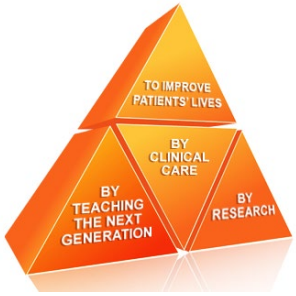
2019 Collaborative Research Symposium
Duke/SingHealth/Duke NUS
Partners in Academic Medicine
August 16, 2019

(Supported by the Duke Office of Duke-NUS Affairs)

Musculoskeletal Sciences Academic Clinical Program

SingHealth / Duke-NUS



AND

Department of Orthopaedic Surgery

Duke University School of Medicine

Department of Orthopaedic Surgery
Duke University School of Medicine

SingHealth DukeNUS ACADEMIC MEDICAL CENTRE

Duke Orthopaedic Surgery and SingHealth/Duke-NUS Musculoskeletal Sciences Collaborative Research Symposium

August 16, 2019
Duke University
Inter-Professional Education Building
311 Trent Drive
Room 1250 (1st floor)

8:00-9:00 a.m. Welcome

Benjamin A. Alman, MD
James R. Urbaniak Professor and Chair
Department of Orthopaedic Surgery
Duke University School of Medicine

Tan Mann Hong, MBBS, FRCS, FAMS
Chair, Musculoskeletal Sciences Academic Clinical Programme
Adjunct Associate Professor, Duke-NUS Medical School
Chairman, Division of Musculoskeletal Sciences,
Singapore General Hospital
Head & Senior Consultant, Musculoskeletal Tumour Service,
Singapore General Hospital

Symposium Goals

Michael "Luke" James, MD FAHA FNCS
Associate Professor, Anesthesiology and Neurology
Clinical Research Liaison, Duke-NUS Affairs
Duke University School of Medicine
Associate Professor of Clinical Sciences
Duke-NUS Medical School

Howe Tet Sen, MBBS, FRCS, FAMS
Vice Chair of Research
SingHealth/Duke-NUS Musculoskeletal Sciences ACP
Senior Consultant, Orthopedic Surgery
Singapore General Hospital
Adjunct Associate Professor
Duke-NUS Medical School

SPEAKERS: Please remember to bring your presentation on a flash drive. The meeting is on a tight schedule so please do not expect to be able to connect your own laptop.

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Schedule	Faculty	Presentation title
9:00 a.m. - 9:06 a.m.	Chen Yongqiang Jerry, MBBS, FRCS	Fixed Bearing Unicompartmental Knee Arthroplasty: Evolving Indications
9:06 a.m. - 9:12 a.m.	William Jiranek, MD	Can we use gene sequencing technology to identify bacteria in Prosthetic joint infections?
9:12 a.m. - 9:18 a.m.	James Mok, MBBS, FAMS (Plastic Surgery)	Non-invasive home management neurostimulation solution for relieving venous stasis and edema in lower limbs
9:18 a.m. - 9:24 a.m.	Erich S. Huang, MD, PhD	Deep Care Management
9:24 a.m. - 9:30 a.m.	Francis Wong Keng Lin, MBBS, MMED (Ortho)	Cell-free regenerative therapies for cartilage regeneration
9:30 a.m. - 9:36 a.m.	Blake Reid Boggess, D.O.	MILES study and clinical uses of orthobiologics.
9:36 a.m. - 9:42 a.m.	Lincoln Liow Ming Han, MBBS, MMED (Ortho)	Biomechanics of kinematic and mechanical aligned total knee arthroplasty
9:42 a.m. - 9:48 a.m.	Gurpreet Baht, PhD	Ageing and the role of circulating factors in fracture healing
9:48 a.m. - 9:54 a.m.	Adrian Ooi, MBBS MMED (Surg) MRCS (Ed) Fams	Abstract title: Bridging the Gap - The SingHealth Plastic Surgery Cadaver Program and Clinical Translation
10:00 a.m. – 10:30 a.m.	**Break (Coffee service in Lobby)**	
10:30 a.m. – 10:36 a.m.	Linda Carime Cendales, MD	Vascularized Composite Allotransplantation Program at Duke
10:36 a.m. – 10:42 a.m.	Kang Yong Chiang, MD	Biomechanics of the Hand and Surgical Applications
10:42 a.m. – 10:48 a.m.	Louis E. DeFrate, PhD	Imaging in Joint Mechanics
10:48 a.m. – 10:54 a.m.	Dr. Hamid Rahmatuallah Bin Abd Razak, MBBS, (Ortho Surg)	A Novel Mechanical Model of Osteoarthritis
10:54 a.m. – 11:00 a.m.	Janet Prvu Bettger, D.Sc	Leveraging technology to optimize health and functioning: VERITAS trial implications on policy, research and practice
11:00 a.m. – 11:06 a.m.	Chung Sze Ryn, MBBCh BAO (NUI), MMED (Surg)	Microvascular anastomosis with fish-mouth suturing and adhesive sealants

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11:06 a.m. – 11:12 a.m.	Shyni Varghese, PhD	Biomaterials Enabled Translational Regenerative Medicine
11:12 a.m. – 11:18 a.m.	Chau Hong Him Dickson, MBBS, MRCS (Edin), MMed (Ortho)	Cognitive Computing applied in Tele-Rehabilitation Surveillance and Diagnostics
11:18 a.m. – 11:24 a.m.	Amy L. McNulty, PhD	Meniscus-Derived Matrix Scaffolds to Promote the Integrative Repair of Meniscal Defects
11:24 a.m. – 11:30 a.m	Dr. Jiang Lei, MBBS, MRCSEd, MMED, (Orthopaedic Surgery)	Neuroprosthetics in Spinal Cord Injury
11:30 a.m. – 11:36 a.m.	Chew Khong Yik, MBBS, FAMS (Plastic Surgery)	**TBD**
11:36 a.m. – 1:15pm	**Speakers Lunch**	
1:15 p.m. – 3:15 p.m. **SCHOOL OF NURSING BUILDING** (see floor plans handouts for conference room locations)	**Work Group Breakouts:** Self-selected investigative teams meet to create collaborative projects, defining milestones and identifying funding sources.	**Work Groups:** Room 1007 (Regenerative Medicine) Room 1013 (Joint/Prosthetics) Room 2010 (MedTech/Device Innovation) Room 2047 (Plastics)
3:15 p.m. – 3:30 p.m.	**Break (Coffee service in Lobby)** Inter-Professional Education Building**)**	
3:30 pm. – 4:30pm.	**Inter-Professional Education Building ROOM 1250**	**Work group presentations for feedback**
3:30 p.m. – 3:45 pm.	Regenerative Medicine group	Regenerative Medicine
3:45 p.m. – 4:00 p.m.	Joint/Prosthetics group	Joint/Prosthetics
4:00 p.m. – 4:15 p.m.	MedTech/Device Innovation group	MedTech/Device Innovation
4:15 p.m. – 4:30 p.m.	Plastics group	Plastics
4:30 pm. – 5:00pm	Michael “Luke" James, MD and Howe Tet Sen, MBBS, FRCS, FAMS	Closing and next steps

