systems for caregiver’s posture used a camera and numerous sensors. However, these systems were considered to have limitation such as place and usability. Then, we have been developing the assistive motion monitoring and feedback
system that uses wearable sensors to prevent lower back pain in caregivers. In this study, we propose estimation method by using insole pressure sensor and inertial measurement unit (IMU) mounted on a trunk.

Methods: The proposed method estimates foot placement using machine learning techniques with feature quantities obtained from insole pressure sensor and IMU mounted on a trunk. In the experiment, we evaluated the root mean square error (RMSE) of the estimated step length during supporting standing-up motion in 100 trial data obtained from 5 participants by 10-fold cross validation. In addition, we compared the RMSE values of three combinations of wearable sensors ("only insole pressure sensor," "only IMU," and "combination of insole pressure sensor and IMU").

Results: The results showed that the RMSE value of the step length estimated by the proposed method using the "combination of insole pressure sensor and IMU" was less than 5% of the body heights. From these results, it is considered that the proposed method can be used in monitoring system to estimate foot placement of caregivers. In addition, we considered that combination of insole pressure sensor and IMU was effective for the proposed method.

Conclusions: We proposed the foot placement estimation method using insole pressure sensor and IMU mounted on a trunk as wearable sensors. The results indicated that the proposed method could be used to estimate foot placement in monitoring system, and combination of insole pressure sensor and inertial sensor was effective for the proposed method.

Abstract Number: ICBME1113

Development of the Standard Brain Artery Structure for Diagnosis Criteria and CFD Control Model

Ko Kitamura, Shunji Mugikura, Makoto Ohta, Hitomi Anzai
Tohoku University, Japan

Cerebral arterial diseases are diagnosed with the interpretation of radiographic images such as MRA and CTA. Medical doctors find diseases based on medical guidelines and their experiences. Currently, quantitative criteria of diagnosis for arterial malformations are lacking. We believe that having the ability to compare the vascular structure between healthy control and patients would allow for a statistical quantification and localization of cerebrovascular defects. The goal of this study is the establishment of the standard structure of brain arteries which is a 3D image model, constructed by normalizing multiple arterial brain images for the use of diagnostic criteria for vascular malformations. To achieve this goal, we already proposed a new method for constructing a standardized cerebrovascular shape: the centerline standardization method.

Computational fluid dynamics (CFD) simulation is widely used for the researches of mechanotransduction, enabling to visualize mechanical stresses on the vasculature. Therefore, the aim of this study is to perform CFD simulation using the standardized cerebral arterial geometry and assess the validity of the standard model for simulation as the control geometry.

Linear registration was performed for MRA images of 40 healthy subjects, and the centerlines of the arteries were acquired, using the image processing software Scikit-image (scikit-image development team). The inscribed circle diameter of the basilar arteries (BAs) was measured. A standard BA was constructed by averaging the X, Y, Z coordinates and the diameter at 21 points that divide the BA into 20 equal lengths. In addition, standard deviations were obtained for X, Y, and Z coordinates. Furthermore, we built a 3D STL geometry using the graphics software Blender (Blender Foundation). In order to make a tubular shape, 81 spheres were linearly interpolated from the coordinate and the diameter of the standard BA, and all those spheres were united. We performed a CFD simulation on the 3D geometry. The simulations were done with STAR-CCM+13.04.010 (SIEMENS, German). The boundary conditions were settled as a rigid wall, blood density, and viscosity (1056 kg/m3, 0.0035 Pa•s), steady Newtonian laminar flow, 165 m/s for inlet flow rate.

We obtained centerline locations and standard deviations of BA from 40 subjects, and also the standardized BA geometry was calculated. Since BAs have relatively large individual differences in shapes, the centerline standardization method is possible to standardize other arteries which have smaller individual differences, for example, internal carotid arteries. It was observed that BA tends to start from either right or left side and goes up to the center of the brain as it approaches the basilar bifurcation. CFD simulation on the standard BA showed a non-parabolic velocity distribution at the outlet.

