Australian & New Zealand Orthopaedic Research Society

ANZORS 25th Annual Scientific Meeting

04-06 October 2019

Program

The John Curtin School of Medical Research (JCSMR),
Australian National University (ANU),
131 Garran Rd, Acton ACT 2601, Australia.

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ANZORS 25th Annual Scientific Meeting

President's Welcome

Welcome to this year's annual ANZORS conference. This year marks the 25th Annual meeting of ANZORS (1995-2019) which is a special occasion and I look forward to celebrating it altogether. This is highlighted also by our social and scientific program, which includes a talk by Past President David Haynes about the history of the Society. It is a pleasure to celebrate this anniversary in the capital city of Australia, visiting Canberra and Australian National University, which has a great history of producing outstanding basic and translational research in the area of orthopaedics.

My warm welcome to our visitors from interstate and overseas to the conference and I look forward to engaging with you throughout the conference. Once again, we are able to offer awards and travel grants thanks to the support of our sponsors.

I would like to extend my thanks to Dr Diana Perriman and Professor Paul Smith, Mr Joe Lynch and Dr Rachel Li for all their hard work this year in preparing for this conference.

The scientific program is a multidisciplinary mix of basic, translational and applied orthopaedic research, which sets ANZORS apart from other societies. ANZORS provides a vibrant, multidisciplinary and informal environment, an excellent terroir for early career researchers and young students to meet with established scientists and professors with a passion for science and orthopaedic research. I share this spirit, this is the way I believe ANZORS has to continue in future. Big problems need multidisciplinary teams to be tackled and this is what we do well at ANZORS, please engage with each other and mingle. Importantly, orthopaedic research needs to receive the funding it deserves. Together we must advocate for it and for the government to distribute it in a more equitable way.

This conference is the first of my three-year tenure as the President of ANZORS. Over the next years I will be engaged in keeping the society growing, strengthen our relationship with other societies, engage further with the International Combined Orthopaedic Research Societies (ICORS) and the International Federation of Musculoskeletal Research Societies (IFMRS). There are achievements I am and we all have to be proud of: the induction of our FIOR Fellows at the recent ICORS 2019 meeting in Canada (Professors Hala Zreiqat, Jill Cornish, Jiake Xu, David Haynes, John Costi and Gerald Atkins); Australia being selected as Guest Nation at the upcoming ORS 2020 meeting in Arizona USA; ANZORS having won the international bid, led by Dominic Thewlis, together with myself, Gerald Atkins and Bogdan Solomon, to host the ICORS meeting in 2025 in Adelaide.

There is still work to be done and I look forward to continue working with the Secretary of ANZORS, Tania Crotti, the Treasurer David Ackland and the Immediate Past President Dominic Thewlis over the next years.

Please enjoy and engage with the great science presented over the next three days and the social sides of the conference program.

Egon Perilli
President, Australian & New Zealand Orthopaedic Research Society
Senior Lecturer, Biomedical Engineering, Medical Device Research Institute, College of Science and Engineering, Flinders University

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ANU prides itself on its international reputation for health and medical sciences research and education. Our influential outreach activities include a national role in promoting research-driven public policy, and strong connections to fundamental biosciences.

ANZORS 25th Annual Scientific Meeting

Committee Members

President Dr Egon Perilli	Senior Lecturer in Bioengineering, The Medical Device Research Institute, College of Science and Engineering, Flinders University
Secretary A/Prof Tania Crotti	Postgraduate Coordinator Manager for the Adelaide Medical School, Co-leader of the Bone and Joint Laboratory, The Faculty of Health and Medical Sciences, The University of Adelaide
Treasurer Dr David Ackland	Senior Lecturer and Deputy Head, Department of Biomedical Engineering, The University of Melbourne
Immediate Past President A/Prof Dominic Thewlis	NHMRC R.D. Wright Fellow and Associate Professor, Centre for Orthopaedic & Trauma Research, The University of Adelaide
2019 Host Organiser Dr Diana Perriman	Research Coordinator for the Trauma & Orthopaedic Research Unit, Senior Lecturer, Australian National University Medical School (ANU)
Prof Paul Smith	Leader of the Trauma & Orthopaedic Research Unit, Professor, Australian National University Medical School (ANU)
Dr Rachel Li	Laboratory Research Lead, Trauma & Orthopaedic Research Unity, John Curtin School of Medical Research, Australian National University Medical School (ANU)

Organising Committee

Local Conference Organising Committee

Dr Diana Perriman, ANU, Co-Chair

Prof Paul Smith, ANU, Co-Chair

Dr Rachel Li, ANU

Mr Joe Lynch, ANU

Dr Egon Perilli

A/Prof Tania Crotti

Dr David Ackland

A/Prof Dominic Thewlis

Scientific Committee

(alphabetical surname order)

Dr David Ackland	The University of Melbourne
Dr Rami Al-Dirini	Flinders University
Dr John Arnold	University of Leeds, UK
Prof Gerald Atkins	The University of Adelaide
Dr Stuart Callary	The University of Adelaide
A/Prof Tania Crotti	The University of Adelaide
Dr Dane Dabirrahmani- Turner	Macquire University
Dr Claudia Di Bella	The University of Melbourne
A/Prof Justin Fernandez	The University of Auckland
Prof David Findlay	The University of Adelaide
Prof Peter Lee	The University of Melbourne
Dr Jiao Jiao Li	The University of Sydney
Dr Rachel Li	Australian National University
Dr ZuFu Lu	The University of Sydney
Dr Saulo Martelli	Flinders University
Dr David Musson	The University of Auckland
Dr Elyse Passmore	The University of Melbourne
A/Prof Nathan Pavlos	The University of Western Australia
Dr Egon Perilli	Flinders University
Dr Diana Perriman	Australian National University
Prof Peter Pivonka	Queensland University of Technology
Dr Bryant Roberts	The University of Sheffield, UK
Dr Dale Robinson	The University of Melbourne
Dr Melissa Ryan	The University of Sheffield, UK
Prof Paul Smith	Australian National University
Dr Corey Scholes	EBM Analytics (NSW)
Prof Bogdan Solomon	The University of Adelaide
Dr Kathryn Stok	The University of Melbourne
A/Prof Ashvin Thambyah	The University of Auckland
A/Prof Dominic Thewlis	The University of Adelaide
Prof Cory Xian	University of South Australia
W/Prof Jiake Xu	The University of Western Australia

ANZORS 25th Annual Scientific Meeting

Travel Grant Recipients

(alphabetical surname order)

ANZORS is proud to support its early career researchers. This year we have awarded 24 travel grants. This represents a significant reinvestment of our funds to support the dissemination of quality orthopaedic research.

Surname	First Name	Institution
Al-Dirini	Rami M A	Flinders University, Australia
Bahl	Jasvir	University of South Australia, Australia
Barzan	Martina	Griffith University, Australia
Bennett	Kieran	The University of Adelaide, Australia
Bucci	Francesca	Flinders University, Australia
Chen	Kai	The University of Western Australia, Australia
FitzPatrick	Anthony	The University of Canterbury, New Zealand
Francis	Sam	The University of Melbourne; St Vincent's Hospital, Australia
Grace	Thomas	The University of Adelaide, Australia
Kabir	Wassif	The University of Melbourne, Australia
Lees	Florence	The University of Adelaide, Australia
Li	Jiao Jiao	The University of Sydney, Australia
Malekipour	Fatemeh	The University of Melbourne, Australia
Muratovic	Dzenita	The University of Adelaide, Australia
No	Young Jung	The University of Sydney, Australia
Ormsby	Renee	The University of Adelaide, Australia
Rapagna	Sophie	Flinders University, Australia
Robinson	Dale	The University of Melbourne, Australia
Russo	Michael	Flinders University, Australia
Shaktivesh	Shaktivesh	The University of Melbourne, Australia
Stapledon	Catherine	The University of Adelaide, Australia
Thomas	Megan	The University of Melbourne, Australia
Yuan	Jun	The University of Western Australia, Australia
Zhang	Xin	The University of Melbourne, Australia

ANZORS 25th Annual Scientific Meeting

Keynote Speakers

Prof Linda Sandell

Past OARSI President; Editor of Journal of Orthopaedic Research; Mildred B. Simon Research Professor and Director of Research; Director, Center for Musculoskeletal Research; Department of Orthopaedic Surgery, Washington University School of Medicine, St. Louis, Missouri, USA

Dr. Linda Sandell is the Inaugural Mildred B. Simon Professor of Orthopaedic Surgery (Research) and Founding Director of the Core Centers for Musculoskeletal Biology and Medicine at Washington University in St. Louis. She has been a leader in the field of orthopaedic research, pioneering the use of molecular biologic techniques, large screening technologies, microscopy, computational biology and genetics to study cell responses to cartilage cell injury, cartilage regeneration, the regulation of gene expression and osteoarthritis. Dr. Sandell has a B.A. in Zoology and a M.S. in Biological Sciences from the University of Denver, and Ph.D. from Northwestern in Biochemistry.
Dr. Sandell was President of the Orthopaedic Research Society and co-founder of the Women's Leadership Forum. She was President of the Osteoarthritis Research Society International (2010- 2013), the Society for Matrix Biology and the Histochemistry Society. She has chaired three Gordon Conferences and founded the Gordon Conference on Cartilage Biology and Pathology. Dr. Sandell has been received numerous awards, in particular, the Kappa Delta Award for Basic Science Research by the American Association for Orthopaedic Surgeons (1992), the Women's Leadership Forum Award (2010) the Alfred R. Shands Jr, MD Award (2015), the Distinguished Investigator Award (2016) by the Orthopaedic Research Society, and Lifetime Achievement Awards from Osteoarthritis Research Society International (2016) and the International Cartilage Repair Society (2017). She is a Fellow of the Orthopaedic Research Society and the International Orthopaedic Research Societies. She is currently the Editor-in-Chief of the Journal of Orthopaedic Research.

A/Prof Tasha Stanton

Associate Professor in Clinical Pain Neuroscience School of Health Sciences, University of South Australia, Australia

Associate Professor Tasha Stanton is a clinical pain neuroscientist at the University of South Australia, Adelaide and Neuroscience Research Australia, Sydney. A/Prof Stanton leads the Pain and Perception laboratory at the University of South Australia and currently holds a National Health & Medical Research Council (NHMRC) Career Development Fellowship. She has received ~$3.4m in competitive research funding, has published >60 peer-reviewed papers, and has been a keynote/invited speaker at >50 national and international conferences. Originally trained as a physiotherapist, her research focusses on perception and pain neuroscience, with a specific interest in osteoarthritis, cortical body representation, somatosensation, multisensory integration, and multimodal illusions. She has received numerous awards for her work including the Ronald Dubner Research Prize from the International Association for the Study of Pain (2016), The Rising Star Award from the Australian Pain Society (2016), the Top 5 under 40 science communicators award from ABC Radio National & UNSW (2016), and The Young Tall Poppy of the Year award (2015).

Prof Rick Sumner

Past ORS President; Professor and Chair, Department of Cell & Molecular Medicine, Rush University, Chicago IL, USA. The Mary Lou Bell McGrew Presidential Professor for Medical Research.

D. Rick Sumner, PhD was trained in biological anthropology and anatomy at the University of Arizona. He was a post-doctoral fellow at Rush University Medical Center, working with Jorge Galante, MD, DMSc, a renowned orthopedic surgeon/scientist who was instrumental in the development of cementless arthroplasty. Dr. Sumner is currently the Mary Lou Bell McGrew Presidential Professor for Medical Research and chair of the Department of Cell & Molecular Medicine at Rush. He is also the director of the Rush MicroCT/Histology Core Laboratory. His primary areas of interest are bone regeneration and implant fixation. He is best recognized for work on bone remodeling around orthopedic implants and developing strategies to improve implant fixation by promoting bone regeneration. Dr. Sumner has been funded through the NIH, the Department of Defense, NASA, several foundations and industry since the late 1980's. He has served on numerous grant review panels and has won several international and national awards, including the Kappa Delta Award from the American Academy of Orthopaedic Surgeons and is a fellow of the American Association for Anatomy. He is currently the principal investigator on two research grants from the NIH and one NIH training grant. He is a member of numerous scientific societies, including the American Association for Anatomy (current President), Orthopaedic Research Society (a past President), International Society of Bone Morphometry (current President), International Federation of Musculoskeletal Research Societies (current Secretary) and the Association of Anatomy Cell Biology Neurobiology Chairs (current Secretary-Treasurer).

Prof Fary Khan

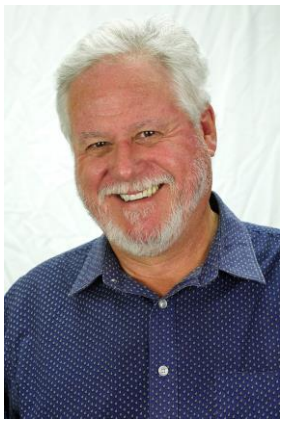
The Royal Melbourne Hospital, Director of Rehabilitation Services and Clinical Director of the Australian Rehabilitation Research Centre, RMH, Australia

Professor Fary Khan is the Director of Rehabilitation Services and Australian Rehabilitation Research Centre, Royal Melbourne Hospital; Clinical Professor, University of Melbourne; Adjunct Professor, Nossal Institute of Global Health and School of Public Health and Epidemiology, Monash University. She is the current Chair of the Disaster Rehabilitation Committee, International Society of Physical and Rehabilitation Medicine; and Chair of Disaster Rehabilitation Special Interest Group, Rehabilitation Medicine Society of Australia and New Zealand. She currently holds over 20 national/international executive positions and over 15 international academic research appointments.

She has a leadership role in rehabilitative care in Australia and extensive experience in evidence-based research, for which she has received numerous awards, including the 2018 ISPRM Sidney Licht Lectureship Award. She has published over 350 scientific papers in academic journals, and is invited speaker at national and international conferences (over 60 presentations in last 5 years). She currently supervises 8 PhD and 3 MD students at the University of Melbourne. She is editor/reviewer for more than ten academic journals.

Prof David Haynes

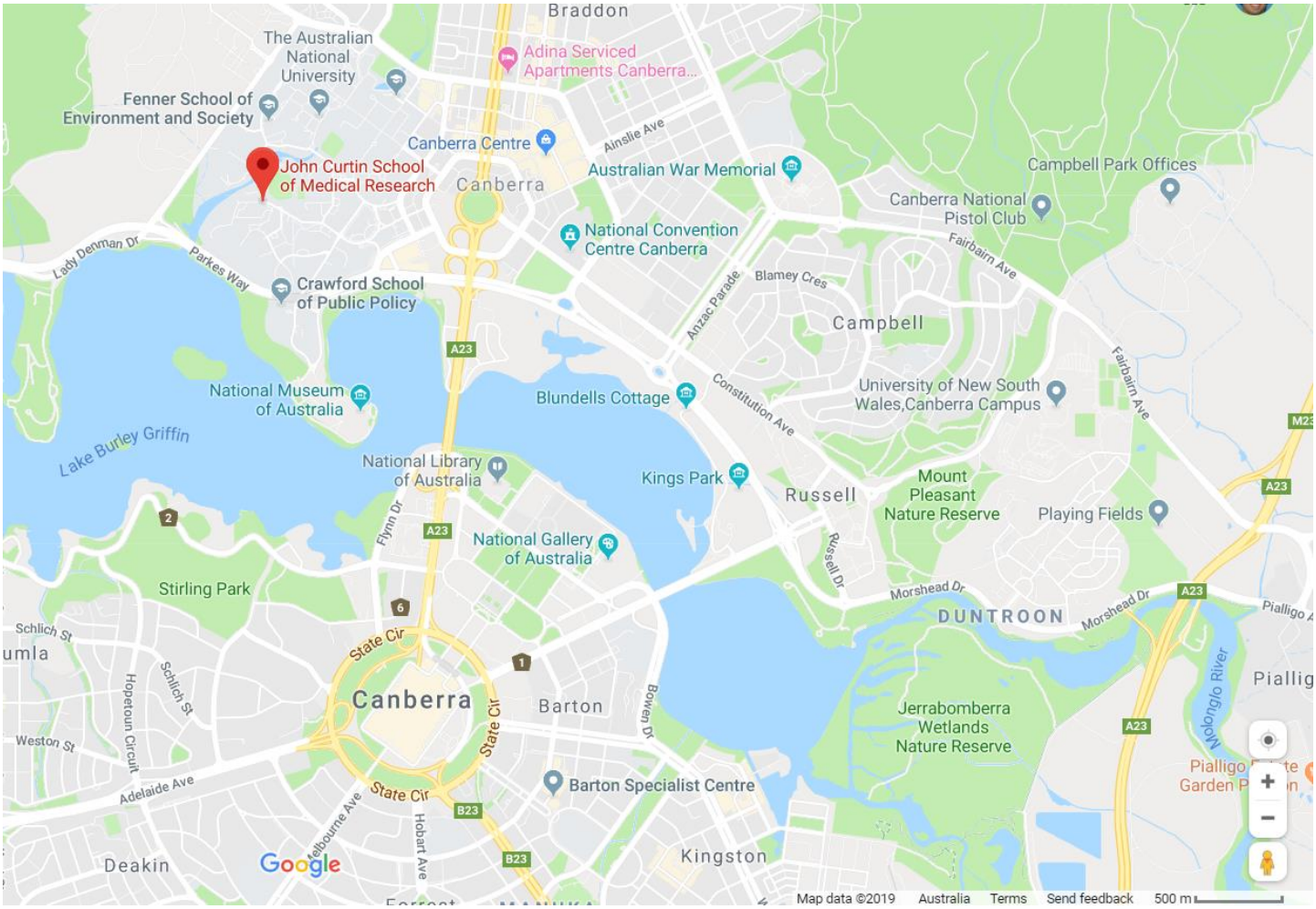
Deputy Head of Adelaide Medical School, University of Adelaide, Australia. Former ANZORS president



Professor David R Haynes has been Head of the Disciple of Anatomy and Pathology, Head of the School of Medical Sciences and Deputy Head of the Adelaide Medical School, University of Adelaide. He has published over 130 publications in respected peer reviewed journals. Over the past two decades he has developed a respected international reputation in the fields of bone pathologies, biomaterials and inflammation. During the 2000's he was Secretary then President of the Australian and New Zealand Society of Orthopaedic Research. In these roles he has help organise more than 7 national and 3 international meetings. Professor Haynes has been chief investigator on more than 17 successful major national and international grants since the early 1990's as well as several other commercially funded studies on pharmacological regulation of inflammatory cytokines, pathogenic bone loss and implant loosening. He also makes a significant contribution to the training of medical students (MBBS), Dental, Health and Medical Science and Nursing students in the Faculty of Health and Medical Sciences. In 2019 he was made a Fellow of the International Orthopaedic Research Societies (FIOR).

Venue

The John Curtin School of Medical Research,
(Finkel Lecture Theatre, ground floor, main entrance),
ANU, 131 Garran Rd, Acton ACT, Canberra, Australia



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25th Anniversary
Australian & New Zealand Orthopaedic Research Society
Australian & New Zealand
Orthopaedic Research Society

PROGRAM

Day 1 (Friday October 04)

Finkel Lecture Theatre, ground floor, The John Curtin School of Medical Research, ANU, 131 Garran Rd, Acton ACT

08:00-08:25	Coffee and registration		
08:25-08.30 **08:30-08:45**	**Welcome: Prof Klaus-Martin Schulte, Chair of Surgery, ANU College of Health and Medicine** **ANZORS President's welcome: Dr Egon Perilli**		
08:45-09:15 Session Sponsor: ANU Session chair: Prof Jiake Xu	**Keynote: Prof Linda Sandell, Washington University School of Medicine, St. Louis, MO, USA** **"Genetic Correlations between Cartilage Regeneration and Degeneration Reveal an Inverse Relationship"**		
09:15-10:15	**First name**	**Surname**	**Abstract title**
Podium 1 Session chair: A/Prof Tania Crotti	Jiake	Xu	New insights into the role of Methionine 199 in the function of Receptor Activator of Nuclear Factor Kappa-B Ligand (RANKL) and bone homeostasis
	Youshui	Gao	Dual effects of miR-136-3p on osteogenesis and angiogenesis to alleviate alcohol-associated osteoporosis via targeting PTEN pathway
	Catherine	Stapledon	A novel investigation into the effects of the Amyloid Precursor Protein on the Osteocyte
	Megan	Thomas	Chondrocyte response to focal unloading in vivo: a differential interference contrast study
	Jun	Yuan	Mitophagy regulates glucocorticoid-induced osteocytic osteolysis
10:15-10:55 Morning coffee & tea; foyer, ground floor, The John Curtin School of Medical Research			
10:55-12:07	**First name**	**Surname**	**Abstract title**
Podium 2 Session chair: Dr Dzenita Muratovic	Kai	Chen	Reactive oxygen species enhances osteoclast activity in steroid-induced osteonecrosis of femoral head
	Jacob	Kenny	Utilising the collaborative cross to investigate genes associated with osteoarthritis progression in mice and humans
	Minhao	Gao	Two types of osteocytes depending on the process of ossification
	Mohammadhossein	Hassanshahi	Icariin attenuates methotrexate chemotherapy-induced bone loss and bone marrow micro-vascular damage in rats
	Peilin	Chen	Compromised cell function and extracellular matrix degeneration in loading-deprived tendon
	Meredith	Harrison-Brown	Limited penetration of cobalt and chromium into the cerebrospinal fluid following metal-on-metal arthroplasty: a cross sectional analysis
12:07-13:20 Lunch & poster viewing (poster viewing will take place between 12:30-13:20) Foyer, ground floor, The John Curtin School of Medical Research			
13:20-13:50 Session chair: Dr Dané Dabirrahmani	**Keynote: A/Prof Tasha Stanton, University of South Australia, Adelaide SA, Australia** **"Osteoarthritis is all about the joint -or is it? Considering new insights from pain neuroscience"**		
13:50-14:50	**First name**	**Surname**	**Abstract title**
Podium 3 Session chair: A/Prof Ashvin Thambyah	Delin	Liu	The expression of DMP1 in mouse central nervous system
	Jiao Jiao	Li	Stem cell therapy for osteoarthritis - Does it work?
	Wassif	Kabir	Functional mechanical testing of native human knee articular cartilage
	Michael	Russo	Lumbar disc herniation failure after multiaxial fatigue
	David	Ackland	Hip abductor muscle volumes are smaller in individuals affected by patellofemoral joint osteoarthritis
14:50-15:30 Afternoon coffee & tea and poster viewing; foyer, ground floor, The John Curtin School of Medical Research			
15:30-16:42	**First name**	**Surname**	**Abstract title**
Podium 4 Session chair: Prof Rick Sumner ***: Orthopaedic Innovation finalist**	Rami	Al-Dirini	Computational efficient method for assessing the influence of surgical variability on primary stability of a contemporary femoral stem in a cohort of subjects
	* Martina	Barzan	Virtual planning and personalised cutting guides for juvenile femoral osteotomies
	* Cheryl	Lee	Biofabrication of human articular cartilage: analysis of genotoxicity, cytotoxicity and chondrogenesis
	* Sam	Francis	Rapid isolation of mesenchymal stem cells to treat clinically significant cartilage defects in one surgical biofabrication procedure
	Joseph	Cadman	A biomechanical comparison of ultra fast-fix and pullout sutures for posterior medial meniscal root tears
	Matthew	Evans	Acromioclavicular joint stabilisation: a biomechanical study of bidirectional stability and strength

18:00-	**Young Investigators Pub-dinner** **Strictly Masters/PhD students only; free meal; must have indicated attendance during registration** **at King O'Malley's Pub (v/gf available), 131 City Walk, Canberra, ACT 2601;** **20 min walk from Conference Venue** **Map: googlemap**

Day 2 (Saturday October 05)

Finkel Lecture Theatre, ground floor, The John Curtin School of Medical Research, ANU, 131 Garran Rd, Acton ACT

08:00-08:15	Coffee & tea		
08:15-09:15	**First name**	**Surname**	**Abstract title**
David Findlay ECR Award Final, Session chairs: Dr Junjie Gao, Dr Diana Perriman ***: Orthopaedic Innovation finalist**	* Young J	No	Effect of Baghdadite substitution on the properties of Brushite cement
	Fatemeh	Malekipur	Spatial distribution of strain in equine distal metacarpal subchondral bone: a microCT-based finite element model
	Dale	Robinson	The application of acoustic emission in the detection of vertebral body fracture
	Renee	Ormsby	Evidence for gender-specific bone loss mechanisms in periprosthetic osteolysis
	* Dzenita	Muratovic	Knee osteoarthritis: presence of bone marrow lesions in subchondral bone indicates increased number and thickness of plate like trabeculae
09:15-09:45 Session chair: Dr Jiao Jiao Li	**Keynote: Prof Rick Sumner, Rush University Medical Center, Chicago, Illinois, USA** **"Bone regeneration and implant fixation"**		
9:45-10:15 Morning coffee & tea; foyer, ground floor, The John Curtin School of Medical Research			
10:15-11:15	**First name**	**Surname**	**Abstract title**
PhD Award Final, Session chairs: Prof Linda Sandell, A/Prof Nathan Pavlos	Jasvir	Bahl	Changes to the hip contact force loading profile following total hip arthroplasty
	Kieran	Bennett	Longitudinal postoperative joint kinematics of tibial plateau fracture patients
	Sophie	Rapagna	Influence of joint alignment in tibal OA vs. controls: cartilage, cortical subchondral bone plate and trabecular bone
	Florence	Lees	Assessment of inflammation, glial cell population and pain-like behaviour in a collagen antibody-induced arthritis mouse model following treatment with Parthenolide
	Xin	Zhang	Effects of ligament sectioning and reconstruction on scapholunate motion during active wrist flexion and extension: a bi-plane X-ray fluoroscopy study
11:15-12:15	**ANZORS AGM** **All delegates welcome (and encouraged) to attend**		
12:30-17:00	**Half day Networking Event.** **(bus transport provided; return back in Canberra by 17:00)** **Pickup: at 12:30 pm, in front of Conference Venue (131 Garran Rd, Acton, ACT 2601)** The National Arboretum Canberra - The Margaret Withlam Pavillon, Canberra, ACT.		
19:00-	**Conference Dinner in the city in historic venue, includes Awards Announcements** Restaurant The Old Parliament House, 18 King George Terrace, Parkes ACT 2600. **Map: googlemap**		

Day 3 (Sunday October 06)

Finkel Lecture Theatre, ground floor, The John Curtin School of Medical Research, ANU, 131 Garran Rd, Acton ACT

08:15-08:45	Coffee & tea; foyer, ground floor, The John Curtin School of Medical Research		
08:45-9:45	**First name**	**Surname**	**Abstract title**
Podium 5 Session chair: Dr Dale Robinson	Shaktivesh	Shaktivesh	Fatigue testing of equine MCII subchondral bone under a simulated training program
	Ali	Entezari	The key role of mechanical stimulation in regeneration of critical-sized bone defects
	Thomas	Grace	The development and reliability of a semi-automated method to split the acetabulum into clinically relevant regions of interest
	Francesca	Bucci	The effect of surgical displacement of the hip joint center on peri-acetabular bone strain and hip contact force while walking: an in-silico examination of a THR patient
	Lianzhi	Chen	Horizontal crack in interface of osteochondral units is a high risk factor of younger age of total knee replacement for obesity-related osteoarthritis
9:45-10:15 Session chair: Dr Catherine Galvin	**Keynote: Prof Fary Khan, Australian Rehabilitation Research Centre, The Royal Melbourne Hospital, VIC, Australia** **"Disaster Management: outcomes of musculoskeletal and neurological Trauma"**		
10:15-10:55 Morning coffee & tea; foyer, ground floor, The John Curtin School of Medical Research			
10:55-12:07	**First name**	**Surname**	**Abstract title**
Podium 6 Session chair: Prof Paul Smith	Nuttaya	Chavalertsakul	Older hip fracture patients with type 2 diabetes mellitus (DM): prevalence, clinical characteristics and in-hospital outcomes
	Charles Changhan	Xu	Admission platelet-to-lymphocyte ratio (PLR) and lymphocyte-to-monocyte ratio (LMR) - two novel independent predictors of in-hospital mortality and myocardial injury in older patients with hip fracture (HF)
	Milad	Ebrahimi	Finding a needle in a sea of needles: accurate patient identification for populating a patient registry within a clinical environment
	Justin	Fernandez	Optimising patellofemoral joint kinematics in knee arthroplasty through personalised implant design
	Joe	Lynch	Shape is a weak predictor of deep knee flexion kinematics in healthy and osteoarthritic knees
	Dané	Dabirrahmani	Anterolateral procedure combined with ACL reconstruction - a biomechanical cadaveric study
12:07-13:20 Lunch & poster viewing (poster viewing will take place between 12:30-13:20) foyer, ground floor, The John Curtin School of Medical Research			
13:20-13:50 Session chair: Dr Egon Perilli	**Keynote: Prof David Haynes, The University of Adelaide, Adelaide, Australia** **"The 25 years history of ANZORS"**		
13:50-14:38	**First name**	**Surname**	**Abstract title**
Podium 7 Session chair: A/Prof Justin Fernandez	Xin	Zhang	A novel dynamic cadaveric wrist simulator for 3-dimensional carpal bone motion measurement using biplane X-ray fluoroscopy
	Catherine	Galvin	Are you mad? You want me to kneel? Comparison of osteoarthritis and healthy knee kinematics while kneeling
	Anthony	Fitzpatrick	Hip implant monitoring through combined acoustic emission and gait analysis
	Diana	Perriman	Gait analysis after gluteal-tendon repair: an age and sex matched comparison
14:38-15:08 Afternoon coffee & tea and poster viewing; foyer, ground floor, The John Curtin School of Medical Research			
15:08-15:44	**First name**	**Surname**	**Abstract title**
Podium 8 Session chair: Dr Martina Barzan	Edmund	Pickering	Where is the load applied in the mouse-tibia model? Insights through finite element modelling.
	Maged	Awadalla	Trabecular bone growth in an adolescent cystic fibrosis rat model: a pilot study
	David	Ackland	Upper limb tasks with humeral axial rotation increase glenohumeral joint translations in patients with anterior instability
15:44-16:00	President's closing address		

POSTERS presented on
Day 1 (Friday October 04)
Foyer, ground floor, The John Curtin School of Medical Research, ANU, 131 Garran Rd, Acton ACT

12:30-13:20	**Lunch break**		
14:50-15:30	**Afternoon break**		
Poster #	**First name**	**Surname**	**Abstract title**
1	Yue	Ding	The effect of ZBTB20 on wear-particle-induced osteolysis in mice
2	Yi	Deng	Gene expression in osteolysis cases examined using RNA Sequencing
3	Junjie	Gao	Endoplasmic reticulum mediates mitochondrial transfer within the osteocyte dendritic network
4	Sara	Farshidfar	Estimation of ligament strains in a healthy, ACL-deficient and reconstructed knee using specimen-specific OpenSim modelling techniques
8	Arjun	Sivakumar	Comparison of simulated and EMG muscle activations between musculoskeletal models in lower limb dynamic simulations of gait
9	Hamed	Shahidian	Biomechanical analysis of medially stabilised knees
10	Manaal	Fatima	What can we learn from the kangaroo knee in relation to treatment of patellofemoral disorders in humans?
12	Holt	Matthew	Anatomical variability of femoral intercondylar notch geometry in patients diagnosed with primary anterior cruciate ligament rupture
15	Emily	Zhong	Quantitative assessment of repair quality in rotator cuff tear: a novel 3-dimensional method using 3T MRI
16	Shabnam	Saadat	A fast registration method for 3D analysis of knee kinematics after total knee arthroplasty
17	Milad	Ebrahimi	Validation of a 3D scanning system for intraoperative anterior cruciate ligament graft geometry determination
18	Catherine	Ngan	Bioprinting skeletal muscle for neuroprosthetic interfacing
20	Ameya	Bhanushali	The variation in radiographic measurements of hip stability between supine and standing radiographs in patients with late DDH
23	Manaal	Fatima	Why does orthopaedic research fail in clinical practice? Generating realistic expectations from 11,000 work hours
24	Mohammad	Ruhullah	Flexible intramedullary titanium elastic nailing of fracture shaft of radius and ulna in children at a tertiary care teaching hospital
25	MacDougal	Cowley	The effect of a quality management system on the integrity of paper-based patient reported outcomes in an orthopaedic registry
26	Corey	Scholes	Younger female patients in total knee arthroplasty: benefits of a rotating platform knee prosthesis with gap balancing technique
27	Corey	Scholes	Patterns in patient reported outcomes revealed by machine learning in patients presenting with symptomatic rotator cuff pathology
30	Corey	Scholes	Rotator cuff repair with increasing age: surgery in patients >70yrs does not lead to adverse outcomes at 6months follow up

Please see next page for posters presented on day 3.

POSTERS presented on
Day 3 (Sunday October 06)
Foyer, ground floor, The John Curtin School of Medical Research, ANU, 131 Garran Rd, Acton ACT

12:30-13:20	**Lunch break**		
14:50-15:30	**Afternoon break**		
Poster #	**First name**	**Surname**	**Abstract title**
5	Hossein	Mokhtarzadeh	A preliminary study: intra-subject variability in dynamic margin of stability during gait
6	Matthew	Holt	Loss of knee extension after ACL reconstruction: what do we know?
7	Ben	Ferguson	Biomechanical analysis of a tissue scaffold and fixation plate used for mandibular reconstruction
11	Hossein	Alemzadeh	Comparison of clinical outcomes between patella resurfacing versus non-resurfacing in primary total knee arthroplasty; a prospective study of 360 cases
13	Sara	Romanazzo	Biomimetic bone precursor nanoparticles enhance angiogenesis and osteogenesis in vitro.
14	Subhajit	Konar	Developing an in vitro system for studying tendon cell response to stiffness and structure
19	MacDougal	Cowley	Can we predict which patients are not fully compliant with patient reported outcomes? An analysis of two thousand patients in clinical practice
21	Chee Han	Ting	Patterns in patient-reported outcomes revealed by machine learning in patients presenting with anterior cruciate ligament rupture
22	Corey	Scholes	Is safe short-stay total knee replacement possible in a regional hospital? Factors associated with hospital length of stay in 362 cases
28	Corey	Scholes	Is short-stay total knee replacement associated with subjective and objective patient function? A prospective observational series with 6 weeks follow up
29	Manaal	Fatima	Effective planning and stakeholder engagement key to registry success: lessons learned from implementation of orthopaedic registries
31	Emily	Zhong	A comparative study of component positioning in total hip arthroplasty by surgical technique, patient positioning and guidance modality
32	Meredith	Harrison-Brown	Do patients need to be followed up annually after metal-on-metal hip resurfacing? An observational cohort study with an average follow-up of 10 years
33	Milad	Ebrahimi	A clinical orthopaedic registry for monitoring outcomes within an upper limb clinic: a quality assessment and baseline report

<u>All</u> posters will be displayed for the whole duration of the conference and presented on either day 1 or day 3 by the author as indicated.


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ABSTRACTS

DAY 1

KEYNOTE 1 – Prof Linda Sandell

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GENETIC CORRELATIONS BETWEEN CARTILAGE REGENERATION AND DEGENERATION REVEAL AN INVERSE RELATIONSHIP

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INTRODUCTION

Objective: The etiology of osteoarthritis (OA) is unknown, however, there appears to be a significant contribution from genetics. We have identified recombinant-inbred strains of mice derived from LG/J and SM/J strains that vary significantly in their ability to repair articular cartilage and susceptibility to post-traumatic OA due to their genetic composition. Here, we report cartilage repair phenotypes in the same strains of mice in which OA susceptibility was analyzed previously, and determine the correlations between phenotypes.

METHODS

We used 12 recombinant-inbred strains, including the parental strains, to test three phenotypes: ear-wound healing (n=263), articular cartilage repair (n=131), and post-traumatic OA induced by DMM (n=53). Genetic correlations between various traits were calculated as Pearson correlation coefficients of strain means.

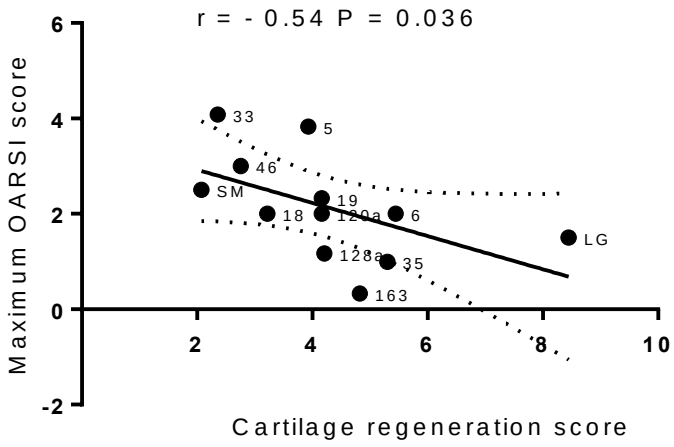
RESULTS

We found a significant positive correlation between ear-wound healing and articular cartilage regeneration (r=0.71;P=0.005). We observed a strong inverse correlation between cartilage regeneration and susceptibility to OA based on maximum (r=-0.54;P=0.036) and summed OARSI scores (r=-0.56;P=0.028) (Figure). Synovitis was not significantly correlated with cartilage regeneration but was significantly positively correlated with maximum (r=0.63;P=0.014) and summed (r=0.70;P=0.005) scores. Ectopic calcification was correlated with cartilage regeneration (r=0.59;P=0.021).

CONCLUSIONS

Using recombinant-inbred strains, our study allows, for the first time, the measurement of genetic correlations of regeneration phenotypes with degeneration phenotypes that are characteristic of post-traumatic OA (cartilage degeneration, synovitis). We demonstrate that OA is positively correlated with synovitis and inversely correlated with the ability to repair cartilage. These results suggest a shift in the risk paradigm for OA from a focus on degeneration to regeneration.

Key words: ear-wound, cartilage injury, Cartilage repair, DMM surgery, synovitis, ectopic calcification



DAY 1

PODIUM 1

NEW INSIGHTS INTO THE ROLE OF METHIONINE 199 IN THE FUNCTION OF RECEPTOR ACTIVATOR OF NUCLEAR FACTOR KAPPA-B LIGAND (RANKL) AND BONE HOMEOSTASIS

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INTRODUCTION

Bone is a connective tissue that undergoes constant remodeling which can be interrupted by the imbalanced activities of bone-resorbing osteoclasts and bone-forming osteoblasts [1]. Osteoclasts are multinucleated cells derived from the monocyte-macrophage lineage. Receptor activator of NF-κB ligand (RANKL), a type II globular transmembrane protein, is indispensable for osteoclast differentiation [2]. A naturally occurring mutation of human RANKL (hRANKL) at amino acid residue M199 within the TNF-like core domain was described in patients with osteoclast-poor autosomal recessive osteopetrosis (ARO) [3]. However, how this mutation affects RANKL function has not been characterized. Here, we hypothesized that hRANKL M199 residue is a structural determinant for ligand-receptor interaction. Understanding the role of M199 in the biology of RANKL may provide new insights for the development of next-generation anti-resorptive drugs.

METHODS

Site-directed mutagenesis was employed to create three rat RANKL mutants, replacing the M200 (rat M199 equivalent residue) with either lysine (M200K), alanine (M200A) or glutamic acid (M200E). MTS was carried out before osteoclastogenesis assay *in vitro* to measure the cellular toxicity. Luciferase reporter assay, RT-PCR, confocal microscopy, western blot, calcium oscillation detection and computational methods were also used to investigate the biological effect of rRANKL mutants. Thermal Shift Assay, western blot and protein binding affinity experiments were later carried out for structural analyses.

RESULTS AND CONCLUSIONS

Mutants M200K, M200A and M200E showed a reduced ability to induce osteoclast formation, osteoclastic polarization as well as bone resorption compared with wild-type rRANKL and did not demonstrate features of competitive inhibition against wild-type rRANKL (**Figure 1A-B**). These mutants all are incapable of activating osteoclast markers and also showed a diminished induction of IκBα degradation, inactivated signaling of NF-κB, NFATc1, AP-1 as well as ARE and blocked calcium flux. Analysis of the spatial distribution of chemical atoms in the crystal structure of mouse RANKL revealed that M198 is a hydrophobic neutral amino acid located within a hydrophobic pocket crucial for protein folding (**Figure 1C**). Mutations in this region can compromise the structural integrity of RANKL and its biological function. After mutation, our western blot results showed the disability of forming RANKL trimeric structure and DSF (Thermal Shift Assay) hinted that mutants are unstructured/disorganized, in which the interrupted interaction to its intrinsic receptors was later verified by binding affinity assay (**Figure 1D**). Taken together, our data showed that M199 in human is a structurally-sensitive residue for RANKL's function, and may represent a therapeutic motif for the development of future generation of anti-resorptive drugs.

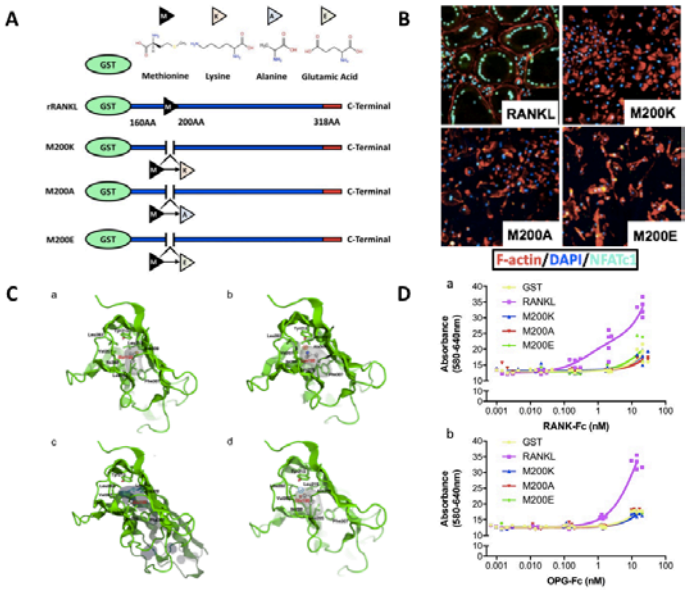

Figure 1. A. The design of three RANKL mutations. B. Mutants did not support osteoclastogenesis. C. Visualization of hydrophobic pocket. D. Receptor-ligand interaction assay.

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DUAL EFFECTS OF MIR-136-3P ON OSTEOGENESIS AND ANGIOGENESIS TO ALLEVIATE ALCOHOL-ASSOCIATED OSTEOPOROSIS VIA TARGETING PTEN PATHWAY

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INTRODUCTION

Alcohol is regarded as one of leading risk factors for osteoporosis. The coupling of angiogenesis and osteogenesis *via* distinct type-H vessels orchestrates the biological process of bone homeostasis. Our previous findings indicated phosphatase and tensin homolog (PTEN) plays a pivotal role in the ethanol-induced anti-osteogenic effect in bone mesenchymal stem cells (BMSCs). Emerging evidence indicates that miR-136-3p plays essential roles in regulating osteogenesis and bone formation.