Benjamin A. Alman, MD
Chair of Orthopaedic Surgery
James R. Urbaniak, MD, Professor of Orthopaedic Surgery
Professor in Cell Biology
Professor in Pediatrics
Professor in the Department of Pathology

Lab Site: https://sites.duke.edu/almanlab/

Dr. Alman is an orthopaedic clinician-scientist whose research focuses on understanding the role of developmentally important processes in the pathologic process involving the musculoskeletal system. The long-term goal of his work is to use this knowledge to identify improved therapeutic approaches to orthopaedic pathologic disorders. He makes extensive use of genetically modified mice to model human disease, and used this approach to identify new drug therapies for musculoskeletal tumors and to improve the outcome of related processes in cartilage, skin, and bone. As part of this work, Dr. Alman generated novel genetically modified mice to study tumors and reparative processes and is using these to develop new therapies. He also works on cellular heterogeneity in bone tumors, such as sarcomas, and how this relates to developmental processes. His lab identified a subpopulation of tumor initiating cells in musculoskeletal tumors, and found that this subpopulation of is responsible for sarcoma self-renewal.

Another focus of the Alman Lab is to determine the regulation of mesenchymal cells in repair processes. Dr. Alman's work on beta-catenin (ß-catenin) using transgenic mice was the first demonstration of the importance of this pathway in fracture repair. More recently, he used lineage-tracing studies to investigate the role of macrophage cells in skin and bone repair, and found a novel role for young hematopoietic cells in rejuvenating fracture repair.

Dr. Alman is the principal investigator on several NIH grants; has more than 175 peer reviewed publications in journals such as *Lancet*, *Cell*, and *Nature Medicine*; and has supervised over 30 graduate students and postdoctoral research trainees in his lab. He was recruited to Duke from Toronto's Hospital for Sick Children in 2013.

Dr. Alman identified somatic mutations resulting in ß-catenin mediated transcription in more than 70% of desmoid tumors. Based on this work, ß-catenin analysis is used to diagnosis this tumor type, and mutational analysis is used as a prognostic test.

Dr. Alman's group found that ß-catenin mediated transcription is activated during the proliferative phase of wound healing and regulates scar size, as well as osteoblast differentiation in fracture repair. He was the first to show that circulating factors regulate fracture healing and ß-catenin during repair, and using parabiosis, found that factors from the blood of juvenile animals can rejuvenate fracture repair.

The first mutation causing enchondromas (a benign pre-malignant cartilage tumor) was identified by Dr. Alman and his research team. Using a mouse expressing the mutation, he identified pathways regulating tumor progression.

Dr. Alman and his group were the first to show that mesenchymal tumors contain a subpopulation of cells with tumor propagating characteristics and that targeting this cell population can be used to treat sarcomas.

Current Projects

- Identification of properties of tumor proagating cells that can be therapeutically targeted in mouse and human sarcomas
- Use of genetically modified mice to determine how novel members in the hedgehog-signaling cascade regulate bone development, growth, cartilaginous neoplasia and the development of osteoarthritis
- Study of interactions between hematopoietic and mesenchymal cells, and the role of novel proteins involved in this interaction in bone and cartilage development, repair, and the rejuvenation of fracture healing
- Discovery of novel therapies for desmoid tumor, a mesenchymal tumor also called aggressive fibromatosis, using cell culture and genetically modified mice.

Tan Mann Hong
MBBS, FRCS (Edinburgh), FRCS (Glasgow), FAMS
Chair, Musculoskeletal Sciences Academic Clinical Programme

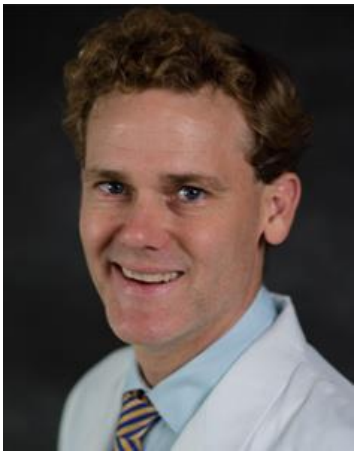
Adjunct Associate Professor, Duke-NUS Medical School
Chairman, Division of Musculoskeletal Sciences, Singapore General Hospital

Head & Senior Consultant, Musculoskeletal Tumour Service, Singapore General Hospital

A/Prof Tan Mann Hong's main interests within orthopaedic surgery are in musculoskeletal tumours, limb sarcomas involving bone and soft tissues, limb salvage surgery, limb reconstructive surgery with mega-endoprostheses and bone allografts, joint replacement surgery, minimally invasive surgery with percutaneous radiofrequency ablation of bone tumours, computer aided surgery in joint arthroplasties and limb reconstruction. In addition, A/Prof Tan also has the longest and largest clinical results for computer navigated TKR from 2007 to present.

As a clinician, A/Prof Tan has made significant contributions in his specialty field. Since 1999, he has been instrumental in establishing SGH as the main referral centre for musculoskeletal tumour surgery and limb salvage reconstructive surgery. A/Prof Tan has cultivated limb salvage surgery in the use of mega-endoprostheses and bone allografts, especially in bone segment replacement for limb sarcomas. He has introduced minimally invasive surgery with percutaneous radiofrequency ablation of bone tumours in Singapore. He also chairs regular sarcoma board conferences with a multi-disciplinary team of oncologists, pathologists and radiologists from the Singapore General Hospital and the National Cancer Centre. These efforts have positively impacted both the safety and quality of clinical care for many musculoskeletal patients.

Michael “Luke" James, MD FAHA FNCS
Associate Professor
Associate Director, Clinical Anesthesiology Research Endeavors
Divisions of Neuroanesthesiology and Critical Care Medicine
Department of Anesthesiology
Associate Director, Brain Injury Translational Research Center
Division of Critical Care and Vascular Neurology
Department of Neurology
Duke University School of Medicine
Faculty, Neuroscience Medicine
Duke Clinical Research Institute
Clinical Research Liaison
Duke-NUS Affairs
Associate Professor of Clinical Sciences
Duke-NUS Medical School
Singapore



Dr. James has an extensive background in neuroanesthesia and neurointensive care and a special research interest in translational and clinical research aspects of intracerebral hemorrhage.