We proposed a standard cerebral arterial structure of BA. The standard BA was constructed by centerline standardization.
method. Furthermore, CFD simulation for the standard structure was performed. The distributions of WSS and the velocity were related to the geometry. The standard vascular structure will enable us to compare the hemodynamics on disease vasculature and control geometry quantitatively.

Abstract Number: ICBME1125

Computational Modeling of Spontaneous Calcium Transients in PDGFRα+ Cells

Yier Li, Martin Lindsay Buist
National University of Singapore, Singapore

Objectives: Spontaneous transient increases in the cytosolic Ca2+ concentration have been reported in platelet-derived growth factor receptor α positive (PDGFRα+) cells. These spontaneous Ca2+ transients have been implicated in the spontaneous transient hyperpolarizations (STHs) of the PDGFRα+ cell membrane potential via activation of small conductance Ca2+ activated K+ (SK3) channels. The STHs in PDGFRα+ cells are passively conducted to smooth muscle cells (SMCs) via gap junctions, which provide electrical coupling between the cells. The stochastic and asynchronous nature of Ca2+ transients is believed to have a tonic inhibitory effect on gastrointestinal (GI) smooth muscle tissue. Methods – A phenomenological model has been developed to describe Ca2+ transients in PDGFRα+ cells as there is no known mechanism for these transients. The model was constructed using published data recorded from PDGFRα+ cells in the murine gastric fundus and distal colon. Tissue level simulations were performed to investigate the tonic inhibition effects of the Ca2+ transients on the GI musculature. Results – The model is able to reproduce the experimental recordings. It predicts that the persistent Ca2+ transients have a net hyperpolarizing effect on smooth muscle tissue. Conclusion – This model demonstrates the feasibility of the proposed approach and provides a platform for understanding the integrative nature of the SMC/interstitial cell of Cajal/PDGFRα+ cell syncytium.

Abstract Number: ICBME1288

Finite Element Analysis for Flows in a Tumor Microenvironment Considering a Leakage to Interstitium: Two-Dimensional Analysis for a Capillary Network with Complex Vessel Shape

Tomofumi Takeda, Suguru Miyauchi, Toshiyuki Hayase
Tohoku University, Japan

In Japan, about half of cancer patients receive chemotherapy of the standard cancer treatments. Because chemotherapy is a systemic treatment, it is necessary to minimize side effects and transport therapeutic agents efficiently to cancer cells. Cancer tissues have singularity to the normal ones, and it increases the interstitial fluid pressure (IFP) and the high IFP makes the transport of anticancer drug inefficient. However, the relationship between an increase in IFP in the tumor microenvironment and the flow field has not been elucidated. In numerical methods for flows in the tumor environment, most of the analyses assume the blood flow as a Poiseuille flow of an one-dimensional model and treat the leakage from the blood vessel as a source in the three-dimensional interstitium region. However, actual tumor blood vessels have many saccular structures and non-uniform blood vessel diameters, and the influence of such blood vessel shape on the flow field in the tumor microenvironment is unknown. Moreover, in the tumor microenvironment, the blood vessel diameter and size of red blood cells are almost the same, so it is considered the influence of red blood cells on the blood flow cannot be ignored. For considering the complex blood vessel shapes and red blood cells, we developed a coupled analysis method of interstitial flow and blood flow considering leakage from blood vessels in our former study. This study applied the proposed method to a two-dimensional flow field of the complex capillary network, and the effect of the blood vessel shape on the flow field was investigated. This study treated the fluid as incompressible Newtonian fluid, and the blood flow, interstitial flow, and permeation on the blood vessel wall were governed by Stokes equation, Darcy law and Starling equation, respectively. The effects of red blood cells were not considered as a preliminary study. The stabilized finite element method was applied because of the same order interpolation function for the velocity and pressure. The governing equations were coupled by summing the weak formulations of Stokes equation and Darcy law and by applying Starling equation to the pressure difference term. The validity of the proposed method was confirmed by one and two-dimensional verification problems. The computational domain was 250×370 μm rectangular domain consisting of the vascular lumen, vessel wall and interstitium. The blood vessel diameter was non-uniform changing between 8 and 10 μm linearly. The triangular element of the finite element discretization was adopted. This study clarified the velocity and pressure fields in the tumor microenvironment with the complex vessel shape. The effect of vessel wall permeability on the flow and pressure fields inside and outside vessel was also clarified. Furthermore, the result was compared with that in the previous study which models the blood flow as one-dimensional flow and leakage as the source in the interstitium, and the effectiveness of the proposed method was confirmed.