METHODS

We used human umbilical vein endothelial cells (HUVECs) cell line and primary BMSCs for *in vitro* investigations. Cells were transfected with miR-136-3p mimic, inhibitor or their respective negative control to regulate microRNA expression. The direct interaction between PTEN and hsa-miR-136-3p was analyzed by luciferase reporter assay. Cell proliferation, osteogenic differentiation and mineralization, and angiogenesis outcome (tube formation assay, transwell assay, scratch wound assay) were evaluated following miR-136-3p regulation. Moreover, the animal model of ethanol-induced osteoporosis was established, followed by histological and immunohistochemical staining, dynamic bone formation and micro-CT scanning collectively used to reveal the relationship between miR-136-3p and PTEN *in vivo*.

RESULTS AND DISCUSSION

Herein, we found the tubular formation and migration of HUVECs to be impaired by ethanol *via* activation of PTEN. Furthermore, ethanol was observed to exert suppressive effect on type-H vessels *in vivo*. Additionally, miR-136-3p in BMSCs was found dramatically decreased during ethanol treatment through miRNA sequencing. By dual-luciferase reporter analysis and fluorescence in situ hybridization (FISH), the rescue effect of miR-136-3p on both angiogenesis and osteogenesis was found to be directly targeting PTEN mRNA. Histological observations and micro-CT findings suggested miR-136-3p could effectively improve bone remodelling and promote type-H vessels formation in the mice model of alcohol-associated osteoporosis.

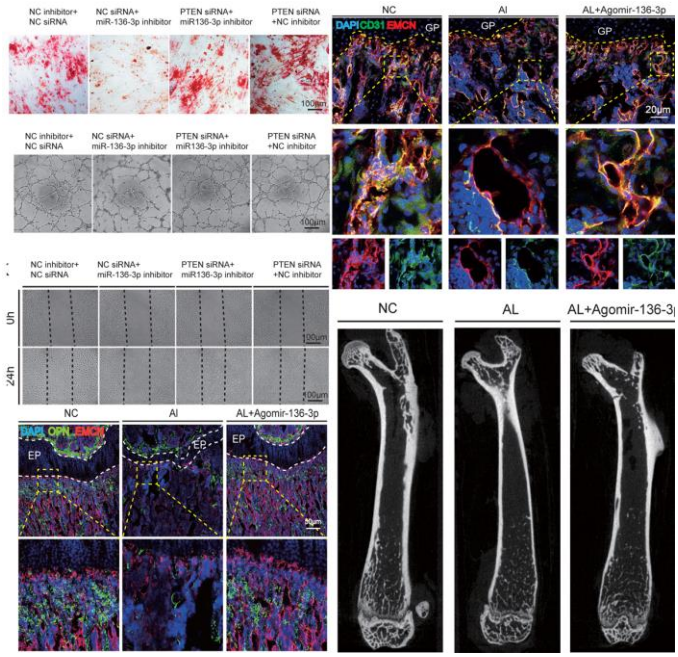

Figure 1: Dual effects of miR-136-3p on osteogenesis and angiogenesis to alleviate alcohol-associated osteoporosis are dependent on PTEN pathway.

CONCLUSIONS

This study is the first to discover the pivotal role of miR-136-3p/PTEN axis in both angiogenesis and osteogenesis and reveal the potential therapeutic effects of miR-136-3p for alcohol-associated osteoporosis. Gene therapy targeting miR-136-3p/PTEN to modulate angiogenesis and osteogenesis might represent a promising strategy for counteracting alcohol-associated bone loss.

A NOVEL INVESTIGATION INTO THE EFFECTS OF THE AMYLOID PRECURSOR PROTEIN ON THE OSTEOCYTE

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INTRODUCTION

The amyloid precursor protein (*APP*) is best characterised in the literature for its role in the pathogenesis of Alzheimer's disease (AD). AD is the most commonly occurring neurodegenerative disease of the ageing population in the western world. Under normal physiological conditions APP can promote neurite outgrowth, plasticity and normal neuronal functioning, however under conditions of inflammation and disease, APP is cleaved, resulting in the development of amyloid beta peptides. Due to their hydrophobic nature, these peptides accumulate around neuronal axons and form amyloid beta plaques, which are thought to be the cause for the initiation of AD. Our group has recently discovered that *APP* is abundantly expressed by bone cells, specifically the osteocyte. The role of *APP* in the bone has not been characterised, therefore the aim of this study was to investigate the effects of synthetic soluble APP_{695} peptide on osteocytes *in vitro*.

METHODS

Soluble APP Preparation: 25µl aliquots at 9mg/ml of sAPP_{695} were diluted to a concentration of 0.5µM in α-MEM (0.5% FCS, 1% ascorbic acid, and 1.8mM potassium phosphate).
Cell culture: Primary osteoblasts were obtained from patients undergoing total hip replacement (THR) for neck of femur fracture (NOF) and differentiated for 28 d until an osteocyte-like phenotype was achieved. Osteocytes were then treated with sAPP_{695} (0 nM, 1 nM and 10 nM) in α-MEM containing B-27 cell growth supplement, for 24, 72 and 96 H. **RNA Extraction & Gene Expression:** RNA was extracted from duplicate wells using TRIZOL reagent (Life Technologies, NY, USA). Complementary DNA (cDNA) was synthesized using iScript (Bio-Rad). Real-time RT PCR was performed using SYBR Green (Qiagen) on a CFX Connect (Bio-Rad). Gene expression was analysed for *BAX*, *BCL-2*, *OPG* and *RANKL* and normalised to *18S*. **Cell Imaging:** Calcein AM and Ethidium Homodimer III fluorescent dyes were added to each treatment and imaged using confocal microscopy (Olympus FV3000). Viable osteocytes stained blue (Calcein AM) and apoptotic cells stained red (Ethidium Homodimer III). **Dead Cell Counts:** Confocal imaging was performed on osteocytes treated with sAPP_{695} at 24, 72 and 96 H. An average of 5 images was taken for each well (2 wells per treatment per time point), red apoptotic cells were counted using Zen Black software (Zeiss). **Statistical Analysis:** Statistical analysis was performed using GraphPad Prism (v7.02). To determine differences between treatment groups, non-parametric Student's T-tests were applied to the datasets.

RESULTS AND DISCUSSION

To determine whether sAPP_{695} induced pro-osteoclastogenic effects, the expression of the pro-osteoclastogenic marker, *RANKL*, to the antagonist, *OPG*, were measured. There was no significant effect on the *RANKL:OPG* mRNA ratio at 24 or 72 H. However at 96 H, *RANKL:OPG* was significantly upregulated at the highest concentration of sAPP_{695} 10 nM p=0.020). The *BAX:BCL-2* ratio is used as a measure of apoptosis in osteoblasts and osteocytes [1]. Following 24 and 72 H treatment with 1 and 10 nM APP_{695}, there was no significant change in *BAX:BCL-2*. However at 96 H, the *BAX:BCL-2* ratio was significantly increased with at both 1 nM ($p = 0.047$) and 10 nM ($p = 0.048$) sAPP_{695} treatments. This indicates that s*APP* induces osteocyte apoptosis in a time-dependent manner. Furthermore, the remaining viable osteocytes are stimulating osteoclastogenesis in response to s*APP*. To determine quantitatively if osteocyte viability was affected with sAPP_{695} treatment, dead cell counts were conducted at each time point. At 24 H, there was a significant increase in death with the 1 nM treatment ($p = 0.048$) and the 10 nM treatment ($p = 0.0006$) when compared to untreated control (0 nM). However at 72 H and 96 H, there was no significant difference in cell death when compared to the untreated control (0 nM). However, the viable cell population was not quantified in this study therefore the percentage of cell death was not measured.

CONCLUSIONS

This novel investigation highlights a role for *APP* with both physiological and pathological functions in the bone. This study suggests that *APP* may have both concentration and time-dependent effects on osteocytes *in vitro*, by activating both apoptotic and pro-osteoclastogenic pathways. However, further investigation is required to determine the clinical implications of *APP* within the bone and its potential as a therapeutic target

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CHONDROCYTE RESPONSE TO FOCAL UNLOADING *IN VIVO*: A DIFFERENTIAL INTERFERENCE CONTRAST STUDY

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INTRODUCTION

Many diseases and injuries of synovial joints result in focal cartilage or osteochondral defects. These conditions are known to lead to degenerative changes within the affected joint and subsequent osteoarthritis (OA) [1,2]. There is evidence that cartilage opposing defects experiences abnormal loading [3] and chondrocytes are thought to be mechanosensitive [4]. Macroscopic "kissing" lesions are observed in cartilage opposing osteochondral defects in horses [5], however there has been little work investigating the histological appearance of these lesions. The aim of this study was to observe how articular cartilage chondrocytes respond to a focal loss of surface contact using an equine model.

METHODS

An osteochondral defect was created in one surface of the midcarpal joint of six adult horses. Two weeks post-operatively the animals began an eight-week treadmill training program. Following this osteochondral samples were collected from the unloaded articular surface directly opposing the defect and from a loaded site immediately adjacent. Control samples were collected from equivalent sites in the sham-operated contralateral limb. Following decalcification 20µm cryosections were cut, wet-mounted and imaged with Differential Interference Contrast microscopy (DIC). These images were used to measure cell aspect ratio (cell length: cell depth) and the degree of clustering based on a previously published scoring system [6] of chondrocytes in the tangential layer of the hyaline cartilage.

RESULTS AND DISCUSSION

Chondrocytes in the tangential cell layer of cartilage immediately opposing the osteochondral defect of treated limbs had lower cell aspect ratios (mean difference = 1.51, P = 0.03) and a greater chondrocyte clustering score (median difference = 2, P = 0.06) than those at the equivalent site in the control limbs (Figure 1). There was no difference between treated and control limbs in the chondrocytes at the adjacent, loaded site.

In this equine osteochondral defect model a focal loss of surface contact resulted in evidence of rounding and proliferation of chondrocytes in the tangential layer of the hyaline cartilage.

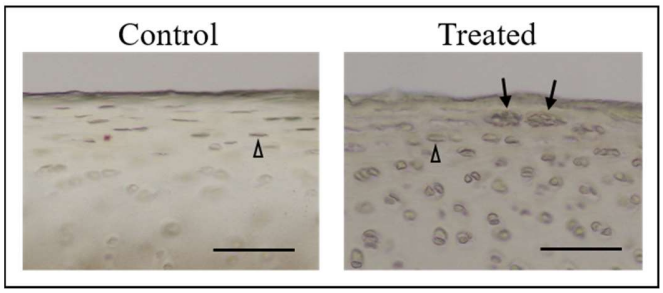

Figure 1: Differential Interference Contrast images of superficial hyaline cartilage from the region opposing the defect in control and treated limbs. Chondrocytes (arrowheads) are rounder and show evidence of clustering (arrows) in the treated limb. Scale bars = 100µm.

CONCLUSIONS

Articular cartilage chondrocytes respond focally to a loss of surface contact. This cellular response may play a role in normal joint homeostasis and in the pathogenesis of OA.

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MITOPHAGY REGULATES GLUCOCORTICOID-INDUCED OSTEOCYTIC OSTEOLYSIS

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INTRODUCTION

Our previous study together with other researches have shown that GC has the capability of inducing autophagy in osteocytes, however, the role of autophagy in GC stressed osteocyte as well as the subsequent outcomes have not been fully illustrated. This study aimed to figure out the possible association between GC-induced osteocytic osteolysis and autophagy, specifically, the mitophagy.

METHODS

Ex vivo primary calvaria culture system and the osteocyte like cell line, MLO-Y4, were employed to observe the effects of GC. Following GC treatment of different doses and time courses, confocal imaging was used to show the changes of extracellular matrix around osteocytes, especially type I collagen composing the lacunae wall and its protease cathepsin K (CTSK). Then, PTEN-induced putative kinase 1 (PINK1) as the mitophagy marker was chosen to verify the existence of mitophagy. To validate the regulation of mitophagy on osteocytic osteolysis, MLO-Y4 cells were transfected with siRNA to knock down PINK1 expression and subsequent changes of genetic expression as well as protein levels of PINK1 and CTSK were determined by real-time PCR and western blotting, respectively.

Figure 1

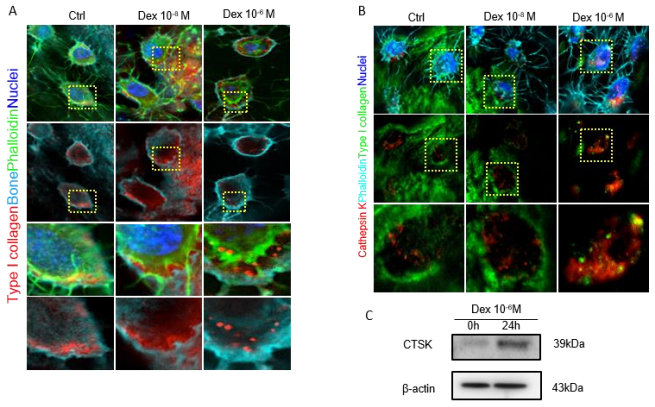

Figure 1: **A&B.** Confocal imaging of *ex vivo* calvaria osteocytes treated with dexamethasone; **C.** Western blot analysis of CTSK in osteocytes.

RESULTS AND DISCUSSION

Abundant type I collagen particles were detected in 10^{-8} M Dex stimulated group, and strikingly accumulated in 10^{-6} M Dex treated group compared with vehicle group (Figure 1A). And an induction of CTSK localized with fluorescence intensities of particle-like collagen was observed in both 10^{-8} M and 10^{-6} M Dex stimulated groups (Figure 1B). Western blot analysis showed consistent increasing of CTSK (Figure 1C). Further examination revealed that PINK1, a marker for stressed mitochondria, was significantly induced by Dex in MLO-Y4 cells (Figure 2A). Transfection of siRNA towards PINK1 resulted in the inhibition of CTSK expression, protein levels of CTSK was also decreased (Figure 2B&C).

Figure 2

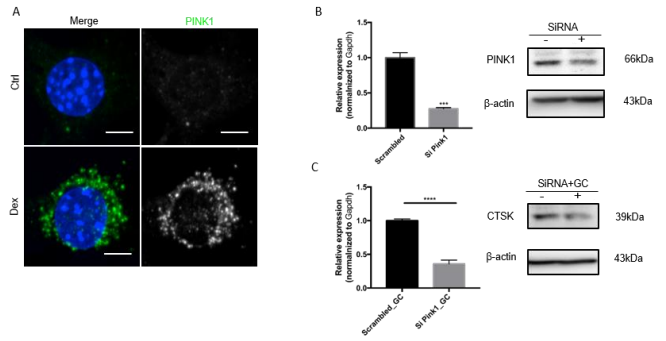

Figure 2: **A.** Confocal imaging for the detection of PINK1 in MLO-Y4 cells; **B.** Real-time PCR and western blotting validating the knocking down of PINK1; **C.** Real-time PCR and western blotting determining the level of CTSK in PINK1 knocking down MLO-Y4 cells.

CONCLUSIONS

GC induces the osteocytic CTSK to degradation extracellular type I collagen, and mitophagy as a possible regulator, plays a crucial role in the activation of CTSK.

ACKNOWLEDGEMENTS

We thank the Centre for Microscopy, Characterization and Analysis for providing confocal imaging facility. We also appreciate support from Early Career Research Small Grant, Faculty of Health and Medical Sciences, The University of Western Australia which was granted to J.-J.G. and the Joint Project Funding for Major Diseases in Shanghai (Grant No.2014ZYJB0301).

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DAY 1

PODIUM 2

REACTIVE OXYGEN SPECIES ENHANCES OSTEOCLAST ACTIVITY IN STEROID-INDUCED OSTEONECROSIS OF FEMORAL HEAD

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INTRODUCTION

Osteonecrosis of femoral head (ONFH) is a progressive bone disorder of the hip which is characterized by subchondral microfractures at early stage and femoral head collapse at late stage [1]. It is widely accepted that excessive osteoclast activity, rather than the necrosis of cells and tissues, causes the loss of bone structural integrity and the collapse of femoral head [2]. However, the mechanisms underlying the activation of osteoclasts in the development of ONFH remain unclear. Accumulating evidence has demonstrated that reactive oxygen species (ROS) can activate osteoclast formation and function. Hence, we hypothesized that high level of ROS may result in the hyperactivation of osteoclasts in the pathogenesis and progression of ONFH.

METHODS

Steroid-induced osteonecrotic femoral heads were collected from patients who received total hip arthroplasty (THA) at the First Affiliated Hospital of Guangzhou University of Chinese Medicine. Each individual femoral head was divided into necrotic and healthy regions. Western Blot (WB) assay and qPCR were performed to examine the osteoclast-specific markers and antioxidant enzymes at both the gene and protein expression levels. To further confirm the relationship between ROS and osteoclasts in the development of ONFH, rats were intramuscularly administered with methylprednisolone (25 mg/kg) to induce ONFH. Dihydroethidium (DHE) was given to the rats 24 hours prior to sacrifice to directly visualize the ROS signal *in vivo*. Histomorphometric analyses and micro-CT were then performed to observe the bone microstructures of the femoral head. WB assay was performed to identify the osteoclastic activity and expression of antioxidant enzymes in the rat femoral heads.

RESULT

Histomorphometric analyses of decalcified human femoral head sections showed that necrotic bones were characterized by an absence of osteocytes within the lacunae and widely surrounded by osteoclasts. QPCR and WB analyses revealed that necrotic bone tissues expressed lower levels of antioxidant enzymes, but higher levels of osteoclast-specific markers compared with the control group.

In the methylprednisolone-treated group, ROS fluorescence intensity of the femoral head was dramatically enhanced in comparison with the control group (**Figure 1A-C**). WB analysis revealed that osteoclast-related proteins (RANKL and cathepsin K) were significantly up-regulated, which was accompanied by a down-regulated expression of antioxidant enzymes, such as heme oxygenase 1 (HO-1), catalase, and SOD1 (**Figure 1D**).

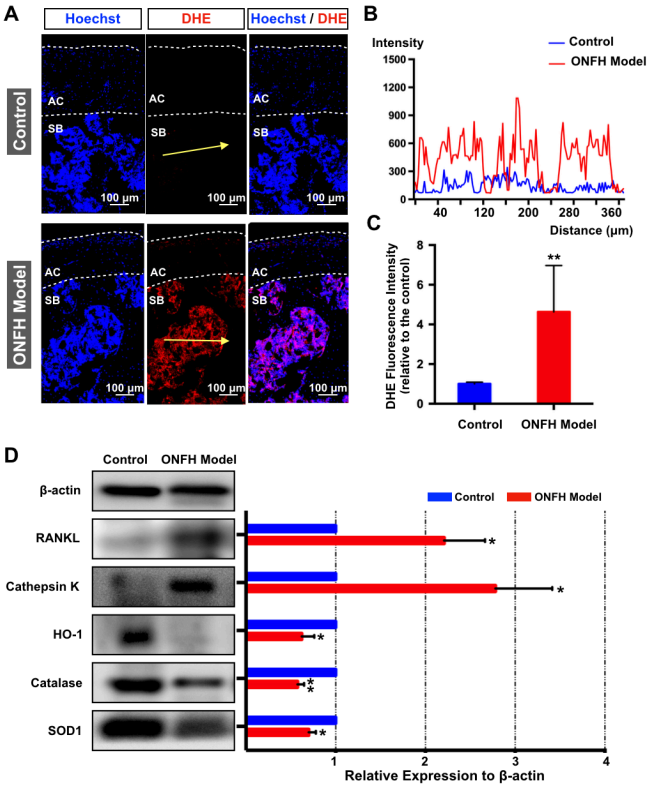

Figure 1(A-C). *In-vivo* ROS fluorescence of femoral head cryosections; (D) the protein expression level of osteoclast markers and antioxidant enzymes in the control group and steroid-induced rat ONFH group. AC, articular cartilage; SB, subchondral bone.

CONCLUSION

Steroid may induce the progression of ONFH by inhibiting the antioxidant enzymes, which may lead to the high level of ROS and subsequent enhancement of osteoclast activity.

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UTILISING THE COLLABORATIVE CROSS TO INVESTIGATE GENES ASSOCIATED WITH OSTEOARTHRITIS PROGRESSION IN MICE AND HUMANS

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INTRODUCTION

Osteoarthritis (OA) is a common degenerative joint disease with a slow progression that affects a significant proportion of the population. Heritable genetic factors have been shown to play a role in spontaneous OA development, with many loci being identified via genome-wide association studies (GWAS), accounting for an estimated 26.3% of the disease trait variance in humans[1]. Despite the success of these human based studies, they are limited by the inability to control for external factors that contribute to the post-traumatic form of the disease. Currently, there is no method for predicting the onset of OA or the rate of progression. Therefore the identification of biomarkers associated with spontaneous OA is of great importance in understanding the mechanism of the disease and to predict the onset and progression of OA.

METHODS

We have utilized the collaborative cross (CC), to assess the severity of knee OA histologically across a spread of ages. Mice >8 months were selected for screening and were analysed as a complete cohort, and a subset of these were analysed as an early onset of OA cohort (8-12 months). Each animal was scored using the OARSI grading scale. Strain representative scores were ranked from lowest to highest and the data used to map genetic loci that were consistently associated with the highest OA scores. Potential candidate genes were analysed further using qPCR, microarray and bioinformatics tools to investigate the expression and any existing role in OA. Assessment of human homologues of the genes identified in the mouse cohort was conducted using the publically available datasets from the UK Biobank[1] and arcoGEN[2] OA cohorts.

RESULTS AND DISCUSSION

The CC mice showed a range of OA phenotypes with a number of strains presenting as potential models of spontaneous OA. Quantitative trait locus mapping of the scores revealed two loci that achieved genome wide significance (Figure 1). Genes that were implicated within these loci were correlated with human GWAS datasets, which were found to be associated with diabetes, hypothyroidism and the immune system. Further investigation of these genes demonstrated expression during osteoblast and chondrocyte formation.

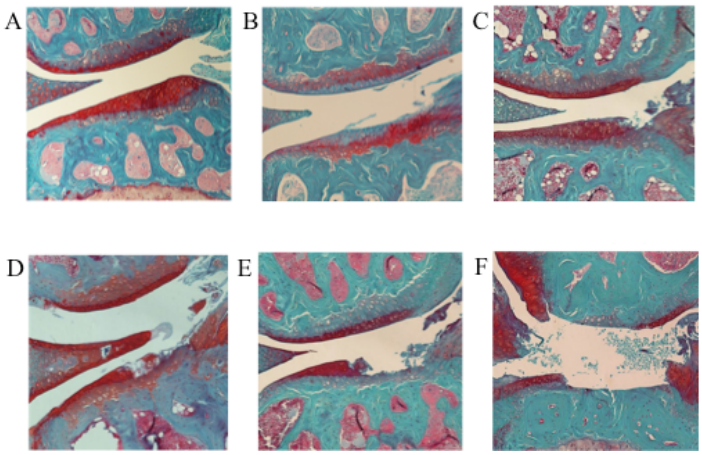

Figure 1: Histological images of OA in the medial compartment. Grade 0 (A), Grade1/2 (B), Grade 3 (C), Grade 4 (D), Grade 5 (E), Grade 6 (F).

CONCLUSIONS

The use of CC mice has proven to be an effective method for investigating the genetic component of OA. The range of OA phenotypes observed in the CC cohort validates the use of highly affected strains as spontaneous OA disease models. Locus mapping revealed several strong candidate genes that that were shown to be associated with human OA GWAS cohorts. These genes were also found to reflect the involvement of diabetes, hypothyroidism and inflammation with OA disease progression. These gene discoveries present potential screening or therapeutic targets, specific to the risk of OA development and age of onset.

ACKNOWLEDGEMENTS

William Tomlinson, Jinbo Yuan, Dian Teguh, Kai Chen, Peter Robbins, Richard Allcock, Kyle Yau.

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TWO TYPES OF OSTEOCYTES DEPENDING ON THE PROCESS OF OSSIFICATION

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INTRODUCTION

There are two essential process of bone formation1. Intramembranous ossification only occurs during the formation of flat bones, while endochondral ossification mainly occurs during cortical long bone development[1]. Intramembranous ossification is mediated by the direct transformation of mesenchymal cells into osteoblasts, while endochondral ossification is chondrocytes-centred, and hypertrophic chondrocytes can become osteoblasts[2]. In both cases, osteoblasts further mature into osteocytes upon the completion of bone formation. During this process, osteocytes alter their morphological features with the formation of dendritic processes that extend towards the mineralizing front6. Meanwhile, the formation of osteocyte lacuna-canalicular system interconnect with neighbouring osteocytes to form an osteocyte network[3]. This sophisticated system enables osteocytes to regulate bone homeostasis.

Given there are distinct differences in the ontogeny of osteocytes during intramembranous and endochondral ossification and evidence that osteocytes in intramembranous and endochondral ossification are directly derived from mesenchymal cells and chondrocyte respectively, we hypothesize that osteocytes, derived from these two different process of ossification have different geometrical and genetic metabolic properties.

METHODS

Calvaria, derived from intramembranous ossification, and femora cortical bone, derived from endochondral ossification, samples were collected from global 4-month mT/mG transgenic mice. The primary osteocytes were imaged by confocal microscopy for the analysis of geometrical properties of osteocytes. High-resolution confocal images allowed the establishment of mathematical models for the analysis of osteocyte geometries. Subsequently, RNA-seq technology was employed for the analysis of genetic differences between calvarial osteocytes and cortical osteocytes. Lastly, 12-month and 18-month old mice samples were collected for confocal imaging to see whether aging has different impacts on osteocytes derived from calvaria and cortical bone.

RESULTS AND DISCUSSION

Our results showed that osteocytes derived from calvaria were geometrically different to that from cortical bones (Fig 1). SIM and geometrical mathematical modelling revealed that calvarial

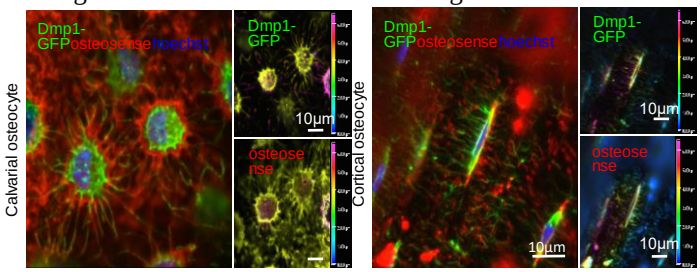

Figure 1: Geometrical properties of calvairal and cortical osteocytes

osteocytes are round shaped with radiated dendritic processes, while cortical osteocytes are spindle shaped with perpendicular dendrites. Calvarial osteocytes are more randomly arranged within the bone matrix, while cortical osteocytes are orderly arranged with paralleled distributions of dendritic network along the axis of cortical bone. Further, mRNA-seq analysis detected 8445 genes were differentially expressed, in which 121 genes were ossification-related. We also observed upregulation of Inppl1, Mapk3, Mtss1, Nf1, Plxnb1, Ptk2b, Smad3, Tacr1 and Bmp5 and downregulation of Alox15, Id1, Tac1, Ranbp3l in cortical osteocytes as compared to that in calvarial osteocytes. The varied expression of these cytoskeleton organization and dendrite development related genes may regulate the morphological differences of osteocytic cell bodies and dendrites. Finally, we showed that aging mainly affects the cortical osteocytes but not calvarial osteocytes. Aging causes distortion of osteocyte dendrites, and the deflection of osteocyte cell bodies in cortical bone but not calvarial bone. Together, in this study we suggest that there are two types of osteocytes, depending on the process of ossification.

CONCLUSION

There are two types of osteocytes with different geometrical and genetical properties depending on different ossification processes. Aging has an impact on endochondral ossification derived osteocytes.

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CONFLICT OF INTEREST DECLARATION

The authors declare that they have no conflict of interest

ICARIIN ATTENUATES METHOTREXATE CHEMOTHERAPY-INDUCED BONE LOSS AND BONE MARROW MICRO-VASCULAR DAMAGE IN RATS

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INTRODUCTION

Bone marrow micro-vascular system is composed of sinusoids which are mono-layered with sinusoidal endothelial cells (SECs). Bone marrow sinusoidal endothelium plays a key role in orchestrating various physiological functions including bone formation and bone remodelling. Previous preclinical and clinical studies have shown that cancer chemotherapy can cause bone marrow sinusoidal damage. However, studies on the effect(s) of methotrexate (MTX), which is an anti-metabolite commonly used to treat solid tumours and paediatric cancers, on bone marrow micro-vascular system are inadequate. In addition, as both clinical and preclinical studies have previously demonstrated the significant bone loss following MTX treatment, which currently lacks preventative therapies, therapeutic strategies are urgently needed by which both MTX-induced bone marrow micro-vascular damage and MTX-induced bone loss can be reduced/prevented. Icariin, an herbal flavonoid, has been widely shown to be beneficial for treating many diseases including osteoporosis and cardiovascular dysfunction. This study sought to investigate the preventive effects of icariin during and following MTX treatment in rats.

METHODS

In one study, groups of young adult rats were treated with 5 daily MTX injections (0.75 mg/kg), the effects of MTX on bone marrow micro-vasculature were examined in a time course (days 3, 6, 9, 11, 14, and 21 after the first injection). In another study, groups of young adult rats were treated with 5 daily MTX injections (0.75 mg/kg) with and without icariin oral supplementation (50 mg/kg) till day 9 after the first MTX injection. Histological analyses (H&E and IHC) on bone marrow blood vessel alterations/damages were conducted on left tibia. qRT-PCR assays were also conducted to examine changes in expression of angiogenesis-related genes in the bone. Additionally, *in vitro* studies were performed to investigate the viability, proliferation, tube formation ability, and nitric oxide production of primary sinusoidal endothelial cells with or without treatment with MTX and/or icariin.

RESULTS AND DISCUSSION

Our histological analyses showed that the diameters of bone marrow sinusoids in MTX alone-treated group were significantly enlarged accompanied by apoptosis induction in bone marrow sinusoidal endothelial cells compared to the normal control. Our *in vitro* studies also revealed that MTX is cytotoxic for cultured sinusoidal endothelial cells and can induce apoptosis, associated with upregulation of expression ratio of Bax and Bcl-2 genes and Bax/Bcl-2 expression ratio. Furthermore, it was shown that MTX can negatively affect proliferation of cultured sinusoidal endothelial cells and also inhibit their abilities of migration and formation of micro-vessel like tubes.

In the second study, histological analyses revealed a significant reduction in the bone volume/tissue volume fraction (%) and trabecular number in the metaphysis trabecular bone of MTX treated rats, but no significant changes in trabecular thickness and trabecular spacing. However, the bone volume/tissue volume (%) and trabecular number were found to be significantly higher in MTX + icariin-treated rats than those of MTX alone-treated rats. Gene expression analyses showed that icariin treatment maintained expression of osteogenesis-related genes but suppressed the induction of adipogenesis-related genes in bones of MTX–treated rats. In addition, icariin treatment attenuated MTX-induced dilation of bone marrow sinusoids and upregulated expression of endothelial cell marker CD31 in the metaphysis bone of icariin + MTX-treated rats. Furthermore, *in vitro* studies suggest that icariin treatment can potentially enhance the survival of cultured rat sinusoidal endothelial cells against cytotoxic effect of MTX and promote their migration and tube formation abilities, which is associated with enhanced production of nitric oxide.

CONCLUSIONS

The results of this study suggest that icariin may have potency to reduce MTX-induced bone marrow sinusoidal endothelial cell damage and MTX-induced bone loss. Therefore, icariin may possess a potency to prevent bone loss and maintain angiogenesis in bone marrow during/following MTX treatment.

ACKNOWLEDGEMENTS

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COMPROMISED CELL FUNCTION AND EXTRACELLULAR MATRIX DEGENERATION IN LOADING-DEPRIVED TENDON

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INTRODUCTION

Tendon is a mechanosensitive tissue which bears loading from muscle contraction to bone. Compared to excessive mechanical loading, which is highly likely cause rupture or chronic tendinopathy, insufficient loading also has adverse effect on tendon tissue. However, less studies were involved in investigation of cellular and extracellular changes in loading deprived tendon. In our study, we investigated cellular function of tendon derived stem cells (TDSCs) and collagen component changes in patella tendon under insufficient loading. The results showed collagen degeneration and compromised TDSCs regarding differentiations and proliferation. Also, we interestingly found that the inflammatory cytokines and MMP-13 were increased in loading deprived tendon. The results are promising to develop therapeutic strategies for degenerative tendinopathy in relative patients.

METHODS

Patella tendons of 12-week aged mice were subjected to no mechanical loading by injection of Botulinum Toxin (botox) in quadricep. Histological examinations were performed by H&E staining and polarized microscopic image. Collagen degenerations were detected by Collagen Hybridizing Peptides. Tri-lineage differentiations of TDSCs (osteogenesis, chondrogenesis and adipogenesis) and tenogenesis were examined by qPCR, western blot and relevant staining. MMP-13 and TNF-Alpha were examined by western blot and qPCR.

RESULTS AND DISCUSSION

Our results showed that tendon without mechanical loading was atrophic and had collagen fibers disorientated (Figure 1A, B) more collagen degeneration was detected in botox group as well (Figure 1C). Colony formation and proliferation ability of TDSC was diminished (Figure 2A, B). Furthermore, differentiation capacity of TDSCs was compromised in botox group (Figure 3) towards osteogenesis, chondrogenesis and adipogenesis. Besides, tenogenesis of TDSC was also downregulated which was evidenced by low expression of TNMD and MKX. Interestingly, TNF-a were upregulated in mRNA level and protein level, which might be the indication to the presence of inflammation. As we further investigation, MMP-13 was increased and this might be the reason for the collagen degeneration. On the other hand, MMP-9 which does not play the dominant role in tendon, was unchanged.

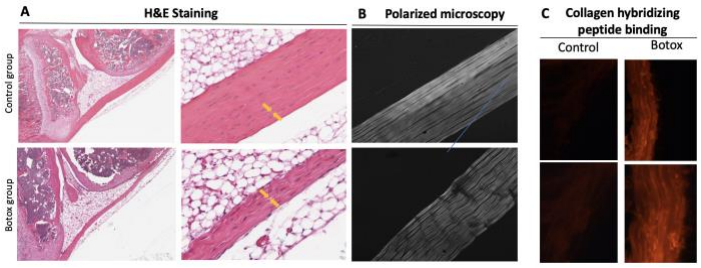

Figure 1. A. H&E staining of patella tendon from both groups. **B**. Polarized microscopic images of patella tendon**. C.** Collagen hybridizing peptides for detection of collagen degeneration.

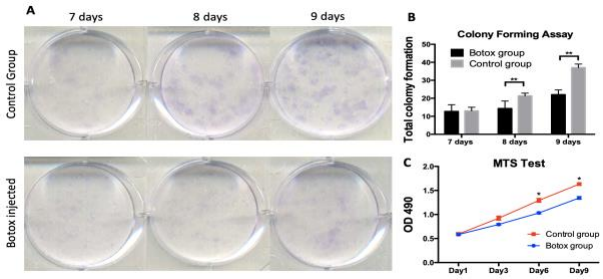

Figure 2. A, B. Colony formation and quantitation. **C**. Proliferation test by MTS.

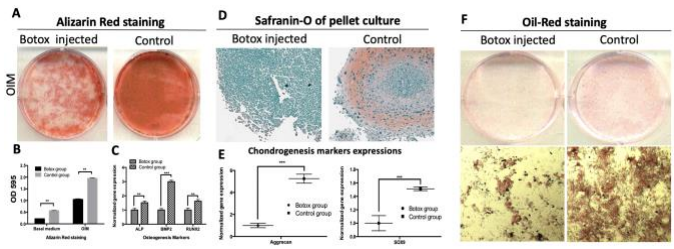

Figure 3. A, B. Alizarin Red for calcium nodule formation and quantitation. C, Expressions of osteogenesis markers. D. Safarinin-O for pellet culture. E. Expressions of chondrogenesis markers. F. Oil-Red staining for lipid formation.

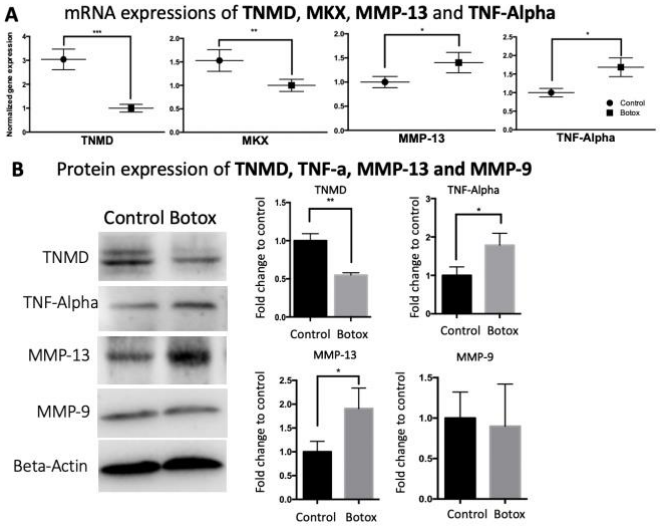

Figure 4. A. mRNA expression of TNMD, MKX MMP-13 and TNF-a. **B**. Western blot and quantitation of TNMD, TNF-a, MMP-13, MMP-9.

CONCLUSIONS

In our study, tendon under insufficient mechanical loading undergo cellular and extracellular changed, including dysfunction compromised cell fate of TDSCs and extracellular collagen degenerations which might be due to the accumulations of inflammation and MMP-13. This study has the potential to provide posssible pathological mechanism of disused tendon and might be favorable for therapeutic development.

LIMITED PENETRATION OF COBALT AND CHROMIUM INTO THE CEREBROSPINAL FLUID FOLLOWING METAL-ON-METAL ARTHROPLASTY: A CROSS SECTIONAL ANALYSIS

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INTRODUCTION

Metal on metal (MoM) implants are known to release metal ions into the bloodstream [1,2]. However, it is not known whether rare reports of implant-related neurotoxicity reflect widespread penetration of ions into the central nervous system [3]. The purpose of this study was to determine the concentration of cobalt (Co) and chromium (Cr) ions in synovial fluid, blood plasma and cerebrospinal fluid (CSF) of patients with metal-on-metal (MoM) implants, and to assess the relationship between implant history and patient characteristics with ion concentrations in CSF.

METHODS

An observational, non-randomised cross-sectional study was conducted with patients presenting to a single surgeon for treatment of degenerative hip and knee conditions. Blood and fluid samples were collected intraoperatively and analysed for proteins and trace elements. Samples below the limit of quantification (5nmol/L) were excluded. Remaining values were stratified into 3 groups; controls (presenting for primary arthroplasty), well-functioning (pre-existing) implant, and hip revisions. Average metal concentrations were compared between groups using Kruskal-wallis ANOVA. Data from patients with quantifiable CSF concentrations were transformed using the Box-Cox method with optimal lambda after removing outliers. A forwards-backwards stepwise multivariable regression model was established incorporating patient demographics and clinical factors.

RESULTS AND DISCUSSION

Overall, the presence of an implant was associated with significantly higher Co and Cr concentrations in plasma, and for Cr concentrations in CSF (Figure 1). In absolute terms, <1% of the levels observed in the joint fluid and <15% of plasma levels appear in the CSF. Multivariable regression models suggested different mechanisms of diffusion between Co and Cr to the CSF, with the presence of an implant not associated with ion levels.

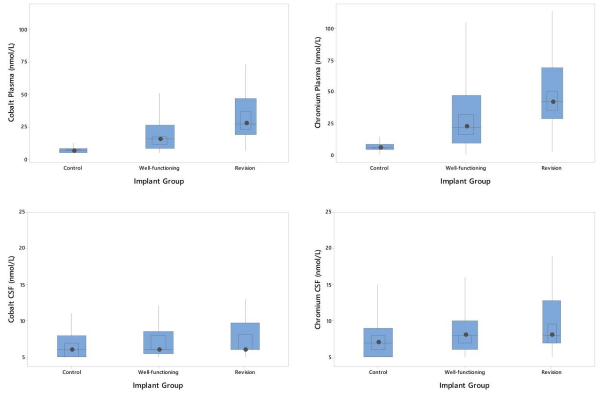

Figure 1: Co and Cr ions in Plasma and CSF compared between implant groups. Boxes represent the interquartile range, and whiskers represent range with outliers excluded.

CONCLUSIONS

The presence of MoM implants is associated with significantly higher plasma levels of Co and Cr but not CSF Co, and the CSF/plasma ratio appears to be nonlinearly influenced by plasma concentration. Co and Cr may be transferred to the CSF by different mechanisms, and their concentrations appears dependent on other factors to be identified. Though higher concentrations of plasma ions are associated with above average concentrations in CSF, thresholds for neurotoxicity remain unclear and require further study.

ACKNOWLEDGEMENTS

We gratefully acknowledge the assistance of Dan Nguyen and Joan Minty for their assistance with data transcription.

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DAY 1

KEYNOTE 2 – A/Prof Tasha Stanton

OSTEOARTHRITIS IS ALL ABOUT THE JOINT – OR IS IT? CONSIDERING NEW INSIGHTS FROM PAIN NEUROSCIENCE

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People are more worried about developing osteoarthritis than many other chronic diseases because they view arthritis as a progressive, incurable, and painful condition. Indeed, pain is the primary reason that people with osteoarthritis (OA) seek care, and pain often limits their function and ability to work.

The classification, prognosis, and management of OA has traditionally been viewed in line with the severity of joint damage (combined, of course, with the clinical presentation of the patient). However, recent advances in pain neuroscience suggest that such a view may be limiting both in terms of our communication about and our treatment of OA.

Pain is complex and is now understood to be an emergent phenomenon that occurs as a protective response when the available information supports the presence of (real or perceived) danger. Critically, such a definition highlights that there are many available inputs – beyond nociceptive input from peripheral sources – that can influence and even initiate pain. For example, by initiating changes in neural activity, emotions, thoughts, and beliefs can profoundly influence the experience of pain. Further, changes in neuroimmune function, which sensitise the nociceptive pathway, occur in persistent pain. Taken together, this means that the pain experienced by people with OA is never a simple 'read-out', so to speak, of the degree of peripheral pathology.

Understanding that there are numerous contributors to the experience of pain in OA is important and has several key clinical implications. First, such knowledge allows us to explore the influence of other contributors to pain, which then opens the door to novel treatment targets. Second, it provides prognostic information to convey to patients, namely that how their knee looks on imaging does not solely dictate their clinical course. Third, such information provides clinicians with important treatment messages for patients. For example, understanding the biology of pain allows us to provide explanations for why exercise might be expected to help a "wear and tear" condition such as OA. This can help to counter negative beliefs of patients who understandably may be asking, "Wouldn't exercise – which induces more wear, and thus tear – actually be bad for my joint"?