After completing residencies in neurology and anesthesiology with fellowships in neurocritical care, neuroanesthesia and vascular neurology, Dr. James joined the Department of Anesthesiology at Duke University and developed a murine model of intracerebral hemorrhage in the Multidisciplinary Neuroprotection Laboratories. Under the mentorship of Drs. David Warner and Daniel Laskowitz, he pursued translatable mechanisms of modifying neuroinflammation after intracerebral hemorrhage to improve long-term functional recovery. In addition, he has used the model to evaluate the potential of several novel therapeutics for translation into human clinical trials. While maintaining an active and productive laboratory, Dr. James engaged in clinical research as a Principal Investigator on several clinical trials involving patients with intracerebral hemorrhage. As part of the Translational Acute Brain Injury Research Center at Duke University, he has been, the Duke site-PI for large, multicenter trials funded by the NIH, including CLEAR- IVH, MISTIE, ERICH, and HI-Def studies. In addition to a research focus in intracerebral hemorrhage, Dr. James has an active clinical practice in neuroanesthesia and neurocritical care. Duke University Hospital consistently handles a high volume of neurovascular and brain tumor neurosurgical cases, which require neuroanesthesia sub specialization. Our small group of neuroanesthesiologists handles patient care and research opportunities during the peri-operative period, as patients move between the emergency department, neurointensive care unit, operative suites, and neurointerventional suites. Dr. James has visited Duke-NUS and SingHealth numerous times. He visited initially on a Duke-NUS Travel Grant Award and then on a 30 day Academic Leave Award. Subsequently he has visited to continue research collaborations with the National Neuroscience Institute in SingHealth as well as to speak at Anesthesiology conferences.

Dr. James serves as the Duke-NUS Clinical Research Liaison. In this role, he works with the Vice Chancellor of Duke-NUS Affairs to maintain existing Duke / Duke-NUS research links and develop new ones in key strategic areas. He oversees the Duke-NUS clinical research fellowship exchange program, the Duke/Duke-NUS pilot grants, travel grants, and the Duke/Duke-NUS/SingHealth mentoring program. Dr. James has established collaborations with SingHealth National Neuroscience Institute and Duke Department of Anesthesiology and has often visited Singapore. He serves as a point of contact for those who already have research collaborations with Duke-NUS and for anyone interested in exploring research possibilities going forward.

Howe Tet Sen, MBBS, FRCS (Edinburgh & Glasgow), FRCS (England), FAMS

Vice Chair, Research
SingHealth/Duke-NUS Musculoskeletal Sciences Academic Medicine Program

Senior Consultant, Orthopaedic Surgery
SingHealth General Hospital

Associate Professor
Duke-NUS Medical School

Dr. Howe Tet Sen is an Orthopaedic Surgeon with an interest in Sports Medicine, Trauma, Minimally Invasive Surgery and Osteoporosis. He completed his MBBS (Singapore) in 1981 and has FRCS degrees from Edinburgh, Glasgow and England. He is fellowship trained at Sports Medicine from the Cleveland Clinic Foundation. He is currently Vice Chair of Research, Musculo-Skeletal ACP at the Singapore General Hospital. His publications can be found here: https://scholar.google.com/citations?user=vbJiXO4AAAAJ&hl=en

Joyce Koh Suang Bee

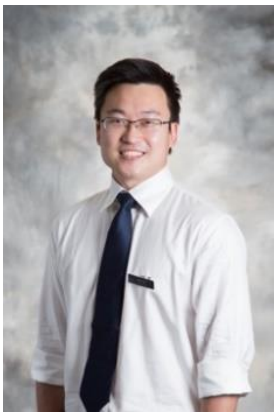
MBBS, FRCS (Edin), FRCSEd (Orth), FAMS
Senior Consultant, Orthopaedic Surgeon, Department of Orthopaedic Surgery
Singapore General Hospital

Dr. Joyce Koh is a senior consultant orthopaedic surgeon at the Department of Orthopaedic Surgery, Singapore General Hospital. She has subspecialty interests in Upper Extremity and Geriatric Trauma care.

Dr Koh has been involved in various educational roles, including as Musculoskeletal Platform director of the Singhealth Surgical Skills Center. She has served on various teaching and administrative roles with AO Asia-Pacific as regional faculty, in driving trauma educational platforms in Singapore, as well as the development of various educational modules.

Research interests include geriartric trauma, atypical femur fractures, novel emerging technologies and health services research She and the local team work closely with Professor Bernard F Morrey and colleagues from the Mayo Clinic, Rochester, MN on the early safety and efficacy trials and clinical implementation of a device for image-guided minimally invasive ultrasonic tenotomy for recalcitrant tendinopathy. Dr Koh also works collaboratively with Prof David Matchar and his team on hip fracture recovery trajectories and the impact of resilience scores on recovery.

Chen Yongqiang Jerry
Associate Consultant, Orthopaedic Surgery
Singapore General Hospital



Title: Fixed Bearing Unicompartmental Knee Arthroplasty: Evolving Indications

Abstract: Introduction: In 1989, Kozinn and Scoot reported the ideal candidate for unicompartmental knee arthroplasty (UKA) based on their clinical experience, including low physical demand patient age > 60 years, non-inflammatory osteoarthritis, mechanical axis of <10 degrees varus or <5 degrees valgus, intact anterior cruciate ligament (ACL), flexion contracture <15 degrees, body weight <82 kg, patellofemoral change not greater than Ahlback Grade II. Other surgeons have added to this list, such as range of motion (ROM) >90 degrees and no previous meniscectomy in lateral compartment. We aim to evaluate if these criteria for fixed bearing UKA are still relevant, based on long term functional outcome scores and implant survivorship.

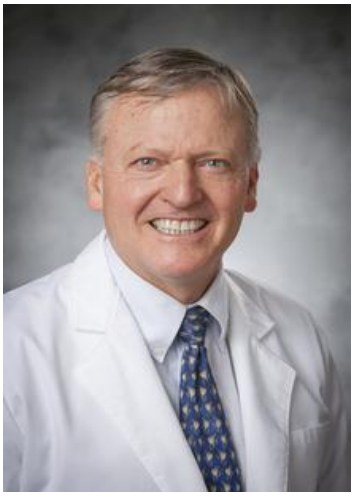
Methods: Ethical approval was obtained from our hospital's ethics committee. Patients diagnosed with isolated end stage medial compartment osteoarthritis and underwent unilateral UKA between 2003 and 2007 were included. All surgeries were performed using the mid vastus approach under tourniquet control. All patients received cemented fixed bearing implants, either Miller-Galante UKA (Zimmer) or Preservation UKA (DePuy Synthes). They were prospectively followed up postoperatively at 6 months, 1 year, 2 years and 10 years. Functional outcomes collected include Knee Society Score, Oxford Knee Score, Short Form-36's Physical and Mental Component Scores, as well as revision surgery to total knee arthroplasty.

Results: Patients ≤55 years had comparable functional outcomes to those age >56 years. The implant survivorship from all-cause revision at 14 years postoperatively were 92.9% and 91.5% respectively. Obese patients (BMI >30 kg/m^2) did experience significant improvement in their function after UKA, although they had poorer long term functional outcomes and implant survivorship compared to those with normal BMI. Those with significant preoperative deformity (varus >10 degrees or flexion contracture >15 degrees) that are passively correctable after bone cuts, also had comparable long term functional outcomes and implant survivorship compared to those with milder preoperative deformity. However, patients with preoperative recurvatum ≥5 degrees experienced poorer functional outcome after UKA. The presence of significant preoperative radiological patellofemoral disease did not affect long term outcome and implant survivorship.