Abstract Number: ICBME1305

Meshless Method for Numerical Solution of Fractional Pennes Bioheat Equation

Hitesh Bansu, Sushil Kumar
Sardar Vallabhbhai National Institute of Technology, India

Fractional calculus has become a hot research topic in many branches of science and engineering during last few decades. The reason is fractional calculus carries some attractive and important advantages. For instance, we can have in-depth and more accurate analysis of the model with the aid of fractional calculus. Because of this advantage in current study, we have implemented the concept of fractional calculus on the Pennes bioheat model with a novel meshless approach. Further, we have introduced two independent discretizations for space and time. Also, we have done the analysis of the behavior of the temperature for the fractional rate of change with respect to space and time.
**Isolation of Paramecium Using a Modernized Electromigration Chip**

**Ashaa Preyadharshini Shunmugam, Javier Gomez Fernandez**  
*Singapore University of Technology and Design, Singapore*

Paramecium is a well-known single celled microorganism that lives in freshwater, brackish and marine water bodies. These are usually 50-300 microns in length and are fully covered with hair-like structures called cilia all around the cell. They are widely been used in schools to study basic cell biology and laboratories as model organisms in various research fields like genetics, evolution biology and cell biology. Recently, paramecium has been studied closely to understand their movement to be bio-mimicked into innovative robots. Even though paramecium has been studied well for years, their isolation process is very old and tedious method. The aim of this project is to improve the isolation process of paramecium using a modernized microfluidic channel and thereby demonstrating the manipulation and control of the movement of paramecium. Galvanotaxis is the innate response of paramecium to an external electric field applied which has been utilized in the isolation method. When electric field is applied in the microfluidic channel, paramecium gets segregated from the rest of the sample and can be collected separately.

**Abstract Number: ICBME1369**

**Survey on "Radiation Dose Structured Report": Management of Medical Radiation Dose**

**Yusuke Oribe, Kiyotaka Iwasaki, Sara Takahashi, Yuka Matsuura, Mitsuo Umezu**  
*Niigata University of Health and Welfare, Japan*

**Objective:** Dose limits for medical exposures are unregulated because patients’ clinical information are regarded to be more beneficial than risks, but justification and optimization of the use of radiation are still required. It becomes mandatory to record and manage medical radiation doses (MRD) on a revision of the Medical Service Act in April 2020 in Japan. The act does not provide specific provisions regarding recording and management of MRD, therefore guidelines by relevant academic societies or organizations will be referred. As an example, Radiation Dose Structured Report (RDSR) which is a kind of structured report defined by Digital Imaging and Communications in Medicine (DICOM) is required in “Guideline for recording medical exposures data” issued by Japanese Society of Radiological Technology. The RDSR has been used for “CT Dose Registry” by American College of Radiology since May 2011, and the data of 1.5 million adults and 800,000 children had been registered in 2 years. In this study, we surveyed the contents of RDSR for recording and management of MRD under the act in Japan.

**Method:** We surveyed the background of recommended using of RDSR and investigated guidelines of academic societies or organizations, reports of Industries Association (JIRA) and International Electrotechnical Commission, and public information issued by Ministry of Health, Labour and Welfare (MHLW).