This presentation will discuss our current knowledge of pain neuroscience in the context of OA. It will explore new findings that suggest that changes in the nervous system, including functional impairment in the processing of nociceptive input, play an important role in osteoarthritic pain. It will also discuss the evidence for changes in the spinal cord and the brain in people with painful knee osteoarthritis, and summarise the evidence for brain-targeted treatment and its effects on pain. Last, it will discuss our role in communicating to people with OA and how we might start and support a revolution to provide a new and redefined public perception of an old disease.

DAY 1

PODIUM 3

THE EXPRESSION OF DMP1 IN MOUSE CENTRAL NERVOUS SYSTEM

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INTRODUCTION

The expression of bone metabolism-related proteins including cathepsin K (CTSK), receptor activator of NF-κB (RANK), receptor activator of NF-κB ligand (RANKL) and Dentin matrix protein 1 (DMP1) are not limited in bone tissues. It has been reported that expressions of these genes were also detected in non-mineralized tissues such as brain. Intriguingly, the expressions of CTSK and RANK in central nervous system (CNS) have predominant roles in learning, memory, cerebral aneurysms formation, body temperature regulation and inflammatory responses. DMP1 as the most classic extracellular matrix protein is considered to express specifically in late stage osteoblasts and osteocytes for regulating bone metabolism and development. However, the specificity, localization and function of DMP1 in CNS are still not clear.

METHODS

To locate the expression of DMP1 we employed mice with Dendra2 green monomeric fluorescent protein, which express 20 times higher fluorescence intensity compare to regular GFP (green fluorescence proteins). We fused Dendra2 to the mitochondrial targeting signal of subunit VIII of cytochrome c oxidase. Mito-Dendra2 can produce fluorescence specifically in mitochondria without affecting function. When crossed with DMP1-Cre mice, DMP1-Cre dependent excision of a floxed stop segment permits expression of mitochondrial green fluorescence in DMP1 positive cells, which enable us to efficiently identify the distribution of DMP1 in brain. To visualize the expression of DMP1, frozen brain sections, immunostaining and confocal microscopy are employed.

RESULTS AND DISCUSSION

Immunostaining and confocal imaging demonstrated that the green fluorescence intensity was highly expressed in CNS including brain and spinal cord. Quantitative analysis of whole brain imaging demonstrate that DMP1 is mainly expressed in cerebellum (21.3%) and olfactory bulb (19%) (Figure 1 & Figure 2), which indicating the expression of DMP1 in brain is mainly regulating the function of motor movements and odor sensitivity. Furthermore, by immunostaining against relative markers of blood vessel and nerves, we revealed that fluorescence signal is co-localized with both blood vessel and nerves in brain. Interestingly, similar association could not be detected in both artery and sciatic nerve, which indicating DMP1 specifically expressed in the blood vessel and nerves of CNS, and DMP1 positive blood vessel and nerves may have their specific role in regulating the metabolism of CNS.

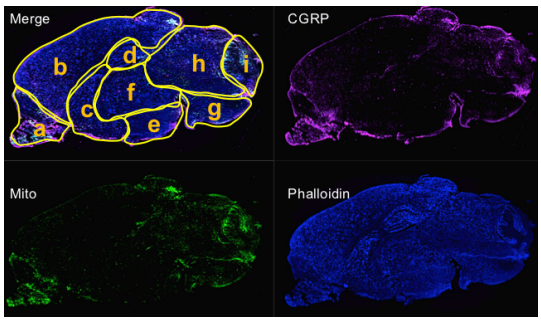

Figure 1: Sagittal plane confocal imaging of DMP1-Cre mouse brain. (a: Olfactory Bulb; b: Cerebral Cortex; c: Ventral Striatum; d: Hippocampus; e: Hypothalamus; f: Thalamus; g: Pons; h: Midbrain; i: Cerebellum)

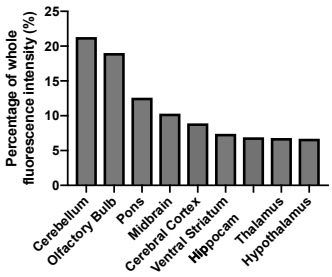

Figure 2: Distribution of fluorescence intensity within sagittal plane of mouse brain

CONCLUSIONS

Besides to mineralized tissues, DMP1 is also significantly expressed in specific blood vessel and neurons of CNS. The existence of DMP1 positive blood vessel and DMP1 positive nerves may have their unique role in CNS.

STEM CELL THERAPY FOR OSTEOARTHRITIS – DOES IT WORK?

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INTRODUCTION

Osteoarthritis (OA) is a leading cause of chronic pain and disability, for which there is no cure. Non-operative treatments are used for pain relief, until an operation is performed to remove the diseased joint. Mesenchymal stem cells (MSCs) have recently brought new hope for treating OA due to their unique secretory functions, which send anti-inflammatory and trophic signals to the surrounding tissues [1]. Interestingly, the few available clinical trials utilising MSCs to treat knee OA have not demonstrated consistent benefits [2]. This study aims to unravel the mechanisms behind this interesting observation using an *in vitro* model of a human osteoarthritic joint. The results of this study can contribute to guiding the development and implementation of novel regenerative therapies for OA.

METHODS

To test whether diseased OA cells can modify the behaviour of MSCs, human synovial fibroblasts (HSFs) isolated from osteoarthritic knee tissues were co-cultured with human bone marrow-derived MSCs in growth, osteogenic and chondrogenic media (simulating the relevant conditions in an osteoarthritic joint) for up to 21 days. To test whether exposing diseased OA cells to MSCs can cause sustained changes in their behaviour and have positive effects on tissue repair, HSFs were either pre-conditioned by co-culturing with MSCs for 3 days (+cHSF), or not pre-conditioned and simply cultured in growth medium (+HSF), and subsequently co-cultured with fresh MSCs in growth, osteogenic and chondrogenic media for up to 7 days. In both experiments, the responses of MSCs were assessed using quantitative RT-PCR (n=4; mean ± SD) and histology (n=2).

RESULTS AND DISCUSSION

MSCs co-cultured with osteoarthritic HSFs (Figure 1A) showed significant upregulation of several markers of inflammation, matrix degradation and tissue degeneration (e.g. MMP2, ADAMTS5). They also showed significantly impaired ability to form new bone and cartilage, through reduced expression of osteogenic (SPP1) and chondrogenic (ACAN) genes, and reduced histological features of differentiated bone (calcium) and cartilage (proteoglycan). These findings suggest that the osteoarthritic joint is a highly inhibitory environment that can increase inflammation in MSCs and significantly impair their regenerative ability. This explains clinical findings where MSCs did not have sustained therapeutic effects for knee OA.

Pre-conditioning the HSFs by exposing them to MSCs did not have any significant positive effects in modifying their behaviour (Figure 1B). HSFs, pre-conditioned or not, caused similar levels of inflammatory marker expression in MSCs in different media types and at different time points (e.g. IL-8). MSCs co-cultured with both pre-conditioned and non-pre-conditioned HSFs also showed impaired chondrogenesis to a similar extent (e.g. SOX9 expression, histology). These findings suggest that short-term exposure of osteoarthritic cells to MSCs is insufficient for sustained modifications to their diseased phenotype. This explains clinical findings where MSCs had some early therapeutic effects for knee OA, but these were not significant when compared to case-matched controls.

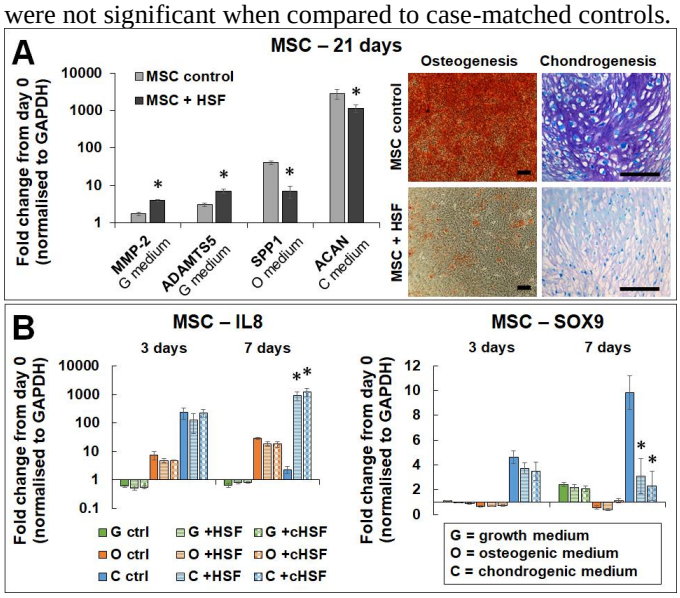

Figure 1: (A) MSCs co-cultured with osteoarthritic HSFs upregulated inflammatory markers (MMP-2, ADAMTS5) and downregulated osteogenic (SPP1) and chondrogenic (ACAN) markers (*P < 0.01), and showed impaired osteogenesis (Alizarin Red S, scale = 500μm) and chondrogenesis (toluidine blue, scale = 200μm). (B) HSFs, pre-conditioned or not, had similar effects on MSCs (*P < 0.001).

CONCLUSIONS

Although MSCs have anti-inflammatory and trophic functions, they could not provide long-term effects in correcting the osteoarthritic joint environment due to adopting the diseased phenotype of the resident cells. Future regenerative therapies for OA should focus on repeated administration of stem cells, or alternatively utilising their secretory products instead.

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FUNCTIONAL MECHANICAL TESTING OF NATIVE HUMAN KNEE ARTICULAR CARTILAGE

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INTRODUCTION

Recapitulation of the complex mechanical properties of native articular cartilage (AC) is essential to ensure the functional durability of tissue engineered cartilage (TEC). Hence, it is crucial to develop methods to quantitatively compare TEC and native AC biomechanics. Under sudden impact, AC behaves as a single-phase, incompressible, elastic solid while under slow-loading, AC exhibits viscoelastic properties [1]. Here, we developed a protocol to conduct a suite of mechanical tests under physiological conditions to examine the impact of cyclic loading on the elastic and viscoelastic properties of human distal femoral AC. This protocol aims to outline laboratory methods and set minimum mechanical benchmarks to aid the assessment and validation of the functional mechanical integrity of TECs in cartilage biofabrication.

METHODS

Osteochondral plugs (n = 9) of 8 mm diameter were harvested with consent from macroscopically normal regions of medial and lateral femoral condyles of patients (n=3) during total knee arthroplasty. The plugs were stored at 4°C in a solution of phosphate-buffered saline with 1% penicillin/streptomycin and protease inhibitors. The surface area and thicknesses of AC were measured using stereomicroscopy and Fiji image processing software. Each plug was immersed in PBS at 37°C (maintained with a heated circulation system) and tested in stages using the Bose ElectroForce BioDynamic 5500 instrument:

(i) A 0.5 mm cylindrical plane-ended indenter was used for three-step stress-relaxation tests (5%, 8% and 10% strain) at 4 indentation sites using a deformation speed of 1 mm/s and relaxation time of 240 seconds.

(ii) Using unconfined compression, dynamic testing was conducted in 4 steps at 3 frequencies (0.1 Hz, 1 Hz and 10 Hz) and 2.5% strain-amplitude. A cyclic compression step (2000 cycles of 20% compression at 4 Hz) was performed between each dynamic test to simulate repetitive joint loading. Equations from viscoelastic theory were used to calculate dynamic moduli [2].

(iii) The compressive modulus was measured at 10-15% strain prior to each compression step.

(iv) Indentation was repeated with the parameters in stage (i) following the last compression cycle.

(v) Poisson ratio was measured using video microscopy and used to calculate Young's modulus. The elastic parameter equilibrium Young's modulus was obtained by applying the stress-strain data to the modified Hayes' solution for finite indentation, which is $E=F(1-v^2)/2awk$ [3].

RESULTS AND DISCUSSION

During indentation, AC was loaded in 80 to 110 milliseconds on average, which is consistent with loading times during human locomotion [1]. The average instantaneous modulus was 0.3 MPa and the average equilibrium Young's Modulus was 0.5 MPa. Wilcoxon matched-pair signed rank tests showed no significant difference (p=0.25) in Young's moduli before and after repetitive compression. On average, the loss factor increased slightly with cyclic compression, suggesting a small amount of intrinsic damping of AC viscoelasticity. On average, the compressive moduli decreased slightly on average both before and after cyclic compression steps.

CONCLUSIONS

The results indicate that native human AC is capable of withstanding thousands of cycles of compression without a significant decrease in elasticity, which emphasizes the durability that tissue-engineered composites require to emulate articular cartilage. The testing parameters and dimensions were chosen to increase reproducibility and practical convenience for TEC testing. The moduli of elasticity and viscoelasticity for native AC also provide benchmarks for the desired mechanical properties of biomaterials used in cartilage biofabrication.

ACKNOWLEDGEMENTS

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LUMBAR DISC HERNIATION FAILURE AFTER MULTIAXIAL FATIGUE

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INTRODUCTION

Repetitive lifting (fatigue) **[1]** and rapid application of high compressive loads (sudden overload) **[2]** can cause intervertebral disc (IVD) injuries and herniation, with posterior lateral herniations potentially impinging nerve roots. In-vitro studies show that fatigue loading involving bending and twisting motions can alter IVD mechanical properties, leading to herniation **[2,3]**. However, no study has been conducted to understand whether fatigue under different combinations of postures (flexion, lateral bending, and axial rotation), places the IVD at greater risk of herniation during sudden overload. Therefore, this study aimed to compare the sudden overload failure stress between three combinations of IVD postures after fatigue, and the effect of fatigue loading on six degree of freedom (DOF) stiffness. It was hypothesized that 6DOF stiffness will be decreased more from flexion and lateral bending motions. Additionally, it was hypothesized that combined flexion and lateral bending will create the lowest failure stress and stiffness during sudden overload.

METHODS

Twenty-four lumbar segments (L4-L5) were dissected from sheep, keeping the facet joint capsules and anterior and posterior longitudinal ligaments intact. 6DOF properties were first measured, followed by 10,000 cycles of combined cyclic fatigue loading at 1 Hz in a hexapod robot **[4]**. Specimens were randomly assigned into one of three combined loading posture groups: 13° flexion, 2° left axial rotation (F+R); 10° left lateral bending, 2° left axial rotation (LB+R); 13° flexion, 10° left lateral bending (F+LB). All groups had a compressive load applied that was equivalent to lifting a 20 kg weight with a straight back and bent knees **[5]**. Measurements of post-fatigue 6DOF properties were then repeated. Specimens were moved to their loading group posture and failed axially at 400 mm/min **[2]**. The percentage changes in 6DOF stiffness after fatigue were calculated relative to before fatigue. A repeated measures ANOVA was performed to determine any significant stiffness differences in 6DOF stiffness before and after fatigue within the loading group. To determine the groups most susceptible to failure, a one-way ANOVA compared failure stress and stiffness between groups ($p<0.05$). Bonferroni tests determined post-hoc significant differences between groups. Failure mode was determined via visual inspection.

RESULTS AND DISCUSSION

Flexion stiffness was significantly reduced for all groups after fatigue: F+R, 86% ($p<0.001$); LB+R, 40% ($p=0.012$); F+LB, 97% ($p=0.004$). Left axial rotation stiffness significantly decreased in flexion groups: F+R, 9% ($p=0.026$); F+LB, 13% ($p=0.040$). Groups loaded in left lateral bending significantly decreased in right lateral shear stiffness: LB+R, 26% ($p=0.008$); F+LB, 38% ($p=0.01$). Left lateral shear significantly decreased for F+LB, 27% ($p=0.017$). Posterior shear significantly decreased for F+LB, 19% ($p=0.031$). There was no significant difference in sudden overload failure stress between the three postures ($p=0.142$). The overall effect of posture was significant for stiffness during the overload failure test ($p=0.045$). LB+R specimens, marginally significantly stiffer than F+LB ($p=0.05$), failed at a lower stress (28.9 MPa), larger than non-fatigued data ($p=0.01$) during sudden overload [6] (Figure 1).

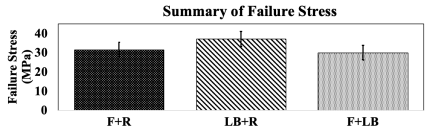

Figure 1. Mean (95% CI) failure stress for each sudden overload posture.

Visually, the two postures that included flexion had higher occurences of posterior or posterolateral herniation. Decreasing IVD stiffness reduces the ability to distribute loads effectively. During flexion and lateral bending postures, the nucleus migrated to the contralateral side. Additionally, lateral bending caused a reduction in shearing stiffness. This reduced ability to resist shearing deformation may lead to IVD annulus tearing from large interlamellar shearing strains. Reduced shearing stiffness and the nucleus migration cause the IVD to become susceptible to herniation during combined lateral bending and flexion.

CONCLUSIONS

Combined flexion and lateral bending fatigue had the greatest effect on 6DOF properties, with significantly decreased flexion and lateral shearing stiffness. Hence, combined flexion and lateral bending motions caused specimens to fail at the lowest stress through posterior and posterolateral herniation. Fatiguing affected the failure mechanics of the IVD and should be considered for in-vitro repetitive lifting and herniation studies. Knowing which DOFs are affected by fatigue can inform muscle strengthen routines to prevent herniation caused by repetitive lifting or sudden overload during occupational and physical activities.

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HIP ABDUCTOR MUSCLE VOLUMES ARE SMALLER IN INDIVIDUALS AFFECTED BY PATELLOFEMORAL JOINT OSTEOARTHRITIS

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INTRODUCTION

The patellofemoral joint (PFJ) is the compartment of the knee most commonly affected by symptomatic osteoarthritis (OA), and can contribute substantially to limitations in physical function associated with knee OA [1]. It has been recently demonstrated that people with PFJ OA walk with increased hip adduction and decreased hip extension during late stance compared to aged-matched controls [2]. While reduced hip abductor muscle strength may be responsible for the increased hip adduction observed during walking, there is currently little evidence linking altered movement patterns during walking with muscle dysfunction in people with PFJ OA. Since a muscle's capacity to generate peak isometric muscle force is a function of its volume, a muscle's volume may be used as an indicator of its force-generating capacity or strength. The aims of the present study were therefore twofold: firstly, to compare the volumes of the hip abductors (specifically, the gluteus medius, gluteus minimus and tensor fasciae latae muscles) in individuals with PFJ OA against those of healthy controls; and secondly, to determine whether a relationship exists between hip muscle volumes and hip kinematics during walking in individuals with PFJ OA and healthy controls.

METHODS

Fifty-one individuals with PFJ OA and thirteen asymptomatic, age-matched healthy controls ≥40 years were recruited. Radiographic severity of OA was assessed using the Kellgren and Lawrence (KL) grading system, adapted to assess the PFJ using skyline X-rays. Inclusion into the OA group required a KL score of ≥1 in the lateral PFJ.

Magnetic resonance (MR) imaging was performed on the most symptomatic leg for the PFJ OA participants and the dominant leg for the healthy controls. Volumes of the gluteus medius, gluteus minimus and tensor fasciae latae were measured from axial images using commercially available software (Amira, FEI Visualization Sciences Group, France) (Fig. 1). Gait experiments were performed on all participants. Three-dimensional locations of retro-reflective markers were measured using a 9-camera video motion analysis system (Vicon, Oxford Metrics Ltd., Oxford) sampling at 120 Hz as participants walked at their self-selected speed. Lower limb joint angles were calculated using inverse kinematics. Pearson correlation coefficients were then employed to assess the relationship between normalized muscle volume and selected kinematic variables, including values for hip joint flexion-extension, adduction-abduction and internal-external rotation angles at the time of contralateral toe off (CTO) and contralateral heel strike (CHS).

RESULTS AND DISCUSSION

Statistically significantly smaller gluteus medius ($p=0.017$), gluteus minimus ($p=0.001$) and tensor fasciae latae ($p=0.027$) muscle volumes were observed in PFJ OA participants compared to controls. Weak correlations were observed between smaller gluteus minimus volume and larger hip flexion angle at contralateral heel strike (CHS) ($r=-0.279$, $p=0.038$) as well as between smaller gluteus minimus volume and increased hip adduction angle at CHS ($r=-0.286$, $p=0.046$).

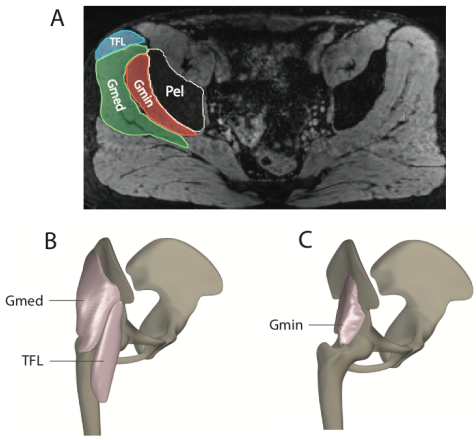

Fig. 1: Representative axial MR image of the pelvis showing delineation of the pelvis, gluteus medius, gluteus minimus and tensor fasciae latae (A) and 3D muscle rendering images for gluteus medius and tensor fasciae latae (B) and gluteus minimus (C).

CONCLUSIONS

Individuals with PFJ OA have smaller gluteus medius, gluteus minimus and tensor fasciae latae muscle volumes when compared with healthy controls. Gluteus minimus is a substantially smaller muscle than gluteus medius and thus has a relatively lower capacity to abduct the hip and support the body against gravity; however, a smaller gluteus minimus muscle volume was associated with increased hip flexion and adduction angles during the late stance phase of walking. A smaller muscle volume results in a reduced capacity for a muscle to generate force and thus, may be considered an indicator of muscle weakness. These results provide evidence for a possible relationship between hip abductor muscle weakness and functional impairments as a consequence of PFJ OA. The current study provides recommendations for hip muscle strengthening interventions for people with PFJ OA.

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DAY 1

PODIUM 4

COMPUTATIONAL EFFICIENT METHOD FOR ASSESSING THE INFLUENCE OF SURGICAL VARIABILITY ON PRIMARY STABILITY OF A CONTEMPORARY FEMORAL STEM IN A COHORT OF SUBJECTS

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INTRODUCTION

Finite element (FE) modelling can provide detailed information on implant stability, however, its computational cost limits the possibility of completing large analyses into the effect of surgical variability in a cohort of patients [1]. The aim of this study was to develop an efficient surrogate model for a cohort of patients implanted using a common cementless hip stem.

METHODS

FE models of implanted femora were generated from computed-tomography (CT) images for 20 femora (11 males, 9 females; 50 -80 years; 52 - 116 kg). An automated pipeline generated FE models for 61 different unique scenarios that span the femur-specific range of implant positions. Peak hip contact and muscle forces for stair climbing were scaled to the donors' body weight and applied to the models [2]. A cohort-specific surrogate for implant micromotion was constructed from Gaussian Process (GP) models trained using data from FE simulations representing the median and extreme implant positions for each femur. A convergence study confirmed suitability of the sampling method for cohorts with 10+ femora. The final model was trained using data from the 20 femora.

RESULTS AND DISCUSSION

The total run time for all models was approximately1,800 CPU hours, out of which approximately 250 CPU hours were required to generate and run the training set. The cohort-specific surrogate model required only 70.3 seconds to train and 1.5 seconds to predict 1,036 unseen cases in the validation set.

The surrogate model was able to predict the micromotion pattern and distribution along the stem cross-sections for a total of 1,036 alignment scenarios (Figure 1(a); $R^2 = 0.81$; RMSE = 20.7 µm), even at the subject-specific level. Also, the micromotion-based ranking predicted using the surrogate models closely match that of the FE models (Figure 1(b)). However, the surrogate models seemed to slightly underestimate the magnitude of the micromotion, with a slope of 0.91 ($R^2_{peak} = 0.89$, and $R^2_{median} = 0.66$).

CONCLUSIONS

Results showed very good agreement between the FE and the surrogate predictions. The total time required for the surrogate model to predict the micromotion range associated the surgical variability was approximately one-eighth of the corresponding full FE analysis. This confirms that developed model is valid and computationally cheaper alternative to full FE analysis when studying implant robustness in cohorts of 10+ femora.

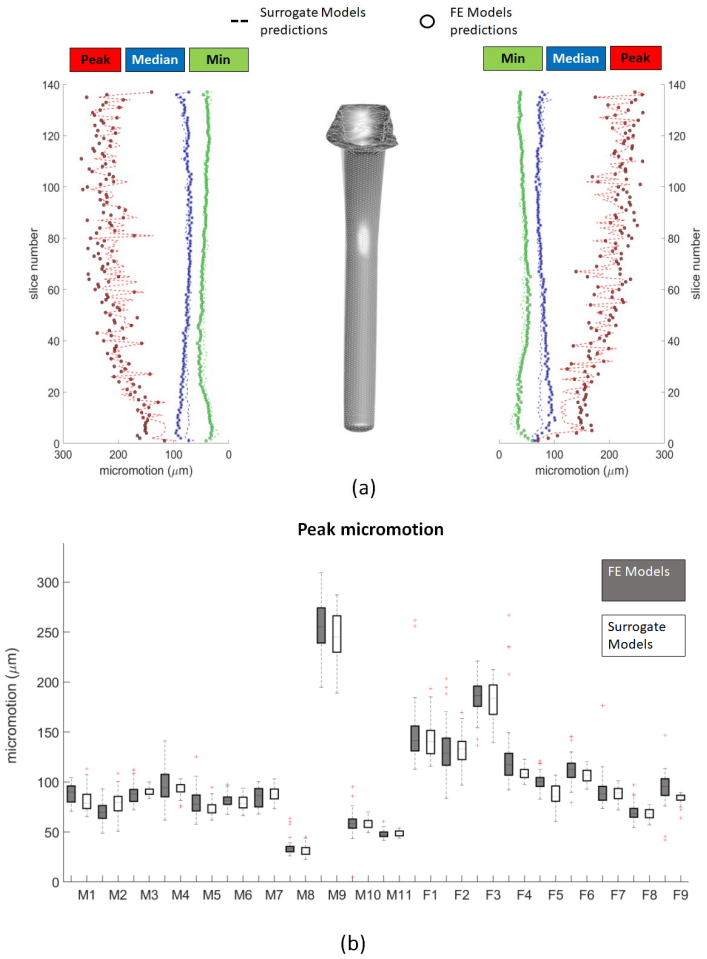

Figure 1: (a) FE (dots) vs surrogate (dashed lines) prediction for the peak (red), median (green) and minimum (blue) micromotion, in each posterior (left) and anterior (right) cross-section, for micromotion values predicted for all femora in the study, (b) individual boxplots for the range of the peak micromotion for all implant positions, where each set of dark and white boxes represent the micromotion range predicted by the FE and the GP surrogate models, for each individual in the study cohort, respectively.

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In the interests of transparency and to help reviewers assess any potential bias, all authors of original research papers are required to declare any competing commercial interests in relation to the submitted work. Referees are also asked to indicate any potential conflict they might have reviewing a particular paper.

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   This study was part of an ARC-linkage project, partially funded by DePuy Synthesis. Rami Al-Dirini was employed as a Research Associate on the ARC-linkage project.

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VIRTUAL PLANNING AND PERSONALISED CUTTING GUIDES FOR JUVENILE FEMORAL OSTEOTOMIES

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INTRODUCTION

Proximal femoral osteotomy (PFO) is a common surgical procedure for hip deformity correction in juvenile patients. The indications include deformity subsequent to Perthes' disease, slipped capital femoral epiphysis or neuromuscular diseases (e.g., cerebral palsy) [1]. PFO is a highly complex procedure involving multi-plane corrections and, consequently, accurate surgical pre-planning is crucial, but typically is only informed by two-dimensional static medical imaging. Therefore, surgery is prescribed and performed with minimal objective understanding of how the deformity affects the pre-operative hip joint kinematics or how the surgery might affect the hip joint and muscular function. The aims of this study were i) to perform virtual surgical simulations to restore normal hip joint anatomy and muscle function, and optimize surgical pre-planning, and ii) to design and manufacture personalized surgical cutting guides using 3D printing to streamline the translation of the virtual plan and enable precise surgical execution.

METHODS

An 18-year-old girl with right hip deformity following slipped capital femoral epiphysis underwent medical imaging. A CT scan of the patient's hips and an MRI scan of her pelvis and full-length femurs were acquired. Three-dimensional pelvis, femurs and glutei muscles were reconstructed using Mimics Research 21.0 (Materialise, Leuven). Femoral neck-shaft angle, femoral anteversion and femoral neck flexion angle were computed for both femurs to determine the required rotational corrections, and two osteotomy planes were defined to facilitate these corrections. To examine the effect of the virtual osteotomy on hip joint function, i) pre-operative and ii) corrected anatomy subject-specific musculoskeletal models were created of the patient's hips [2]. Range of motion and glutei moment arms were computed in OpenSim and compared between the two models. To design the personalized cutting guide, the appropriate implant (OrthoPediatrics, Warsaw, USA) was selected and positioned on the corrected femur and the corresponding initial implant position on the pre-operative femur was determined by reversing the rotational corrections. Adhering to quality control guidelines [3], a personalized cutting guide was designed in 3-matic (Materialise, Leuven) and 3D printed in biocompatible Nylon (Formiga P110, EOS, Germany) for use in surgery.

RESULTS AND DISCUSSION

Three rotational corrections were required to get the right femoral head aligned as the contralateral hip (Fig 1a). Compared to the pre-operative model, the corrected model increased impingement-free range of motion for hip flexion (+35°), hip internal rotation (+27°) and hip abduction (+24°), and increased glutei moment arm lengths (Fig.1b). The increase in moment arm length suggests that the corrected position of the greater trochanter increased the mechanical advantage of the glutei, potentially leading to more efficient movement during activities of daily living. The 3D printed cutting guide fitted and locked onto the 3D printed pre-operative bone surface (Fig. 1c), enabling precise deformity correction.

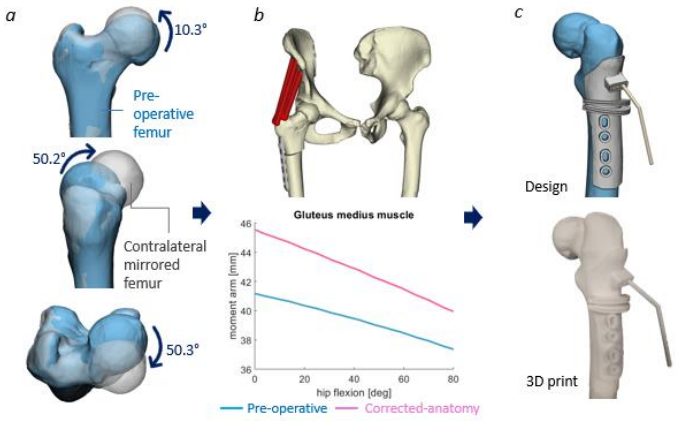

Figure 1: Rotational corrections required to align the pre-operative (blue) to the contralateral (grey) femur (a), corrected-anatomy OpenSim model and pre-operative(blue)/corrected-anatomy (pink) gluteus medius moment arm comparison, and personalized cutting guide design and manufacturing (c).

CONCLUSIONS

The proposed virtual surgery workflow has the potential to improve PFO pre-planning. The manufactured cutting guide will be used in surgery at the Queensland Children's Hospital and may improve surgery efficiency and precision.

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MINGHAO ZHENG ORTHOPAEDIC INNOVATION AWARD 2019, FINALIST

Orthopaedic Innovation Award Statement:

The technology developed in this study allows the clinician to use computer simulations to perform and evaluate multiple surgery options in a digital environment before operating on the patient. Surgery is projected to be quicker, less invasive and more effective. Furthermore, the surgeon will be able to use personalised 3D printed surgical guides, which conform with Therapeutic Goods Administration guidelines regarding custom made medical devices, to ensure precise deformity correction. The efficacy of the planned virtual surgery and personalised cutting guide for the patient described in this study will be presented during the conference.

BIOFABRICATION OF HUMAN ARTICULAR CARTILAGE: ANALYSIS OF GENOTOXICITY, CYTOTOXICITY AND CHONDROGENESIS

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INTRODUCTION

Three dimensional biofabrication allows the creation of tissues using biomaterials and stem cells. Biofabrication of articular cartilage could be used to repair cartilage defects and prevent osteoarthritis. For clinical translation of this technology there is a responsibility to ensure the safety of the biofabrication procedure. Genotoxic and cytotoxic free radicals generated by crosslinking chemistry necessary to harden the printed material after light exposure might impact on cell viability and DNA integrity. Whilst cytotoxic effects have been explored in the literature, reports of genotoxicity in 3D printed bioscaffolds are limited [1,2].

The aim of this study was to develop a test of genotoxicity by detecting DNA double stranded breaks (DSBs) within 3D printed bioscaffold using human adipose derived stem cells (hADSCs) and gelatin methacrylate (GelMa) as a hydrogel material. Subsequently we analysed genotoxicity, cytotoxicity, mechanical properties and chondrogenesis in bioscaffolds with different cross-linking conditions by changing the concentration of the photo-initiator, the molecule that upon light irradiation is responsible for the crosslinking reaction.

METHODS

Immunostaining followed by imaging with confocal microscopy and Western Blotting were used to detect phosphorylated histones (pH2AX), a marker of DSBs. We validated these tests using Valinomycin, a known inducer of DSBs and apoptosis in 2D cell culture. Live/Dead viability test and Cell Titer metabolic assay were used to detect cytotoxicity. Cytotoxic and genotoxic effects of different concentrations of lithium phenyl-2,4,6-trimethylbenzoylphosphinate (LAP) on hADSCs encapsulated within GelMa cross-linked at under 405nm, 100mW/cm^2 for 60 seconds were analyzed using the assays described. Chondrogenesis was analysed with gene and protein expression analysis and mechanical compression tests.

RESULTS AND DISCUSSION

The detection of pH2AX was validated in 2D cell culture upon treatment with Valinomycin. Next, using Live/Dead viability test (Fig. 1A) and Cell Titer metabolic assay (Fig. 1B) we detected a decreasing trend proportional to the increasing concentration of LAP. Immunostaining and Western Blot (Fig.2) revealed an increase in the pH2AX signal, meaning that the photo-crosslinking reaction can impact on both cell viability and genotoxicity. Therefore, we selected the safest crosslinking condition to demonstrate chondrogenic capacity. Our data shows that our biofabrication procedure leads to production of neocartilage in 3D bioscaffold, thus making it an efficient method for the regeneration of articular cartilage.

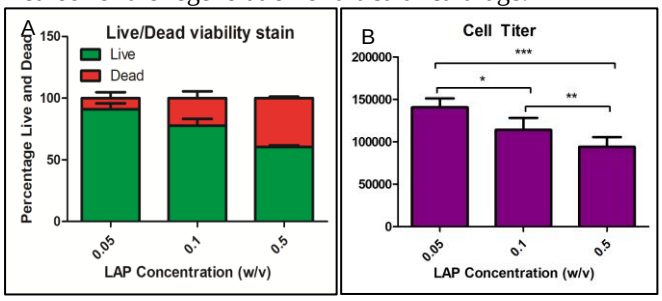

Figure 1. Cell viability analyses. A) Live/Dead stain and B) Cell titer metabolic analysis. */**= p<0.05, ***= p<0.0001

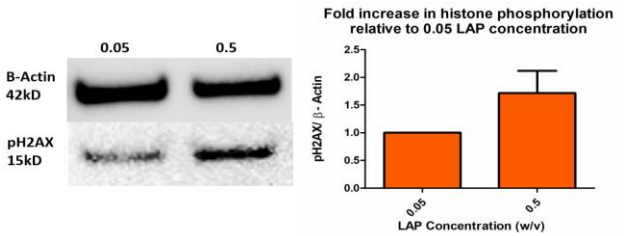

Figure 2: Western blot illustrating pH2Ax signal and densitometric analysis showing pH2AX normalized against B-Actin at different LAP concentrations.

CONCLUSIONS

Cellular cytotoxicity and genotoxicity need to be identified and carefully detected to provide an indication of the safety of the regenerative treatment approach in patients. Overall, we identified a reliable genotoxicity test that can potentially be applied to other biofabrication techniques to ensure the genomic integrity of implanted cells to reduce risk of tumorigenesis.

In addition, we achieved successful chondrogenesis with a low risk biofabrication procedure demonstrating the efficacy and safety of our technique. This technology has the potential for clinical translation where direct printing of these scaffolds into cartilage lesions can replace existing cartilage repair techniques.

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MINGHAO ZHENG ORTHOPAEDIC INNOVATION AWARD 2019, FINALIST

Orthopaedic Innovation Award Statement:

3D Biofabrication of articular cartilage is a safe and efficient technique to repair cartilage defects. It could prevent osteoarthritis and relieve significant morbidity in our population. Our method of analysing the safety of the biofabrication procedure, has not been applied in 3D scaffolds before and can henceforth be used to test the safety of all biofabrication procedures. It is an important step in clinical translation of this technology. No patent has been filed.

RAPID ISOLATION OF MESENCHYMAL STEM CELLS TO TREAT CLINICALLY SIGNIFICANT CARTILAGE DEFECTS IN ONE SURGICAL BIOFABRICATION PROCEDURE

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INTRODUCTION: Biofabrication is a strategy addressing cartilage repair by generating bioscaffolds composed of materials and stem cells [1]. A major barrier to clinical translation is the need for cell expansion in a laboratory which leads to concerns with the use of animal serum-based media, ethical regulation and sterility [2-3]. Furthermore, In *vitro* cell expansion requires an extra procedural step leading to surgical reimplantation of tissue using a down line second procedure which increases recovery time, risk and patient burden.

Here, we present a one-step surgical repair technique for chondral repair using a pure stem cell population (Figure 1), this is achieved by:

A) Developing a rapid 85-minute isolation protocol of human Adipose-Derived Mesenchymal Stem Cells (hADSCs) from the Infrapatellar Fat Pad (IFP)

B) Identifying the minimal concentration of hADSCs laden in a GelMa/HA hydrogel required to produce neocartilage

C) Determining if clinically significant cartilage defect sizes can be treated using a rapidly derived pure stem cell population and the minimal hADSCs concentration identified

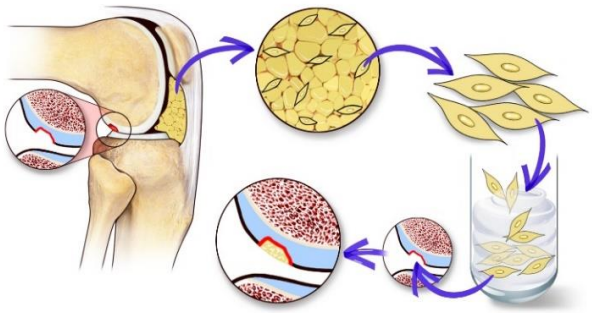

Figure 1: Proposed single-stage chondral repair concept

METHOD: IFP was opportunistically harvested and processed using either the 85 -minute rapid or >27-hour standard (control) isolation protocol. Live cell count, cell viability, cell adherence percentage and the total hADSCs count was calculated. Immunophenotyping and a 3-week chondrogenic assay was performed. Next, 1cm^2 bioscaffolds were fabricated using three hADSCs concentrations (representing 12.5, 25 and 50% of the healthy chondrocyte concentration) laden in a GelMa/HA hydrogel, after 3 weeks of chondrogenic stimulation GAG/DNA quantification, chondrogenic gene expression, immunostaining and imaging was performed.

RESULTS: The rapid 85-minute isolation approach yielded a comparable cell count, viability, adherence percentage and hADSCs count to the control isolation approach. Flow cytometry showed comparable profiles in both groups consistent with the hADSC phenotype and chondrogenic differentiation was also comparable in both rapid and control groups after 3-weeks as evidenced by GAG/DNA quantification and qPCR data. The GAG content, chondrogenic gene expression and ECM accumulation after 3 weeks is highest in the 5.0 million hADSC/ml concentration bioscaffold group (50% of the healthy chondrocyte concentration).

DISCUSSION AND CONCLUSION: Our rapid 85-minute hADSCs isolation protocol is comparable to standard lab protocols. The minimum hADSCs concentration required to produce successful chondrogenesis in a GelMa/HA hydrogel is 5.0 million hADSC/ml. We identify that cartilage lesions up to 224 µl (224 mm^3) in volume can be repaired in one surgical operation using this concentration and the number of non-expanded hADSCs that can be rapidly isolated. These novel findings pave the way for future clinical progression of one-step cartilage repair treatment options using pure stem cells.

ACKNOWLEDGEMENTS The authors acknowledge support from The Australian Research Council Industrial Transformation Training Centre (ARC-ITTC) in Additive Biomanufacturing, the Medical Technologies and Pharmaceuticals (MTPConnect) Bio MedTech Horizons program, the Royal Australasian College of Surgery and The University of Melbourne Seeding Grants.

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MINGHAO ZHENG ORTHOPAEDIC INNOVATION AWARD 2019, FINALIST

Orthopaedic Innovation Award Statement:

We have developed and validated a novel rapid 85-minute hADSCs isolation protocol Using this protocol we prove that we can repair chondral defects in one surgical operation. These findings pave the way for future clinical progression of novel one-step cartilage repair treatment options using pure stem cells. There is current discussion surrounding patent options, no patent has been filled yet.

A BIOMECHANICAL COMPARISON OF ULTRA FAST-FIX AND PULLOUT SUTURES FOR POSTERIOR MEDIAL MENISCAL ROOT TEARS

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INTRODUCTION

Meniscal root repairs are critical in restoring knee function following a complete meniscal root tear. The common suture pattern for fixing the meniscal horn is the Two Simple Stitches pattern. However, this is prone to suture cutout. Various more complex suturing patterns offer improved suture cutout loads[1,2] but are technically difficult to perform in a trans-tibial procedure[3]. The Ultra Fast-Fix™ may provide an alternative method for securing the meniscal horn, without the technical challenges associated with some suturing techniques. This study compares the biomechanical properties of a posterior medial meniscus trans-tibial root repair consisting of two Ultra FasT-Fixes™ with the Two Simple Stitches pattern.

METHODS

Ten pairs of cadaveric medial menisci were dissected and the posterior horn secured with either two Ultra Fast-Fixes™ (UFF) or two simple stitches (TSS). Each construct was mounted in a mechanical testing machine (Instron Illinois, USA) and subjected to preloading with 2 N for 10 seconds, then cyclic loading from 5N to 20N for 1000 cycles at a frequency of 0.5Hz. The menisci were then loaded to failure at 0.5mm/s.

RESULTS AND DISCUSSION

All biomechanical results are presented in table 1. The average yield load and stiffness were similar for both constructs. The elongation after cyclic loading is greater for the UFF. The displacements at yield load and ultimate failure were also higher for the UFF. The ultimate failure load of the UFF construct was also significantly higher.

To maintain biomechanical function of the meniscus, the accepted threshold for elongation is 3mm[1,2,4]. Both constructs had elongations within this limit.

The significant differences in elongation and displacements are due to the different mechanisms for securing the tissue. The UFF creates a loop around the meniscal fibres and cinches onto the tissue with increasing load, explaining the higher elongations, displacements and ultimate failure load. In contrast, the TSS pattern relies entirely on the intrinsic strength of the meniscal tissue. These differences are further highlighted in the mode of failure results. Most UFF constructs failed when the sutures broke. All the TSS constructs failed by suture cut-out.