Discussion and Conclusion: With improved implant designs and better understanding of UKA using long term results, the indications and contraindications of UKA have evolved over the last three decades. We recommend UKA as an effective treatment modality for patients with isolated end stage medial compartment osteoarthritis and good ROM of the knee. Contraindications are limited to: 1) inflammatory arthritis; 2) previous meniscectomy in lateral compartment; and 3) preoperative recurvatum ≥5 degrees.

Bio: Dr. Jerry Chen currently works in the Department of Orthopaedic Surgery at Singapore General Hospital. He graduated with Bachelor of Medicine, Bachelor of Surgery (MBBS) from Yong Loo Lin School of Medicine in 2010 and obtained his Fellowship of the Royal College of Surgeons (FRCS Orth) from Edinburgh in 2018. During his training years, he was awarded Best Resident Award and Inspiring Resident Educator Award. He also published more than 45 scientific papers during his residency years and received over $500,000 of grant funding. Dr Jerry Chen sees himself as an outstanding surgeon partnering leading research institutions to be at the cutting edge of technological advancements, so as to improve patients' health care.

William A. Jiranek, MD, FACS
Professor of Orthopaedic Surgery



Title: Can we use gene sequencing technology to identify bacteria in Prosthetic joint infections?

Abstract:

Bio: Dr. Jiranek joined the Department of Orthopaedic Surgery in May 2017 from Virginia Commonwealth University Health System where he was Chief of Adult Reconstruction in the Department of Orthopaedic Surgery and Chief of Musculoskeletal Health in the Neuroskeletal Center for Health and Performance and Professor of Orthopaedic Surgery. Dr. Jiranek's clinical practice focuses on the treatment of hip and knee joint disorders and arthritis. His research interests include tissue-guided restoration of articular cartilage of the knee, joint infections, the body's immune response to biomaterials and innovative practice and funding models. Dr. Jiranek is also a past president of the American Association of Hip and Knee Surgeons.

James Mok
MBBS, MRCS(Ed), MMed(Surgery), FAMS (Plastic Surgery)
Associate Consultant Plastic Surgeon
KK Women's and Children's Hospital

Title: Non-invasive home management neurostimulation solution for relieving venous stasis and edema in lower limbs

Abstract: Revene is non-invasive, compact, on-demand home management solution for relieving venous stasis and edema in lower limbs of patients with early stages of chronic venous insufficiency and for prevention of deep vein thrombosis.

Current preventative therapy is the compression stocking, which is difficult to wear, tight and hot. 80% of patients are non-compliant to compression. For chronic venous ulcer sufferers, this results in 70% ulcer recurrence rate within 2 years. Our device looks to improve preventative treatment compliance in order to reduce ulcer recurrence, and to prevent deep vein thrombosis.

Retrograde neuromuscular electrical stimulation via the posterior tibial nerve is able to safely, comfortably and effectively improve lower limb venous return via stimulation of the superficial and deep posterior calf muscles. Current wired neuromuscular electrical stimulation devices only activate the superficial calf muscles to promote venous return. Our design to activate the superficial and deep calf muscles via the posterior tibial nerve is intended to improve venous return in a wearable, easy to comply device.

Bio: Dr James Mok is a Plastic Surgeon at KK Women's and Children's Hospital, Singapore. His subspecialty interests are paediatric plastic, aesthetic surgery and medical device development. His field of work has included 1) active, occlusive dressings for massive burn victims 2) wound closure device for abdominal dehiscence 3) biochemical sensors to monitor tissue survival after surgery.

Dr Mok aspires to revolutionise fem-tech and baby-tech in his current sphere, by transforming palpable patient needs through high impact inventions and translating them for better patient outcomes.

Erich S. Huang, MD, PhD
Co-Director, Duke Forge (center for health data science)
Director, Duke Crucible (data science accelerator)
Assistant Dean for Biomedical Informatics
Division of Translational Bioinformatics
Department of Biostatistics & Bioinformatics
Department of Surgery
Duke University School of Medicine

Title: Deep Care Management

Abstract: Value-based reimbursement models provide potential avenues for aligning reimbursement with quality care delivery. At the same time, such models require robust analytic capabilities. Erich Huang and his team have worked with Duke Health's Accountable Care Organization, Duke Connected Care (DCC), to apply deep learning to the care management of their attributed population.

Duke Connected Care's "Deep Care Management" is a platform that uses an inferential prediction engine based on a special class of deep learning called "Deep Poisson Factor Modeling" (DPFM) that combines the interpretability found in traditional topic models with deep hierarchies of hidden binary units. The engine incorporates raw Medicare Shared Savings Program (MSSP) claims data in tandem with electronic health record (EHR) data abstracted out of Duke's Epic data warehouse. Claims provide awareness of events that trigger medical charges while EHR data provide more granular information about a patient's encounters.

Key takeaways:

- Dynamic machine learning as a means for operationalizing "learning healthcare"
- Requirement for interdisciplinary teams to make such complex data science platforms successful
- The importance of building "platforms" as opposed to "applications". The Project will only be as successful as it is extensible

Bio: Erich Huang, MD, PhD, is co-director of Duke Forge. Dr. Huang received his PhD and MD degrees from Duke University. There, his doctoral work comprised applying machine learning tools to model cancer signaling pathways. Moving into the world of clinical medicine, Dr. Huang trained in Duke's Surgery Residency Program. After completing his chief residency, Dr. Huang joined the faculty of Duke's Department of Surgery. In 2011, he was recruited to be director of Cancer Research by Sage Bionetworks in Seattle, Washington. There, he led efforts in building a cloud-based platform and tools for Open Science and open cancer data science challenges. There he was funded by the Sloan Foundation for developing scientific provenance APIs. Extensions of that work were funded by the NIH's Big Data to Knowledge program when Dr. Huang was recruited to be the first faculty member in Duke's Division of Translational Biomedical Informatics. He is a Sidney Kimmel Cancer Research Foundation Translational Scholar Awardee, an IBM Faculty Awardee, and a Burroughs Wellcome Fund Regulatory Science Awardee.

Francis Wong Keng Lin
MBBS (Singapore), MRCSEd, MMed (Orth), MCI (NUS), FRCSEd (Orth), FAMS
Associate Consultant, Department of Orthopaedic Surgery, Sengkang General Hospital
SingHealth Duke-NUS Musculoskeletal Sciences Academic Clinical Programme
PhD Candidate, Department of Orthopaedic Surgery, Yong Loo Lin School of Medicine, National University of Singapore

Title: Cell-free regenerative therapies for cartilage regeneration

Abstract: Damaged articular cartilage has an inherently limited capacity for self-regeneration and repair. Patients with knee cartilage injuries have significant morbidity and pain on activity. The natural history of untreated knee cartilage injuries typically shows increased pain and function which limits their daily functions. In professional athletes, chondral injuries of the knee may lead to potentially deleterious effects on their player careers. Long term untreated chondral injuries will eventually lead to an increased risk of developing osteoarthritis. Whilst MSCs or chondrocytes are considered the gold standard of clinical use for cartilage repair, they have a limited cellular capacity for self-renewal, proliferation and differentiation with increasing donor age. Increasingly, clinical and animal studies are suggesting that the therapeutic efficacy of MSCs in tissue repair is likely mediated by the trophic factors secreted by MSCs, instead of their differentiation potential. MSC exosomes are nano-sized, cell-secreted bi-lipid membrane vesicles of about 40-100nm present in the MSC secretome, consisting of proteins, nucleic acids and lipids, and have been found to possess potent immunomodulatory and regenerative properties. As extracellular components, they are considered non-viable and can be stored at -80°C for up to 6 months without loss of bioactivity.