**Result:** The use of RDSR was recommended in the “Diagnostic Imaging Industry calls on Healthcare IT Vendors to Support IHE dose reporting workflow for CT” agreed by Japan, US, and European industrial groups since 2010. According to the notification of MHLW published on March 12, 2019, only the equipment exposing relatively high radiation dose such as fluoroscopy, CT, and Positron-Emission-Tomography are required to control MRD. The medical exposures were evaluated by RDSR mentioned in the guidelines by the relevant academic...
A fenestrated stent-graft is a promising device used for blocking blood flow into a thoracic aortic aneurysm, while preserving blood flow to supra-aortic branches. However, ineffective seal near supra-aortic branches, especially in aortic curved arches, may induce endoleak.

Objectives: One approach for training a Brain-Computer Interface (BCI) decoder for cursor control assumes that the subject always intends to move in a straight line towards the target. In practice, intended movement direction may not be directed straight at target, leading to mislabelling of output. This may impair the learning of accurate decoder parameters. We propose that training with a subset of data where discrepancy between assumed movement direction and intended movement direction is small can improve decoding. We show that in joystick control, where intended movement direction can be inferred from joystick direction, better decoders can be trained using a subset of data with smaller discrepancies.

Methods: We used data recorded from a Non-Human Primate (NHP) that was implanted with a 100 channel microelectrode array. The NHP used a joystick to perform an 8 direction centre-out cursor task. We computed 500ms firing rates for each channel and trained linear discriminant analysis (LDA) models using either joystick direction or ReFITed directions (direction from current position to target). Joystick and ReFITed directions were mapped to 8 discrete directions. We used only the data when NHP was moving cursor to the target. Data was selected using the criteria that the continuous joystick direction (unmapped) was pointed at the target within a certain cut-off angle. Finally, we tested the LDA model on a validation set and evaluated its performance by computing the mean angle difference between the predicted direction and the joystick direction.

Results: When training with ReFITed directions, mean angle difference in 15 experimental days decreased when using cut-off angles between 15° and 90°. Using an optimal cut-off angle of 30°, mean angle difference decreased on average by 3.46° or 9.43%. This involves a decrease in mean angle difference in 11 out of 15 experimental days. In contrast, when training with joystick directions, mean angle difference monotonically increased as cut-off angle decreased.

Conclusions: If the intended movement direction is known or can be predicted well, decoder training can be improved by selecting a subset of data with the criteria that intended movement direction is pointed at the target within a certain cut-off angle. This approach may be extended to neural control without joystick by using decoder output to select data. This approach also reduces the amount of training required, which may be useful in situations like real time online calibration.

Abstract Number: ICBME1286

Quantification of Blood Vessel Wall Property and Clinical Interpretation of the Result to Presume the Potential Endoleak Risk

Junya Kozaki, Kazuma Nakamura, Kota Shukuzawa, Mitsuo UmezU, Kiyotaka Iwasaki
Waseda University, Japan

Background and objectives: A fenestrated stent-graft is a promising device used for blocking blood flow into a thoracic aortic aneurysm, while preserving blood flow to supra-aortic branches. However, ineffective seal near supra-aortic branches, especially in aortic curved arches, may induce endoleak.
Objective: Statistical multiple linear regression (MLR) technique uses several explanatory variables to predict the outcome of a response variable. The goal MLR is to model the linear relationship between explanatory (independent) and response (dependent) variables. A MLR model is built with the help of TensorFlow, which is equipped with a vast array of Application Programming Interfaces to perform machine learning algorithms. In this study, Range of Motion/ROM [response variable] of the cervical spinal column (C2-T1) is predicted by treating ligament strain, facet forces, resultant load and endplate stresses as explanatory variables.

Methods: The general line equation for MLR is, 
\[ Y_i = \beta_0 + \beta_1 x_{i1} + \beta_2 x_{i2} + \beta_3 x_{i3} + \beta_4 x_{i4} + \epsilon \]

Where Yi is predictior variable (i=1 to n (number of data rows) ) \( \beta_0 \) is intercept \( \beta_1, \beta_2, \beta_3, \beta_4 \) are slope coefficients for \( x_1, x_2, x_3 \) and \( x_4 \). \( \epsilon \) is error term that reduces as number of epoch increases and remains least and constant at one point.