Both constructs also demonstrated similar Stiffness and Yield Loads. This suggests that the strength of the two constructs is comparable and further suggests that the primary difference lies in the mechanism of securing the meniscal tissue.

During testing, maintaining tension on the UFF construct while fitting it into the testing jig was difficult. This loss of tension may have resulted in relaxation of the cinching mechanism, possibly contributing to higher elongation. It is hypothesised that this problem may be mitigated in the surgical scenario through the use of appropriate techniques to apply and maintain the appropriate tension through the trans-tibial tunnel.

CONCLUSIONS

The Ultra FasT-Fix™ construct may represent a viable alternative to the TSS suture pattern, if for technical reasons TSS suture pattern cannot be used.

ACKNOWLEDGEMENTS

Smith and Nephew funded this study and provided all hardware.

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Table 1: Comparison of Biomechanical properties for meniscus root fixation constructs. Values are displayed as mean ± standard deviation (p-value compared with TSS)

Construct	Elongation after Cyclic Loading (mm)	Yield Load (N)	Displacement at Yield Load (mm)	Ultimate Failure Load (N)	Displacement at Ultimate Failure (mm)	Stiffness (N/mm)
TSS	1.18 ± 0.40	82.49 ± 14.17	4.43 ± 1.13	94.29 ± 7.99	5.82 ± 1.18	24.55 ± 4.05
UFF	1.93 ± 0.55 (0.004)*	91.99 ± 13.07 (0.19)	6.31 ± 2.27 (0.018)*	114.17 ± 9.93 (0.0003)*	10.42 ± 4.62 (0.017)*	24.40 ± 4.25 (0.89)

*statistically significant

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In the interests of transparency and to help reviewers assess any potential bias, all authors of original research papers are required to declare any competing commercial interests in relation to the submitted work. Referees are also asked to indicate any potential conflict they might have reviewing a particular paper.

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Smith and Nephew funded the study and donated all hardware.
Chris Vertullo, the primary surgeon, was also receiving grant funding from Smith and Nephew at the time the study was conducted.

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ACROMIOCLAVICULAR JOINT STABILISATION: A BIOMECHANICAL STUDY OF BIDIRECTIONAL STABILITY AND STRENGTH

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INTRODUCTION

The acromioclavicular (AC) joint facilitates stable vertical, horizontal and rotational motion of the clavicle during normal shoulder function. While many AC joint injuries can be managed non-operatively, surgical treatment for AC joint dislocation is known to restore joint motion, reduce pain and result in normal shoulder function. A previous *in vitro* study has demonstrated the importance of the coracoclavicular (CC) ligament complex in maintaining vertical stability of the AC joint, and that the AC joint capsule plays a critical role in horizontal stability [1]. The purpose of this biomechanical study was to evaluate the horizontal and vertical stability of the dislocated AC joint after reconstruction using 3 surgical techniques and compare the results to those of the native AC joint. Specifically, we aimed to compare bidirectional stability of the AC joint after repair using the single–clavicular tunnel technique, double–clavicular tunnel technique, and the double-clavicular tunnel technique with additional suture across the AC joint. Since the double-tunnel technique allows anatomical placement of the suture pulleys to replicate the structure of the native CC ligaments, we hypothesized that this approach would provide greater AC joint stability than the single tunnel technique.

METHODS

Twenty-four fresh-frozen shoulders were obtained from human cadavers. Each specimen was dissected free of all soft tissue, leaving the AC joint capsure and CC ligaments intact. Specimens were fixed to an Instron test machine by potting the medial half of the clavicle in a hollow mounting fixture and the scapula in a cylindrical mounting platform using dental cement. Eight inctact AC joint specimens were first tested as controls. The AC capsule and CC ligaments of all specimens were then divided and randomised into three treatment groups: a single clavicular tunnel (Group A), a double clavicular tunnel (Group B), and a double clavicular tunnel plus suture fixation across the AC joint (Group C) (Fig. 1). Each specimen underwent cyclic loading by translating the clavicle in the anterior, posterior, and superior directions relative to the acromion, with a peak load of 70N at 1 Hz over 500 cycles.

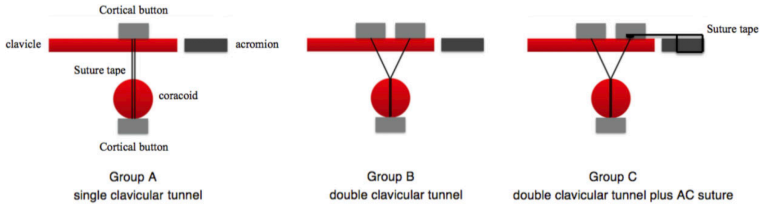

Figure 1: Schematic diagram of 3 surgical repair constructs (Groups A-C) utilizing cortical buttons to anchor suture

Load to failure translation was then performed in the superior direction. Construct stiffness was calcualted at each load increment during cyclic loading in each direction, as well as stiffness and load to failure during pull-out testing.

RESULTS AND DISCUSSION

There was a significant decrease in joint stiffness with time for all test groups, including controls, during cyclic loading in each direction ($p<0.05$) (Fig. 2). Compared with controls, all three treatment groups demonstrated equivalent stiffness and displacement in the vertical plane. In the horizontal plane, all three treatment groups demonstrated significantly decreased stiffness, increased displacement, or both when compared with controls ($p<0.05$). When all treatment groups were compared, no treatment arm proved superior regarding stiffness or displacement in either plane. Load-to-failure testing of the three treatment groups in the vertical plane demonstrated construct strength and stiffness comparable with previous reports for the native AC joint. The mode of failure was predominantly fracture at the point of fixation to the testing apparatus.

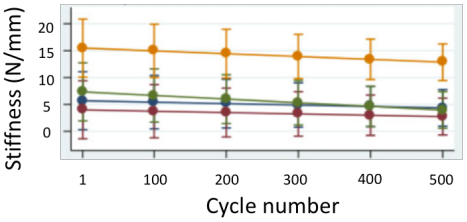

Figure 2: Mean stiffness of repair constructs (Groups A-C) and control specimens during cyclic displacement in the anterior direction

CONCLUSIONS

There is no difference in bidirectional strength and stability between the single– and double–clavicular tunnel techniques for coracoclavicular reconstruction of the AC joint. The addition of a stabilizing suture across the AC joint does not improve horizontal stability in the absence of repair of the AC joint capsule. This laboratory study provides evidence of the importance of the AC joint capsule and associated soft tissues in affording horizontal stability to the AC joint. Information from this and subsequent studies utilising a bidirectional AC joint loading model can influence the choice of surgical procedure in the clinical treatment of AC joint dislocations.

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DAY 2

David Findlay Early Career Researcher (ECR) Award Finalists

EFFECT OF BAGHDADITE SUBSTITUTION ON THE PROPERTIES OF BRUSHITE CEMENT

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INTRODUCTION

Brushite cements for bone filling applications have gathered increasing research attention recently due to their ability to partially resorb *in vivo* and support bone tissue growth [1]. There is however limited literature on strategies addressing the issues regarding the acidity and low radiopacity of brushite cements. The acidic reaction can detrimentally impact host bone tissue response; and the elemental composition of brushite is similar to human bone, hence the ability to distinguish both under conventional x-ray imaging is difficult. In this study, we hypothesize that through the approach of substituting of beta-tricalcium phosphate (β-TCP) with baghdadite ($Ca_3ZrSi_2O_9$) in the brushite cement formulation, we would be able to synthesize brushite cements with enhanced *in vitro* biocompatibility and radiopacity of the cement without loss in mechanical strength.

METHODS

Brushite cement mixtures were prepared by substituting the β-TCP reactant with baghdadite at various concentrations (0, 5, 10, 20, 50 wt%, labelled BC, BCB5, BCB10, BCB20, BCB50 respectively), and mixed with monocalcium phosphate anhydrous, in 0.1 M sodium pyrophosphate solution [2].

RESULTS AND DISCUSSION

There was a statistically significant increase in compressive strength for up to 20 wt% substitution of β-TCP with baghdadite, with BCB10 exhibiting the highest compressive strength at 21.1 ± 4.1 MPa, compared to 12.1 ± 3.9 MPa for pure brushite cement (**Figure 1a**). In addition, x-ray visibility in the form of equivalent aluminium sample thickness increased linearly with baghdadite substitution of β-TCP (**Figure 1b**). These results indicate cementitious reactivity of the baghdadite in the brushite cement formulations.

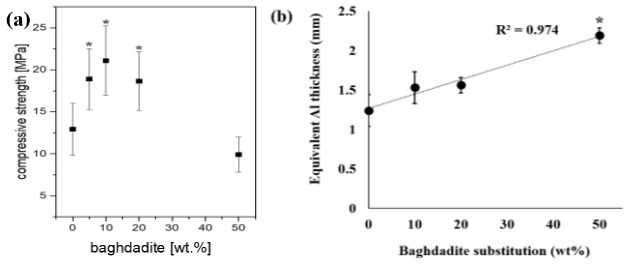

Figure 1: (a) Compressive strength and (b) x-ray aluminum equivalent thickness with different amounts of baghdadite substitution of β-TCP in brushite cement. *: $p < 0.05$ vs pure brushite cement.

Based on the mechanical strength results, BCB50 was omitted for *in vitro* primary human osteoblast (HOB) studies. The pH of the culture media conditioned with BC, BCB5, BCB10, and BCB20 prepared for cytotoxicity tests as per outlined in ISO/EN10993 were measured to be 6.47, 6.57, 6.73, and 7.02 respectively. Culture media conditioned BCB10 and BCB20 exhibited almost half the phosphorus ion levels (362.9 ppm and 349.1 ppm respectively) compared to those conditioned with BC (709.5 ppm). MTS assay absorbance values at 490 nm indicating *in vitro* HOB proliferation for BCB10 and BCB20 samples were significantly higher than BC and BCB5 samples for both the day 1 and day 7 time points (**Figure 2**). Baghdadite substitution in brushite cements showed a strong reduction in acidity and phosphate release, and may hence be responsible for the better HOB cytocompatibility of the BCB10 and BCB20 cements observed [3, 4].

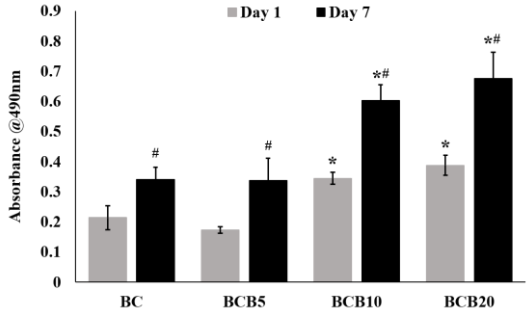

Figure 2: MTS assay absorbance values recorded for primary human osteoblasts cultured in media conditioned with 200 mg/mL of BC, BCB5, BCB10, and BCB20. #: $p < 0.05$ vs day 1 absorbance values of the corresponding material; *: $p < 0.05$ vs BC and BCB5 at the corresponding cell culture time point.

CONCLUSIONS

This study has demonstrated that up to 20 wt% baghdadite substitution of β-TCP is a useful strategy to improve both radiopacity and *in vitro* HOB cytocompatibility of brushite cements without compromising its mechanical properties. This strategy may be used concurrently with other reported protocols to further optimize the formulation of brushite-based cements.

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MINGHAO ZHENG ORTHOPAEDIC INNOVATION AWARD 2019, FINALIST

Orthopaedic Innovation Award Statement:

Brushite cements are currently being used clinically to fill irregular-shaped bone defects. However, brushite cements cause the surrounding aqueous environment to be acidic, thus detrimentally impacting surrounding bone tissue growth. Brushite cements are also similar to bone in elemental composition, thus difficult to distinguish using x-ray imaging. This study shows that substituting baghdadite into the brushite cement formulation can enhance biological properties of brushite cements by reducing both its acidity and phosphate ion release, as well as able to enhance radiological properties. This strategy has the potential to impact current brushite cement formulations used in the clinical setting.

SPATIAL DISTRIBUTION OF STRAIN IN EQUINE DISTAL METACARPAL SUBCHONDRAL BONE: A MICROCT-BASED FINITE ELEMENT MODEL

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INTRODUCTION

Focal microdamage and adaptation in the subchondral bone (SCB) subjected to intensive cyclic loading are important factors that contribute to SCB failure and joint degeneration. The associated increased bone turnover likely due to targeted remodeling results in spatial heterogeneity in the SCB tissue mineral density (TMD) and mechanical properties[1,2]. In this study, we developed micro computed tomography (µCT)-based finite element (FE) models of SCB from the third metacarpal (MC3) condyles of racehorses. Our objective was to quantify the spatial distribution of strain within SCB which had adapted to intensive cyclic loading *in vivo*.

METHODS

Cartilage-bone plugs (Ø=6.5mm, length=10mm) from the distopalmar condyles of n=8 Thoroughbred racehorses were extracted and scanned (4µm, µCT50, Scanco Medical) to measure bone TMD and resampled to 40µm to develop µCT-based FE meshes. Previously, we found a gradient in the axial stiffness (K) in the superficial SCB (4mm) of these specimens when tested in unconfined compression perpendicular to the cartilage surface (ε=2.3%, ε̇=46%/s). Real-time planar deformations were imaged (1000 frames/s) (Fig. A). The 2 mm of bone closest to the articular surface (superficial SCB: SSB) deformed almost three times the underlying 2 mm SCB (Deep SCB: DSB)[2]. To implement this apparent-level bone stiffness gradient at a tissue-level in FE models, we chose TMD as a tissue-level microstructural property of the bone to associate the stiffness gradient with, because $\frac{TMD_{DSB}}{TMD_{SSB}}$ correlated with $\frac{K_{DSB}}{K_{SSB}}$ (r=0.87, p=0.01). We then pooled TMD and K of SSB and DSB to realize a TMD-elastic modulus (E) for the SCB plugs:$E\ (MPa) = -77869.8 + 95.1TMD\left(\frac{kg}{m3}\right)$(r=0.83,p<0.000) (Fig. B), and assigned a tissue-level E to each finite element based on its TMD (Fig. D). Quasi-static compression of n=8 µFE models was simulated (ABAQUS) with unconfined and confined boundary conditions, to compare with experimental results and estimate tissue strains, respectively. Cartilage was simulated as incompressible, neo-Hookean hyperelastic (Poisson's ratio=0.49, shear modulus=40MPa). 90th percentiles of compressive and tensile strains were calculated for finite elements within SSB and DSB of an inner cylinder of Ø=3 mm.

RESULTS AND DISCUSSION

Unconfined compression FE models simulated a stiffness gradient like those of the experiments (Fig. C). When confined, the applied 30MPa compressive stress through the articular cartilage, which represents the joint surface pressure during a gallop, generated an overall strain of 0.9 ± 0.3 % in the SCB. This strain distributed non-uniformly across the SCB (Fig. E, F) with peak compressive strains of 2.05±1.03 % within the 2 mm SCB below the cartilage, which were 3.45±2.25 times of that within its underlying 2 mm SCB. The gradient of tissue-level material properties led to tensile strains of 0.40±0.21 % in the SCB beneath cartilage. The location of high strains corresponds to the common area of fatigue-induced microdamage in equine metacarpal condyles[3].

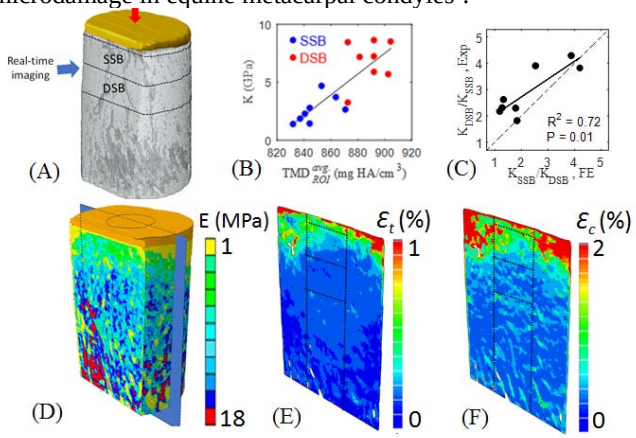

Fig.: (A) 3D reconstructed µCT image of a cartilage-bone indicating SSB and DSB, (B) linear regression between K and TMD, (C) correlation between FE-predicted and experimental results, (D) FE model with the E distribution and the inner ring, (E, F) tensile and compressive strain in a SCB vertical slice.

CONCLUSIONS

A novel outcome of this study was the estimation of spatial distribution of strains within the SCB with a tissue mineral density and porosity distribution highly adapted to high impact loading *in vivo*. These results provide insight into understanding the mechanism of adaptation, and joint failure.

ACKNOWLEDGEMENTS

Racing Victoria Limited/Victorian State Government.

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THE APPLICATION OF ACOUSTIC EMISSION IN THE DETECTION OF VERTEBRAL BODY FRACTURE

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INTRODUCTION

Vertebral fractures are a persistent injury typically associated with osteoporosis in the elderly and traumatic incident in younger individuals. These fractures are severely detrimental to quality of life, as evidenced by high rates of neurological and functional deficit [1]. Whilst the prevention of these injuries is critical, the study of vertebral fracture initiation and progression has been largely limited to experimental quasi-static loading of cadaveric spines. The application of more realistic dynamic loads is challenging, since localised bone fractures are difficult to quantify in real time. The aim of this study was to evaluate whether acoustic emission (AE) sensors may be used to identify isolated trabecular fractures and more severe fractures sustained by the vertebral body during dynamic compression.

METHODS

Twenty sets of three-vertebra specimens were prepared from the lumbar spines of fifteen male cadavers (age: 61.5±9.8 years). Two miniature AE sensors (S9225; Physical Acoustics Corp., USA), were attached to the centre vertebral body, each sampled at 2 MHz. The outer vertebrae were potted and attached to a testing machine that applied compression at 1 m/s. Each specimen was repeatedly compressed with increasing amounts of displacement until a fracture was observed visually or identified according to a stiffness change. The precise nature of the fracture was evaluated using pre- and post-test CTs (resolution: 0.1 mm). Parameters obtained from each test included: peak compressive force (Fz), maximum drop in compressive force (ΔFz), peak of AE signal ($AE_{amplitude}$), area under AE signal ($AE_{exposure}$) and the duration of intense AE activity ($AE_{duration}$).

Based on the CT image analysis, the final test of each specimen was classified as either: Category 1: No fracture, Category 2: Isolated trabecular fracture, or Category 3: Combined cortical and trabecular fracture. The initial compression tests were also classified as Category 1 due to their low magnitude (2.1±0.6 kN). The ability of each test parameter to identify each fracture outcome was determined using the area under the receiver operating curve (AUROC).

RESULTS AND DISCUSSION

The greatest AUROC for classification between Category 1 and 2 was for $AE_{duration}$ (0.98, 95% CI: 0.94-1.00) (Table 1). When distinguishing between these categories, each AE parameter had a mean AUROC that was greater than those derived from force measurements. However, when classifying between Category 1 and 3, the variable ΔFz provided ideal classification with a mean AUROC of 1.00. Measurements of force and AE wave pressure for a representative Category 3 test are provided in Figure 1. These results clearly depict intense AE activity prior to the peak compressive force, which suggests an accumulation of trabecular bone damage precedes a cortical fracture involving a drop in the compressive force.

Table 1: AUROC for each parameter used to classify between the fracture categories.

Parameter	Category 1 from Category 2 AUROC (95% CI)	Category 1 from Category 3 AUROC (95% CI)
$AE_{amplitude}$	0.95 (0.88-1.00)	0.98 (0.93-1.00)
$AE_{exposure}$	0.97 (0.91-1.00)	0.98 (0.95-1.00)
$AE_{duration}$	0.98 (0.94-1.00)	0.98 (0.95-1.00)
F_z	0.90 (0.78-1.00)	0.87 (0.75-1.00)
ΔF_z	0.87 (0.66-1.00)	1.00 (1.00-1.00)

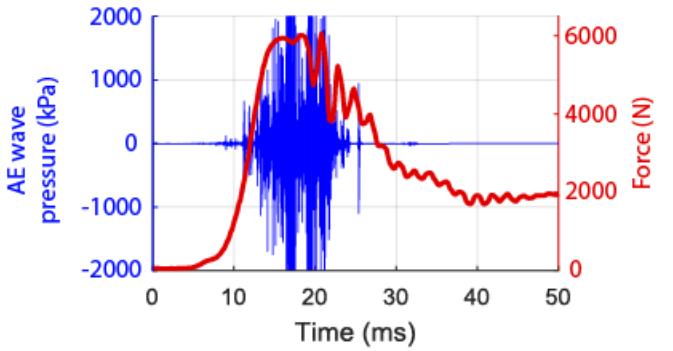

Figure 1: AE wave pressure and compressive force of a representative specimen classified as Category 3.

CONCLUSIONS

This study demonstrates the effective ability of AE sensors to identify localised trabecular bone fractures from dynamic loading. It is believed that an accumulation of these isolated fractures precedes a combined cortical and trabecular fracture characterised by a significant loss in the vertebral body stiffness. These more severe vertebral fractures may be readily identified using parameters calculated from load cell readings.

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EVIDENCE FOR GENDER-SPECIFIC BONE LOSS MECHANISMS IN PERIPROSTHETIC OSTEOLYSIS

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INTRODUCTION

Osteolysis adjacent to total hip replacement (THR) prostheses is a major cause of their eventual failure. Periprosthetic osteolysis is associated with the production of bioactive particles, produced by wear of articulating prosthesis surfaces. Wear particles invade the peri-prosthetic tissue, inducing inflammation and bone resorption. Previous studies have shown that osteocytes, the most numerous cell type in mineralised bone, can respond to wear particles of multiple orthopaedic material types. Osteocytes play important roles in bone resorption, regulating bone resorption by osteoclasts, and directly through osteocytic osteolysis. In this study, we performed histological analysis of bone biopsies obtained from male and female patients undergoing either primary THR surgery or revision THR surgery for aseptic loosening

METHODS

Patients were recruited into this study with informed written consent and ethics approval by the Human Research Ethics Committees of the Royal Adelaide Hospital and the University of Adelaide. Forty patients undergoing either primary THR for osteoarthritis or revision THR for aseptic loosening associated with radiographic evidence of periprosthetic osteolysis, were recruited at the Royal Adelaide Hospital. Patient cohorts (n=20/group) were age matched and included comparable numbers of males and females. Intraoperative trephine biopsies were taken from the periacetabular bone prior to reaming for insertion of the acetabular component, in primary THR patients, and after removal of the failed implant and the granulomatous tissue, in the patients undergoing revision THR. The biopsies were formalin fixed for 48 H and decalcified (10% EDTA/1% paraformaldehyde) for 2 weeks. Sections (5 µm) were stained with toluidine blue and imaged using NanoZoomer (20x, Hamamatsu Photonics). Osteocyte parameters were quantified using Image J software by manual tracing around osteocyte lacuna perimeters and bone perimeters using a Bamboo Pen and Touch (Wacom, Kazo). Statistical differences between the osteocyte parameters, were assessed using Student's t-tests (GraphPad software v7.02).

RESULTS AND DISCUSSION

Histological analysis of the bone biopsies showed metal wear particles evident within granulomatous tissue adjacent to the bone. Particles of either metal or UHMWPE were observed by microscopy in 15 of the 20 biopsies taken from the patients in the revision cohort; in 5 patients' samples both particle types were detected (3 female, 2 male). Furthermore, metal particles were visually detected within Haversian canals as well as on the surface of the bone. Evidence of osteocyte lacunae coalescence was also observed in the revision THR biopsies. Histological analysis of the bone biopsies showed significantly increased osteocyte lacunar area (Lac.Ar) and percentage lacunar area/bone area (%Lac.Ar/B.Ar) in revision THR bone with confirmed osteolysis, compared to bone biopsies from primary THR. Analysis by patient gender showed significantly increased Lac.Ar, indicative of osteocytic osteolysis, was specific to female revision samples. Conversely, male but not female revision THR biopsies displayed increased %Lac.Ar/B.Ar, compared to male primary THR bone, suggesting increased osteoclastic resorptive activity at the bone surface in males.

CONCLUSIONS

In conclusion, this study provides evidence that osteocytes may contribute to the development of osteolysis by activating resorptive pathways in response to wear particles, contributing to the aseptic loosening of implants, in a gender-specific manner.

ACKNOWLEDGEMENTS

The authors would like to thank the nursing and surgical staff of the Orthopaedic and Trauma Service at the Royal Adelaide Hospital for their help in collecting patient bone specimens.

Table 1: Patient demographics for Primary and Revision THR cohorts

THR Cohort	Age range	Average age	N	Gender	Age range	Average age
Primary THR	70-89	75	n= 20	Male (n=10)	70-84	75
				Female (n=10)	70-89	76
Revision THR	69-89	80	n= 20	Male (n=10)	69-87	79
				Female (n=10)	69-81	80

KNEE OSTEOARTHRITIS: PRESENCE OF BONE MARROW LESIONS IN SUBCHONDRAL BONE INDICATES INCREASED NUMBER AND THICKNESS OF PLATE LIKE TRABECULAE

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INTRODUCTION

Both animal and human studies indicate that changes in subchondral bone play an important role in the initiation and progression of osteoarthritis (OA). Bone marrow lesions (BMLs) in the subchondral bone have been identified by magnetic resonance imaging (MRI) as biomarkers of pathology in OA, and strongly associate with the severity of OA clinical symptoms and structural degeneration. It has been noted that the use of bone metabolism-altering therapies resulted in the reduction of BML size, together with a reduction in pain and cartilage volume loss. However, very little is known about the bone microstructure within BML zones in OA subchondral bone. The aim of this study was to evaluate the rod-and-plate microstructure of subchondral trabecular bone, in conjunction to changes in the subchondral plate and overlying cartilage, in human tibial plateaus with and without tibial BMLs, in comparison to non-OA controls, by applying a novel individual trabecula segmentation (ITS) technique.

METHODS

Tibial plateaus were collected from 22 OA patients aged 49-79 years undergoing knee arthroplasty and from 11 non-OA cadaver donors aged 44-89 years without bone disease. All specimens were scanned by MRI to identify BMLs and Micro CT was used to characterize the microstructure of the subchondral trabeculae. The specimens were then processed for cartilage histology and OARSI grading.

RESULTS AND DISCUSSION

BMLs have been identified in 14 (64%) of OA tibial plateaus (OA-BML group) and the remainder were tibial plateaus with no BML (OA-no BML group). All BMLs were identified in the anterior medial subregion.

When compared to controls, the medial compartment from OA subjects without BMLs had a lower rod bone volume fraction (rBV/TV), ($p<0.0001$) and rod trabecular number (rTb.N), ($p=0.002$); the plate bone volume fraction (pBV/TV) and plate trabecular number (pTb.N) did not differ. The subchondral bone of OA tibial plateaus containing BMLs was characterized by increased plate bone volume fraction (pBV/TV), ($p=0.003$), plate trabecular number (pTb.N), ($p=0.04$), and both rod and plate trabecular thickness (rTb.Th and pTb.Th) ($p<0.0001$ for both). Anterior medial subregion representing BML bone is characterized by a greater number of plate and rod-like trabeculae ($p<0.0001$ for all parameters) compared with posterior medial (no BML) bone. These differences also associated positively with increased histological OARSI grade within the BML region.

This study shows that in established knee OA, both the extent of cartilage damage and trabecular microstructural alteration in the subchondral bone depended on the presence of a BML. Thus, use of BMLs as MRI image-based biomarkers may inform on the severity of disease in established OA.

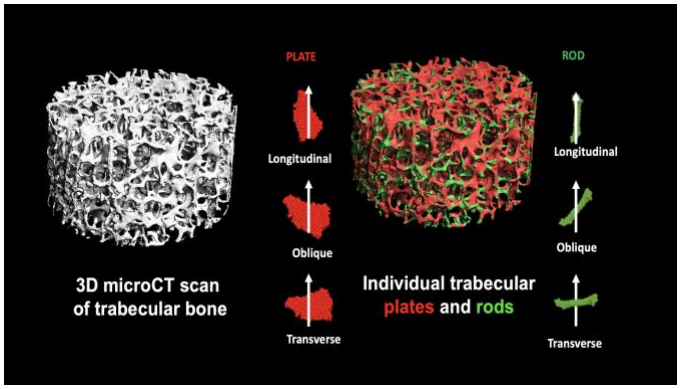

Figure 1: Left;3D micro CT scan of trabecular bone. Right; Individual Trabecula Segmentation ITS analysis

CONCLUSIONS

Since, BMLs appear to inform on the degree of structural difference in the subchondral bone, these features in combination with ITS-based analysis of rod-and-plate microstructure changes of subchondral bone can potentially be used in evaluation of OA progression and may assist in staging OA with respect to disease severity.

MINGHAO ZHENG ORTHOPAEDIC INNOVATION AWARD 2019, FINALIST

Orthopaedic Innovation Award Statement:

In established knee-osteoarthritis, bone marrow lesions (BMLs) are in close association with clinical symptoms and loss of cartilage volume. In this study we applied a novel ITS (individual trabecular segmentation) analysis of rod-and-plate microstructure changes and found that the presence of a BML defines the changes in both the subchondral bone and cartilage, which in turn relate to the severity of the disease. BMLs may therefore provide surrogate biomarkers that can discriminate OA subtypes or severity, for example helping to triage candidates for joint replacement surgery or conservative, non-surgical treatment, or be used as therapeutic targets, and response to treatment.

DAY 2

KEYNOTE 3 – Prof Rick Sumner

BONE REGENERATION AND IMPLANT FIXATION

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Implant fixation to the host bone is a prerequisite for long-term survival of total joint replacements. Indeed, a major cause for revision surgery is aseptic loosening of implants. For implants placed without the use of bone cement, implant fixation takes advantage of injury-induced bone regeneration in which the newly forming bone forms a bond between the host skeleton and the implant.

There has been considerable effort at optimizing implant design to promote secure fixation. Notable areas of research include designing appropriate surface characteristics of the implant, including porous coatings and other surface treatments. The importance of bone regeneration is apparent and this recognition has motivated several groups to study the process of bone regeneration in the context of placement of total joint replacement implants.

Part of the surgical procedure is to create a bed into which the implant is placed. This surgery injures the bone which mounts a biological response involving repair. Bone healing in general falls into one of two categories: endochondral and intramembranous bone regeneration. Bone repair during total joint replacement is intramembranous. Thus, studies of intramembranous bone formation and regeneration are relevant to the biology of implant fixation. In essence, there "happens" to be an implant placed at the site of injury. If the implant has the appropriate surface characteristics, is mechanically stable and in close contact with the host bone tissue, then the newly formed "repair" bone forms a mechanical connection to the skeleton. This tissue can adapt mechanically to the new loading environment and remodel over time, thereby providing a long-lasting means of mechanically fixing the implant to the host bone.

We and many others have spent considerable effort in determining how this biological process can be enhanced. Major approaches include the use of locally delivered growth factors and systemically delivered drugs. For instance, we showed over two decades ago that local delivery of transforming growth factor-beta led to considerable increase in bone regeneration and implant fixation[3]. Since then, other locally applied growth factors such as bone morphogenetic protein have also been found to enhance bone regeneration and implant fixation. A few years ago, we showed that sclerostin antibody, the most recently approved new drug for osteoporosis, given systemically led to enhanced implant fixation[4].

While the biology of intramembranous bone regeneration is less well-explored than endochondral repair, we now have a detailed time-course of gene expression during the repair process[5]. Essential findings were that nearly one-third of known genes in the rat model were differentially expressed following mechanical ablation of the femoral medullary canal and that specific biological processes and pathways had distinct temporal patterns. In another study, we showed in a mouse model that the volume of intramembranous bone regeneration following ablation of the marrow is a heritable trait independent of the heritability of intact bone phenotypes, suggesting the existence of independent genetic programs for bone healing and development[1].

Another area of interest is early detection and treatment of aseptic loosening in total joint replacement. We have identified a novel combination of urine markers that have high ability to predict future loosening[2]. If these (or other) markers can be verified it might be possible to prevent or even reverse loosening with the use of anabolic agents. An even more recent approach is to dampen the inflammatory response to implant-derived particles by manipulating the gut microbiome. We are currently in the midst of performing experiments on both approaches.

ACKNOWLEDGEMENTS

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   In addition to government and philanthropic funding, the projects described herein were supported by research grants to my institution from two commercial entities.

DAY 2

PhD Award Finalists

CHANGES TO THE HIP CONTACT FORCE LOADING PROFILE FOLLOWING TOTAL HIP ARTHROPASTY

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INTRODUCTION

Hip joint loading is purported to play an important role in the primary stability of implants following total hip arthroplasty (THA) [1]. Previous studies have reported hip contact forces in patients before and after THA but have been limited to comparing the hip contact forces alone without considering the temporal nature of the loading profile [2]. Evidence of altered loading profiles has been shown in patients following THA, whereby a single peak pattern, instead of a normal double peak pattern is observed [3]. This suggests that the temporal profile may provide a better understanding of altered hip joint loading after THA than the magnitude of the force alone.

We aimed to determine the change in hip contact force peaks and temporal profile before and up to six months post-THA. It was hypothesized that patients would demonstrate a more normal double-peak loading profile after THA, irrespective of any changes to peak hip joint contact forces.

METHODS

Forty-three participants awaiting primary THA for osteoarthritis were recruited from a large metropolitan hospital (mean age: 65 SD 14 years; BMI: 30 SD 5 kg/m^2). Gait analysis was performed pre-operatively, and at six weeks, three months and six months after THA. A generic lower-limb musculoskeletal model (Gait2392) was scaled to individual anthropometries using the Musculoskeletal Atlas Project. Subject specific hip joint centre locations were obtained from computed tomography before and after THA and used to update the scaled musculoskeletal models. Joint angles and muscle forces were calculated and used as inputs to determine hip joint contact forces in OpenSim.

The number of peaks in the loading profile was determined using the first derivative of the signal during stance, whereby a peak was indicated by zero-crossing points. Where a double-peak was identified, a linear effects mixed model analyses compared the change in hip contact force magnitude over time. With evidence suggesting an association between reduced gait speeds and altered loading [4], independent sampled *t*-test was used to test the difference in gait speed between single and double-peak observations.

RESULTS AND DISCUSSION

For double-peak observations, significant main effects were identified for the magnitude of the first peak (p=.002) but not the second peak (p=.081). *Post hoc* pairwise comparisons identified an increase at three and six months compared to six weeks (mean difference: 0.49 SD 0.12 BW p = < .001 and 0.31 SD 0.14 BW, p = .031, respectively), however values were comparable to before surgery at six months (mean difference: 0.08 SD 0.21 BW) (Figure 1A). Pre-operatively, single peak hip contact force profiles were observed for 11 patients (26%). Four continued to show a single peak at 6 months (Figure 1A). Patients with a single peak profile walked slower at all time points compared to patients with a double-peak (Figure 1B).

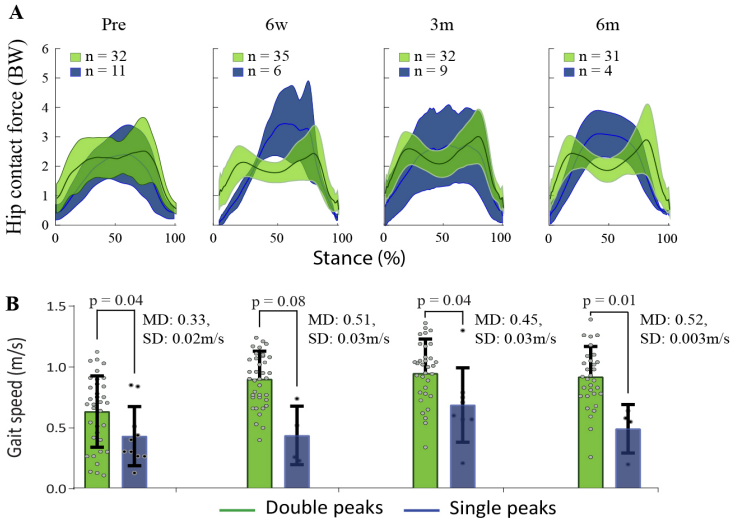

Figure 1. (A) Hip joint loading profiles for single and double peak observations. (B) Difference in gait speed for single and double peak observations over time. MD: mean difference; SD: standard deviation

CONCLUSIONS

Despite no change to the magnitude of the hip contact force over time, THA enabled patients to walk at greater speeds, resulting in a more normal double-peak loading profile.

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LONGITUDINAL POSTOPERATIVE JOINT KINEMATICS OF TIBIAL PLATEAU FRACTURE PATIENTS

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INTRODUCTION

Tibial plateau fractures (TPFs) affect the articular surface of the knee and are associated with poor long-term outcomes [1]. The time course of lower limb kinematics, which can be seen as a surrogate for functional capacity, with postoperative recovery at both the early and late stages of recovery has not previously been investigated. Investigation into all lower limb joints provides a description of the functional compensation of the lower limb as a system when recovering from a TPF. The aim of this study was to investigate if the kinematics of the affected side changes over the first two years postoperative.

METHODS

Eighteen patients with TPFs were recruited from the Royal Adelaide Hospital. Open reduction internal fixation surgery was performed [2]. Patients were instructed to weight bear immediately after surgery, as tolerated. Gait analyses were performed postoperatively within two weeks, at six weeks, three and six months, and at one and two years, using standard motion capture techniques. A generic full-body musculoskeletal model [3] was scaled using static trial marker data in MAPClient [4]. Rigid body motion was reconstructed using inverse kinematics, and bilateral joint angles for the operated limb were calculated in the sagittal plane for the ankle, knee and hip during walking [5]. From this, the kinematic variables were investigated, namely: hip, knee and ankle angles, specifically the range of motion (ROM); the angle at toe off (TO), peak ankle dorsiflexion and plantarflexion and maximum knee flexion during swing. A linear effects mixed model tested changes in kinematic variables with time as a repeated measure. The level of significance was set at 0.05.

RESULTS AND DISCUSSION

Group mean hip, knee, and ankle angles during walking were compared between time points (Figure 1). Significant effects were identified for five kinematic variables over time: hip ROM ($p=<0.001$), knee ROM ($p=0.004$), ankle ROM ($p=0.017$), hip angle at TO ($p=<0.001$) and maximum knee flexion angles ($p=0.004$). Post-hoc pairwise comparisons showed statistically significant increases between 12 and 26 weeks in hip ROM (32° to 39°, $p=0.002$), knee ROM (42° to 51°, $p=0.02$), maximum knee flexion angle (51° to 60° $p=0.017$) and ankle ROM (20° to 24°, $p=0.036$). Between 26 weeks and one year, a significant improvement was shown in the hip angle at TO (-12° to -19°, $p=0.002$). No effects were identified for: hip, knee, and ankle initial contact angles; maximum knee angles during stance, and maximum ankle dorsiflexion and plantarflexion angles ($p>0.05$).

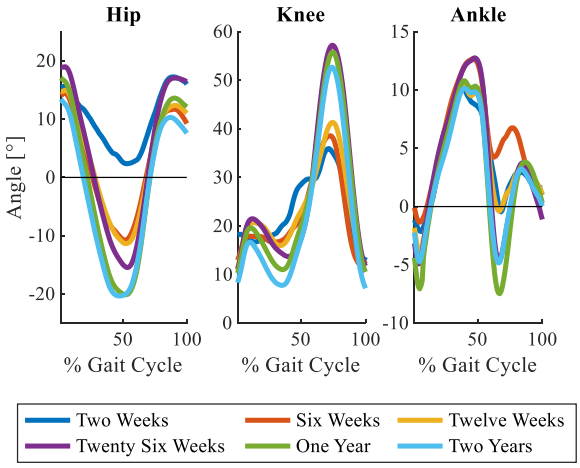

Figure 1 Mean sagittal plane hip, knee and ankle joint angles during gait for TPF patients from two weeks to two years.

CONCLUSIONS

Our results indicate that by 26 weeks post-surgery, TPF patients demonstrate significant improvement in their lower limb joint kinematics, with little further change evident up to two years. To our knowledge, this is the longest duration of longitudinal investigation into the postoperative joint kinematics of TPF patients, and the results provide insight into the functional improvements of patients who begin weight bearing immediately after surgery.

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INFLUENCE OF JOINT ALIGNMENT IN TIBAL OA VS. CONTROLS: CARTILAGE, CORTICAL SUBCHONDRAL BONE PLATE AND TRABECULAR BONE

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INTRODUCTION

Variations in knee joint alignment have been linked to regional changes observed in tibial cartilage and subchondral bone in knee osteoarthritis (OA) [1,2]. However, reports on cortical subchondral bone plate (SBP) and subchondral trabecular bone (STB) differences between OA and non-pathological joints are conflicting [3, 4]. Moreover, the effect of joint alignment on cartilage morphology (thickness), the SBP and the underlying STB remains unexplored [1].

This study aimed to use micro-CT imaging to quantify tibia cartilage thickness, SBP thickness and STB microarchitecture in end-stage knee OA patients with varus- or valgus-aligned joints, comparing them to control (non-OA) knees.

METHODS

Participants: Tibial plateaus were retrieved from 25 knee-OA patients (68±7 years, 90±18 kg; varus-aligned (n=18), valgus-aligned (n=7); knee arthroplasty; classified as varus- or valgus-aligned from pre-operative radiographs) and from 15 cadavers (62±13 years, 83±16 kg; controls) free of musculoskeletal disease in the examined joint.

Micro-CT: The entire plateaus were micro-CT scanned (17.4 µm/voxel, model 1076, Skyscan-Bruker, Belgium). From the micro-CT images, cartilage thickness (Cg.Th), cortical SBP thickness (Pl.Th) and the STB bone volume fraction (BV/TV) were analysed in four cylindrical subregions of interest (ROIs, 10mm diameter, 3-5mm length), in anteromedial (AM), anterolateral (AL), posteromedial (PM) and posterolateral (PL) condyles (Fig.1.a, b, c). Medial-to-lateral (M:L) Cg.Th ratios, M:L Pl.Th ratios and M:L BV/TV ratios among the 4 ROIs were also explored (Fig.1).

Statistics: Cg.Th, Pl.Th, STB BV/TV and their M:L ratios for the varus-OA and valgus-OA group were compared to controls (Kruskal-Wallis and Bonferroni-adjusted Mann-Whitney U-tests). Statistical significance, $p<0.05$.

RESULTS AND DISCUSSION

Age and body mass were not significantly different between OA and controls.

Compared to controls, varus-OA showed significantly lower Cg.Th in AM ROI (-59%, $p<0.05$), but higher laterally (up to +63%); whereas in valgus-OA it was higher medially (+56% in PM ROI, $p<0.05$). In controls the Cg.Th M:L ratios were close to unity (range: 0.8-1.1, Fig.1.a), in varus-OA they were all below unity (0.2-0.6, $p<0.05$) and in valgus-OA they were similar to or higher than in controls (up to +40%).