Bio: Dr Francis Wong has a strong interest in orthopaedic tissue regeneration and is actively involved in clinical trials involving autologous bone marrow mesenchymal stem cell (BM-MSC) therapy, where autologous BM-MSC with hyaluronic acid were injected into knees with chondral defects. This strong interest in new discoveries within orthopaedic tissue regeneration especially, in the field of cartilage regeneration, has led him to take up a part-time PhD in NUS, looking at effects of Mesenchymal Stem Cell Exosomes in combination with Hyaluronic Acid as a cell-free therapeutic treatment option for functional cartilage repair.

Blake Boggess, DO, FAOASM
Professor
Duke University School of Medicine
Duke Sports Medicine Team Physician

Title: The MILES Study and Clinical use of Orthobiologics

Abstract: The clinical use of Mesenchymal stem cells has demonstrated promise across all facets of medicine, including orthopedics and sports medicine, where early results have exhibited the potential for enhanced cartilage, tendon and meniscal healing. These results have increased demand among patients of all ages. Several high-profile professional athletes, including National Football League, National Basketball Association and Major League Baseball players have sought these relatively new cell-based therapies for sports-related injuries.

The MILES (**M**ulticenter tr**I**al of stem ce**L**l th**E**rapy for o**S**teoarthritis) study is a randomized multicenter trial comparing the efficacy of corticosteroid control to mesenchymal stem cell preparations from autologous bone marrow concentrate (BMC), adipose derived stem cells in the form of Stromal Vascular Fraction (SVF), and third party human mesenchymal stem cells manufactured from umbilical cord tissue for the treatment of unilateral Knee Osteoarthritis (OA).

Bio: Dr. Boggess received his undergraduate degree from Brigham Young University, where he ran varsity track for four years. He attended medical school at Midwestern University in Chicago and graduated in 2000. Dr. Boggess did his residency and sports medicine fellowship at Duke University where he has been full time faculty for the past 15 years.

His clinical and research interests are musculoskeletal ultrasound, regenerative medicine and non-operative orthopedics. He is a recognized leader in educating other physicians in the use of musculoskeletal ultrasound and orthobiologic procedures. He has directed over 34 ultrasound courses nationally and internationally including Russian, China, Cuba and Taiwan.

Lincoln Liow Ming Han, MBBS, DWD(CAW), MRCSEd, MMED(ORTHO), FRCSEd (ORTH)
Registrar, Department of Orthopaedic Surgery, Singapore General Hospital
Lieutenant Colonel, Navy Medical Service, Singapore Armed Forces
Diving and Hyperbaric Medicine Consultant, Navy Medical Service, Singapore Armed Forces

Title: Biomechanics of kinematic and mechanical aligned total knee arthroplasty

Abstract: Mechanical alignment TKA (MA-TKA) aims to restore a neutral mechanical alignment by positioning the tibial and femoral components perpendicular to each bone's mechanical axis. Although good midterm to long-term implant survivorship is associated with MA-TKA, patient dissatisfaction remains high. To address this high dissatisfaction, kinematic alignment (KA) TKA was introduced, allowing restoration of the original, native, varus lower limb alignment of 2 to 3 degrees. MA-TKA and KA-TKA differences have been reported in multiple clinical outcomes and gait analysis studies and the results are mixed.

TKA with medial pivot liner represents another approach to restore normal knee motion and function by having a more constrained medial articulation and unconstrained lateral articulation. There are limited clinical reports describing outcomes of TKA with medial pivot liner. There is a paucity of biomechanical knowledge regarding the use of medial pivot articulation in KA-TKA, specifically its effects on the knee kinematics and collateral ligaments strain behaviours.

We are planning to investigate the knee joint biomechanics in KA-TKA with medial pivot liner. This is a cadaver study using 16 paired lower limb specimens. Strains and kinematic data are recorded for intact knees and TKA groups during knee flexion-extension cycles using a robotic biomechanical tester. The knowledge gained will enhance the understanding of knee kinematics and collateral ligaments strain behaviours after medial pivot KA-TKA. The results and analyses may help to validate the current medial pivot liner design or allow design improvement. This will hopefully lead to improved knee function, clinical outcomes, implant survivorship and higher patient satisfaction.

Bio: Dr. Lincoln Liow is an Orthopaedic Surgical Registrar at Singapore General Hospital. He is also a Singapore Armed Forces Consultant in Diving and Hyperbaric Medicine. He was selected to undergo an Orthopaedic Biomechanics Research Fellowship at Massachusetts General Hospital (MGH), Harvard Medical School (HMS), Boston, United States of America under the supervision of a leader in orthopaedic biomechanics, Dr. Li Guoan, PhD, Director of the Bioengineering lab at MGH/HMS. He has worked on multiple orthopaedic biomechanics projects and published widely on in-vivo knee biomechanics using dual fluoroscopic and biplanar radiography. His work on Bicruciate retaining total knee arthroplasty was nominated for the New Investigator Recognition Award (NIRA) during the 2016 Orthopaedic Research Society Annual Meeting and awarded the Jacques Duparc Award at the 2019 European Federation of National Associations of Orthopaedics and Traumatology (EFORT). Dr. Liow is a keen clinician-academician, has published >50 peer reviewed articles and serves as an editorial board member / reviewer for several top-ranked Orthopaedic journals. He is also interested in the use of artificial intelligence in Orthopaedic imaging, immunopathology of osteoarthritis and clinical outcomes-based research.

Dr. Gurpreet S. Baht, Ph.D.

Assistant Professor,
Department of Orthopaedic Surgery,
Department of Pathology,
Duke Molecular Physiology Institute
Duke University

Title: Aging and the role of circulating factors in fracture healing

Abstract: Age is a well-established risk factor for impaired bone fracture healing. We have previously demonstrated that youthful circulation is able to rejuvenate aged bone fracture healing. From this work, we have developed a list of “rejuvenating factors” and a list of “aging factors”. Here, we identify a role for apolipoprotein E (ApoE) in age-associated impairment of bone fracture healing and osteoblast differentiation. In both humans and mice, circulating levels of ApoE increase with age. Using an AAV-based siRNA system, we decreased circulating levels of ApoE protein in 24-month-old mice and demonstrated that, as a result, fracture calluses from these aged mice displayed enhanced bone deposition and mechanical strength. Our results demonstrate that circulating ApoE is an aging factor that inhibits bone fracture healing by altering osteoblast metabolism, thereby identifying ApoE as a new therapeutic target for improving bone repair in the elderly.