The python environment interfaced with ABAQUS was programmed for determining ROMs across all functional spine units. The dataset was generated from a human cervical spine finite element model (C2-T1). The data was trained, and a model was initially created. Then an unknown data was tested on this model to predict ROM. Machine learning was used to find ROMs for all conditions that are difficult and cumbersome to run on FEA software every time. The final mathematical model explained the relationship between independent and response variables. The degree of relation between independent and dependent variables was determined by the coefficient of determination, R-squared. Root Mean Square Error (RMSE) measured the error between data sets by comparing predicted and observed values.

Results And Conclusion: The dataset was split as 90% training data and 10% testing data, and the R-squared and RMSE values were 0.94 and 0.77. As an improvement in the accuracy of the model, weights can be assigned to every dependent variable. In a weighted regression procedure, more weight is given to observations with smaller variance because they provide more reliable information about the regression function than those with larger variances. Thus, the MLR model successfully helps in predicting the ROM [response variable] of a whole cervical model (C2-T1) by considering ligament strain, facet forces, resultant load and endplate stresses as the explanatory variables. This initial study has shown the effectiveness of combining conventional FEA for modeling the human cervical spine under complex/combined sagittal and lateral bending loads that exist in day-to-day environments with the machine learning process and laying a foundation for future research for medical applications.

Acknowledgements: Supported by Dassault Systemes Foundation, India; Department of Neurosurgery, Medical College of Wisconsin, USA; and VIT, Chennai, India.
Abstract Number: ICBME1418

Irregularity of Forearm Rotation Movement in Patient with Parkinson’s Disease Scans Without Evidence of Dopaminergic Deficit (SWEDD)

Yoon Hyeok Choi, Ji-Won Kim, Yu-Ri Kwon, Ki-Wook Moon, Do-Young Kwon
Konkuk university, Korea

Introduction: It was reported that some of patients clinically diagnosed with Parkinson’s disease (PD) have a normal dopamine transporter scan. This neurological condition has been referred to as scans without evidence of dopaminergic deficit (SWEDD). It is important to quantitatively differentiate patient with SWEDD from patients with PD because they have similar clinical characteristics. Irregular movement is one of clinical feature in PD. Therefore, this study investigated difference between patients with PD and patients with PD in irregularity of forearm rotation movement.

Method: Twenty-three patients with SWEDD and 23 patients with PD participated in this study. A custom-made angular velocity measurement system based on gyro sensor (CG-L53, NEC/Tokin, Japan) was used for measurement of forearm rotation movement. All subjects were instructed to perform pronation-supination movement of wrist for 15 s as rapidly as possible and with as large an amplitude as possible. Angular velocity signals were recorded at 250 Hz sampling frequency. Coefficient of variation (CV) of angular velocity was calculated to represent the irregularity of forearm rotation due to the interruptions or hesitations in ongoing movement. Trend of the movement from the repetitive oscillating signals was derived from the averaged value for 1-second window sliding. Then, the mean and standard deviation of the averaged values were calculated, and the CV was defined as the ratio of the standard deviation to the mean.

Result: SWEDD groups had less irregular angular velocity in comparison with PD groups during forearm rotation (p < 0.05).

Conclusion: This result indicates that PD groups have greater forearm movement variability caused by hesitations, arrests or pauses in ongoing movement as compared to SWEDD groups. This study demonstrated the feasibility of differentiating patients with SWEDD from patient with PD. Quantitative irregularity of forearm movement could aid the clinician in identifying potential SWEDD patients.

Acknowledges: This work was partly supported by the Technology development Program of MSS (No.52588829) and the National Research Foundation of Korea (NRF) funded by the Ministry of Education (No.2018R1C1B6008083).
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