Pl.Th was significantly higher in varus-OA medially compared to controls (up to +117%), whereas it was higher laterally in valgus-OA (up to +110%). Similarly, BV/TV was higher medially in varus-OA (up to +49%, $p<0.05$) and higher laterally in valgus-OA (up to +76%, AL, $p<0.05$), compared to controls.

In varus-OA, the M:L Pl.Th ratios were all above unity (range 1.4-2.0) and higher than in controls (0.8-1.8, Fig.1.b); in valgus-OA they were closer to unity (0.8-1.0) and lower than controls. Similarly, in varus-OA, the M:L BV/TV ratios were all above unity (1.6-2.4) and higher than controls (0.9-2.1, Fig.1.c); in valgus-OA, they were lower than in controls (up to -48%, AM:AL and PM:AL, $p<0.05$) and closer to unity (0.8-1.1).

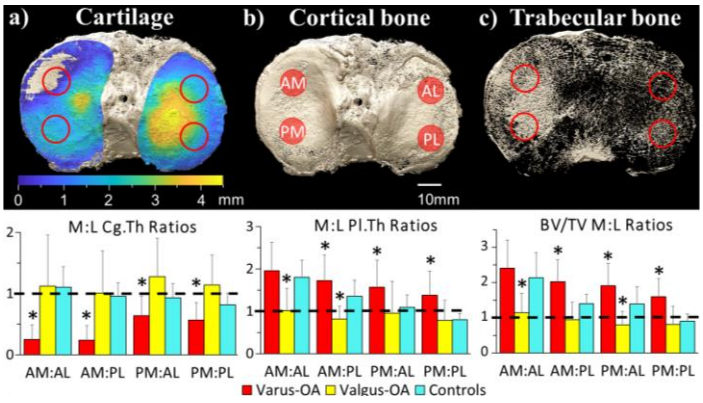

Figure 1: Top: micro-CT 3D rendering of a right tibial plateau (varus-OA), showing cartilage (a), cortical SBP (b) and STB (c). Bottom: average M:L Cg.Th ratios, M:L Pl.Th ratios and M:L BV/TV ratios. Error bars= standard deviation; dashed line indicates unity; *$p<0.05$ versus controls.

CONCLUSIONS

OA and non-OA tibias differ significantly in Cg.Th, Pl.Th and STB microarchitecture depending on joint alignment, suggesting that joint structural changes in OA may reflect differences in medial-to-lateral load distribution upon the tibial plateau. These findings may contribute to improve our understanding of the disease.

ACKNOWLEDGEMENTS

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ASSESSMENT OF INFLAMMATION, GLIAL CELL POPULATION AND PAIN-LIKE BEHAVIOUR IN A COLLAGEN ANTIBODY-INDUCED ARTHRITIS MOUSE MODEL FOLLOWING TREATMENT WITH PARTHENOLIDE

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INTRODUCTION

Rheumatoid arthritis (RA) is a chronic autoimmune disease characterised by inflammation of the joint, synovial hyperplasia and damage of cartilage and bone. Pain is often associated with joint destruction with an increased level of nociceptor sensation, a common symptom seen in patients considered to be in remission. The neuroimmune relationship between the immune system and the brain has been suggested as playing a key role in the formation and maintenance of persistent pain in RA [1]. Pro-inflammatory transcription factors e.g. nuclear factor-kappa B (NF-κB) have been found to be involved in inflammatory hypersensitivity [2] and induction of genes responsible for generating injury-responsive cytokines in glial cells [3]. Parthenolide (PAR) works through inhibition of NF-κB and has been found to have anti-inflammatory properties in collagen-induced arthritic rats previously [4]. In this work, it was thus hypothesised that PAR would lead to decreases in paw inflammation and glial reactivity within the brain and spinal cord of mice with inflammatory-induced arthritis.

METHODS

A mild model of collagen antibody induced arthritis (CAIA) was induced [5]. CAIA mice were treated with either PBS (vehicle) or PAR (1 or 4mg/kg). Clinical paw inflammation was scored in all paws. Mechanical allodynia was assessed by von Frey behaviour testing. Brain and spinal cords were harvested. Periaqueductal grey (PAG) and rostral ventromedial medulla (RVM) regions of the brains and spinal cord were selected for analysis of nociceptive signaling regions. Glial reactivity was determined by immunohistochemical detection of GFAP (Astrocyte marker) and IBA1 (Microglia marker). Statistical analysis was performed using area under the curve and Mann-Whitney test to compare control to untreated CAIA mice and untreated CAIA mice to PAR treated CAIA mice ($P<0.05$).

RESULTS AND DISCUSSION

Paw inflammation was greater in the CAIA group compared with control ($P<0.003$) and significantly greater in CAIA compared with CAIA+1mg/kg PAR ($P=0.032$) or CAIA+ PAR 4mg/kg ($P=0.017$). Spinal expression of GFAP and IBA1 was significantly increased in CAIA mice compared with control ($P<0.0293$, $P=0.0007$ respectively). IBA1 levels were significantly reduced in CAIA when treated with 4mg/kg PAR ($P=0.0013$). PAG and RVM regions GFAP positive cells were significantly higher in CAIA compared with control in both the PAG and RVM ($P<0.0001$, $P=0.0006$ respectively); 1 mg/kg PAR and 4 mg/kg PAR treated CAIA mice had statistically decreased GFAP compared to CAIA in both the PAG ($P<0.0001$, $P<0.0001$ respectively) and RVM ($P=0.0004$, $P=0.001$ respectively). There was a significant increase in GFAP positive cells in CAIA+1 mg/kg PAR compared to 4 mg/kg PAR treated groups within the PAG but not the RVM ($P=0.02$). The number of IBA1 positive cells were significantly higher in CAIA compared with control in both the PAG and RVM ($P<0.0001$, $P=0.0007$ respectively); 1mg PAR and 4mg PAR treated CAIA mice had statistically decreased IBA1 compared to CAIA in both the PAG ($P=0.0044$, $P<0.0001$ respectively) and RVM ($P=0.0260$, $P=0.01$ respectively). There was a significant increase in IBA positive cells in CAIA+1 mg/kg PAR compared to 4 mg/kg PAR treated groups within the PAG but not the RVM ($P=0.02$).

CONCLUSIONS

The present results support the hypothesis that glial reactivity is increased in CAIA mice and decreased by PAR treatment. Both 1 mg/kg and 4 mg/kg PAR was effective at reducing the reactivity of both microglial (IBA1) and astrocytic (GFAP) populations within the lumbar spinal cord, PAG and RVM. Further directions include exploring new strategies to investigate pain-like behavior in the CAIA mouse model e.g. the catwalk and examining NF-κB expression levels to further clarify the involvement of NF-κB signaling in RA specific pain.

ACKNOWLEDGEMENTS

This project was kindly funded by Arthritis Australia (TC, MH, EP). AD, CSP Scholarship (FL) RTP Scholarships (BW)

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A NOVEL DYNAMIC CADAVERIC WRIST SIMULATOR FOR 3-DIMENSIONAL CARPAL BONE MOTION MEASUREMENT USING BIPLANE X-RAY FLUOROSCOPY

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INTRODUCTION

The wrist, which is one of the most complex joints in the human body, is comprised of the radiocarpal, midcarpal and distal radioulnar and is represented by over 15.2% of upper limb injuries [1]. At present, evaluation of dynamic wrist function in cases of ligament damage and after surgical intervention remains challenging due to the complex interaction between muscle loading and the resulting carpal bone motion. The aim of this study was to develop and validate a dynamic cadaveric wrist motion simulator that is capable of reproducing accurate and physiologically meaningful active wrist motions that are repeatable at both macroscopic and carpal bone levels.

METHODS

Seven fresh-frozen wrists were harvested from human cadavers (age: 72±15 years) and radiographically screened for joint abnormalities. The wrist joint capsule was opened dorsally and radio-opaque beads in clusters of three implanted into the scaphoid, lunate and capitate bones. Computed tomography (CT) scans of the specimens were reconstructed and used to register bead to bone positions.

A custom-designed computer-controlled dynamic wrist simulator was developed and employed for reproducing active wrist motion by applying physiological loading to tendons of the wrist prime mover muscles using six stepper-motor-driven actuators (Parker Hannifin Corp., Cleveland, USA) (Fig. 1). The forearm was disarticulated at the elbow and fused in neutral supination by means of two Steinmann pins. The radius and ulnar were vertically mounted in a potting block, and steel cables instrumented with 1DOF load cells (Dacell Inc., Korea) attached to the prime mover muscles that were detached from their origins. These included the flexor carpi ulnaris and radialis, extensor carpi radialis brevis and longus, extensor carpi radialis, and abductor pollicis longus.

Sinusoidal motion profiles of dynamic wrist flexion-extension (± 30°), radial-ulnar deviation (± 20°) and their superposition (dart thrower's motion) were performed by applying muscle forces that minimised the sum of squares of muscle activations [2]. Global wrist motion, measured in real-time using a high-speed video motion analysis system comprising four cameras (Vicon, Oxford, UK), was used as a position feedback to update the muscle forces. This was achieved by tracking triads of retroreflective markers rigidly attached to the radius and third metacarpal. The control system was implemented in LabVIEW (National Instruments, Austin, USA) and employed a decentralized adaptive controller and a quadratic programming optimizer for muscle force estimation, with additional feedforward of the tendon velocities estimated using a kinematic model of the wrist. Carpal bone motions were measured using a biplane fluoroscopy system that had a dynamic root mean square (RMS) accuracy of 0.168° in rotation and 0.039 mm in translation. Repeatability of simulated motions was measured at the global wrist joint-level and carpal-bone level using RMS errors in angles and positions.

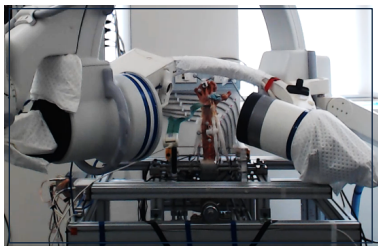

Figure. 1: Photograph of cadaveric wrist simulator and bi-plane fluoroscopy system imaging a wrist specimen undergoing dynamic wrist flexion

RESULTS AND DISCUSSION

Simulated flexion-extension, radial-ulnar deviation and dart thrower's motion resulted in sub-degree RMS errors in global wrist motion, sub-millimeter and sub-degree repeatability in carpal bone motion, and sub-Newton tendon force repetability (Table 1).

Table 1: The rms (RMSE), maximum absolute error of the position control (Max ABSE), mean repeatability of the global wrist joint angle and carpal bone motion, the applied tendon forces for flexion-extension (FEM), radial-ulnar deviation (RUD) and dart thrower motion (DTM).

Wrist Motion	RMSE (deg)	Max ABSE (deg)	Rep. global motion (deg)	Rep. carpal motion		Rep. tendon force (N)
				Translational (mm)	Rotational (deg)	
FEM	0.09	0.26	0.02	0.03	0.19	0.13
RUD	0.15	0.38	0.03	0.03	0.19	0.18
DTM	0.18	0.48	0.04	0.03	0.18	0.23

CONCLUSIONS

The present study introduced a novel dynamic wrist simulator that demonstrates strong repeatability of simulated global wrist motions and local motions of carpal bones using dynamic x-ray fluoroscopy. This apparatus has applications in evaluating the effect of injury and surgical reconstruction on wrist function.

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DAY 3

PODIUM 5

FATIGUE TESTING OF EQUINE MCIII SUBCHONDRAL BONE UNDER A SIMULATED TRAINING PROGRAM

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INTRODUCTION

Subchondral bone (SCB) is prone to injury when subjected to high magnitude cyclic (fatigue) loading as occurs in racehorses. Previously researchers have studied the fatigue behavior of equine third metacarpal (MCIII) subchondral bone under a constant load and frequency [1]. But during exercise SCB is typically subjected to varying loads [2]. We aimed to determine the mechanical response of SCB of the MCIII under more realistic loading conditions which included all loads likely to be experienced during a fast-workout for a racehorse.

METHODS

Subchondral bone plugs (n=12, diameter = 6.5 mm, length =6.8 mm) were harvested from left and right medial condyles of n=12 racehorses. Plugs were scanned with microCT and images were processed for tissue mineral density (TMD in $gmHAcm^{-3}$) and bone volume fraction (BVTV) using CTAnalyser (SkyScan 1172; Bruker microCT N.V., Kontich, Belgium). The fatigue loading included various stress levels and frequencies that represented the loading conditions during a typical fast workout of a racehorse (Figure 1). The loading was repeated until the failure of each specimen. Relative energy loss was defined as the ratio of energy loss (area enclosed by stress-strain curve) to absorbed energy (area underneath stress-strain curve). Cox proportional hazards regression models were used to estimate the instantaneous probability (hazard) of SCB failure as a function of time and covariates. The unit of 'time' was modelled by loading cycle. Hazard ratios (HR) and their 95% confidence intervals (CI) are reported. Statistical significance was set at $P<0.05$.

RESULTS AND DISCUSSION

The mean ± standard deviation for total cycle to failure were 70,186 ± 58,870 (18.30 ± 15.70 training workouts) for n=12 specimens. All specimens failed under loading equivalent to a slow or fast gallop. Fatigue life (cycles to failure) was greater in specimens with higher BVTV (p=0.013, HR=0.77, 0.63-0.95), higher TMD (p-value=0.001, HR=0.95, 0.92-0.98), higher initial modulus (p<0.001, HR=1.00, 0.99-1.00) and lower relative energy loss (p<0.001, HR=1.25, 1.14-1.37).

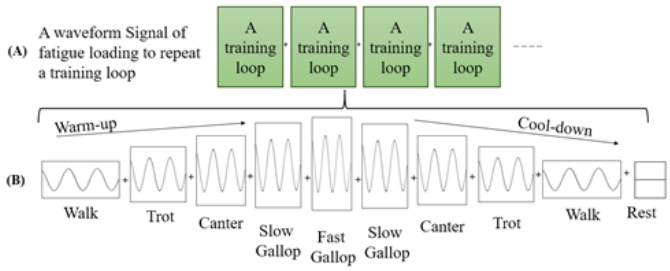

Figure 1: A) A waveform signal indicating the repetition of a training loop (1 fast-workout); B) loading cycles within a training loop, includes warm-up and cool-down phase.

CONCLUSIONS

The response of the equine MCIII SCB under simulated training loads demonstrated the importance of the highest speeds in the development of SCB injury. This is similar to observations in live horses where catastrophic failure most commonly occurs during high speed galloping. Under a loading protocol similar to a typical fast workout training, SCB that was initially stiffer, had a higher BVTV and TMD and lower energy loss prior to failure was more resistant to cyclic loading.

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THE KEY ROLE OF MECHANICAL STIMULATION IN REGENERATION OF CRITICAL-SIZED BONE DEFECTS

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INTRODUCTION

Mechanical strains created by the substrate have been extensively linked to cellular responses and regenerative outcomes in numerous experimental studies [1, 2]. In the case of bone scaffolding in load-bearing anatomical sites such as critical-sized segmental defects, the magnitude of strain generated in the scaffold can be influenced by the physiological loads within the defect site. Moreover, the choice of fixation device used to stabilize the scaffolding system can significantly affect strain distribution and subsequent mechanical stimulation in the scaffold. One main challenge is how to effectively evaluate proper mechanical stimulation generated in a bone scaffold in vivo. In the present study, finite element method (FEM) is implemented to characterize the mechanical strain and its effect on bone formation in ceramic scaffolds implanted in critical-sized segmental defects in sheep tibia.

METHODS

The Sr-HT-Gahnite scaffolds with similar compositional and architectural properties were implanted into critical-sized segmental defects in sheep tibia. After 12 months, all sheep were sacrificed and explants were harvested for histological evaluation. Although all surgical procedures were performed under similar conditions for all sheep, the X-ray images revealed some variation in the arrangement of the fixation plate and screws as well as the quality of the bone-implant interface in different sheep.

Finite element method (FEM) was implemented to create case-specific numerical models [3] mimicking the in vivo loading regime under walking condition for each sheep, taking into consideration the location of the scaffold and the arrangement of the fixation construct, as determined from the X-ray images.

RESULTS AND DISCUSSION

The finite element analyses enabled prediction of the total strain energy by simulating the pattern of load transfer into each scaffold. The case-specific numerical models demonstrated a direct correlation between the total strain energy and the amount and pattern of the newly formed bone in each scaffold (Figure 1). The results collectively suggested that new bone formation proceeded better in the defects with significant and evenly distributed loads at physiologic level.

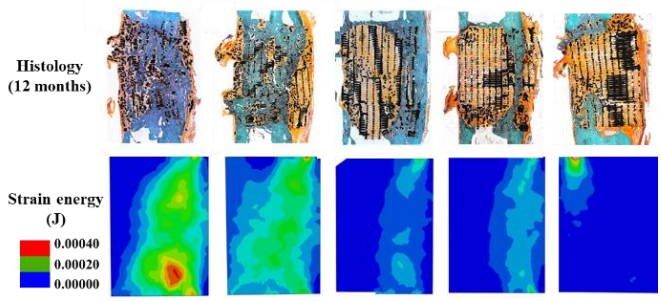

Figure 1: Histological images of whole sections (top panel) are included for comparison with the numerical results of total strain energy in the longitudinal cross-section at the center of each scaffold (bottom panel).

CONCLUSIONS

The in-silico modeling of strain energy distribution in the scaffolds revealed the importance of surgical fixation and mechanical loading on long-term bone repair regeneration. Uneven strain distribution or low strain due to improper load transfer or implant instability, which might result from variations in surgical fixation, could have considerable negative impacts on bone healing.

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THE DEVELOPMENT AND RELIABILITY OF A SEMI-AUTOMATED METHOD TO SPLIT THE ACETABULUM INTO CLINICALLY RELEVANT REGIONS OF INTEREST

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INTRODUCTION

Implant loosening is the most common cause of total hip arthroplasty (THA) implant failure in Australia [1] and is often associated with acetabular peri-prosthetic osteolysis [2]. Splitting the acetabulum into regions of interest (ROI), which correspond to ROIs proposed by Paprosky [3], and quantifying the extent of lysis within these ROIs could assist with surgical planning when revision surgery is required. The aim of this study was to develop a semi-automated method for achieving this. In addition, the intra-operator reliability of the approach was tested as some user input is required. This testing was performed for CTs of the native hip as well as unilateral and bilateral cases with a physically simulated osteolytic lesion.

METHODS

Semi-automated ROIs: Splitting of the acetabulum into three ROIs (anterior, superior and posterior) required segmentation and 3D reconstruction of a pelvis. Points around the acetabular rim (AR) and the Anterior Superior Iliac Crest and the Pubic Tubercle anterior landmarks (AL) (Figure 1A) were located manually on the 3D reconstruction of the CT and exported as coordinates. The 3D model and landmarks were input into the custom written code which applied an acetabular sphere fit via the Pratt method using the AR coordinates and a local patient-specific coordinate system based on the center of this sphere and the AL coordinates (Figure 1A). The sphere radius was increased by 40% before the sphere was split into thirds and the containing areas exported (Figure 2B).

Reliability tests: To test the intra-operator reliability, the above method was repeated three times for three CTs (pre-op, unilateral and bilateral). CTs were taken of a fresh frozen cadaver on which these operations were performed. A single simulated lytic lesion was created in the left acetabulum for the unilateral and bilateral cases and later segmented in addition to the pelvis (Figure 1C). The coefficient of variation (CoV) of the ROIs between repeats was calculated for the average Hounsfield units (HU), volume (mm^3), volume of lysis (mm^3), and extent of lysis (missing bone as a percentage of total bone that should be present). As the lysis was confined to the superior region of the acetabulum, these values were only comparable for this ROI.

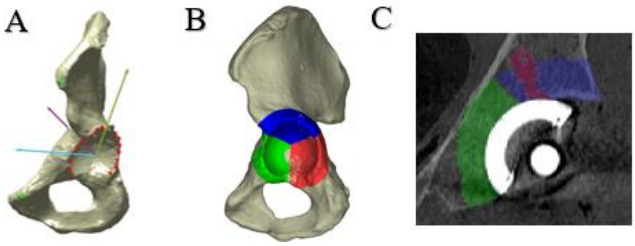

Figure 1: (A) AL/AR coordinate points and local coordinate system (B) Acetabulum split into ROIs (C) ROIs (anterior & superior) over original CT alongside segmented osteolysis.

RESULTS AND DISCUSSION

The CoVs for each region for each CT are presented in Table 1. The CoVs indicate good reliability of the method [4]. Variability increased for all measures with number of implants, with exception to the extent of lysis. As the lytic lesion was generated during surgery using a drill it extends further than those generally seen in real life scenarios. If the volume was confined to the superior ROI then the lysis volume CoV would remain low for increasing implants. The effect of the volume extending outside the ROI has little effect when being taken as a percentage of the entire volume. This suggests that this parameter would be a reliable indicator of lysis within the ROIs upon validation of the lysis segmentation accuracy.

CONCLUSIONS

This study presents a new semi-automated method, with good intra-operator reliability, for splitting the acetabulum into ROIs corresponding to the Paprosky Classification. Further work will explore the inter-operator reliability and the accuracy of this technique for lytic volume estimation.

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Table 1: Coefficients of variation (%) after three repeats of average Hounsfield units in ROI, volume of ROI, volume of bone loss in ROI and extent of bone loss in ROI.

	Pre-Op			Unilateral			Bilateral		
	Anterior	Superior	Posterior	Anterior	Superior	Posterior	Anterior	Superior	Posterior
Average Hounsfield Units	2.36	0.69	2.28	7.49	3.36	3.23	6.34	3.01	2.02
ROI Volume	5.38	0.99	2.83	7.55	9.64	8.59	10.37	14.95	11.27
Volume of Bone Loss	-	-	-	-	8.78	-	-	15.22	-
Extent of Bone Loss	-	-	-	-	3.34	-	-	3.20	-

THE EFFECT OF SURGICAL DISPLACEMENT OF THE HIP JOINT CENTER ON PERI-ACETABULAR BONE STRAIN AND HIP CONTACT FORCE WHILE WALKING: AN IN-SILICO EXAMINATION OF A THR PATIENT

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INTRODUCTION

Post-surgical changes of HJC location result in poor hip function and increased rate of loosening of the acetabular component [3]. Experimental studies have shown that superior and superolateral HJC displacements cause a significant increase in hip joint forces [2] and peri-acetabular strain [4]. However, current information is limited to selected loading cases and directions of HJC displacement. The aim of this study was to investigate the effect on peri-acetabular strain of changes of HJC location in different directions while walking. The analysis was completed for a severe mono-lateral osteoarthritic patient by combining CT imaging, motion analysis, finite-element (FE) and musculoskeletal modelling.

METHODS

The participant was a male (61 age male, with 167 cm height and 69.92 kg weight; BMI 25.07) with severe hip osteoarthritis, who received a Zimmer Trilogy at the Royal Adelaide Hospital (Adelaide, Australia). Trajectories of skin-mounted reflective markers and ground reaction forces were recorded pre-operatively while walking (VICON, Oxford Metrix Limited, U.K., 100Hz). Pre- and post-operative dual-energy CT images were obtained (SOMATON, Siemens Healthineers, Germany) and segmented (ScanIP, Simpleware Ltd., UK). The HJC location was defined as the center of the sphere that best fit the acetabular surface (NMSBuilder, IOR, Italy) for the healthy hip and mirrored to determine the HJC in the severely osteoarthritic hip. The musculoskeletal model was the instance that best matched the participant's marker position and skeletal geometry in a public statistical musculoskeletal model (MAP Client, University of Auckland, New Zealand). The post-surgical change of the HJC was measured from the pre- and post-operative CT images and applied to the musculoskeletal model in antero-posterior (AP), medio-lateral (ML) and infero-superior (IS) directions. Hip joint contact forces were estimated through static optimization and assumed to generate on the acetabulum a Hertzian pressure distribution. The hemipelvis model was a linear tetrahedral mesh with locally isotropic material properties. The Bone Mineral Density (BMD) map was obtained by calibrating the images assigning BMD = 0 g/cm^3 to soft tissue and BMD = 1.73 g/cm^3 to compact bone regions. The elastic modulus for the trabecular bone was calculated using published equations [5]. The cortical layer was modelled using shell elements (E = 17 GPa; μ = 0.3). The model was constrained at the sacroiliac and pubic-symphysis articulations. The distribution of hip contact pressure was applied to the acetabulum. Bone strains were calculated for 12 frames of walking using an explicit FE solver (ABAQUS, Dassault Systemes, USA). Bone strain and hip contact forces obtained by displacing HJC were compared to those obtained for natural HJC position (ANOVA, Matlab, Matworks, USA, $\alpha = 0.05$).

RESULTS AND DISCUSSION

The HJC displacement was 12.4 mm, consistently with earlier clinical measurements (14.0 ± 4.9 mm) [2]. The peak bone strain was found at the time of the peak hip contact force. The native HJC led to a peak contact force and bone strain equal to 1654 N and 5078 με, respectively. ML and IS displacement of the HJC caused statistically significant changes (p = 0.02 – 0.04) of both the peak joint force and bone strain, which varied by 5 – 9% and 4 – 6%, respectively; AP displacement results were non-significant. Both ML and IS displacements caused a supero-lateral displacement of the center of pressure. Results confirm previous studies [2,3], in which ML displacement increases hip contact forces and acetabular strains, and extend the validity to the IS displacement.

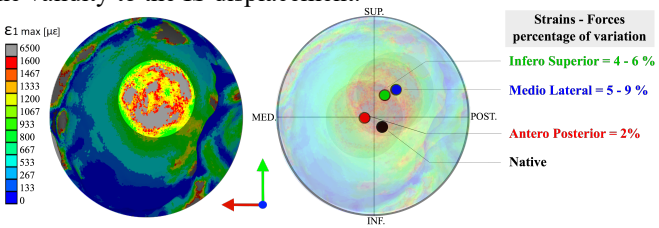

Figure 1: Left: The acetabular region exceeding $\varepsilon_1 = 0.0016$. Right: The location of the center of pressure for the native HJC and after AP, IS, ML displacements of the HJC.

CONCLUSIONS

HJC displacements in medio-lateral and infero-superior direction cause a superolateral displacement of the centre of pressure and increase in the joint contact force and bone strain. These results might be used to reduce acetabular loosening risk. Further studies are necessary to understand the generality of the present conclusion in conjunction with the effect of the acetabular implantation on peri-acetabular bone strain.

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HORIZONTAL CRACK IN INTERFACE OF OSTEOCHONDRAL UNITS IS A HIGH RISK OF YOUNGER AGE OF TOTAL KNEE REPLACEMENT FOR OBESITY-RELATED OSTEOARTHRITIS

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INTRODUCTION

Osteoarthritis (OA) is a chronic disease leading to joint pain and dysfunction. Obesity accelerates OA development by biomechanical and biochemical mechanisms. We hypothesis that obesity accelerates OA development by breaking the homeostasis of osteochondral unit.

METHODS

We collected a cohort of 616,496 cases, including OA patients' age, BMI and gender, from Australia Orthopaedic Association National Joint Replacement Registry (AOANJRR) and British National Joint Registry (NJR) to investigate the correlation between BMI and the age of patients. Due to geographic convenience, we collected 88 cases of end-stage OA patients receiving TKR in Western Australia to analyze the effect of BMI on pathological changes of osteochondral units. Cylindrical bone specimen, including articular cartilage and underlying subchondral bone, were extracted from center of medial and lateral side of tibia. Micro-CT, histomorphometric measurements and immunohistochemistry analysis were performed to analyze effect of BMI on pathological changes in osteochodral units.

RESULTS AND DISCUSSION

Of the 88 patients, the age of patients receiving TKR is negatively associated with BMI ($p<0.01$, $R^2=0.171$). Cartilage degradation assessed by OARSI grading system showed less cartilage degradation was associated with increased BMI in both medial and lateral sides (Figure A). However, we observed a new pathological change of horizontal crack, surrounded by cartilage degradation, filled in cartilage/bone fragments, fibrosis infiltration and erythrocytes, was observed (Figure B). And its frequency is increased in patients with increased BMI in both medial and lateral side of tibia plateaus. In subchondral bone, active bone formation, evidenced by increased osteoid formation, with elevated levels of osteoid thickness ($p<0.01$), osteoid volume ($p<0.01$) and osteoid surface ($p<0.01$), was observed in patients with increased BMI in both medial and lateral side (Figure A). Immumohistochemistrical staining showed increased TGF-β1 were cumulated in the STB in obese patients (Figure A).No alterations of bone resorption and microstructure were shown to be related to BMI. Data from registries demonstrated a significantly progressive fall in the age at patients received TKR and BMI across all the subgroups (Figure C). The mean age of patients with BMI ≥40kg/m2 showed 8 years younger than patients with BMI ≤25kg/m2. Even though the less degradation is shown in obese patients, the observation of increased horizontal crack in obese patients may explain their younger ages when they underwent TKR. Based on these results, we raised a hypothesized model "shear-stress inducing horizontal crack in osteochondral interface" for explaining the younger age for TKR surgery in OA patient with obesity (Figure D).

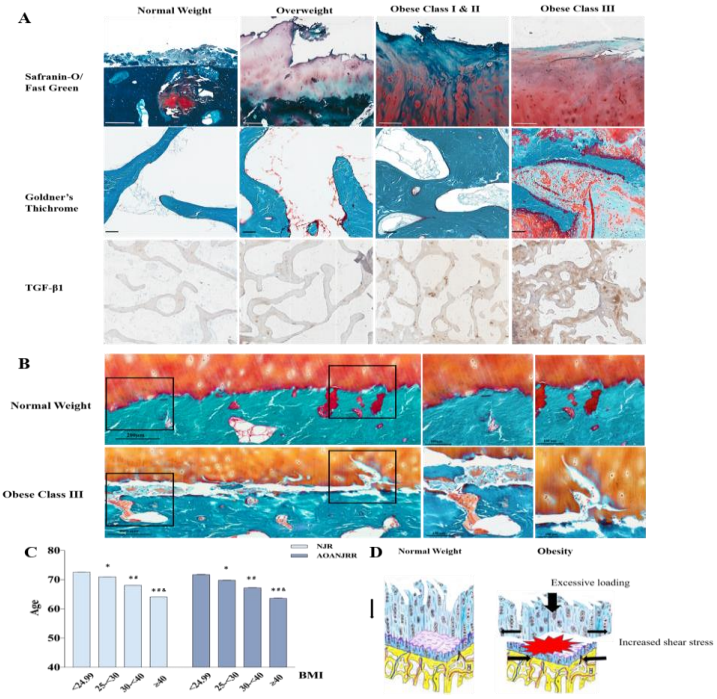

Figure (A). Histological and immumohistochemistrical images in osteohndral units of medial side from OA tibial plateaus. (B) Comparison of normal-weight and obese patients who are with and without horizontal cracks in the osteochondral interface (C) Data from registries showed patients with higher BMI underwent TKR at their younger age. (D) Mechanical model of shear stress induced by morbid obesity causing the deterioration of the interface between calcified cartilage and hyaline cartilage.

CONCLUSIONS

This study demonstrated a new pathological changes in the osteochondral unit in osteoarthritic tibia plateaus. Even though the less degradation is shown in obese patients, the increased frequency of the horizontal crack may explain a younger age of obese patients undergoing TKR. Increased osteoid was observed in patients with increased BMI, which could be explained the increased TGF-β1 expression. Based on the results, we raised a hypothesized model "shear-stress inducing splitting of osteochondral interface" for explaining the younger age for TKR surgery in OA patient with obesity.

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DAY 3

KEYNOTE 4 – Prof Fary Khan

DISASTER MANAGEMENT: OUTCOMES OF MUSCULOSKELETAL AND NEUROLOGICAL TRAUMA

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Disasters (both natural and man-made) are escalating worldwide, human exposure and/or impact on population and society from these disasters are intensifying, due to factors such as climate change, population growth, urbanization, density within living area, mass population displacements, poorly planned infrastructure etc. With increasing numbers of disaster survivors, there is more demand for services (including rehabilitation needs, which are often unmet) as many have complex and long-term disabling injuries (such as musculoskeletal, spinal cord and/or traumatic brain injury, crush and peripheral nerve injuries, burns, amputation etc.) relative to mortality.

Inadequate rehabilitation services limit people's ability to recover following treatment, fully participate in society and look after themselves. In recent years, many countries have recognized the importance of disaster planning, preparedness and management capacity; however, rehabilitation services have not yet been prioritized. Unfortunately, major disparities and gaps exist amongst countries, and those with a high disaster-risk tend to have low coping capacity and a large population vulnerable to calamities living in more exposed areas. Despite growing demand, rehabilitation services and workforce are still limited in many disaster-prone countries, implying significant burden of rehabilitation for individuals (their families) and community. There is strong consensus that medical rehabilitation is integral to disaster management, should be initiated acutely during emergency response and included in the continuum of care over a longer-term until treatment goals are achieved; and survivors successfully integrated into society.

This presentation will highlight current developments in trauma and disaster rehabilitation; challenges in the implementation of WHO guidelines and key future perspectives. Strategies will include strong leadership and effective action from national and international bodies for comprehensive rehabilitation-inclusive disaster responses.

DAY 3

PODIUM 6

OLDER HIP FRACTURE PATIENTS WITH TYPE 2 DIABETES MELLITUS (DM): PREVALENCE, CLINICAL CHARACTERISTICS AND IN-HOSPITAL OUTCOMES

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INTRODUCTION

Data on the impact of DM on hospital outcomes in orthogeriatric patients are scarce and controversial [1-3]. We aimed to assess the prevalence, clinical characteristics and hospital outcomes in older hip fracture (HF) patients with DM with regard to its severity.

METHODS

Among 1515 consecutive orthogeriatric patients admitted in 2012-2015, there were 601 (39.7%) with HF in whom we analysed the demographic, clinical, laboratory characteristics and hospital outcomes: (1) length of hospital stay (LOS), (2) high postoperative inflammatory response (HPIR, CRP ≥150mg/L after the 3rd postoperative day), (3) post-operative myocardial necrosis (evidenced by cardiac troponin [cTnI] rise), (4) all-cause mortality and (5) need to be discharged to a residential care facility (RCF).

RESULTS AND DISCUSSION

The mean annual prevalence of DM was 21.4% in the total orthogeriatric cohort and 19.8% among HF patients. HF patients with and without DM did not differ by mean age and pre-morbid residence but the proportion of males was higher in the DM group (39.5% vs. 28.6%, p=0.026) (Table1). Compared to the non-DM patients, subjects with DM more often had pre-existing cardio- and cerebrovascular diseases, and chronic kidney disease (CKD). The DM patient manifested a significantly prolonged LOS: ≥10 days in 72.3% vs 57.3% (p=0.003) and ≥20 days in 36.1% vs 23.2% (p=0.005). Of 119 diabetic patients 34 (28.6%) were diet controlled, 52 (43.7%) used oral hypoglycaemic agents and 33 (27.7%) required insulin (IDDM). The IDDM patients compared to the diet controlled group were significantly younger (80.5 vs. 84.7 years, p=0.029), more often had coronary artery disease (48.5% vs. 20.6%, p=0.021), history of myocardial infarction (18.2% vs. 2.9%, p=0.054), CKD (60.6% vs. 29.4%, p=0.02), higher HbA1c levels (7.7% vs. 5.9%, p<0.00001), more often developed myocardial injury (63.6% vs. 41.2%, p=0.01) and overt myocardial infarction (15.2% vs. 0%, p=0.025).

CONCLUSIONS

Subjects with DM comprise about 20% of hospitalised older HF patients and have a significantly prolonged hospital stay. The severity of DM is associated with prevalent cardiovascular and renal comorbidities predisposing to high incidence of post-operative myocardial injury. Specific strategies need to be implemented to prevent perioperative complications in DM patients undergoing hip surgery.

ACKNOWLEDGMENTS

No conflict of interest to declare.

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Table 1: Clinical characteristics and hospital outcomes in hip fracture patients with and without type 2 diabetes mellitus.

Characteristics and Outcomes	Non-DM	T2DM			
	Total (n = 482)	Total (n = 119)	Diet controlled (n = 34)	OHG (n = 52)	IDDM (n = 33)
Age, years (mean ± SD)	82.8 ±8.7	81.9 ±8.4	84.7 ±6.6	81.0 ±9.2[2]	80.5 ±8.7[2]
Male, n (%)	138 (28.6%)[1]	47 (39.5%)	14 (41.2%)	18 (34.6%)	15 (45.5%)
CAD, n (%)	99 (20.5%)[1]	40 (33.6%)	7 (20.6%)	17 (32.7%)	16 (48.5%)[2]
MI, n (%)	33 (6.8%)[1]	16 (13.4%)	1 (2.9%)	9 (17.3%)	6 (18.2%)
CHF, n (%)	44 (9.1%)[1]	20 (16.8%)	6 (17.6%)	7 (13.5%)	7 (21.2%)
CVA, n (%)	39 (8.1%)[1]	19 (16.0%)	6 (17.6%)	7 (13.5%)	6 (18.2%)
CKD, n (%)	108 (22.4%)[1]	48 (40.3%)	10 (29.4%)	18 (34.6%)	20 (60.6%)[2]
HbA1c, % (mean ± SD)		6.7 ±1.4	5.9 ±1.0	6.8 ±1.3[2]	7.7 ±1.3[2]
HPIR, n (%)	283 (58.7%)[1]	85 (71.4%)	25 (73.5%)	34 (65.4%)	26 (78.8%)
LOS ≥10 days, n (%)	276 (57.3%)[1]	86 (72.3%)	24 (70.6%)	34 (65.4%)	27 (81.8%)
LOS ≥20 days, n (%)	112 (23.2%)[1]	43 (36.1%)	12 (35.3%)	18 (34.6%)	13 (39.4%)
Myocardial injury, n (%)	195 (40.5%)	54 (45.4%)	14 (41.2%)	17 (32.7%)	21 (63.6%)[2]
Overt MI, n (%)	30 (6.2%)	11 (9.2%)	0	6 (11.5%)	5 (15.2%)[2]

Only statistically significant data presented.
[1]P<0.05, comparison with total T2DM group,
[2]P<0.05, comparison with diet controlled group.

Abbreviations:
DM, diabetes mellitus; T2DM, type 2 DM; OHG, oral hypoglycaemic agent; IDDM, insulin dependent DM; CAD, coronary artery disease; MI, myocardial infarction; CHF, chronic heart failure; CVA, cerebrovascular accident; CKD, chronic kidney disease (GFR ≤60 mL/min/1.73m²), CRP, C-reactive protein; HPIR, high postoperative inflammatory response; LOS, length of stay; myocardial injury defined as cardiac troponin I (cTnI) ≥0.06µg/L or ≥25ng/L; overt MI defined as cTnI ≥1.0µg/L or ≥500ng/L.

ADMISSION PLATELET-TO-LYMPHOCYTE RATIO (PLR) AND LYMPHOCYTE-TO-MONOCYTE RATIO (LMR) - TWO NOVEL INDEPENDENT PREDICTORS OF IN-HOSPITAL MORTALITY AND MYOCARDIAL INJURY IN OLDER PATIENTS WITH HIP FRACTURE (HF)

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INTRODUCTION

Early prognosis of hospital outcomes in older HF patients is important to stratify the level of care and appropriate management, but remains very difficult. The aim of this study was to investigate the prognostic significance of admission PLR and LMR, two parameters which have recently been reported as predictors of adverse outcomes in various (mostly oncological) diseases [1-3], but were not evaluated in HF patients.

METHODS

We analyzed prospectively collected data on 1,291 consecutive patients with HF (mean age 82.9 ± 8.7[SD] years, 73.5% females) in regard to in-hospital all-cause mortality and post-operative myocardial necrosis (assessed by cardiac troponin I rise). Multivariate stepwise logistic regression analyses were performed with cutoffs for PLR >280 (the fourth quartile) and for LMR <1.1 (the first quartile). The receiver operating characteristic (ROC) was used to assess the predictive values of these ratios.

RESULTS AND DISCUSSION

Both PLR and LMR on admission were significant indicators of developing post-operative myocardial injury (odds ratio [OR] 1.49 and 1.77, respectively) and hospital mortality (OR 2.29 and 2.31, respectively); the ORs remained unchanged after adjustment for 17 variables, each of which showed a significant association with these outcomes on univariate analyses (Table 1). ROC demonstrated reasonable predictive values, especially when PLR or LMR were combined with other characteristics such as age (>80 years), chronic kidney disease, elevated PTH, history of myocardial infarction, dementia (ROC 0.707 - 0.742). PLR predicted in-hospital all-cause mortality with 43% sensitivity, 75% specificity, 96% negative predictive value, and LMR predicted mortality with 43%, 76%, and 96%, respectively.

CONCLUSIONS

Both PLR (>280) and LMR (<1.1) are significant, independent prognostic indicators of poor outcomes and could potentially be used for stratification of older hip fracture patients on admission.

ACKNOWLEDGEMENTS

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CONFLICT OF INTEREST DECLARATION: None

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Table 1: Prognostic value of platelet-to-lymphocyte ratio (PLR) and lymphocyte-to-monocyte ratio (LMR) in predicting hospital all-cause mortality and myocardial injury (with cardiac troponin rise) in older patients with hip fracture

Outcome	Model	PLR		LMR	
		OR [95%CI]	ROC	OR [95%CI]	ROC
Hospital death	Non-adjusted	2.29 [1.35, 3.89]	0.592	2.31 [1.37, 3.90]	0.591
	Adjusted	2.31 [1.34, 3.97]	0.726	2.07 [1.20, 3.59]	0.742
Myocardial injury	Non-adjusted	1.49 [1.15, 1.93]	0.539	1.77 [1.37, 2.30]	0.555
	Adjusted	1.60 [1.18, 2.19]	0.707	1.49 [1.12, 1.98]	0.712

Adjusted for all clinical (n=7) and laboratory (n=10) variables which were significant on univariate analyses ($p < 0.05$).
Abbreviations: OR, odds ratio; CI, confidence interval; ROC, receiver operating characteristic.

FINDING A NEEDLE IN A SEA OF NEEDLES: ACCURATE PATIENT IDENTIFICATION FOR POPULATING A PATIENT REGISTRY WITHIN A CLINICAL ENVIRONMENT

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INTRODUCTION

Data quality in orthopaedic registries remains an ongoing challenge for evidence-based practice change. Clinical registries are complex systems vulnerable to transcription issues, logical inconsistencies, missing information, duplicate records and measurement errors [1]. Tracking patients for clinical purposes is difficult, and even more challenging for registries with specific eligibility criteria, categorisation parameters, high patient volume and short deadlines. This report describes the accuracy of a semi-automatic system developed to categorise patients for inclusion into a quality-controlled registry within a hospital department.

METHODS

A quality-controlled registry was planned and implemented for one surgeon within a hospital department, comprising six observational cohorts presenting with shoulder and knee pathologies. A semi-automated process to continually identify patients attending orthopaedic outpatient clinics for the first time, presenting for surgery, or returning patients was established with a one-week turnaround (Figure 1A). The recommendation to flag a patient for the registry to clinic or theatre staff was established by comparing consult and surgical lists from electronic medical records to information held in the registry database (Socrates v3.5. Ortholink, Aus).