Bio: Gurpreet Baht, Ph.D., is an Assistant Professor in the Department of Orthopaedic Surgery and Department of Pathology and is a faculty member of the Duke Institute of Molecular Physiology. Dr. Baht’s work focuses on bone health, specifically understanding fracture repair in the context of aging.

The Baht Lab uses mouse models to investigate the process of bone fracture healing and osteoblast differentiation. The current research themes within the lab aim to understand how cellular metabolism and inflammation effect aged bone healing.

Adrian Ooi, MBBS MMed (Surg) MRCS (Ed) FAMS

Adj A/Professor of Plastic Surgery
Program Director, SingHealth Plastic Surgery
Singapore General Hospital

Title: Bridging the Gap - The SingHealth Plastic Surgery Cadaver Program and Clinical Translation

Abstract: It can be argued that the main premise of surgical research is its translatability to clinical practice. One of the mainstays of surgical research and education continues to be the cadaver lab. Here, intricacies of human musculoskeletal anatomy and neurovasculature can be dissected to aid in developing new procedures and techniques. The refinement of vascular injection techniques have further aided in detailed cadaveric study. This talk is centered around the cadaver program at SingHealth Plastic Surgery, including how it is run, the benefits it brings, the research it produces and its application to surgical procedures.

Bio: Dr Ooi is a Consultant Plastic Surgeon in the department of Plastic, Reconstructive and Aesthetic Surgery at the Singapore General Hospital. He is also the Program Director for SingHealth Plastic Surgery, a consultant head and neck reconstructive surgeon in the SingHealth Duke-NUS Head and Neck Disease Center, and Adj Asst Professor at Duke-NUS medical school. He completed medical school in London, and his general and plastic surgery training in Singapore. He has done fellowships in Reconstructive Microsurgery at the University of Chicago and in Aesthetic Surgery at the Wellington Hospital, London.

His clinical interests encompass the spectrum of reconstructive microsurgery, with particular emphasis on post-oncological reconstruction of the head and neck, breast and extremities. He also has a special interest in lymphedema and VCA surgery. His aesthetic surgery interests are primarily of the face and neck.

His research interests include basic, clinical and translational work. The former includes projects and grants for non-invasive flap monitoring using enhanced imaging methods, and bridging nerve gaps utilizing fascicular turnover flaps, for which he received an outstanding presentation award from the American Society for Reconstructive Microsurgery. The latter includes setting up a comprehensive free flap database within SingHealth, developing an in-house computer aided design facility and cadaveric/clinical studies into anatomy and plastic surgical techniques.

Linda C. Cendales, M.D.

Associate Professor of Surgery
Duke Health Scholar
Director, Vascularized Composite Allotransplantation
Duke University Medical Center

Title: Vascularized Composite Allotransplantation Program at Duke

Abstract: Vascularized composite allotransplantation (VCA) is a recently introduced option for limb replacement and reconstruction of tissue defects. Essentially all immunosuppressive regimens reported to date in clinical VCA have used calcineurin inhibitors (CNIs). Accordingly, most VCA recipients have experienced CNI–related side effects. As VCA is typically employed for non-life-threatening conditions, the tolerance for chronic side effects such as those inherent in the use of CNIs is reduced, which makes alternatives to CNIs desirable for VCA

Belatacept is a B7-specific fusion protein that mediates CD28-B7 costimulation blockade (CoB). It has been developed as a CNI replacement in kidney transplantation. We have been the first to show that Belatacept prevents rejection in a non-human primate VCA transplant model of our design. Thereafter, we translated belatacept to the clinic, showing for the first time in clinical hand transplantation that CNI conversion to belatacept could be successfully deployed to reverse CNI–based nephrotoxicity. We have now designed a clinical trial combining depletional induction with transient CNI exposure to test whether a belatacept-based immunosuppressive regimen can be used *de novo,* minimizing chronic exposure to CNIs and their inherent chronic side effects. We reported on the first case of a hand transplant recipient who underwent *de novo* belatacept-based treatment in combination with lymphocyte depletion and short-term CNI exposure with transition to a CNI-free regimen.

Bio: Dr. Cendales is the only person in the United States to have completed formal fellowship training in both Hand and Microsurgery and Transplant Surgery. Dr. Cendales established and published a model of VCA in nonhuman primates and has one of the largest experiences in VCA in non-human primates reported in the scientific literature. She organized the first international symposium on VCA histopathology at the International Banff Conferences on Allograft Pathology leading to the published classification system now used as a standard for clinical reporting of rejection worldwide. Dr. Cendales established the VCA program at Duke and led the multi-disciplinary team that performed North Carolina's first unilateral and the first bilateral hand transplants in May 2016 and in November 2018 respectively. Dr. Cendales is the Principal Investigator of clinical and translational studies in VCA funded by the Department of Defense. Dr. Cendales is the Immediate Past-President of the International Society of Vascularized Composite Allotransplantation Society (ISVCA), the Chairwoman of the Organ Procurement and Transplantation Network / United Network for Organ Sharing (OPTN/UNOS) Vascularized Composite Allograft (VCA) Committee, the Co-Chair Elect of the American Transplant Congress, and the Chairwoman of the American Society of Transplantation VCA Advisory Board.

Kang Yong Chiang, MD

Associate Consultant
Department of Hand and Reconstructive Microsurgery
Singapore General Hospital

Title: Biomechanics of the Hand and Surgical applications

Abstract: The hand is a compact organ engineered to transmit force, provide sensory input, and extend cerebral dexterity. Many aspects of mechanics of the hand remain undiscovered. In the biomechanics lab in Singapore General Hospital, tendon, skin and bony mechanics are studied to provide insights to injury patterns, influence surgical techniques and surgical innovation. High speed videography and advanced computing has enabled progression in motion analysis and video magnification. We hope this can be applied to motion analysis of the hand.

Bio: Kang Yong Chiang, MD is a Hand and Reconstructive Microsurgeon in Singapore General Hospital. He graduated from Yong Loo Lin School of Medicine, and completed Hand Surgery residency program in 2017. His research focus had been on clinical research and surgical innovation. He joined Singhealth in 2018, and is currently developing his interests in surgical applications of tissue mechanics in the hand. He also has interests in integrating video technology to education and research in the hand.

Louis E. DeFrate, PhD
Frank H. Bassett III, M. D. Associate Professor of Orthopaedic Surgery
Associate Professor in the Department of Mechanical Engineering and Material Science
Associate Professor in the Department of Biomedical Engineering
Affiliate of the Regeneration Next Initiative

Title: Imaging in Joint Mechanics

Abstract:

Bio:

Lab Site: sites.duke.edu/defratelab/

The DeFrate laboratory applies engineering principles to study clinically-relevant problems involving the musculoskeletal system. In particular, they evaluate in vivo biomechanics using advanced radiographic and MRI techniques, which enables them to investigate soft tissue structure, composition, and function in healthy and diseased states.

Our laboratory applies engineering principles to study clinically-relevant problems involving the musculoskeletal system. In particular, we evaluate in vivo biomechanics using advanced radiographic and MRI techniques, which enables us to investigate soft tissue structure, composition, and function in healthy and diseased states. We develop volumetric models of joints (including the ankle, knee, shoulder, and spine) and soft tissue structures (such as ligaments, tendons, articular cartilage, and intervertebral discs) from 3D MRI scans and use custom software to evaluate mechanical function during in vivo loading (activities of daily living, walking running, strenuous exercise, etc.). We also use optical motion analysis to capture joint-level kinematics during dynamic motions (gait, landing) and simultaneously acquire high-speed biplanar radiographs to evaluate concurrent soft tissue deformations. By combining these data with MRI sequences that non-invasively quantify tissue composition as well as local and systemic biomarkers of tissue metabolism, we can perform a full-spectrum analysis of joint biomechanical health.

Hamid Rahmatullah Bin Abd Razak, MBBS, GDFM, MRCS (Glasg), M Med (Ortho Surg), MFSTEd FRCSEd (Ortho), FRCSGlasg (Tr & Orth), FAMS (Orth Surg)

Associate Consultant
Department of Orthopaedic Surgery, Sengkang General Hospital
SingHealth Duke-NUS Musculoskeletal Sciences Academic Clinical Programme

Title: A Novel Mechanical Model of Osteoarthritis

Abstract: Current animal models of knee osteoarthritis (OA) involve commonly either an anterior cruciate ligament transaction (ACLT) or a medial meniscus tear (MMT). These models involve intra-articular surgery and incite post-surgical inflammation. At best, they represent secondary knee OA. However, It is known that 80% of knee OA is primary. There is therefore a current gap in developing an animal model that better replicates primary knee OA, and at the same time is cheap, ready available and easy to use in experiments. To address this gap, a novel mechanical model of knee OA in rats has been developed based on a surgically induced varus tibial malalignment. This model has shown that OA changes can be developed in the rodent knee joint without intra-articular surgery. This model can be developed and validated further to be used in multiple studies evaluating mechanical factors in knee OA development and to study the effect of interventions in primary knee OA.

Bio: Dr Hamid Razak is a first-year Associate Consultant. He has published close to 60 scientific articles in peer-reviewed journals to date. Having extensively performed clinical research, Dr Hamid is now focussing on translational biomechanic research. He is currently pursuing a MD (Res) in Orthopaedic Biomechanics at Imperial College London where he is experimenting on new animal models for osteoarthritis. He is also involved with research evaluating the effects of multiligament reconstruction on the native biomechanics of the knee joint using a 6 degree-of-freedom robot arm. Upon his return to Singapore, Dr Hamid hopes to spearhead a biomechanics workgroup to translate laboratory findings to meaningful patient care.

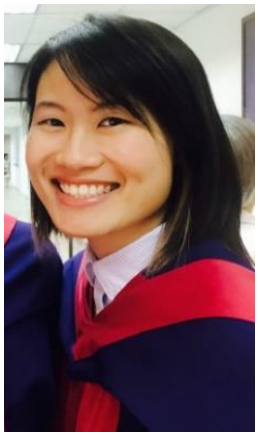
Janet Prvu Bettger, Sc.D. (science doctorate), M.Sc.
Associate Professor of Orthopedic Surgery and Nursing
Co-Director, Duke Clinical and Translational Institute Accelerator Core
Faculty Director, Duke-Margolis Center for Health Policy Undergraduate Initiatives

Title: Leveraging technology to optimize health and functioning: VERITAS trial implications on policy, research and practice

Abstract: Several factors challenge access to specialized therapists prior to or after surgery. Digital health technology can directly address many barriers. Rigorous effectiveness and implementation research are lacking and widespread adoption is limited. We conducted the VERITAS RCT with unilateral TKA patients to examine the effect of a virtual exercise therapy program (digitally simulated avatar coach, in-home 3D biometrics and tele-rehabilitation with a physical therapist) versus traditional therapy in the home or outpatient clinic on healthcare costs and clinical outcomes. Benefits found in this study of 287 adults suggest virtual exercise programs with clinical oversight should be considered for use with patients after TKA. However, a significant amount of research is needed to guide implementation, adaptations to type and dose of therapy facilitated by technology, translation to other populations, and the interface with national policies for value-based care.

Bio: Dr. Bettger's research is dedicated to establishing real world evidence aimed to improve health care quality and policies that reduce the burden of disease and disability. As a health services researcher and implementation scientist, her research extends from observational studies to randomized and pragmatic trials. She has studied implementation of several integrated care models in several countries to improve the transition home from the hospital. She has also studied implementation of primary care and community-based models of care that can prevent functional decline. She has partnered with experts in Singapore on stroke systems health services research, and implementation research, and worked on large cluster randomized trials to improve evidence-based care in Brazil, Peru, Argentina, US and China.

Chung Sze-Ryn, MBBCh BAO (NUI), MRCS (Edin), MMed (Surg)
Senior Resident (Hand & Reconstructive Microsurgery, Singapore General Hospital)
Adjunct Research Fellow (DUKE-NUS)



Title: Microvascular anastomosis with fish-mouth suturing and adhesive sealants.

Abstract: End-to-end anastomosis through conventional interrupted sutures is time consuming, introduces inflammatory trauma, and raises the risk of microvascular complications by exposure to subintimal structures. The four corner sutures based on fish-mouth suturing technique aims to achieve intima apposition with sealing ensured by peripheral tissue adhesive application. Twenty anastomoses were carried out on bilateral common iliac arteries in ten New Zealand white rabbits, where conventional interrupted technique was compared to four corner fish-mouth technique with tissue adhesive. Our results show that the mean anastomosis time for the fish-mouth group reduced by 16% with both groups achieving 100% patency. Both groups had similar scores of inflammation and fibrosis despite the choice of a known inflammatory tissue adhesive. This is a pilot study using adhesive sealants (2-octyl cyanoacrylate) for vessel anastomosis. We are currently working with Nanyang Technology University Singapore in exploring new adhesives for vessel anastomosis.

Bio: Dr. Chung Sze-Ryn is a Senior Resident in Department of Hand and Reconstructive Microsurgery in Singapore General Hospital and an Adjunct Research Fellow at DUKE-NUS. She received her medical degree from Royal College of Surgeons in Ireland and her MRCS from the University of Edinburg in United Kingdom. Upon obtaining her medical degree, she completed her internship in Singapore, and subsequently joined the Singhealth Hand Residency program in 2013. She received her Master of Medicine degree in Surgery from National University of Singapore in 2016. She is passionate about microsurgery and research, especially in the field of clinical research. She hopes to collaborate with like-minded researches across all disciplines to improve outcomes and change clinical practice for the better.