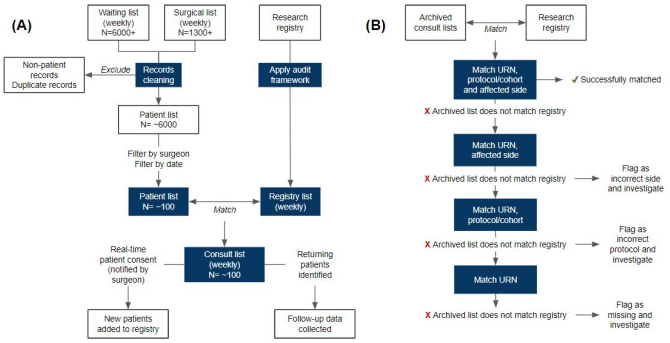

Figure 1: (A) Process to identify patients for inclusion into the registry, with automated steps highlighted in blue. (B) Process for establishing accuracy of patient capture.

Accuracy was assessed by cross-matching archived consult lists to patient labels in the registry, comparing unit record numbers (URNs), protocol/cohort labels and affected side, and sending to a research assistant for manual review (Figure 1B).

RESULTS AND DISCUSSION

More than ~6000 patient records were fed into the consult list generation process and filtered to ~100 patients per week. Returning patients of interest were flagged in the consult list for data collection at required time points. New patients eligible for research were identified and consented before being added to the registry on the consult day. Registry capture rates after quality checks in the last fortnight increased by up to 17%, and in combination with a quality system, capture rates achieved 100% for all cohorts, with first-pass accuracy of 83-100% (Figure 2).

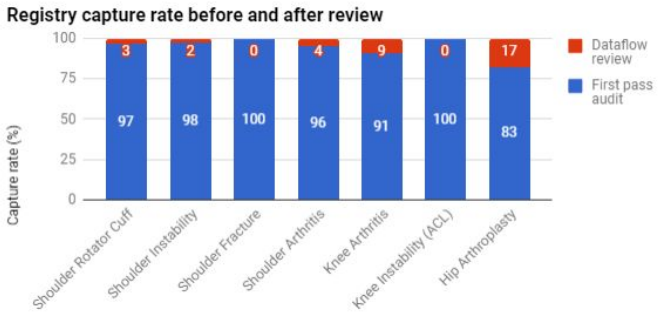

Figure 2: Registry capture with a semi-automated inclusion and quality check processes

CONCLUSIONS

A semi-automated, integrated process to continually identify patients of interest to an orthopaedic registry within a metropolitan hospital department can achieve first-pass accuracy of >80% and with human oversight, provides 100% accuracy in providing clinic staff with patients for followup in the treatment pathway.

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CONFLICT OF INTEREST DECLARATION

In the interests of transparency and to help reviewers assess any potential bias, all authors of original research papers are required to declare any competing commercial interests in relation to the submitted work. Referees are also asked to indicate any potential conflict they might have reviewing a particular paper.

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1. The author(s) did receive payments or other benefits or a commitment or agreement to provide such benefits from a commercial entity.

MC, ME and CS are paid employees of EBM Analytics, which provides quality management systems for patient registries.

2. A commercial entity paid or directed, or agreed to pay or direct, any benefits to any research fund, foundation, educational institution, or other charitable or nonprofit organization with which the authors are affiliated or associated.

N/A

OPTIMISING PATELLOFEMORAL JOINT KINEMATICS IN KNEE ARTHROPLASTY THROUGH PERSONALISED IMPLANT DESIGN

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INTRODUCTION

Arthroplasty is an effective procedure for end-stage knee osteoarthritis, when conservative measures have failed. However, 20% of knee arthroplasty patients are not satisfied with the procedure [1] and the patellofemoral joint is the leading source of problems. Patella tracking using modern TKR designs is in contrast to the native knee, especially in terms of coronal plane kinematics [2], and is primarily a result of the articulating surfaces of the patella button on the trochlear groove. It remains unclear whether the shape of the trochlear groove in arthroplasty designs preserve the normal knee function. This study investigates the differences between native knee patellofemoral kinematics, a common knee arthroplasty design and an optimised design.

METHODS

Firstly, a finite element (FE) model of the native knee was developed from MRIs of a healthy male [3]. Bones were treated as rigid-bodies, cartilage as deformable and ligamentous soft tissue as non-linear springs. The model was validated against cadaveric load-displacement laxity profiles [4] and against weight-bearing MRIs of 0°, 30° and 60° flexion. Secondly, a TKR model was developed using a Vanguard design and was prescribed using x-ray fluoroscopy kinematics, muscle forces and *in vivo* contact forces from an instrumented knee [5]. Finally, an optimised TKR design was developed with a novel patella track oriented laterally throughout the trochlea, implanted *in silico* and FE models of coronal plane kinematics performed. Patellar tracking from all models was compared as the knee went through flexion from 0° to 65°.

RESULTS AND DISCUSSION

Comparing the results of these models revealed that there is a significant ***medial*** translation in the *TKR* knee, which agrees with [4,6] but is in contrast to the *Native* knee. The *Native* patella tracked ***laterally*** with mean 3mm (range 1-4mm) throughout flexion. In contrast, the *TKR* patella tracking was significantly different ($p<0.01$), moving 6mm ***medially*** from full extension to 65° flexion. The *optimised TKR* design showed ***lateral*** patella tracking (mean 2mm; range 1.8-3.0 which was not significantly different ($p=0.48$) from *Native* patella tracking (Figure 1).

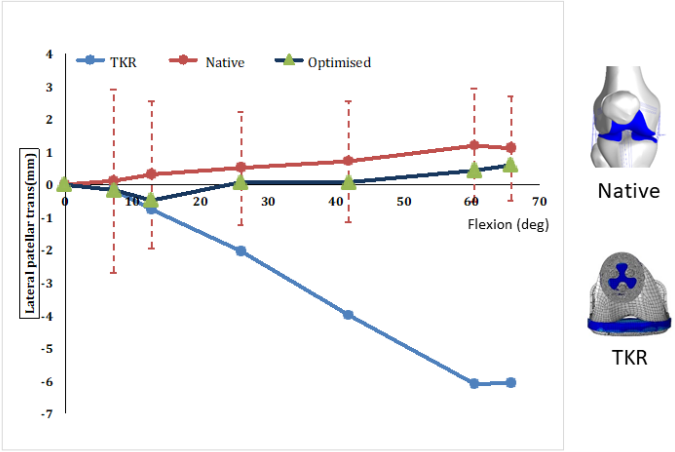

Figure 1: Comparing medial-lateral patellofemoral translation (mm) in the TKR, native and optimised knee from full extension to 65° flexion. Positive translation is lateral.

CONCLUSIONS

This study suggests that existing TKR designs may not preserve natural trochlear groove anatomy and have long term implications on knee function. This suggests that future designs should revisit the shape of the trochlear groove in femoral components and be informed by natural knee anatomy. This may explain why PFJ problems are common. The abnormalities in tracking were due to the geometry of the trochlea groove and therefore could be improved by modifying the design.

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SHAPE IS A WEAK PREDICTOR OF DEEP KNEE FLEXION KINEMATICS IN HEALTHY AND OSTEOARTHRITIC KNEES

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INTRODUCTION

Knee OA is associated with bony shape changes, pain and loss of function. Patients avoid, or have trouble, performing demanding deep-flexion activities such as squatting or kneeling [1]. Clinically, bony shape is used to estimate disease severity (x-rays) and restoration of joint shape following total knee replacement (TKR) is an assumption for improved functional outcomes. Although tibiofemoral morphology has been associated with kinematics of the tibiofemoral joint in early flexion and gait, there is no research examining these relationships in deep flexion or in OA [2,3]. Therefore, the aim of this study was to examine the association between tibiofemoral joint shape and kinematics during deep knee flexion in patients with and without OA.

METHODS

61 healthy participants and 58 patients with end-stage knee OA received a 3D CT scan of their knee. Participants completed full flexion kneeling while being imaged using single-plane fluoroscopy. A statistical shape model (SSM) was generated for the tibiofemoral joint by performing a Principal Component Analysis (PCA) on aligned healthy and OA bony meshes generated from the CT Scans. Six DoF kinematics were measured by registering a 3D static CT onto 2D dynamic fluoroscopic images. Kinematic variability was captured using bivariate functional principal component analyses (bfPCA). One bfPCA model was created for each DoF and included both OA and healthy kinematics. Data used in the bfPCA was represented as a function of flexion and visualised using reconstructed angle-angle or position-angle plots. Principal components (modes) and subsequent weights accounting for 90% of the variation in the both the shape model and bfPCA models were retained. Random Forest Regression models were created to test the ability of bony shape, BMI, sex, and group to predict kinematics.

RESULTS AND DISCUSSION

The first 7 modes of the SSM and up to three modes of the bfPCAs captured >90% of the variation. The ability of the random forest models to predict kinematics from shape were low, with no more than 50% of the variation being explained in any model. Kinematic prediction errors were high, ranging between 24.2% and 29.4% of the data indicating that additional predictors need to be identified. The predictors which best predicted of maximal flexion and kinematic bfPCA's were a combination of group, BMI and either shape modes 2 or 6. Shape features within these modes included large bony expansions on the posterior-medial femur and tibia, an increase in the coronal and posterior tibial slope, flattening of the femoral condyles, and changes in the condylar radii (Figure 1).

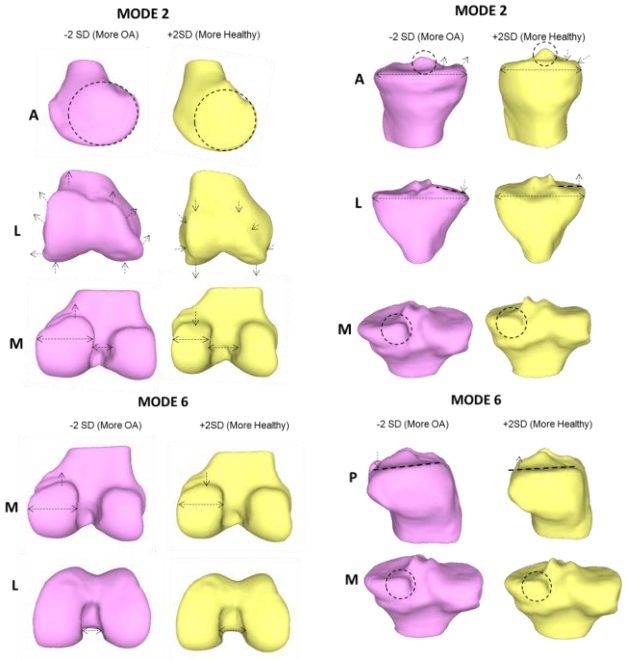

Figure 1. Shape variations captured within the second (top) and sixth (bottom) mode of the statistical shape model perturbed minus (OA) and plus (Healthy) two standard deviations away from the mean shape.

CONCLUSIONS

Bony knee shape was a weak predictor of deep knee flexion kinematics with only 50% of the kinematic variability explained and with high prediction errors. The results suggest that other factors may be more important in driving deep knee flexion kinematics. These findings have implications for the expectations placed on high flexion TKR design. Further research should investigate how factors such as soft tissue envelope influences kinematics and the effect of different TKR designs on knee kinematics.

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2. A commercial entity paid or directed, or agreed to pay or direct, any benefits to any research fund, foundation, educational institution, or other charitable or nonprofit organization with which the authors are affiliated or associated.

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ANTEROLATERAL PROCEDURE COMBINED WITH ACL RECONSTRUCTION – A BIOMECHANICAL CADAVERIC STUDY

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INTRODUCTION

It has been suggested that after an ACL injury, a combined ACL reconstruction and anterolateral procedure can provide better clinical outcomes with respect to anterolateral rotational stability [1-3]. There are a number of different anterolateral procedures which have shown promising outcomes. These include the anterolateral ligament reconstruction (ALL) as well as the lateral extra-articular tenodesis (LET). However, it is currently unclear which procedure provides best rotational stability whilst restoring the native knee kinematics. This study aims to directly compare a number of different, commonly used anterolateral procedures in combination with ACL reconstruction, in a series of cadaveric knees. It was hypothesised that LET procedures provide more rotational restraint but are less physiological than ALL procedures.

METHODS

Ten fresh-frozen cadaveric knees were used for this study. All knees were free of deformity, osteoarthritis and previous surgery. Retroreflective fiducial markers were attached to pins fixed to both the femur and tibia of each specimen for purposes of registration and motion tracking. Surgery was performed by a single surgeon. The following conditions were successively applied for each knee: (1) Intact, (2) ACL deficient knee, (3) combined ACL and ALC deficient knee, (4) isolated ACLR, (5) combined ACLR and ALLR (6) combined ACLR and modified Ellison (7) combined ACLR and modified deep Lemaire (8) combined ACLR and modified superficial Lemaire, (9) combined ACLR and modified MacIntosh. Knee kinematics were recorded for 3 cycles and 3 trials during passive knee flexion, with the knee internally rotated (IR) at 5Nm with a torque rig. Kinematics were recorded over the range of 0° to 90° knee flexion using Vicon 3D motion capture system (Vicon, LA, USA). Anteroposterior translation was also tested by way of the Lachman test (30° flexion) and anterior tibial drawer test (90° flexion) by using a dynamometer set at 90Nm.

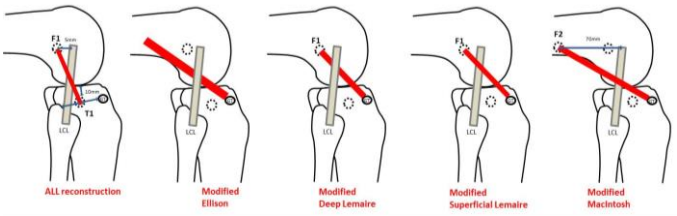

Figure 1: ALL and LET procedures: ALL, Modified Ellison, Modified Deep Lemaire, Superficial Lemaire and MacIntosh.

RESULTS AND DISCUSSION

Removing the ACL induced IR laxity as did the combined ACL plus anterolateral deficient knee ($p<0.001$). Although the general pattern of kinematics was similar to intact, the isolated ACLR did not restore the kinematics to the native state and exhibited residual rotational laxity. The combined ACLR + ALLR (0-90° flexion) as well as the combined ACLR + modified Ellison (0-40° flexion) best restored kinematics to the intact state. The combined ACLR with modified superficial and deep Lemaire as well as modified Macintosh created an overconstrained IR kinematics, which did not behave similar to the intact state.

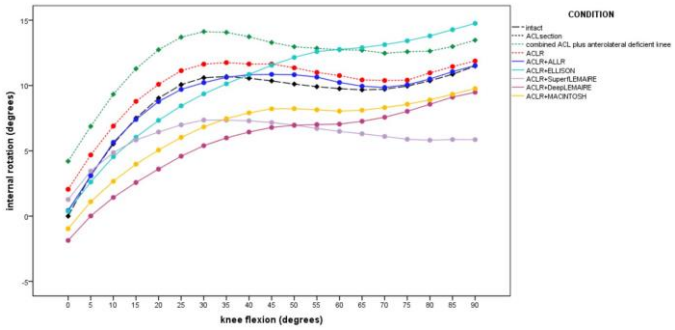

Figure 2: Internal rotation over the full flexion range under different surgical conditions.

The ACL deficient knee displayed increased anterior-posterior laxity at 30° and 90° degrees of flexion ($p=0.01$). Isolated ACLR reduced the laxity at 30° and 90°. At 30°, the addition of the anterolateral procedures did not make any difference to the isolated ACLR. But at 90° flexion, the modified superficial Lemaire was the only procedure that induced an additional decrease in AP laxity, compared to isolated ACLR ($p=0.032$).

CONCLUSIONS

The isolated ACLR did not restore the IR kinematics to the intact state, suggesting that this procedure alone would not fully address rotational laxity after an anterolateral injury. Addition of either the ALLR or Ellison would assist in restoration of rotational kinematics.

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DAY 3

KEYNOTE 5 – Prof David Haynes

THE HISTORY AND PEOLE OF 25 YEARS OF ANZORS

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My presentation will aim to cover not just ANZORS history but the people that made it. Some of the very early history is vague but many interesting facts have emerged. Images from meetings of people from the past 20 years been unearthed and carefully selected.

ANZORS spans 25 years of the most active and diverse period of orthopaedic research in history. Australia and New Zealand orthopaedic researchers have played a significant role in this and the part ANZORS has played has been crucial. It has not only provided a platform to present findings and views but has encouraged more than a generation of Australian and New Zealand orthopaedic researchers to reach their impressive potential. Most importantly ANZORS has provided an inviting environment for young orthopaedic researchers to develop their "voice" in research locally and worldwide. Although the conference environment is relaxed the discussions are often in depth and not without polite vigor emphasising the passion so many of us have for orthopaedic research. ANZORS has provided 3 important things. Firstly, it has always encouraged young researchers to present their findings and develop their careers. Secondly, it has provided a platform for early and mid career researchers to network and develop fruitful collaborations. Thirdly, it has allowed senior researchers the opportunity to mentor impressive younger researchers and meet old friends at least once a year.

In its infancy ANZORS had very humble beginnings when founded within the Australian Orthopaedic Association (AOA). Low membership early on meant it almost ceased to exist in the late 1990's. and it was only due to the hard work of a few dedicated individuals that it survived. In the 2000s ANZORS grew enough to survive independently of the AOA. Successful meetings with our Kiwi partners in New Zealand were started and we participated in several international meetings. During 2010's ANZORS grew even further to become mature stable organization respected on the world stage. This is evidenced by the fact that ANZORS was chosen by ICORS to host 2025 International Combined Orthopaedics Research Societies (ICORS) meeting to be held in Adelaide, South Australia. In addition, Australia was chosen as the Guest Nation for ORS 2020 in Phoenix (8-11 February 2020), Arizona, USA. The future of ANZORS looks bright as the next generation of Australian and New Zealand orthopaedic researchers drive it into an exciting future. However, I hope a brief look in the rear vision mirror, such as in this presentation, will be helpful to put things in perspective as we drive forward.

DAY 3

PODIUM 7

A NOVEL DYNAMIC CADAVERIC WRIST SIMULATOR FOR 3-DIMENSIONAL CARPAL BONE MOTION MEASUREMENT USING BIPLANE X-RAY FLUOROSCOPY

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INTRODUCTION

The wrist, which is one of the most complex joints in the human body, is comprised of the radiocarpal, midcarpal and distal radioulnar and is represented by over 15.2% of upper limb injuries [1]. At present, evaluation of dynamic wrist function in cases of ligament damage and after surgical intervention remains challenging due to the complex interaction between muscle loading and the resulting carpal bone motion. The aim of this study was to develop and validate a dynamic cadaveric wrist motion simulator that is capable of reproducing accurate and physiologically meaningful active wrist motions that are repeatable at both macroscopic and carpal bone levels.

METHODS

Seven fresh-frozen wrists were harvested from human cadavers (age: 72±15 years) and radiographically screened for joint abnormalities. The wrist joint capsule was opened dorsally and radio-opaque beads in clusters of three implanted into the scaphoid, lunate and capitate bones. Computed tomography (CT) scans of the specimens were reconstructed and used to register bead to bone positions.

A custom-designed computer-controlled dynamic wrist simulator was developed and employed for reproducing active wrist motion by applying physiological loading to tendons of the wrist prime mover muscles using six stepper-motor-driven actuators (Parker Hannifin Corp., Cleveland, USA) (Fig. 1). The forearm was disarticulated at the elbow and fused in neutral supination by means of two Steinmann pins. The radius and ulnar were vertically mounted in a potting block, and steel cables instrumented with 1DOF load cells (Dacell Inc., Korea) attached to the prime mover muscles that were detached from their origins. These included the flexor carpi ulnaris and radialis, extensor carpi radialis brevis and longus, extensor carpi radialis, and abductor pollicis longus.

Sinusoidal motion profiles of dynamic wrist flexion-extension (± 30°), radial-ulnar deviation (± 20°) and their superposition (dart thrower's motion) were performed by applying muscle forces that minimised the sum of squares of muscle activations [2]. Global wrist motion, measured in real-time using a high-speed video motion analysis system comprising four cameras (Vicon, Oxford, UK), was used as a position feedback to update the muscle forces. This was achieved by tracking triads of retroreflective markers rigidly attached to the radius and third metacarpal. The control system was implemented in LabVIEW (National Instruments, Austin, USA) and employed a decentralized adaptive controller and a quadratic programming optimizer for muscle force estimation, with additional feedforward of the tendon velocities estimated using a kinematic model of the wrist. Carpal bone motions were measured using a biplane fluoroscopy system that had a dynamic root mean square (RMS) accuracy of 0.168° in rotation and 0.039 mm in translation. Repeatability of simulated motions was measured at the global wrist joint-level and carpal-bone level using RMS errors in angles and positions.

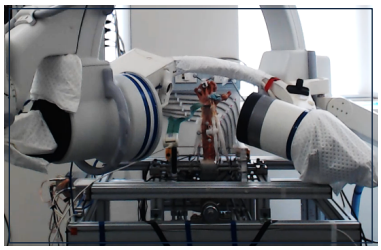

Figure. 1: Photograph of cadaveric wrist simulator and bi-plane fluoroscopy system imaging a wrist specimen undergoing dynamic wrist flexion

RESULTS AND DISCUSSION

Simulated flexion-extension, radial-ulnar deviation and dart thrower's motion resulted in sub-degree RMS errors in global wrist motion, sub-millimeter and sub-degree repeatability in carpal bone motion, and sub-Newton tendon force repetability (Table 1).

Table 1: The rms (RMSE), maximum absolute error of the position control (Max ABSE), mean repeatability of the global wrist joint angle and carpal bone motion, the applied tendon forces for flexion-extension (FEM), radial-ulnar deviation (RUD) and dart thrower motion (DTM).

Wrist Motion	RMSE (deg)	Max ABSE (deg)	Rep. global motion (deg)	Rep. carpal motion		Rep. tendon force (N)
				Translational (mm)	Rotational (deg)	
FEM	0.09	0.26	0.02	0.03	0.19	0.13
RUD	0.15	0.38	0.03	0.03	0.19	0.18
DTM	0.18	0.48	0.04	0.03	0.18	0.23

CONCLUSIONS

The present study introduced a novel dynamic wrist simulator that demonstrates strong repeatability of simulated global wrist motions and local motions of carpal bones using dynamic x-ray fluoroscopy. This apparatus has applications in evaluating the effect of injury and surgical reconstruction on wrist function.

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CONFLICT OF INTEREST DECLARATION

In the interests of transparency and to help reviewers assess any potential bias, all authors of original research papers are required to declare any competing commercial interests in relation to the submitted work. Referees are also asked to indicate any potential conflict they might have reviewing a particular paper.

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   This research project was partially funded by Medartis AG (Switzerland)

ARE YOU MAD? YOU WANT ME TO KNEEL?
COMPARISON OF OSTEOARTHRITIS AND HEALTHY KNEE KINEMATICS WHILE KNEELING

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INTRODUCTION

Hip and knee osteoarthritis is the 11th highest contributor to disability in Australia and ranks amongst the top ten causes of disability worldwide[1]. The lifetime risk of the disease is now 14%[2]. Knee osteoarthritis (OA) produces pain and loss of joint function, a slow erosion of the ability to perform activities of daily living. Those with knee OA avoid high-flexion tasks such as kneeling--finding it one of the most challenging activities. This research is a cross-sectional study of the kinematics of knee motion while kneeling. It aims to, for the first time, quantify the differences of in *vivo* kneeling knee kinematics in six-degrees-of-freedom (6DOF) between those with and without knee OA.

METHODS

We recruited healthy (44) and knee OA (56) participants (all over 50 years). Each participant's knee CT scan (3D) was 'registered onto their 'kneeling knee' single-plane fluoroscopy (2D), using the in-house 3D/2/D registration algorithm called Orthovis. Orthovis produced kinematic data in 6DOF as quantified by the Grood and Suntay coordinate system[3]. A calibration grid was used to minimise out-of-plane errors. One-way MANCOVAs with covariate BMI, compared the kinematic variables (with respect to flexion); anterior/posterior, medial/lateral, compression/distraction, internal/external, valgus/varus position, displacement and rate-of-change (/°flexion).

RESULTS AND DISCUSSION

Age and sex were similar between groups ($p > 0.05$). Kinematic differences between the groups are reported as pairwise comparisons (95%CI), and all values refer to the movement of the femur relative to the tibia while kneeling into flexion. OA knees had -12.8° (-17.0°, -8.6°) less maximum flexion. OA femurs at 120° flexion, were -4.6° (-7.7°, -1.4°) more externally rotated, and at maximum flexion were 8.3 (5.0, 11.5) mm more anterior and 4.0 (1.6, 6.2) mm more medial. Over the flexion range, 120° to maxium flexion, OA femurs translated 5.8(2.8,8.9) mm less posteriorly and 1.39 (0.6, 2.1) mm more into distraction (Figure 1).

It appears that healthy knees initially distract and then compress towards deeper flexion, whereas OA knees after approximately 128° continue to distract (Figure 1).

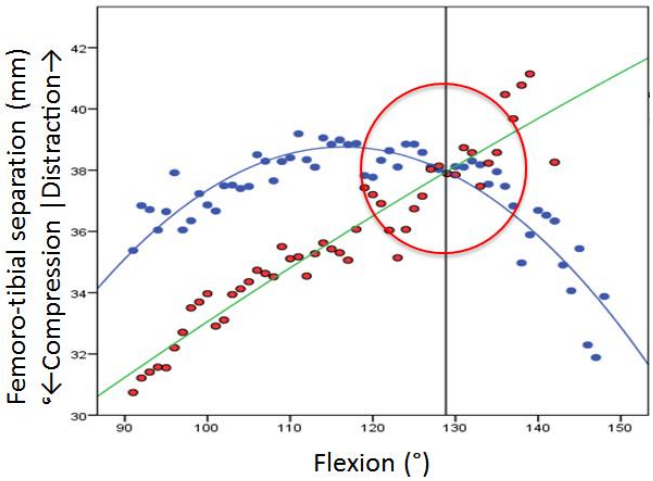

Figure 1: Femorotibial separation, demonstrating a parabolic profile in healthy knee compression/distraction and a linear profile for OA knees. ●: Healthy knees, ●: OA knees.

CONCLUSIONS

Knee OA changes kneeling knee kinematics. This study is the first comparison of such a large number of participants, so strongly matched for age and gender. Our results may help in the design of conservative management programs.

ACKNOWLEDGEMENTS

Zimmer Biomet supported this research through the Clinical Research Grant

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Zimmer Biomet Clinical Research Grant

HIP IMPLANT MONITORING THROUGH COMBINED ACOUSTIC EMISSION AND GAIT ANALYSIS

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INTRODUCTION

Early diagnosis of total hip arthroplasty (THA) implant deterioration may allow proactive surgical intervention and improve patient outcomes. Acoustic Emission (AE) monitoring of THA implants utilizes ultrasonic receivers to record implant vibrations during dynamic patient motion [1]. These acoustic emissions can provide insight into implant failure modes and potentially be used as a diagnostic indicator for future patients.

This study aims to provide increased insight into the *in-vivo* condition of THA implants and develop a diagnostic tool to supplement existing diagnostic methods. Previous results have shown that audible THA AEs are likely induced by interactions at the implant's main bearing interface as opposed to other interfaces such as the trunnion Morse taper [1,2]. Furthermore, this study also seeks to provide new insight by including gait analysis to better understand the implant failure mechanics.

METHODS

Ultrasonic sensors are utilized for *in-vivo* AE monitoring of THA patients during walking, to capture the implant vibrations emitted. In parallel, three inertial measurement units (IMUs) and 3D motion capture with incorporated force plate data are used to record patient limb motions. These limb motions are then linked to a simple lower-limb biomechanical model using OpenSim to estimate joint angles during AE monitoring. Ethical approval was obtained from the New Zealand Upper South A regional ethics committee (URA/10/11/075).

AE monitoring data has been collected from 120 THA patients in total. However, to date, only three THA patients have undergone the simultaneous collection of AE and gait data. For these three patients, their recorded AE data was synchronised in time with the corresponding force plate and estimated hip joint angle data. The synchronised data of the walking motions was then plotted against the percentage of gait cycle. One complete gait cycle was defined from heel strike (0%) until subsequent heel strike of the same foot (100%). Due to laboratory constraints, force plate data was available for only a single stance phase during each walking test and the hip angle was able to be reliably estimated for approximately 1.5 gait cycles per walking test.

RESULTS AND DISCUSSION

Initial results from the synchronised AE and gait data has indicated consistency between the occurrence of AEs and stages of the gait cycle. Figure 1 shows the synchronised AE, ground reaction force, and hip angle data for three gait cycles of a single walking test. It was observed from Figure 1 that an audible squeak occurred during terminal stance (between approximately 30-40% of the gait cycle) of two consecutive gait cycles. Consequently, the hip joint angle during the audible squeaking was transitioning through approximately 5°-15° extension. Comparable observations to those seen in Figure 1 were also observed in eight further walking tests for the same THA patient. Furthermore, AEs from repeated walking tests of a second patient consistently showed AEs of substantial magnitude to occur only during stance phase, despite having no audible AEs occur.

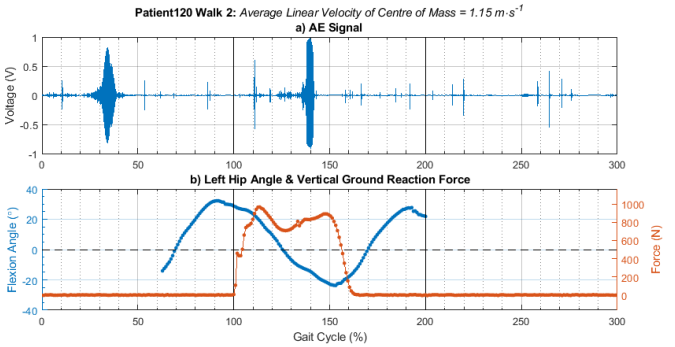

Figure 1: a) THA AE signal of three consecutive walking gaits, from a single test, synchronized with b) hip flexion angle and ground reaction force.

CONCLUSIONS

The initial results from the combined AE and gait analysis are promising. Substantial AEs, including audible squeaking, has been observed to occur only during the stance phase of the gait cycle with audible squeaking only observed during rapid changes in hip angle. While the initial dataset has been limited to only three patients, it is anticipated that ongoing research will verify these observations and continue to show promise of the diagnostic potential of the AE monitoring technique.

ACKNOWLEDGEMENTS

Funding from the Marsden fund is gratefully acknowledged.

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GAIT ANALYSIS AFTER GLUTEAL-TENDON REPAIR: AN AGE AND SEX MATCHED COMPARISON

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INTRODUCTION

Background: Gluteal-tendon repair (GTR) is performed for gluteus medius and minimus tendon tears. These tears are primarily detected in a subset of patients with greater trochanteric pain syndrome (GTPS) who do not respond to non-surgical modalities such as physiotherapy and corticosteroid injections. The disability and pain associated with GTPS has been reported to be the same as end stage hip osteoarthritis for which replacement is recommended [1]. Recent reports indicate that the outcomes after GTR are good but only patient reported outcome surveys have been evaluated and most have only included short-term follow-up [2,3,4,5]. Three-dimensional gait analysis after GTR has never been reported although data on GTPS patients indicate that they have greater hip-adduction moment, greater pelvic obliquity, and less ipsilateral trunk lean in stance [6]. The aim of this study was to compare the gait characteristics of GTR patients with healthy age and sex matched controls.

METHODS

Motion analysis technology including 12 camera Vicon, Oxford Metrics Ltd, Oxford, UK) with 24 retroreflective markers; and ground reaction force data sampled at 1000Hz were used to measure the gait characteristics of 25 GTR patients and 29 healthy controls. Gait was measured over repeated 7 metre walks. A generalised linear model was used to compare stride length, velocity, hip-adduction moment, and range of movement in hip adduction, hip internal rotation, pelvic obliquity and trunk lean, of both cohorts throughout stance.

RESULTS AND DISCUSSION

There were no differences between the groups for hip-adduction moment, pelvic obliquity, hip adduction and hip internal rotation (Figure 1). GTR patients had a shorter stride length (mean difference - 0.1 m; 95% CI - 0.1 to 0.0; p=0.031) and reduced walking velocity (mean difference - 0.1 m/s; 95% CI -0.2 to 0.0; p=0.015). The GTR group demonstrated significantly less ipsilateral trunk lean at first-peak hip-adduction moment (mean difference 1.6 degrees; 95% CI 0.3 to 2.8; P=0.016), the mid-stance minimum hip-adduction moment (mean difference 1.4 degrees; 95% CI 0.1 to 2.6; p=0.029), and the second-peak hip-adduction moment (mean difference 1.6; 95% CI 0.5 to 2.8; p=0.06). However, there were no significant differences in hip-adduction moment, or range of movement in hip adduction, hip internal rotation, or pelvic obliquity displacement at any of these three gait locations.

CONCLUSIONS

There were no significant differences between GTR and control participants for hip-adduction moment and pelvic obliquity, which are factors affected by GTT. Slower walking speed, smaller stride length and reduced ipsilateral trunk lean may reflect persistence of pre-existing gait abnormalities in patients after surgical repair. The findings suggest that GTR can return the gait characteristics of GTT patients to a status similar to matched healthy controls.

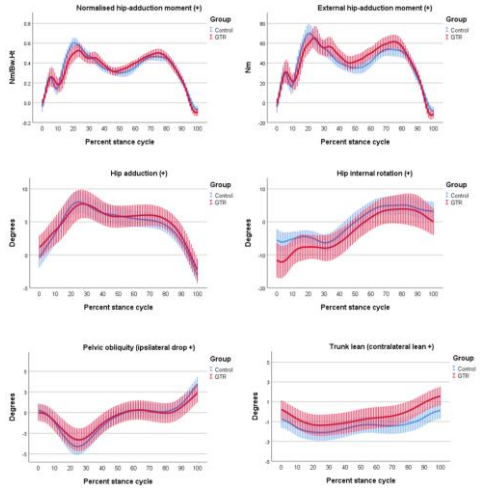

Figure 1: Group means for biomechanical gait variables. Data are shown for GTR (red) and control (blue). Group means (solid line) with 95% CI (error bars) are shown.

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DAY 3

PODIUM 8

WHERE IS THE LOAD APPLIED IN THE MOUSE-TIBIA MODEL? INSIGHTS THROUGH FINITE ELEMENT MODELLING

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INTRODUCTION

The mouse-tibia loading model [1] has become the gold standard for investigating bone adaption and is a powerful tool in the exploration of interventions aimed at osteoporosis. In this, an *in vivo* loading regime is mechanically applied to the mouse tibia. Localised adaption of the cortical and trabecula bone can be measured. Often, this is replicated *in silico* through finite element modelling (FEM), providing deeper insights into the link between adaption and localised stresses and strain (a key component of Frost's mechanostat [2]).

However, the FEM approach is problematic, as its predictions are highly dependent on how load is applied to the tibia. Differences in loading can results in large differences in the predictions of the FEM model. While some studies [3] have investigated this, the question of the where load is applied in the mouse-tibia model remains an open question. In this work, we seek to answer this question by investigating the relationship between load location and strain, comparing against experimental values.

METHODS

Female C57BL mice were used. Prior to experimentation, micro-CT slices were recorded. Following micro-CT, strain gauges were attached to the medial and lateral surface of the tibial diaphseal mid-shaft, proximal to the junction with the fibula, in line with the method used by De Souza [1]. The lower leg was mounted in a loading apparatus with the ankle and knee securely held by two cups. Loads were applied, up to 10 N, and the results strain gauge readings were recorded.

Using the micro-CT slices, the 3D geometry of the tibia was reconstructed through an in-house code. The volume was meshed through a direct voxel meshing approach where each voxel was transformed into an eight-node brick element. Nodes of the distal end were fixed. While the physiological loading at the proximal end is complex, it can be simplified to a single load at a representative location. A 10 N load was applied to the proximal end at selected coordinates. The load position was varied to quantify the relation between load location and strain measured at gauge locations. This is described in Figure 1a.

RESULTS AND DISCUSSION

The FEM modelling showed that the strains at each gauge location were highly dependent on the load location. This is significant as it demonstrates that failure to correctly identify the load location will results in erroneous prediction. To demonstrate this, Figure 1b-c shows the differing strain predictions for two different load locations.

This can be extended by modelling the gamut of potential load locations. In doing so, the effective load location can be ascertained, being the location with the minimum deviation between experimental and FEM strain values. This requires strain readings from a minimum of two gauges.

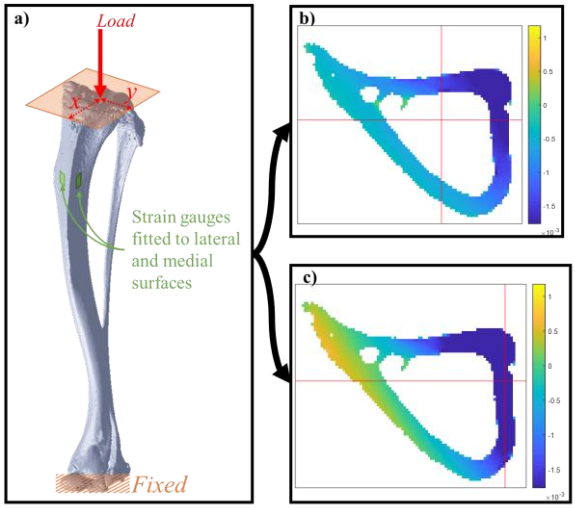

Figure 1: a) Schematic of the FEM model showing the variable load location, b-c) example strain predictions for two different load location (red cross-hair is a projection of the load location).

CONCLUSIONS

FEM modelling, coupled with *in* vivo data from two strain gauges can be used to determine the load location in the mouse-tibia loading model. Our results show that failure to correctly identify the load location will lead to erroneous results. We recommend that future works incorporate this technique to ensure valid predictions.

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TRABECULAR BONE GROWTH IN AN ADOLESCENT CYSTIC FIBROSIS RAT MODEL: A PILOT STUDY

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INTRODUCTION

Patients with cystic fibrosis (CF), multiorgan genetic disease, have an increased frequency of bone fracture compared to healthy subjects [1]. This is more pronounced in adolescent CF females where the fracture frequency is higher compared than their male counterparts and healthy females [1]. Recently, a CF rat animal model was developed at Robinson Research Institute. CF rats exhibit delayed CF related pancreatic and gut pathology and do not spontaneously develop lung disease [2], so can be used to investigate bone development in the absence of indirect secondary affects (e.g. lung, gut or pancreatic disease). Recently, a reduction in bone content compared to their healthy littermates was found in juvenile CF rats (3-6 weeks) [3]. It is unknown if this transfers into adolescence, a development stage where fractures are observed in CF humans. The aim of this study was to investigate if the reduced bone growth is seen in adolescence, by comparing CF rats to their heterozygote (Het) littermates. Pilot results obtained at the Australian Synchrotron (AS) are presented.

METHODS

Het and *CFTR* knockout Sprague-Dawley rats (n=10 each) developed using CRISPR. All experiments were conducted at the AS Imaging and Medical beamline (Clayton, VIC) as part of an ongoing study. The protocol was approved by the Uni Adelaide and the AS animal ethics committees.

Animals were humanely killed by Sodium Pentobarbital overdose, micro computed tomography (μCT) scans of the tibiae were performed (energy of 30 keV) at an isotropic pixel size of 19 μm and cross-sections were reconstructed. The trabecular bone volume of interest (VOI) was selected starting 1 mm below the lower end of the growth plate, extending distally for 3 mm [4] and the following bone morphometric parameters quantified: trabecular bone volume fraction (BV/TV), trabecular number, trabecular thickness and separation (CT Analyser, Skyscan-Bruker, Belgium) [4]. Associations between BV/TV and age (Kendall's Tau) and differences in BV/TV among groups at a given time point (Mann-Whitney) were investigated. Statistical significance was set to $p<0.05$. Other statistical techniques are being evaluated.

RESULTS AND DISCUSSION

The female CF rats did not show changes in BV/TV over time (Kendall's Tau= 0.25, P= 0.54 (Fig. 1.A) between weeks 11 and 15, with BV/TV reaching maximum values of 22%; whereas the female HET (16 weeks) exhibited almost double the BV/TV values (range 31% - 40%, Fig.1A). When combining females and males, at 13 weeks the BV/TV values between CF and Het did not differ (Fig.1B, red circle; BV/TV Het: 12±1%; BV/TV CF= 17±3%; P> 0.05), but at later weeks the BV/TV was significantly lower in CF (dashed circle) compared to Het (dotted circle) (Het: 13±3%; CF: 34±4%; P=0.001) (Fig. 1.B), as also highlighted in the micro-CT 3D reconstructions (Fig.2).

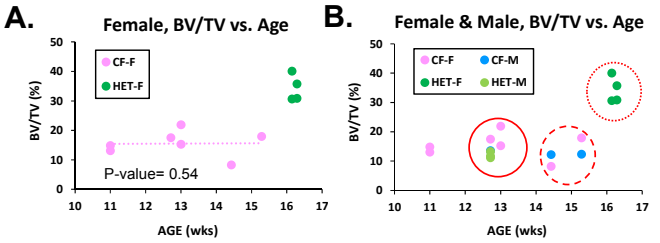

Figure 1: Slowed trabecular growth in the right tibia of CF rats compared to Het. * denote P<0.05. CFF, CFM, HETF, & HETM: CF female, CF male, Het female, and Het male, respectively.

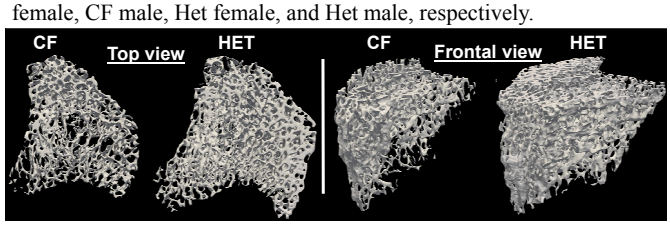

Figure 2: 3D proximal tibia trabecular bone density, CF vs. Het (15 and 16 weeks of age, respectively).

CONCLUSIONS

The results in this pilot study indicate that in adolescence, CF knockout rats have reduced trabecular bone growth compared to Het rats. Future studies would use the same techniques to evaluate various therapies for preventing CF fractures.

ACKNOWLEDGEMENTS

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UPPER LIMB TASKS WITH HUMERAL AXIAL ROTATION INCREASE GLENOHUMERAL JOINT TRANSLATIONS IN PATIENTS WITH ANTERIOR INSTABILITY

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INTRODUCTION

Loss of normal osteochondral concavity compression during humeral motion can contribute to recurrent anterior shoulder instability, further soft-tissue damage, and defects to the glenoid rim in more than 80% of anterior instability cases [1]. Left untreated, recurrent instability has been shown to result in in higher incidence of moderate and severe arthropathy compared with those managed with surgery [2]. The aim of this study was to use computed tomography (CT) to quantify glenohumeral joint position in patients with recurrent anterior shoulder instability. Accurate measurement of glenohumeral joint position during activities of daily living in anterior instability patients is clinically relevant, and may indicate pathologic glenohumeral translation patterns, as well as regions of the glenoid prone to larger than usual joint-contact forces.