Shyni Varghese, PhD
Professor of Biomedical Engineering, Mechanical Engineering & Materials Science and Orthopaedics Surgery
Duke University

Title: Biomaterials Enabled Translational Regenerative Medicine

Abstract: Reciprocal interactions of cells with their microenvironment are fundamental to multiple cellular processes necessary for tissue development, homeostasis, and regeneration. It is becoming increasingly apparent that while the extracellular environment normally maintains tissue homeostasis, but when negatively perturbed, it may also contribute to disease progression and age-dependent pathologies. In this talk, I will discuss our efforts to delineate the role of the extracellular matrix on cellular responses relevant to tissue repair, stem cell differentiation, and disease progression. In this talk, I will discuss our efforts to delineate the role of the ECM on various cellular responses relevant to tissue regeneration and disease progression. First, I will briefly talk about our efforts to create synthetic analogs of the ECM to direct stem cell commitment *in vitro* and *in vivo* and employ such engineered matrices as a platform to understand the molecular mechanism underlying stem cell differentiation commitment (Shih et al., PNAS 111: 990, 2014; 114: 5419 2017; Kang H et al., Biomacromolecules 16: 1050, 2015). Second, I will talk about our recent efforts to engineer self-healing lubricants to mitigate joint injuries mediated post-traumatic osteoarthritis. I will end by briefly introducing our efforts to develop vascularized tissue and healthy and disease tissue models *in vitro* as a technological platforms to study basic concepts and screen drug and small molecules.

Bio: Shyni Varghese, Ph.D., is a Professor of Biomedical Engineering, Mechanical Engineering & Materials Science, and Orthopaedics Surgery at Duke University. She is also the inaugural MEDx investigator at Duke University. Prior to moving to Duke she was a Professor of Bioengineering at University of California, San Diego with affiliations in NanoEngineering, Materials Science and Institute of Engineering in Medicine. Dr. Varghese's research is at the interface of biologically inspired materials and stem cells. Dr. Varghese has co-authored over 100 peer-reviewed research articles, covering a wide range of interdisciplinary topics in stem cells, smart biomaterials, biologically inspired systems, and regenerative medicine. Her research activities have also resulted in over 12 patent disclosures. Examples of ongoing research activities in her laboratory involve developing functional biomaterials such as self-healing materials; technologies to improve stem cell based therapies including stem cell differentiation, cell transplantation, activating endogenous stem cells, engineered functional tissue grafts; and organ-on-a chip systems. She serves on various scientific bodies and is also on the editorial board of a number of journals and a consultant to various biotech companies. She is currently serving as an associate editor of Biomaterials Science (an RSC journal).

Chau Hong Him Dickson, MBBS, MRCS (Edin), M Med (Ortho)
Senior Resident, Singhealth Orthopaedic Residency Program
Medical Officer (Major), Headquarters Medical Corps. Singapore Armed Forces

Title: Similar radiological results with accelerometer-based navigation versus conventional technique in total knee arthroplasty.

Abstract:

Bio: Dr Dickson Chau is an Orthopaedic Senior Resident. He was awarded a military scholarship and in his military medical work has driven policies and participated in operations related to Humanitarian Aid, Disaster Relief, and Specials Operations Medical Ops. Dr. Dickson's research interests are in MedTech and his current projects include application of 3D printing and mobile-apps to orthopaedic education, and is currently applying for grants for tech-in-community to pilot wearable enabled remote musculoskeletal rehabilitation, and medical innovation collaboration grant between orthopaedics and radiology to develop an intraoperative surveillance device.

In his free time, Dr Dickson is a pro bono medical advisor to a Telemedicine start-up registered with the Ministry of Health regulatory sandbox, teaches computer coding to underprivileged children, and writes code to automate resident administrative tasks.

Amy L. McNulty, PhD
Associate Professor of Orthopaedic Surgery
Associate Professor of Pathology
Duke University School of Medicine

Title: Meniscus-Derived Matrix Scaffolds to Promote the Integrative Repair of Meniscal Defects

Abstract: Meniscal tears have a poor healing capacity, and damage to the meniscus is associated with significant pain, disability, and progressive degenerative changes in the knee joint that lead to osteoarthritis. Therefore, strategies to promote meniscus repair and improve meniscus function are needed. The objective of this study was to generate porcine meniscus-derived matrix (MDM) scaffolds and test their effectiveness in promoting meniscus repair via migration of endogenous meniscus cells from the surrounding meniscus or exogenously seeded human bone marrow-derived mesenchymal stem cells (MSCs). Both endogenous meniscal cells and MSCs infiltrated the MDM scaffolds. In the absence of exogenous cells, the 8% MDM scaffolds promoted the integrative repair of an in vitro meniscal defect. Dehydrothermal crosslinking and concentration of the MDM influenced the biochemical content and shear strength of repair, demonstrating that the MDM can be tailored to promote tissue repair. These findings indicate that native meniscus cells can enhance meniscus healing if a scaffold is provided that promotes cellular infiltration and tissue growth. The high affinity of cells for the MDM and the ability to remodel the scaffold reveals the potential of MDM to integrate with native meniscal tissue to promote long-term repair without necessarily requiring exogenous cells.

Bio: The long-term goals of the McNulty Lab are to develop strategies to prevent osteoarthritis and to promote tissue repair and regeneration following joint injury. In order to achieve these goals, we need to understand the mechanisms necessary for tissue repair and regeneration and how they are altered with aging and joint injury. Specifically, Dr. McNulty's lab is working to enhance the integrative repair of meniscus to restore meniscal function and decrease the risk of osteoarthritis development. The lab has identified IL-1 and TNF as inhibitors of integrative meniscal repair and are developing novel methods to suppress inflammation and the downstream mediators of these cytokines to promote tissue repair. Furthermore, Dr. McNulty and her team are working to understand the pathways that are activated by normal and injurious mechanical loading of joint tissues and how these mechanotransduction pathways are altered during aging. A greater understanding of alterations in mechanosensitive signaling mechanisms with aging and injury will likely reveal potential targets to prevent tissue degeneration and osteoarthritis. In addition, the following specific research areas are currently being investigated: 1) improving meniscus repair using a meniscus-derived matrix allograft; 2) mechanotransduction in meniscus health and repair; 3) the interplay between mechanical and biological signals in meniscus health and injury; and 4) rejuvenation of aging chondrocytes to enhance reserve and prevent osteoarthritis.

Jiang Lei, MBBS, MRCSEd, MMed (Orthopaedic Surgery)
Senior Resident, Orthopaedic Surgery
Singhealth

Title: Neuroprosthetics in Spinal Cord Injury

Abstract: Spinal cord injury is a debilitating condition with poor functional recovery despite modern surgical advances. The development of neuroprosthetics can potentially change the paradigm of spinal cord injury management and restore motor function via interfacing electrodes. The talk describes the challenges facing the use of neuroprosthetics in spinal cord injury patients and summarizes the different strategies that may be used to in the implantation of neuroprosthetics. The use of a novel wireless neuroprosthetic device in a non-human primate model will be described, demonstrating the stimulation of grip strength via signals proximal to a site of nerve injury in the primate model and its potential use in spinal cord and nerve injury patients.

Bio: Dr Jiang Lei is a clinician-scientist senior resident from the Singhealth Orthopaedic Surgery residency programme. His previous research included clinical studies validating prognostic scores for hip fracture mortality as well as the effect of lumbar fusion on total hip arthroplasty outcomes. His specialty interest is in spinal surgery and his research interests include the use of neuroprosthetics in spinal cord injury, working closely with the National University of Singapore.

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