METHODS

Four patients with recurrent anterior shoulder instability were recruited (mean age: 27 years), as well as one patient with recurrent posterior instability (age: 23 years) and one healthy control (age: 31 years). Patients with anterior and posterior instability had no significant glenoid bone loss (<15%) measured on CT-scans in the en-face view. All subjects had their entire glenohumeral joint scanned in a CT (Multitom Rax, Seimens, Germany) using a low-dose configuration, with a voxel size of 2mm^3. Subjects had their shoulder scanned while holding their upper limb in five contrasting positions corresponding to activities of daily living: (i) 90º abduction (ii) 90º flexion (iii) 90º abduction and full external rotation (ABER) (iv) lift-off position (representing full internal rotation), and (v) neutral position with maximum external rotation (NER). 3D reconstructions of the glenohumeral joint were created by segmenting the CT image datasets (Mimics, Materialise, Belgium). Glenohumeral joint positions were defined by the position of a sphere fitted to the humeral head and expressed relative to a glenoid-fixed coordinate system on axes normalised to glenoid radius. The glenoid origin was defined by the centre of a circle fitted to the glenoid rim, with the superior direction defined by a line between the infra- and supra-glenoidal tubercles, and the anterior direction perpendicular (3 o'clock position of a right shoulder).

RESULTS AND DISCUSSION

For the anterior instability patients, lift-off and ABER resulted in a mean 3.3±4.0mm and 2.6±3.2mm of anterior glenohumeral joint translation, respectively. NER resulted in a mean 3.3±2.6mm of anterior joint translation. In contrast, 90º abduction and 90º flexion resulted in little anterior joint translation (mean: 1.0±4.2mm and 0.2±2.4mm, respectively). For the anterior instability patients, small amounts of superior joint translation were observed at 90º abduction and 90º flexion (0.8±2.8mm and 1.6±1.6mm, respectively) while lift-off produced 2.4±4.6mm of superior translation. For the posterior instability patient, 90º flexion of the shoulder resulted in posterior dislocation of the glenohumeral joint. Joint translations were overall almost negligible for the control subject.

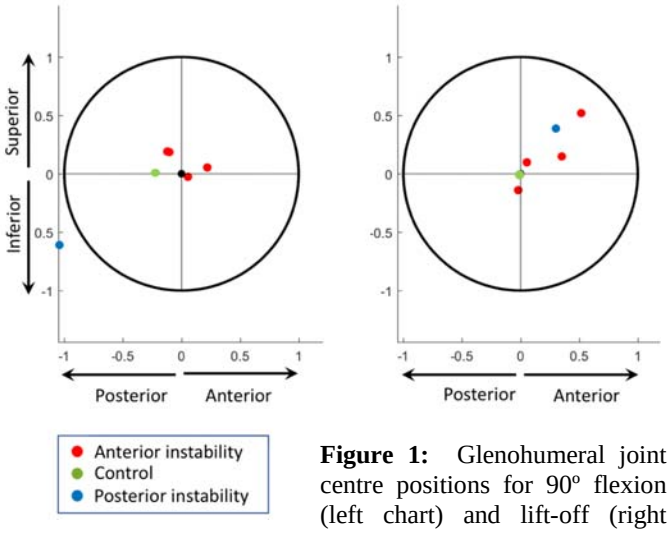

Figure 1: Glenohumeral joint centre positions for 90º flexion (left chart) and lift-off (right chart) shown on normalized axes for the anterior instability patients, posterior instability patient and control subject

CONCLUSIONS

Patients with anterior instability of the shoulder exhibit greater glenohumeral joint translation when activities of daily living are performed with humeral axial rotation compared to planar elevation tasks. This may be because of the increased glenohumeral joint shear produced by the rotator cuff muscles in the axially rotated humerus. Overall, glenohumeral joint translations are larger in patients with anterior instability, suggesting greater abnormal joint-contact loading, which may ultimately contribute to increased risk of instability injury and arthropathy.

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DAY 1

POSTERS

THE EFFECT OF ZBTB20 ON WEAR-PARTICLE-INDUCED OSTEOLYSIS IN MICE

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INTRODUCTION

Arthroplasty has become the most effective treatment for severe joint diseases [1]. Revision surgeries are still counted 7% patients within 10 years after primary arthroplasty, and particle-induced peri-prosthetic osteolysis is one of the main causes for performing revision surgeries [2]. Wear particles released from surfaces of implants play a critical role in osteolysis, which can be phagocytized by macrophages. ZBTB20 functions as a transcriptional repressor. In a recent study, ZBTB20 was demonstrated to inhibit IκBα transcription, promoting NF-κB activation [3]. Some researches has proved that wear particles can stimulate PRRs, especially TLR2/4, leading to activation of NF-κB pathway and production of TNF-α and IL-6. Since IκBα is a crucial component in NF-κB pathway and the upstream of TNF-α and IL-6, we hypothesized that ZBTB20 is a vital regulator in macrophage activation and particle-induced osteolysis.

METHODS

H&E staining and IHC on clinical synovial membrane specimens, then RNA-Seq transcriptome data of RAW264.7 macrophages stimulated with titanium (Ti) particles was generated to explore potential key molecules in the process of osteolysis. Cluster analysis and protein interaction network were performed using STRING database. shRNA and overexpression lentivirus were constructed, and expression of TNF-a, IL-6, IFN-β, IRF-3 as well as NF-κB pathway was determined. Local lentivirus injection, local macrophage injection and bioluminescence (BLI) imaging were performed on calvaria of mice, and bone resorption was assessed.

RESULTS AND DISCUSSION

Wear particles appeared in the H&E staining slices of synovial membrane around aseptic loosening prosthesis, while the expression of TNF-α and IL-6 in aseptic loosening groups increased (Fig 1A). We generated mRNA profiles of RAW264.7 treated with Ti particles using Illumina HiSeq 4000. Protein-protein interaction network showed that IκBα was a key molecule in RAW264.7 stimulated by Ti particles (Fig 1B). Major part of p65 translocated into nucleus in particle-stimulated macrophages (Fig 1C).
Particle-induced p-IKKβ and p-p65 decreased in ZBTB20-knockdown macrophages, while protein level of IκBα aggrandized in ZBTB20-knockdown macrophages (Fig 2A). Transfected RAW264.7 macrophages were injected on crania combined with Ti particle, and BLI signals originating from the calvaria region can be clearly detected (Fig 2B). Micro-CT 3D reconstructed images were performed (Fig 2C).

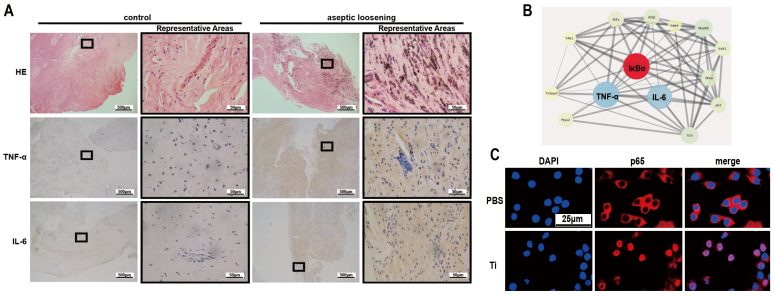

Figure 1. (A) H&E staining and IHC of synovial membranes. (B) Cluster analysis according to STRING database. (C) RAW264.7 macrophages were treated with Ti particles, and immunofluorescence showed p65 translocated into nucleus.

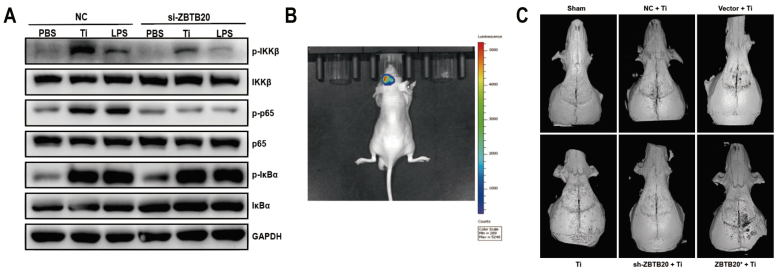

Figure 2. (A) Immunoblot in lysates of si-ZBTB20 or NC macrophages stimulated with Ti particles or LPS. (B) Images of BLI after the injection of RAW 264.7 reporter cell combining with Ti particles. (B) Micro-CT 3D images.

CONCLUSIONS

We demonstrated that ZBTB20 positively regulated IRF-3 and NF-kB signal pathway, playing a positive role in macrophage activation and osteolysis induced by Ti particles in vitro and in vivo. Thus, our findings identified ZBTB20 as a potential therapeutic target for aseptic prosthesis loosening.

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GENE EXPRESSION IN OSTEOLYSIS CASES EXAMINED USING RNA SEQUENCING

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INTRODUCTION

The failure of total joint replacement due to osteolysis frequently requires revision surgery. Previous studies on osteolysis have been limited by examining pre-specified genes and pathways. This study presents an RNA Sequencing (RNAseq) analysis of human bone and synovial tissue samples using High-throughput RNAseq. This is the first *in vivo* investigation of the entire transcriptome in patients with osteolysis.

METHODS

This study was approved by the Human Research Ethics Committee of Australian National University and ACT Health (Ref# 2009/040). Seventy-six bone and synovial tissue samples that would otherwise be discarded from patients undergoing primary total joint replacement (n=36) and revision joint replacement for osteolysis (n=28). High-throughput RNAseq was performed on total RNA extracted from the samples. RNAseq data were analysed using several steps: alignment, quality control, obtaining genomic features per sample and summarizing the data across samples for subsequent comparisons between samples.

RESULTS AND DISCUSSION

Differential expression analysis showed 755 down regulated genes and 731 up regulated genes in patients undergoing revision joint replacement vs. primary joint replacement. Differences occurred in 15 pathways, including those responsible for regulation of bone remodelling and metabolism, for example: Wnt signaling, inflammatory, IL-JAK-STAT, angiogenesis, extra cellular matrix, insulin receptor recycling. Interestingly, 23 genes were aberrantly expressed in both subgroups of revision hips and knees.

CONCLUSIONS

Our results provide a valuable resource for the potential identification of novel biomarkers associated with bone loss, which may be targeted to prevent and treat osteolysis.

ENDOPLASMIC RETICULUM MEDIATES MITOCHONDRIAL TRANSFER WITHIN THE OSTEOCYTE DENDRITIC NETWORK

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Intercellular mitochondrial transfer has attracted a great deal of attention for its major role in the regulation of tissue damage, tissue homeostasis, inflammation and resistance to cancer chemotherapy. Osteocytes are an excellent model to investigate the mechanism of mitochondrial transfer, since osteocytes form an inter-connecting network through their dendritic processes. We demonstrated, in primary murine osteocytes with photo-activatable mitochondria (PhAM) floxed and in MLO-Y4 cells, mitochondrial transfer in the dendritic networks, visualized by high resolution confocal imaging. Normal, healthy osteocytes transferred mitochondria to adjacent metabolically stressed osteocytes depleted of functional mitochondria and restored their metabolic function. Remarkably, the coordinated movement and transfer of mitochondria within the dendritic network rely on endoplasmic reticulum (ER)-mitochondria contact, predominantly mediated by mitofusin 2 (Mfn2), a GTPase that tethers ER to mitochondria. A decline in Mfn2 expression with age occurs concomitantly with impaired mitochondrial distribution and transfer in the osteocyte dendritic network. These data show a previously unknown function of ER-mitochondrial contact in mediating mitochondrial transfer, and provides a mechanism to explain the complex homeostasis of osteocytes.

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ESTIMATION OF LIGAMENT STRAINS IN A HEALTHY, ACL-DEFICIENT AND RECONSTRUCTED KNEE USING SPECIMEN-SPECIFIC OPENSIM MODELLING TECHNIQUES

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INTRODUCTION

Of the several ligaments in the knee joint, the anterior cruciate ligament (ACL) has the highest rate of injury during dynamic activities [1]. Anterolateral knee injuries lead to residual rotational laxity and isolated Anterior Cruciate Ligament Reconstruction (ACLR) have shown to have limited restoration to intact knee kinematics. Thus, an anterolateral procedure may be necessary in combination with an ACLR [2]. This study aimed to predict and compare the strain levels of knee ligaments of a specimen-specific OpenSim model under anterolateral procedures performed in combination with ACLR during applied passive movements.

METHODS

A previous controlled laboratory experiment was undertaken using a fresh-frozen lower limb of a 46-year male cadaver. Knee kinematics were recorded for the following states: intact joint, ACL-sectioned, ACLR and anterolateral ligament reconstruction (ALLR) using a 3D optoelectronic motion analysis system (Vicon, LA, USA) from 3 cycles through 0 to 120° of passive knee flexion, with an applied 5Nm of internal rotation (IR) torque. The limb was CT and MRI scanned before and after testing. Bone and cartilage geometries were segmented and created using Amira 6.7.0 (Thermo Fisher Scientific, Carlsbad, USA) and Geomagic Studio 2012.1.0 (Geomagic, USA) software. Joint centres and bony landmarks were also calculated from segmented CT images.

The tibiofemoral joint of a generic OpenSim model [3] was replaced by a new six degrees of freedom knee joint to simulate the specific cadaveric limb (Figure 1). Twelve ligament bundles were included in the knee model: anterior cruciate ligament (aACL, pACL), posterior cruciate ligament (aPCL, pPCL), medial collateral ligament (aMCL, iMCL, pMCL, aDMCL, pDMCL), lateral collateral ligament (LCL), popliteofibular ligament (POPL) and anterolateral ligament (ALL). Ligament insertion points were derived from CT. To avoid penetration of bones with the ligament bundles, wireframe wrapping surfaces were included in the model. Ligaments were modelled as linear, elastic soft tissues with defined resting length, resting strain and force at unit elongation based on the literature [4]. Kinematics and torque were applied to the model, as per the experiment, and ligament force values obtained. Ligament strains were calculated based on stress-strain relationship of the predefined ligament model [5] and validated using the literature [4].

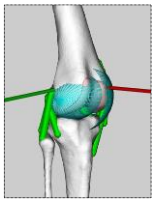


Figure 1: OpenSim specimen specific knee model.

RESULTS AND DISCUSSION

The ACL and PCL bundles generally followed linear strain pattern while other ligaments represented parabolic strain patterns, through the range of passive flexion (Figure 2).

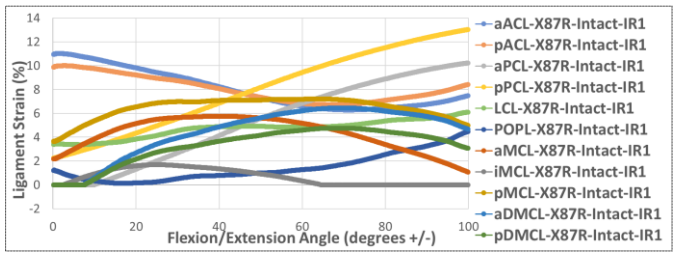
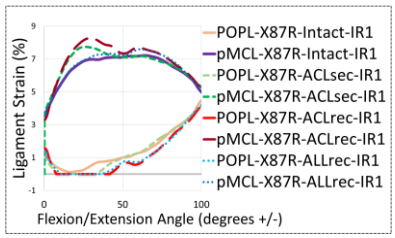


Figure 2: Percentage of all ligament strain vs flexion angle in the intact knee

When comparing the injured vs ACLrec vs ALLrec knee, the pMCL and POPL, showed the most deviation from the intact strains, at 29.7˚ and 35.6˚ of knee flexion for ACLrec and ALLrec, respectively. The pMCL in ACLsec and ACLrec followed the same pattern with two peaks at around 30˚ and 58˚ of knee flexion. The pMCL in ALLrec also followed the same pattern as intact, characterised by a plateau. In all states, the highest strains were observed in the pPCL at maximum flexion angle (Figure 3).



CONCLUSIONS

In this pilot study, the ALLrec technique better mimicked strain values of the intact ligaments in comparison with the ACL reconstructed state.

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COMPARISON OF SIMULATED AND EMG MUSCLE ACTIVATIONS BETWEEN MUSCULOSKELETAL MODELS IN LOWER LIMB DYNAMIC SIMULATIONS OF GAIT.

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INTRODUCTION

Musculoskeletal (MSK) modelling is commonly used in the biomechanical analysis and dynamic simulations of gait. Inconsistencies in simulated muscle activations between different MSK models have been highlighted and are not clearly understood [1]. It has been suggested that the Gait2392 model is sufficient in the gait analysis of healthy individuals [2], however, a shortcoming may lie in anatomical detail where all muscle paths, including those which wrap to bone and retinacula are represented by line segments. Some studies have shown more anatomically detailed models to yield more reliable simulations of muscle activations when compared to the gait 2392 [2]. The Rajagopal Full Body, yet to be compared against previous MSK models is derived from the lower body model by Arnold et al and magnetic resonance images of 24 healthy individuals to reflect the lower limb musculature of young healthy individuals in the simulation of gait [3]. This study aims to compare simulated muscle activations from the Gait 2392 and Rajagopal Full Body Models, and investigate if the inclusion of arm segments affect any muscle forces.

METHODS

Three dimensional (3D) recorded for 15 muscles of the lower extremity for a single healthy individual. Using the MAP-Client [4] to scale an articulated statistical shape model using motion capture markers, patient-tailored MSK models were generated for the Gait2392 and Rajagopal Full body models. Inverse kinematics, inverse dynamics and static optimization were performed on 19 walking trials to produce simulated muscle activations for the Gait2392, Rajagopal (no upper limb tracking) and Rajagopal (with upper limb tracking) models using OpenSim [5]. To compare simulated and experimental EMG muscle activations, simulated activations were normalized to the maximum activation over an entire gait cycle. The EMG activations were also normalized to their peak excitations. A cross correlation analysis was then performed for each muscle where to compare similarity between simulated and experimentally acquired EMG muscle activations. A mean cross correlation coefficient was then calculated for each muscle by averaging coefficients across all trials for each of the three models.

RESULTS AND DISCUSSION

Average simulated muscle activations and EMG activations for 15 muscles of the lower limb are shown in (Figure 1). The peak cross correlation coefficients for all analysed lower limb muscles ranged between r = 0.534 - 0.955. For all models, peak correlation coefficients were lowest for the Bicep Femoris and Gluteus Maximus. Simulated muscle activations for the Rajagopal full body model did not change with the inclusion of arm segments.

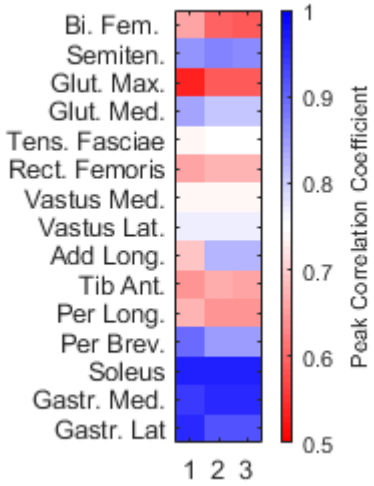

Figure 1: Peak Cross Correlation Coefficients between muscles for (1) Gait2392, (2) Rajagopal, without arms and (3) Rajagopal, with arms.

CONCLUSIONS

Our result showed that both the Gait2392 and Rajagopal models are capable of producing simulated muscle activations with good correlation to experimental EMG activations for muscles of the lower limb in a young healthy individual. Including movements of the upper limb in these simulations did not result in increased correlation between simulated and experimental activations. In the presence of pathology, the accuracy of a MSK model's simulated muscle activations is unclear.

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BIOMECHANICAL ANALYSIS OF MEDIALLY STABILISED KNEES

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INTRODUCTION

Evidence shows that Total Knee Arthroplasty (TKA) is the most reliable treatment for late-stage osteoarthritis (OA) [1]. To date, several studies demonstrated that TKA using medial pivot knee prosthesis can improve function of the knee joint [2]. Demanding daily living activities such as stair negotiation have been shown to be challenging for OA and TKA patients due to high loading on the joint [3]. The aim of this study was to investigate the influence of a medially stabilised knee implant on the kinetics of the knee joint during stair negotiation.

METHODS

Eight participants (67.5±7.2 yrs) with severe knee OA receiving a medially stabilised knee prosthesis (GMK Sphere, Medacta International) underwent 3D motion analysis during stair ascent and descent approximately two weeks prior and six months after surgery. All implantation procedures and patient recruitment process were performed by a single surgeon. Kinematic and kinetic data were acquired using motion capturing system with eight cameras (VICON, Oxford-UK) and three force plates (Kistler, Winterthur, Switzerland), respectively. Subjects were asked to walk at their self-selected pace on stairs without using handrails, and repeat trials up to three times depending on their ability. Kinematic and kinetic data were filtered using a low pass 4th order Butterworth filter at 6 Hz and 40 Hz, respectively. Subject-specific musculoskeletal models were developed for each patient in Opensim [4] using a modified version of Gait 2392 model. The knee joint moments in sagittal, frontal and transverse planes during stance phase were computed for every pre-op and post-op trial following inverse kinematics and inverse dynamics, and then averaged for each patient. Joint moments were normalised by body weight*height. Paired sample t-tests were used to determine differences between OA and TKA groups (SPSS, v25). At this stage, only stair ascent data was analysed for presentation.

RESULTS AND DISCUSSION

No statistical differences were found between groups for the knee joint moments during stair ascent (Figure 1), although marked individual improvements were seen in at least half of the participants. Knee moments in the TKA group were generally characterised by less abrupt gradient changes. Overall the adduction moment and internal rotation moment were lower in the TKA group compared with the OA group. The lower flexion moment in the OA group during the first half of the stance phase reflects the stiffer knee joint in the sagittal plane during stepping up activity [3]. The reduced adduction moment in the TKA group during stair ascent indicates that patients have accommodated to demands of stair ambulation in the frontal plane. The reduced internal rotation moment in the TKA group compared to the OA group during stair ascent is likely related to the reduced demand by the joint due to the articulating surface geometry of the implant.

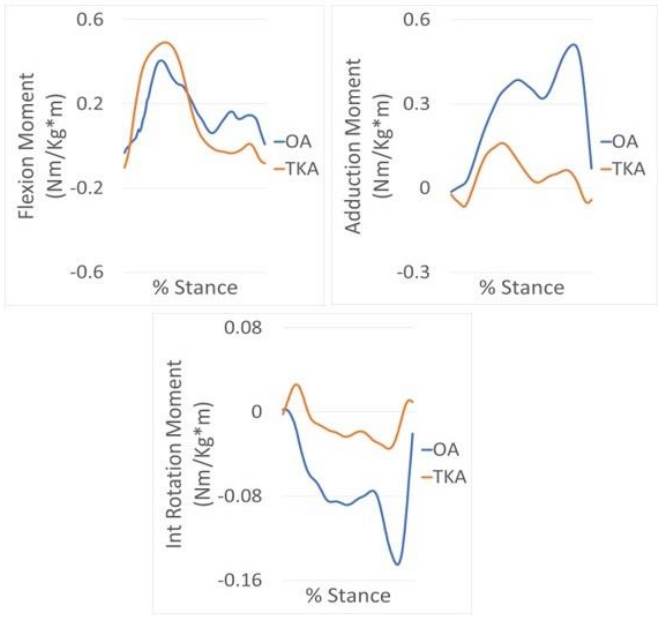

Figure 1: Characteristic knee joint moments in three anatomic planes for stair ascent.

CONCLUSIONS

Six months after receiving the implant, individuals demonstrated some improvements in knee function. The results need to be further investigated with regards to individual limb height and biomechanical strategies.

ACKNOWLEDGEMENTS

The authors would like to acknowledge Medacta International for funding part of this study.

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> This study was partially funded by Medacta International.

WHAT CAN WE LEARN FROM THE KANGAROO KNEE IN RELATION TO TREATMENT OF PATELLOFEMORAL DISORDERS IN HUMANS?

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INTRODUCTION

There is limited understanding of how patella realignment or patellectomy to surgically manage patellofemoral pain (PFP) affects the knee biomechanics [1]. By analysing marsupials like kangaroos (Macropodidae) that naturally lack an ossified patella, actionable biomimetic insight for the management of end-stage PFP in humans can be gained. This study aimed to lay the foundation for a multi-stage investigation, by establishing the static biomechanical profile of the Macropodidae stifle to inform the inputs and factors requiring consideration for future dynamic analyses.

METHODS

Four hindlimbs from two professionally culled specimens (eastern grey, *Macropus giganteus*) were sourced from Queensland, Australia. Approval from an Animal Ethics Committee was not required for this research. Volumetric CT and MRI sequences were obtained for the specimens, from which three-dimensional models of the stifles were created. (Figure 1A-B). Two limbs were dissected to visualise the insertion points, origins and lines of action of the quadriceps muscles and the knee extensor mechanism. Static measurements were obtained from the three-dimensional models to establish the biomechanical profile.

RESULTS AND DISCUSSION

The results confirmed structural differences in the Macropodidae stifle with lack of an ossified patella, which was replaced by a fibrocartilaginous pad resembling that of a shoulder rotator cuff (Figure 1C) The lack of patella may have had an impact on the moment arm length, which was lower (~29mm) than previously reported for human adult cadaver specimens [2] and in-vivo using MRI (~45mm) [3] at the same flexion angle. A prominent tuberosity suggests higher mechanical advantage within Macropodidae stifles, with a tibial tuberosity projection index of 17.9 (length of the tuberosity relative to tibial length), compared to an average of 10.3 in adults [4]. A shorter femur in the Macropodidae stifles (200mm vs 425mm in data for males [5]) has important implications for muscle cross-sectional area and volume, but the comparable torque generated at the knee requires further clarification in a dynamic model with realistic loading inputs.

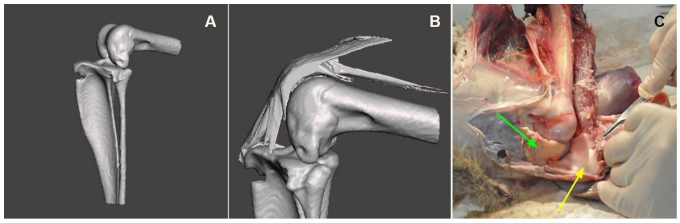

Figure 1: Three-dimensional models of the femur and tibia (A) were assembled with the knee extensor mechanism (B). Dissection of the extensor mechanism (yellow arrow) revealed a cuff-like thickening and a fat pad (green arrow) instead of an ossified patella (C).

CONCLUSIONS

The ability of the Macropodidae stifle to achieve a considerable mechanical advantage without a patella provides insight into options for modifying knee function in the context of PF disorders. However, the findings suggest that altering PF biomechanics, particularly when compensating for a reduced mechanical advantage, may be more complex than simply replicating a prominent tuberosity as found in Macropodidae. The present study has quantified a biomechanical profile of the Macropodidae stifle and revealed key structural and functional differences relative to the human knee. The data reported in this study can be used to inform the inputs and constraints of future comparative analyses from which important lessons can be learned for the human knee.

ACKNOWLEDGEMENTS

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ANATOMICAL VARIABILITY OF FEMORAL INTERCONDYLAR NOTCH GEOMETRY IN PATIENTS DIAGNOSED WITH PRIMARY ACL RUPTURE

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INTRODUCTION

The intercondylar notch houses the ACL and is a key consideration with respect to graft sizing and placement in ACL reconstruction [1]. Accurate geometric characterisation of the intercondylar notch may therefore be of value to preoperative planning, however there is inconsistency in the literature regarding the anatomical variance in intercondylar notch morphology in patients undergoing ACL reconstruction [2,3]. The aims of this study were to i) describe the three-dimensional characteristics and sources of anatomical variability in the geometry of the intercondylar notch in an ACL-injured sample using contemporary imaging techniques and ii) assess the relationship between patient factors and anatomical variability of the notch in the context of impingement risk.

METHODS

A retrospective analysis of preoperative MRI for 49 patients clinically diagnosed with ACL rupture was performed. The scans were examined in the axial plane using an online PACS viewer and notch width and angle assessed at multiple slices, as well as anteroposterior depth, notch height and calculated total volume. A principal component analysis was performed to prioritise the sources of variability within the sample. A multivariable linear regression was performed to assess the relationship between patient factors (age, height, weight, sex), while controlling for imaging parameters such as slice thickness, and principal component loadings.

RESULTS AND DISCUSSION

Notch geometry described normal distributions for all but notch volume, height and distal angle (Figure 1). Three principal components were identified that explained 80% of the total variance and corresponded to shape (PC1), size in the coronal plane (PC2) and size in the sagittal plane (PC3). Patient factors displayed significant ($P<0.05$) relationships to PC loadings, however the total variance that remained unexplained in each model remained substantial. Variation in activity level amongst participants may be factor worthy of future investigation [4]. Nevertheless, the relationship between intercondylar notch geometry and patient demographic or anthropometric characteristics requires further study.

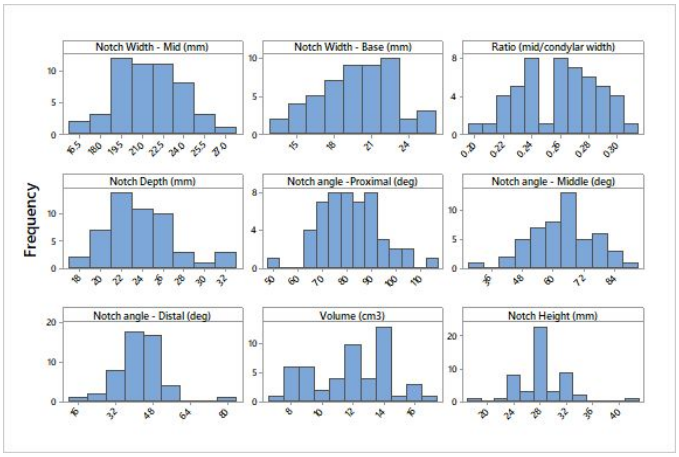

Figure 1: Anatomical variation of intercondylar notch characteristics in patients presenting with ACL rupture

CONCLUSIONS

Intercondylar notch characteristics vary considerably within ACL-injury patients with shape, as well as size in the coronal and axial planes, explaining the majority of variability. While patient factors are associated with notch characteristics, further work is required to identify the correct combination of factors to accurately predict notch geometry for planning ACL reconstruction.

ACKNOWLEDGEMENTS

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QUANTITATIVE ASSESSMENT OF REPAIR QUALITY IN ROTATOR CUFF TEAR: A NOVEL 3 DIMENSIONAL METHOD USING 3T MRI

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INTRODUCTION

Biomechanical testing has found that surgical repair of a torn rotator cuff (RC) triple row (TR) sutures yields superior results compared to the double row (DR) method [1]. However, clinical evidence demonstrating improved structural integrity of TR repair is lacking, particularly with respect to 3D assessment of repair quality [2]. Here we describe a novel imaging pipeline using graphical user interfaces (GUIs) for the quantitative assessment of RC repair quality.

METHODS

T2* weighted MRI scans were obtained with 5 echo times on 8 patients that received RC repair. An open-source GUI [3] was used to create parametric maps of relaxation times, which was validated using T2* relaxation principles [4]. A second GUI was created to overlay the original scan over the composite image in order to segment a region of interest (Figure 1A), and visualise high T2* relaxation values with a heat map (Figure 1B). Differences among group means were assessed using a one-way analysis of variance.

RESULTS AND DISCUSSION

Validation of the first GUI revealed 100% agreement between the GUI and manual calculations using relaxation principles. Preliminary analysis for one patient with a TR repair revealed regions of high T2* relaxation times that coincided with the repair site in three-dimensional space (Figure 1C).

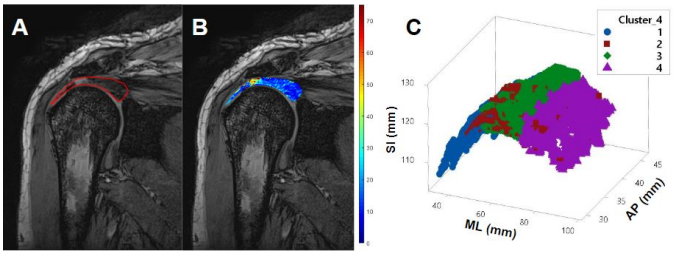

Figure 1: (A) Segmented region of interest; (B) Pixel intensity visualised on the relaxation image; (C) 3D representation of RC based on T2* relaxometry grouped by similar values.

Median relaxation time compared between pixel clusters was significantly higher (P<0.001) at the repair site compared to other clusters (Figure 2). The pilot results demonstrate feasibility of the proposed pipeline in determining regions of high T2* relaxation times that anatomically correspond to the surgical repair site, indicative of higher water content and suboptimal tissue quality [5] in this region.

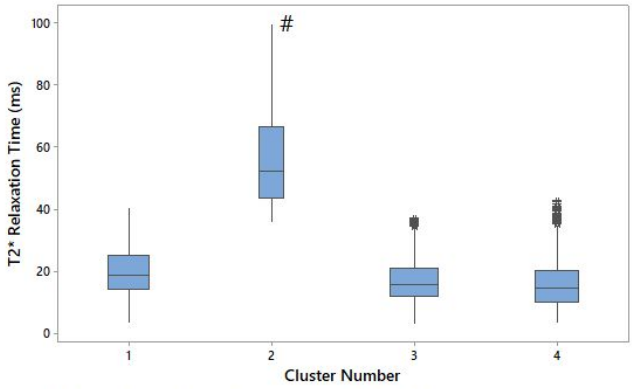

Figure 2: Higher median relaxation in Cluster 2 coincided with the repair site. #Denotes significant difference to other clusters (P<0.001)

CONCLUSIONS

We demonstrate a novel method of quantitative 3D assessment of tissue quality that can not only be used to quantitatively compare surgical repair methods to treat a torn RC, but can also be applied to other soft tissues.

ACKNOWLEDGEMENTS

The research was supported by the QEII Hospital Orthopaedic Research Fund

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ML is a paid employee of QLD Xray, which provided support for scans and protocol development.

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A FAST REGISTRATION METHOD FOR 3D ANALYSIS OF KNEE KINEMATICS AFTER TOTAL KNEE ARTHROPLASTY

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INTRODUCTION

Image registration has applications in different areas of medical image analysis. It can be used to assist the investigation of joint kinematics in conditions such as ligament injury, osteoarthritis, and after joint replacement. Analysing the 3D movement of joints after total knee arthroplasty (TKA) surgery is crucial as the correct position and relative movement of knee implants will significantly impact the success of the surgery. Multi-modal image registration techniques are generally divided into the three categories of feature-based, intensity-based and a combination of these two methods. However, most proposed methods are not very accurate or computationally expensive, or invasive, and this research area is still insufficient.

METHODS

We proposed a non-invasive and robust 3D model to 2D single-plane fluoroscopy image registration method for human knee joints. The method does not require tantalum beads to be implanted into the bone before the image capturing process, and does not need any postoperative CT scan because the 3D models designed for implants for an individual can be used in the registration. As a result, it has become possible to perform 3D TKA analysis any time after the surgery simply by taking single-plane radiographs, which allows the patient free motion in the plane between the x-ray source and the image intensifier. This method is based on a new multi-modal similarity measure edge position difference (EPD) [1] accompanied with a steepest descent optimization method. EPD is a fast similarity measure, which is based on the minimum difference between the position of binary edge images. In the first step of the proposed registration method, the input data is pre-processed. In the pre-processing process distortion correction and a 2D digitally reconstructed radiograph (DRR) projection are applied on the fluoroscopy image and the 3D volume respectively. These are followed by image binarization, and computation of an outline of the implants. The method, then, uses a coarse-to-fine registration steps to find the best transformation parameters to align the model and the x-ray images to be registered.

RESULTS AND DISCUSSION

The proposed method was compared with the method in [2] based on the SCV similarity measure. The two methods were used to perform 3D to 2D registration on clinical data captured at the Canberra Hospital, Australia. Figure 1 shows the mean success rate of registration for the femoral and tibial components in the fluoroscopy frames of the data. As can be seen, the proposed method had a higher success rate when compared to the SCV method. Regarding computation time, the proposed method is almost 4.5 times faster than the SCV method.

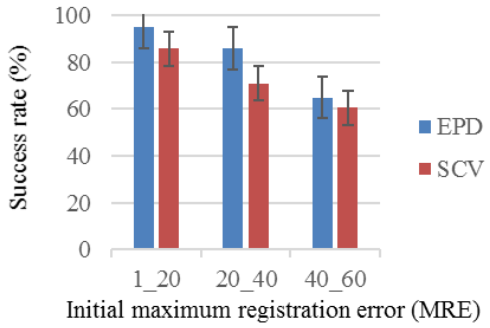

Figure 1: The success rate of the EPD and the SCV methods.

CONCLUSIONS

The proposed method is a non-invasive and efficient registration method. It uses EPD similarity measure, accompanied with a steepest descent optimization method. The experimental results show that the proposed method is not only robust but also fast.

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Dr. Perriman and Professor. Smith report grants from Zimmer Biomet, during the conduct of the study.
Professor. Scarvell, Professor. Pickering and Mrs. Saadat have nothing to disclose.

VALIDATION OF A 3D SCANNING SYSTEM FOR INTRAOPERATIVE ANTERIOR CRUCIATE LIGAMENT GRAFT GEOMETRY DETERMINATION

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INTRODUCTION

A significant factor in determining long-term patient outcomes and revision rates after anterior cruciate ligament (ACL) reconstruction is graft geometry, with graft impingement or re-rupture affecting 15-20% of patients after surgery [1]. However, literature regarding the effect of size and geometry of graft tendons on patient outcomes is relatively scarce, due to time and sterility requirements impeding the ability to measure grafts intraoperatively. This study aimed to provide a preliminary validation of a 3D scanning system as a novel approach to determine graft geometry intraoperatively.

METHODS

Four cadaver bovine tendon grafts were sourced to simulate human autograft specimens, and were subjected to the conventional 500N tensile force for one minute prior to measurement to simulate intraoperative processes. Two observers independently measured the physical volume using Archimedes' principle, and the length and diameter of the grafts using vernier calipers. The grafts were scanned using a professional 3D scanning system, the Artec Space Spider (Luxembourg) and processed using the included software. Regression and t-test analysis determined the correlation between measurements obtained from the physical and 3D scanner methods. Inter-observer agreement was determined by Bland-Altman analysis [2].

RESULTS AND DISCUSSION

The 3D scanner generated STL files in near real-time, which were later processed using the associated software to produce 3D models of the bovine tendons (Figure 1). Strong correlation ($p<.05$) between physical methods of measurement and the 3D scanning system was found across all dimensional properties: graft volume yielded an average bias of -1.2% when physically measured volume was compared to the scanner output, graft diameter yielded an average bias of -0.8%, and graft length yielded an under-weighted mean relative difference for both observers of -3.2 and -2.9%. Negligible variation between observers (<1%) indicated a high degree of repeatability in the measurements.

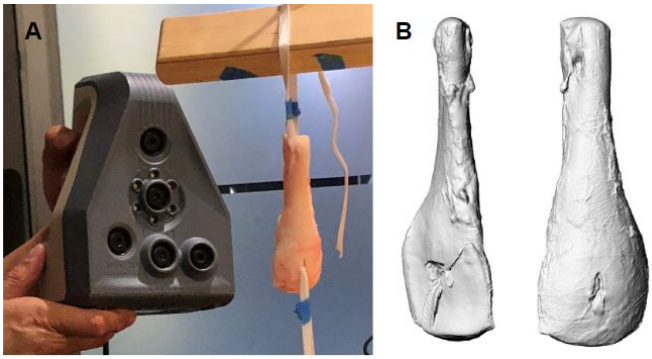

Figure 1: The Artec Space Spider used to scan the bovine grafts (A), and the resulting 3D models of a tendon (B)

Further work to implement the proposed method involves piloting the 3D scanner intraoperatively in order to: 1) verify that the scanning time and procedure does not interrupt or prolong the surgery, 2) ensure the rig used for vertical graft placement meets sterilisation requirements, and 3) determine logistical feasibility of the methods (cost, insurance requirements, training).

CONCLUSIONS

This study is a first in attempting to determine ACL graft geometry via 3D scanning methods for intraoperative use. The findings reveal a strong correlation between physical methods of determining geometry and a 3D scanning approach, and suggest that the proposed method is suitable for graft imaging and modelling.

ACKNOWLEDGEMENTS

The authors wish to acknowledge Ben Tam from Qubic (Sydney, Australia) for demonstrating use of the 3D scanner and assisting with the model preparation.

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BIOPRINTING SKELETAL MUSCLE FOR NEUROPROSTHETIC INTERFACING

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Presenting Author: Catherine GY Ngan cgy.ngan@gmail.com

INTRODUCTION: Motorised prosthetic devices can serve as important rehabilitative tools after losing a limb. These technologies utilise a range of mind-prosthetic interfacing strategies to provide intuitive motor control. Current methods are hampered by delicate neural biology, leading to premature device failure. This work presents a bioprinting approach to tissue engineering skeletal muscle, with early *in vivo* evidence of innervation and vascularisation. This is a proof-of-concept study for the development of a muscle-based bioelectrode system, to harness activity from residual nerves for intuitive prosthetic control.

METHODS: A bioprinting technique was established to tissue engineer functional skeletal muscle using a gelatin methacryloyl (GelMA) bioink. The bioprinted muscle was implanted into the nude rat to assess its capacity for innervation and vascularisation. The tissue construct was supplied by a surgically formed arteriovenous loop and transected femoral nerve. The triad of muscle, vasculature and nerve was housed in a customised 3D printed chamber as a bioelectrode prototype, designed for grafting onto transected peripheral nerves after limb amputation. *In vivo* electrophysiology and histology was performed to assess neural integration and vascularisation.

RESULTS AND DISCUSSION

Primary mouse myoblasts were bioprinted into cell-laden GelMA fibres with high cell viability. The maturation of these cells was characterised by morphology and molecular analysis over two weeks *in vitro*. The printed constructs were shown to be functional with calcium imaging and multielectrode array recordings *in vitro*. The muscle was then implanted in customised 3D-printed chambers supplied by an AV loop and transected femoral nerve into the nude rat. After 2 weeks *in vivo*, preliminary data suggested the presence of muscle activity as a direct consequence of neural activation via a cuff electrode around the femoral nerve. Immunohistochemistry revealed remarkable tissue maturity, with sarcomeric striations and peripherally placed nuclei in organised bundles of muscle fibres (Figure 1).

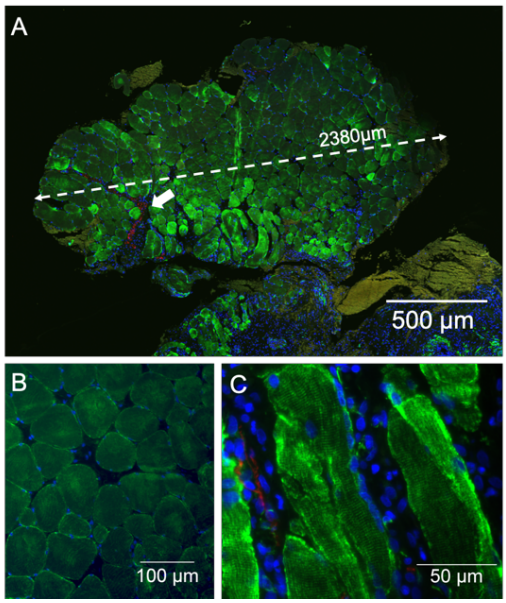

Figure 1: Histology of mature skeletal muscle. Sections stained for desmin (green), B3T (red) and DAPI (blue). A) A 2.38mm wide specimen. Arrow points to neural sprouting within this muscle bundle. B) Transverse-section and C) longitudinal-section of mature myofibres.

CONCLUSIONS: This study developed a bioprinting technique for tissue engineering functional skeletal muscle for applications in the neuroprosthetic interface. Although the work presented is in the frontier stages of development, it is proof-of-concept for a muscle-based bioelectrode system and brings the dream of mind-controlled motorised prosthetic limbs closer to everyday reality.

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THE VARIATION IN RADIOGRAPHIC MEASUREMENTS OF HIP STABILITY BETWEEN SUPINE AND STANDING RADIOGRAPHS IN DYSPLASTIC HIPS

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INTRODUCTION

Developmental dysplasia of the hip (DDH) is a condition resulting in insufficient acetabular coverage of the femoral head. Radiographic evaluation is most commonly performed on supine radiographs. However, the surgeon needs to correct acetabular coverage for the functional, standing position. To appreciate the potential measurement variation and identify contributing factors, the aims of this study were 1) to compare the anterior and posterior acetabular coverage measured in supine and standing positions in patients with hip dysplasia, 2) to investigate any correlation between pelvic tilt and measurements of acetabular coverage, 3) to determine the difference between specialised software results and manual measurements, 4) to determine the influence of software corrections for pelvic rotation, and 5) to determine the interobserver error for all measurements.

METHODS

Preoperative supine and standing radiographs were retrospectively analysed from 37 consecutive patients (43 hips) from a single centre, two surgeon (DWH and LBS) cohort. Anterior (AC) and posterior coverage (PC), the lateral centre edge angle (LCEA), acetabular inclination (AI), Sharp Angle (SA), pelvic tilt (PT), femoro-epiphyseal acetabular roof (FEAR) index, femoro-epiphyseal horizontal angle (FEHA), leg length discrepancy (LLD) and pelvic obliquity (PO) were analysed using the Hip2Norm® software and manual measurements on the Carestream Vue Motion Patient Archiving and Communications System (CareStream Vue). Measurements taken using Hip2Norm® were recorded uncorrected and corrected for pelvic rotation.

Variation between supine and standing results was determined by the Mann-Whitney U test, and correlation between pelvic tilt and other measurements was determined by Spearman's correlation. Intra-class correlation (ICC) was used to compare the difference between software and manual results. ICC was also used to determine interobserver error.

RESULTS AND DISCUSSION

AC, PC, LCEA, AI, SA and PT were able to be measured by all methods in 43 dysplastic hips. FEAR, FEHA, LLD and PO were only able to be measured manually in 27 dysplastic hips.

AC ($p=0.0053$), PT ($p<0.0001$) and LLD ($p=0.0001$) demonstrated significant variation between supine and standing radiographs (Figure 1). Other measurements did not vary significantly between postures. However in all measurements except the SA, PO and LCEA, there were at least 20% of cases that demonstrated moderate variation (>5 degrees).

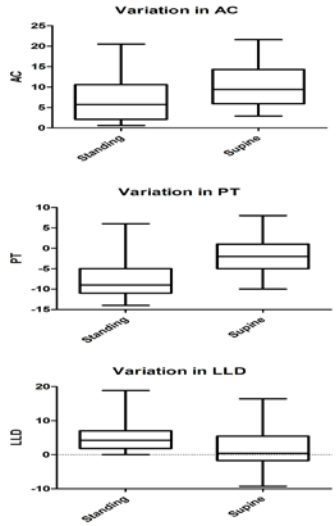

Figure 1: Graphs showing the statistically significant variation of AC, PT and LLD measurements between standing and supine radiographs.

There was positive correlation between PT and AC (Spearman's rho correlation coefficient=0.3733, $p=0.0162$). No other measurements demonstrated a correlation with PT.

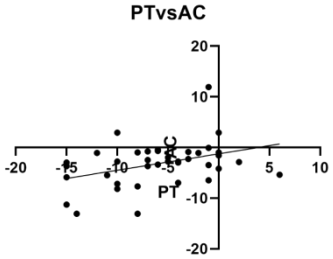

Figure 2: Correlation between PT and AC.

Uncorrected Hip2Norm® and manual methods demonstrated variable agreement for different measurements. LCEA and SA demonstrated good agreement (ICC 0.612 and 0.674 respectively), while AI agreement was poor (ICC 0.149). Uncorrected and rotation corrected Hip2Norm® methods also demonstrated variable agreement for different measurements. AC demonstrated the best agreement (ICC 0.932) and SA had the worst (ICC 0.262). The interobserver error was excellent for all software and manual measurements.

To appreciate the variation in hip coverage measurements in a large number of individual cases, surgeons should routinely use both supine and standing radiographs to plan surgical corrections. The positive correlation between PT and AC makes this particularly important in patients with considerable variation in PT. There was some discrepancy between software and manual measurements which needs further investigation

WHY DOES ORTHOPAEDIC RESEARCH FAIL IN CLINICAL PRACTICE? GENERATING REALISTIC EXPECTATIONS FROM 11,000 WORK HOURS

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INTRODUCTION

Real-life observational studies are essential to determine whether patients in routine practice are achieving expected outcomes [1]. Time and financial demands however, as well as a lack of supportive research infrastructure are challenges facing researchers in clinical practice [2]. We aim to report on the reasons why, and the extent to which time and financial resources are strained in clinical practice when conducting orthopaedic research.

METHODS

We reviewed research projects that were in progress at one research organisation at any stage during the period of 01 Jan-31 Dec 2018, conducted under sponsorship and collaboration with clinical partners. Observational clinical studies were assessed for proposed budget, actual cost, planned timeline and final time to delivery. Project-specific time data and general attendance at work was extracted from the project management software (Intervals, .

RESULTS AND DISCUSSION

A total of 11,640 work hours were tracked for 11 research staff members. Of the 55 research projects identified, 21 (38%) were observational clinical studies with 1362 hours (12%) tracked to them during the review period. Studies that went overtime by up to 4 times the expected timeframe (Figure 1A) were typically commenced with stakeholder affirmation that all data was available and ready to analyse, but this was not the case when executed. Studies with budget blowout by more than 3-4 times the original amount (Figure 1B) were a result of either scope creep, or the involvement of in-house staff that required additional training or coordination. Some adequately planned studies (concept and methods viability checked, with a study plan agreed upon by stakeholders) came under budget by up to 50%, however, they were still overdue by 2-3 times their original timeline.

These findings reveal key issues when conducting clinical orthopaedic research, that is often oversimplified and under resourced. A full-time in-house staff member spending 75% of their time on research has ~1300 hours available, which is often spread across multiple projects, amongst other administrative duties. Internal factors affecting project completion include a lack of dedicated resources, staff turnover and scope creep. External factors include delays in the ethical approval process, low patient recruitment rates or high patient drop-out.

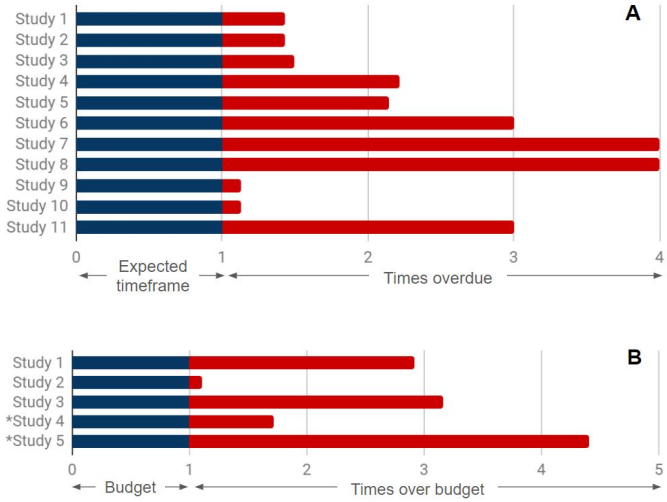

Figure 1: Studies were up to (A) 4 times overdue and (B) 4 times over budget for a number of reasons.
**Denotes studies still in progress, but already over budget.*

CONCLUSIONS

Observational clinical studies can be expensive and time-consuming, but stakeholders are not always aware of this. Lack of planning and limited research experience often lead to unrealistic expectations of what can be achieved in a set budget or timeframe..

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   The clinical partners mentioned in this investigation sponsored the analysed studies, but no support or materials were received from them in relation to this investigation or the preparation of this abstract.

FLEXIBLE INTRAMEDULLARY TITANIUM ELASTIC NAILING OF FRACTURE SHAFT OF RADIUS AND ULNA IN CHILDREN AT A TERTIARY CARE TEACHING HOSPITAL

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INTRODUCTION

Displaced fracture shaft of both bone forearm in children can still managed with close reduction and cast application. If, it has failed or remain inadequately reduced after closed reduction require intramedullary fixation to achieve functional outcome. This study assesses the functional outcome of treating displaced fracture shaft of both bone forearm in children with intramedullary flexible titanium elastic nail.

METHODS

79 children aged 3 to 15 years with displaced fracture of shaft of both bone forearm underwent flexible titanium elastic nail.

Image intensifier was adjusted to obtain appropriate AP and lateral views of forearm. We used flexible nail of 0.5 mm smaller than the calculated size. The radial and ulna nail with its proximal 5mm pre-bent was bent to about 15 to 30 degrees for easy passage of the pin through the medullary cavity.

Stability of the fracture was accessed postoperatively. If the fracture was stable then simple sling is applied for 5 days, if fracture was unstable then long arm posterior plaster slab was applied for at least 4 weeks. The patient was instructed to avoid excessive loading of the involved limb until adequate callus formation is observed on radiographs at four weeks and is advised to refrain from sports for 6-8 weeks. Physiotherapy was started as early as possible. The patients were followed up for a period of 12 months.

RESULTS

Close reduction followed by nailing was possible in 71 patients, while 8 patients required open reduction through mini incision of both the radius and ulna fracture prior to nailing. 74 patients had excellent results and 5 patients had good results. 13 patients had minor complications including skin irritation over prominent hardware; superficial nail insertion site infection was noted in our study. 2 patients had a restriction of 20° of pronation and 10° of supination, 2 patients restriction of 15° of pronation and 1 patient had 8° volar angulation at the radial bone with limitation of 5° supination. All fractures were united in acceptable alignment by an average 9 weeks and nails were removed at an average of 6 months.

DISCUSSION

Up to 25% of complete forearm fractures displaced during the follow-up and may require a second intervention [1]. Several authors have suggested that a reduction is unacceptable if the patient has an angular deformity >10° or complete displacement [2]. Parameters for accepting rotational malalignment range from 30°-45° to none and some authors have noted that rotational remodeling is not predictable [2].

In our study most 70% (55/79) of the middle third shaft of forearm fractures treated with flexible intramedullary nail in which showed angular deformity >15º in radiograph at the time of admission. Daruwalla et al. [3] recommended operative intervention for midshaft and proximal forearm fractures with angulations >10° because of limited remodeling potential in these areas of the bone. Given the potential failure of non operative management (1.5% to 31%) and the importance of minimizing angular deformity to preserve normal forearm rotation, operative management of pediatric forearm fracture has been increasingly popular.

Flexible intramedullary nailing is preferred fixation method Flexible intramedullary nails as shown in the present study where 74(94%) patients had excellent results and is comparable with other similar study.

CONCLUSIONS

Flexible nailing leads to more versatile and efficient application of internal fixation for fracture shaft of both bone forearm, which permits early mobilization and return to the normal activities of the patients, with very low complication rate.

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THE EFFECT OF A QUALITY MANAGEMENT SYSTEM ON THE INTEGRITY OF PAPER-BASED PATIENT REPORTED OUTCOMES IN AN ORTHOPAEDIC REGISTRY

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INTRODUCTION

Value based healthcare, whereby care practitioners are reimbursed relative to patient outcomes as opposed to services provided, relies heavily on the collection of accurate patient-reported outcomes (PROMs) at key moments within the treatment pathway. Although the advent of electronic PROMs collection has reduced the risk of errors permeating through an orthopaedic registry dataset [1], paper capture remains the standard in many sites responsible for registries monitoring considerable patient volumes. What is neglected in the contemporary literature is discussion regarding the quality of data being reported and used to make significant practice changes. The purpose of this study was to report on the effect of a novel quality management system, within a department registry, on data quality captured using paper-based PROMs.

METHODS

A quality controlled clinical patient registry was implemented for one surgeon within a public hospital department. Patients presenting with shoulder or knee pathology eligible for surgical intervention were recruited to the registry and asked to complete paper forms at their clinic visits, before and after surgery. Registrars administered the forms and scanned them to electronic form for entry into the registry database (Socrates v3.5, Ortholink Pty Ltd, Aus). Quality assessment was performed at scheduled intervals (3 months) and the data stored in the database compared to the original paper version.

RESULTS AND DISCUSSION

A total of 1436 paper forms were collected and verified over a 12month period. The quality management system detected errors in 8 - 12% of forms per quarter, with issues attributed to data entry from paper to electronic database, patients filling out the form incorrectly or missing responses such that the questionnaire was incomplete and a score could not be calculated (e.g. Figure 1). Corrections applied to PROMs data improved PROMs completeness by 3.5 - 16% per quarter. Although paper-based forms remain the mainstay of orthopaedic patient registries, errors present in the data remain under-recognised. Despite previous reports of data quality in a hospital registry [2], this is the first study to demonstrate the effect of an integrated quality management system on patient-reported outcomes collection in a public hospital department.

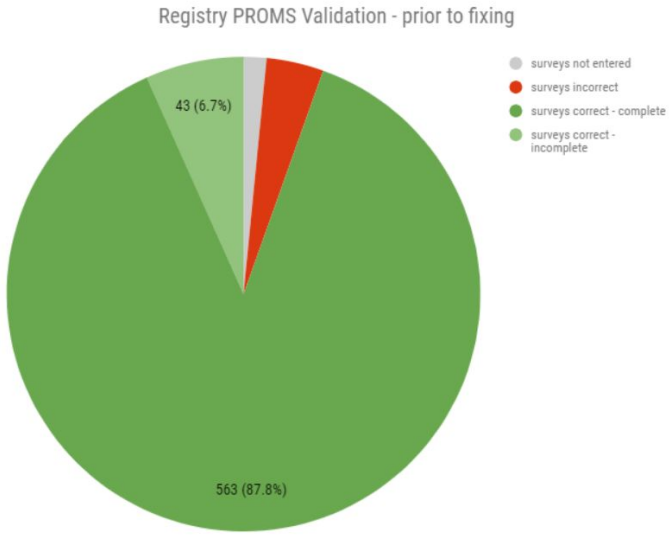

Figure 1: Example validation check for one quarter of data capture within the patient registry

CONCLUSIONS

The addition of a quality management system improves data quality in the collection of PROMs using paper. Future work should focus on the improvements in data quality and patient compliance associated with transition to electronic data capture, as well as hybrid models in populations where electronic capture is not viable.

ACKNOWLEDGEMENTS

The research was supported by the QEII Hospital Orthopaedic Research Fund

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YOUNGER FEMALE PATIENTS IN TOTAL KNEE ARTHROPLASTY: BENEFITS OF A ROTATING PLATFORM KNEE PROSTHESIS WITH GAP BALANCING TECHNIQUE

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INTRODUCTION

Knee malalignment resulting in increased angular and torsional forces have been associated with increased risk of OA progression [1] and decline in physical function [2]. The increased incidence in lower limb malalignment in women [3] may contribute to earlier onset of arthritis, necessitating earlier need for total knee arthroplasty (TKA). The younger and female disposition may lead to subsequent challenges with respect to choice of suitable knee prosthesis, with designs lacking compensation of aberrant torsional forces potentially leading to malrotation of components and ultimately unsuccessful TKA [4]. We hypothesise a rotating bearing knee (RBK) design for TKA with gap balancing technique may improve outcomes and survivorship in individuals where significant torsional abnormalities contribute to knee pathology.

METHODS

Retrospective analysis of a single-surgeon practice was performed. A total of 1442 procedures comprising rotating bearing knee designs were cross-matched with manufacturer records. Clinical outcomes (complications, reoperations) were linked to patient-reported outcome measures (KSS-function, OKS). Regression models were used to determine relationships between patient age, gender and reported outcomes.

Cumulative percent revision was reported by the Australian Orthopaedic Association National Joint Replacement Registry (AOANJRR) and compared between the senior author and national data for other total knee designs.

RESULTS AND DISCUSSION

Preliminary analysis of the available data revealed significant improvements in general health, knee pain and function, with significant interactions between age and gender for OKS at 12months, in particular for females under the age of 55. A cumulative revision rate of 3.2% at 5 years and 4.8% at 13 years was determined for this cohort, with significantly lower revision rates noted in females patients (Figure 1). Younger patients aged <55 demonstrated superior survivorship compared with AOANJRR data for fixed bearing designs.

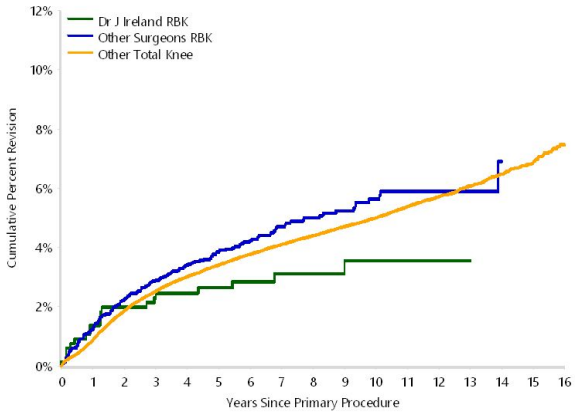

Figure 1: Cumulative percent revision of primary total knee replacement in females for present cohort using RBK with gap balancing technique, compared to general RBK designs and other total knee designs.

CONCLUSIONS

The RBK design incorporated in this single-surgeon practice provided good functional outcomes and encouraging revision rates for the younger and female patient demographic. A rotating bearing prosthesis with gap balancing technique may be considered as a first line option for this subgroup of patients.

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   The research herein forms part of a clinical research registry which receives sponsorship funding from manufacturing orthopaedic company (Exactech Inc. USA) to identify trends in performance of implants used for hip and knee replacement surgery.

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PATTERNS IN PATIENT REPORTED OUTCOMES REVEALED BY MACHINE LEARNING IN PATIENTS PRESENTING WITH SYMPTOMATIC ROTATOR CUFF PATHOLOGY

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INTRODUCTION

Patient reported outcome measures (PROMs) are considered a key pillar of value-based healthcare, as they can provide a comprehensive assessment patients using minimal resources [1]. A key assumption is that results of PROMs are accurately aligned to the clinical condition of the patient (descriptive), and to the clinical decision to pursue a particular treatment option (predictive). A large assortment PROMs have been described, including measures intended to be condition-specific and those intended to gauge overall general health [2]. For rotator cuff pathology, reports of patient outcomes are highly variable regarding both the specific PROMs used, and the combination of PROMs recorded at a given time point [3]. There is also little information regarding relationships between baseline PROMs and the pathology present in the shoulder. The aim of this study was to establish the relationship between responses to different PROMs collected at initial presentation for patients with symptomatic rotator cuff pathology.

METHODS

Data was extracted from a prospective patient registry incorporated into a metropolitan private upper limb surgery practice. All patients were clinically assessed by one of two fellowship trained shoulder surgeons. Patients completed the Veterans RAND 12 Item Health Survey (VR-12), the American Shoulder and Elbow Society standardised assessment (ASES) and Oxford Shoulder Score (OSS) questionnaires independently at the time of initial presentation. Every patient presenting with symptomatic rotator cuff pathology deemed appropriate for intervention (either operative or nonoperative) was included. A multivariate clustering model was used to identify subgroups based on similarity of responses to the questionnaires, and nominal logistic regression was performed to determine relationships between cluster membership and patient age, gender, BMI, insurance status, rotator cuff tear presence and number of symptomatic pathological processes identified.

RESULTS AND DISCUSSION

A sample of 353 patients were extracted, with 260 (74%) available for analysis after filtering for missing PROMs. Four subgroups (clusters) were identified in the sample. Patients in Cluster 1 had the best outcomes for all PROMs, Cluster 2 patients had low scores for all PROMs, and Cluster 3 patients had higher scores for ASES and OSS, but lower VR-12 mental component. Cluster 4 returned low ASES and OSS, but higher VR12 mental component scores. Regression analysis identified gender, insurance status, tear type (partial, full or re-tear), and presence of other concurrent shoulder pathology as significant ($P<0.05$) discriminatory factors between clusters.

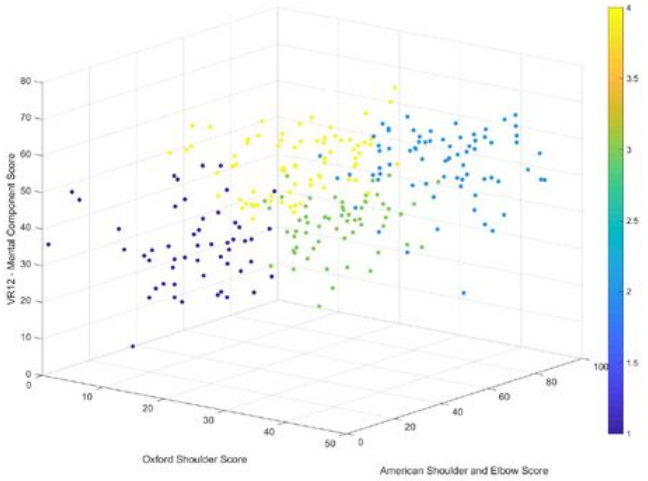

Figure 1: Illustration of patient responses organised by cluster and plotted in three-dimensional space

CONCLUSIONS

The combination of both condition-specific and general health PROMs was able to identify 4 distinct patient groups at baseline presentation of rotator cuff pathology. Identifying such contextual data is likely to be useful for the meaningful interpretation of post treatment PROMs.

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ROTATOR CUFF REPAIR WITH INCREASING AGE: SURGERY IN PATIENTS >70YRS DOES NOT LEAD TO ADVERSE OUTCOMES AT 6MONTHS FOLLOW UP

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INTRODUCTION

The treating surgeon faces a difficult series of decisions when treating an elderly patient with a symptomatic rotator cuff tear (RCT). Despite general acceptance that surgical repair in these patients is at elevated risk of poor outcomes [1,2], the contemporary literature is limited in its scope and lacks consensus on the issue [3-5]. The aim of this study was to determine whether arthroscopic cuff repair (ACR) in patients with increasing age (>70yrs) demonstrate worse retear incidence, rehabilitation compliance, or patient-reported outcomes at 6 months follow up.

METHODS

Patients electing to undergo ACR with a single surgeon between 2010 and 2016 were recruited prospectively to a clinical registry maintained by the practice. Patient records with a minimum of 6months follow up were included in the present analysis. Clinical and baseline patient reported outcome measures (PROMs; Constant, Oxford Shoulder Score, OSS, Western Ontario Rotator Cuff index, WORC) were collected preoperatively, while pathology and treatment details were recorded intraoperatively. Retear incidence at 6, 12 and 24 weeks was assessed using ultrasound. Rehabilitation compliance was self-reported at the above intervals (none, partial, full) and PROMs were reassessed postoperatively.

RESULTS AND DISCUSSION

A sample of 689 ACR records were retrieved from the registry for analysis, with 61.5% male (N = 424) and 14.4% aged >70yrs at time of surgery (N = 99; 73yrs IQR 71-76). Group 1 (N = 590) were aged 59yrs (IQR 52-64) and did not differ to Group 2 in terms of gender distribution, symptom onset rate, symptom duration, or baseline PROMs. Group 2 also demonstrated a significantly higher incidence of partial retears at 6months (14.8% vs 7.5%, P = 0.02), but no difference in full retear incidence (6.8% vs 4.1%, P = 0.26). No difference in rehabilitation compliance at 3months was observed between groups, however Group 2 demonstrated superior OSS (2 pts, 95%CI 0-3, P = 0.02) and WORC (7.8pts, 95%CI 3.3 - 12.3, P < 0.01) scores at 6 months. In addition, age was significantly associated with postoperative WORC (rho = 0.24, P <0.01), while age (OR 0.95, 95%CI 0.91 - 0.99) and tear size (Grade 4 OR 0.06, 95%CI 0.01 - 0.35) were associated with reduced retear incidence.

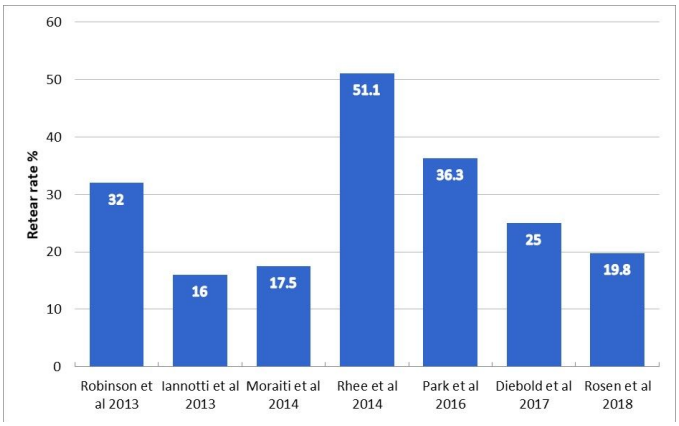

Figure 1: Retear incidence for older (>65yrs) patients in the literature compared to present results

CONCLUSIONS

ACR outcome in patients with increased age is comparable if not better than younger patients, with equivalent full retear incidence and superior postoperative outcomes. Patients should not be excluded from surgery on age alone and other factors, such as tear size, may be important determinants of retear risk within 6months of surgery.

ACKNOWLEDGEMENTS

The authors gratefully acknowledge Theresa Johnson and Christopher Howitt for their assistance with data collection.

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DAY 3

POSTERS

A PRELIMINARY STUDY: INTRA-SUBJECT VARIABILITY IN DYNAMIC MARGIN OF STABILITY DURING GAIT

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INTRODUCTION

Intra-subject variability in gait was shown to affect postural stability[1]. Several biomechanical parameters have been used to provide a measure of stability during walking i.e. center of pressure excursion or center of mass (CoM) motion in different anatomical plans. Traditionally, stable gait is assumed when CoM projection is within the base of support (BoS); however, such a measure does not include CoM speed. A review of current measures are provided in [2]. Margin of stability (MoS) has been used to measure level of stability in ML or AP directions considering extrapolation of CoM and normalized CoM velocity with respect to BoS. Though MoS has been used in normal and perturbed gaits, it is unclear how MoS alters in different sessions i.e. its intra-subject variability during perturbed gait [3]. Thus, using CAREN (**C**omputer **A**ssisted **R**ehabilitation **EN**vironment) system, we developed a protocol to measure dynamic MoS during walking and perturbation at different sessions. CAREN is a complex biomechanical system to study multisensory system of human balance during gait with a virtual reality environment and 6DoF controllable platform. We hypothesized that intra-subject variability of MoS is large in both ML and AP directions specially during perturbation.

METHODS

We recruited five young (26±2yrs old, weight=65±4kg, height=173±7cm) students from the University of Melbourne. The participants signed the consent form from an approved ethics protocol. The participants performed an initial warm-up trial first for 2 minutes. They could rest for about 1 min between trials. The gait speeds (2, 4, & 6 km/hr.) were randomized and the subjects walked on a split-belt treadmill. Following the warm-up, the subjects walked without any perturbations before performing walking with perturbations. We simulated forward and backward falls in CAREN. Each trial took 2 mins while 4 random perturbations were applied. Perturbations included left or right side while forward or backward trips were simulated by accelerating or decelerating the relevant belt. These trials were repeated 5 times for each subject in different sessions. The preliminary outcomes of intra-subject variabilities are presented here. We recorded four intervals of 7 seconds during each 2-minute trial. The 7s duration was selected as 2s before the perturbation to 5s after to have enough gait cycles for further analyses.

RESULTS AND DISCUSSION

There is a large intra-subject variability in different sessions, however, on average, this variability before and after perturbations did not significantly change (Fig. 1). Dominant leg showed fewer median changes following the perturbation which may indicate the importance of laterality in falls. We believe that more data is required to investigate our hypotheses thoroughly. We aim to expand upon these preliminary findings and study the effects of different speeds and perturbations on gait parameters specifically MoS.

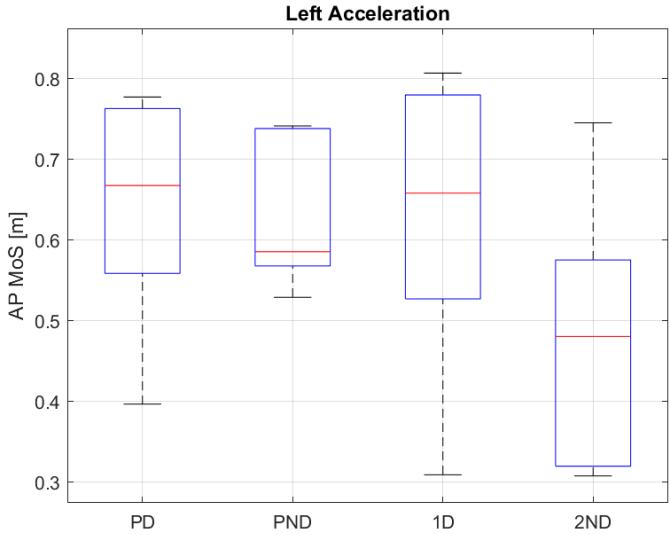

Figure 1: An example of Margin of Stability (MoS) in AP direction for one subject performing 5 sessions. PD: Previous Dominant initial contact, PND: Previous Non-Dominant before perturbation, and 1D: 1st Dominant initial contact, 2ND: 2nd Non-Dominant contact after perturbation.

CONCLUSIONS

Our findings indicate that there might be an intra-subject variability in MoS during gait, however, we could not find significant differences with our limited number of subjects. Our future studies will include more subjects and other aspects of gait performance and perturbations in other anatomical planes.

ACKNOWLEDGEMENTS

We would like to thank The University of Melbourne for funding and Motek Link for technical advice.

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LOSS OF KNEE EXTENSION AFTER ACL RECONSTRUCTION: WHAT DO WE KNOW?

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INTRODUCTION

Loss of extension (LOE) or knee extension deficits are a potential complication following anterior cruciate ligament (ACL) rupture, and subsequent treatment with surgical reconstruction [1,2] or nonoperative treatment [3]. However, the change in post-treatment knee extension and the incidence of patients presenting with measurable LOE, remains largely unknown. Furthermore, there is a lack of consistent information in the literature to establish a reasonable benchmark for treatment with respect to reducing the incidence of extension loss in patients diagnosed with ACL rupture. The aim of this review therefore was twofold: 1.To establish the trajectory of knee extension recovery in patients diagnosed with ACL rupture, and 2. To determine the incidence of knee extension deficits during early and late stages of recovery.

METHODS

The protocol for the systematic review [4] was registered on the PROSPERO international prospective register of systematic reviews prior to commencement. A systematic search was conducted in PubMed for English language papers in publication as of April 2018, with no restrictions on publication year. Studies were screened and assessed for eligibility by two independent reviewers as per PRISMA guidelines. All study designs that reported incidence of knee extension loss or quantified knee extension during passive or active measurement underwent quality assessment and data extraction.

RESULTS AND DISCUSSION

Preliminary analysis revealed 4082 articles retrieved using the initial search criteria. Eligible studies spanned a variety of designs and quality. Knee extension after ACL rupture was measured at variable time points in a passive pose (muscles relaxed) or during active locomotion, with studies varying greatly in the method of measurement, the task of interest and poor descriptions of how full extension was standardised.The incidence of knee extension deficits varied with age, treatment/surgical technique and injury to treatment period (Figure 1), with a mean LOE incidence of ~6 to 12% at early and late stages of recovery after reconstruction surgery respectively.

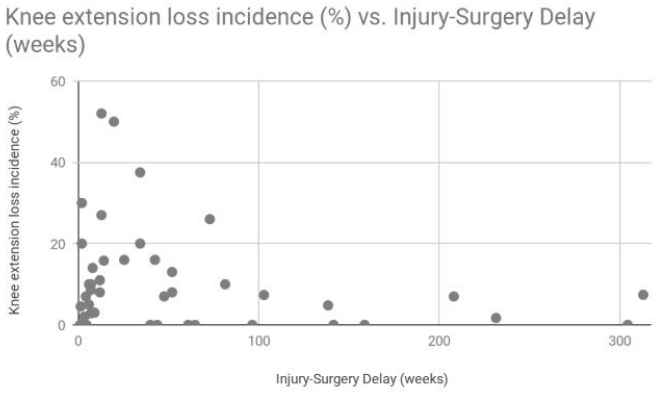

Figure 1: Relationship between loss of extension incidence and injury-surgery delay following ACL reconstruction.

CONCLUSIONS

The terms knee extension deficit or loss of extension were limited by poor standardisation across the literature. Preliminary analysis identified evidence of the incidence and factors associated with loss of extension after ACL reconstruction; however the trajectory of knee extension deficits were difficult to infer due to discrepancies in measurement techniques and patient population variation. Future work should focus on a standardised framework for postoperative monitoring of knee extension recovery after ACL reconstruction

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BIOMECHANICAL ANALYSIS OF A TISSUE SCAFFOLD AND FIXATION PLATE USED FOR MANDIBULAR RECONSTRUCTION

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INTRODUCTION

The reconstruction of segmental mandibular defects through the use of tissue scaffolds and fixation devices remains a major challenge for maxillofacial rehabilitation. Controlled mechanobiological environment signifies an important condition for proper cell differentiation, proliferation and bone regeneration. However, biomechanical stabilisation of the tissue scaffold with respect to the surrounding bone is crucial to preventing fibrous tissue formation, which can inhibit bone regeneration and rapid healing from implantation.

Titanium (Ti-6Al-4V) fixation plates and screws have a high mechanical strength, making them suitable for providing biomechanical stabilisation to the tissue scaffold and mandibular system. However, an unintended consequence of using metallic plates is that they can cause stress shielding, potentially leading to the reduction in bone density where the physiological loading is removed from the bone by the implanted metallic plate. Often, stress shielding can be caused by the stiffness mismatch between titanium and bone [1].

Stress shielding can also cause less uniform stress distribution within the scaffold, which can result in stress concentrations and potentially lead to fracture of the load-bearing scaffold as well as disrupted bone regeneration. Uneven stress distribution is more critical to the mandibular structure due to its highly sophisticated biomechanics in comparison with other bones in the body such as long bones, which are mainly subjected to longitudinal loads.

The objective of this study is to analyse the distribution of stress in a mandibular scaffold – bone system by using numerical methods. It will specifically assess the role of the fixation plate in influencing the mechanobiological conditions for ensuring tissue regeneration. The result is expected to provide a guideline for the design of both the fixation plate and the scaffold for mandibular tissue engineering.

METHODS

The patient specific computer tomography (CT) data is used to create the mandible model using ScanIP with site-dependent heterogeneous material properties (Fig. 1). The specific Hounsfield Units (HU) values and associated bone density were used to derive the Young's modulus at different sites of the mandible.

The tissue scaffold is designed in Solidworks for additive manufacturing (Robocast). Orthotropic configuration of struts is adopted to construct the detailed scaffold structure. The scaffold is fit to the mandibular bone profile.

The model reconstructed in ScanIP is transferred to commercial code Abaqus for finite element analysis, which will determine the stress and strain energy distribution in both mandibular bone and scaffold under mastication. The mechanical load carried by the fixation device is characterized by examining its effects on the biomechanical environment of the bone and scaffold.

RESULTS AND DISCUSSION

Preliminary findings of this study indicate that the attachment of the fixation plate can alter the distribution of stress in the scaffold. High stress regions (coloured in green) occurred on the lower margin of the scaffold and less stress (coloured in blue) is experienced in the middle and upper areas (see Fig. 1).

The areas of high stress concentration (lower margin of the scaffold) may be of a higher risk of failure under loading. The geometry and configuration of the fixation construct may be optimised to reduce stress concentration in the lower margin of the scaffold, thereby stabilising the scaffolding system more effectively. In addition, the optimised fixation system results in a more homogenous strain distribution and consequently better bone formation outcome.

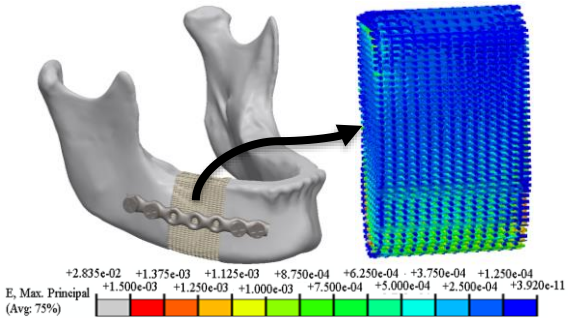

Fig. 1: Scaffold/fixation plate for mandibular reconstruction (left); and stress in scaffold under mastication (right)

CONCLUSIONS

The fixation plate largely affects the mechanical conditions of scaffold and bone in the mandible. The results can help optimise the design of the system for additive manufacturing.

ACKNOWLEDGEMENT

Australian Research Council (ARC) Training Centre for Innovative BioEngineering.

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COMPARISON OF CLINICAL OUTCOMES BETWEEN PATELLA RESURFACING VERSUS NONRESURFACING IN PRIMARY TOTAL KNEE ARTHROPLASTY; A PROSPECTIVE STUDY OF 360 CASES

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INTRODUCTION

Recently, TKA has been found to achieve a high rate of clinical success, and an important issue in TKA is whether the procedure should include patellar resurfacing. The aim of this study was to compare clinical outcomes between patellar resurfacing and nonresurfacing in total knee arthroplasty (TKA).

METHODS

Data from osteoarthritis patients who underwent TKA, and were followed up for ≥ 4.5 years were analysed retrospectively. Patients were divided into two groups: patellar nonresurfacing group and patellar resurfacing group. In the Nonresurfacing group, the partial lateral facet of the patella was removed, the patella was reshaped to match the trochlea of the femoral prosthesis and circum patellar denervation was performed. In the resurfacing group, the patella was resurfaced with a cemented component. Clinical outcomes included incidence of anterior knee pain, Knee Society Score, patient satisfaction, revision rate and radiographic findings. Fisher's exact test was used to assess nominal data including the incidence of AKP, patient satisfaction score, and revision rate. P values < 0.05 were considered to be statistically significant.

RESULTS AND DISCUSSION

Totally 360 patients were evaluated including 198 cases assigned to the nonresurfacing group and 162 to the resurfacing group. Mean age of two groups had statistically significant difference but BMI showed not to be statistically significant different between two groups. There was significant difference between two groups for measured clinical outcomes such as Oxford Knee Score (OKS). Clinical outcomes for patellar nonresurfacing, including patelloplasty and circumpatellar denervation, showed to be different to those for patellar resurfacing, in TKA.

CONCLUSIONS

Patellar nonresurfacing (including removal of patellar osteophytes, patellar partial lateral facetectomy and circumpatellar denervation) can obtain satisfactory outcomes in TKA. In addition, patellar nonresurfacing can easily be converted to patellar replacement, if AKP cases.

ACKNOWLEDGEMENTS

The authors of this study acknowledge helps of Mirhosseini hospital staff for gathering data.

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Table 1: Tables may extend across both columns, and those should be included at the bottom of the proceeding.

Variables	Resurfacing Group N=162	Non-Resurfacing Group N= 198	P-value
Age	59.83±0.89	58.7±0.7	0.003
BMI[a]	24.84±0.33	24.51±0.35	0.184
Surgery Duration	76.7 ± 29.5	72.7 ± 32.6	0.072
OKS[b]	39.56±0.36	37.21±0.31	0.000
OKSA[c]	22.89±0.59	21.02±0.31	0.000
OKSF[d]	17.09±0.18	16.19±0.19	0.000

BIOMIMETIC BONE PRECURSOR NANOPARTICLES ENHANCE ANGIOGENESIS AND OSTEOGENESIS IN VITRO.

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INTRODUCTION

Calcium phosphates are inorganic compounds composed of calcium cations and phosphate anions, naturally found in approximately 60% of all human bones in the form of semi-crystalline carbonated hydroxyapatite nanocrystals, and responsible for bone stiffness. Due to their osteoconductive and chemical similarity to the inorganic part of the bone, calcium phosphates have been widely used as the backbone formulation to fabricate synthetic bone grafts for the treatment of bone defects [1]. Here in, we have developed a novel type of calcium phosphate nanoparticles (NPs) (CaP), by mimicking bone forming precursors particles involved in the bone mineralization process. CaP nanoparticles are amorphous and porous with the hospitable structure to be doped with various bioactive elements or incorporated with large and small biomolecules. Moreover, to promote vascularization, which is a crucial step in bone repair, we have incorporated a trace amount of lithium ions between calcium and phosphate atoms of CaP, labeled as Li-CaP [2].

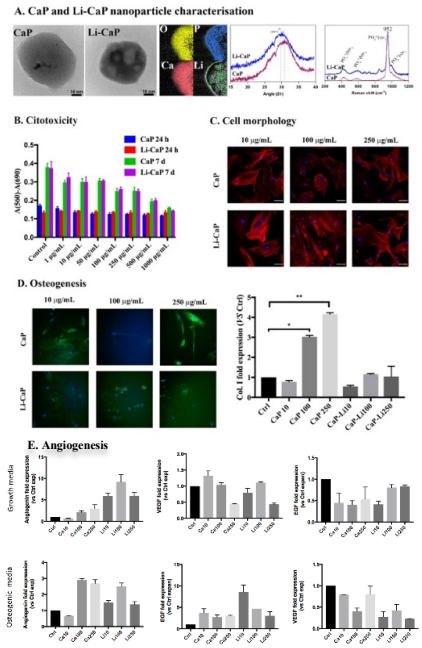

Figure 1:NPs characterization (A), hMSC co-culture with CaP and Li-CaP cell viability (B), cell morphology (C), and cell differentiation (D, E). Scale bars: 100 μm.*p<0.001, **p<0.0004.

METHODS

Human bone marrow-derived stem cells (hMSC) were seeded at 5000 cells/cm^2 on standard tissue culture plates. After 24 h, either CaP or Li-CaP were added at different concentrations, to assess cell viability, cell adhesion, and osteogenic differentiation.

RESULTS AND DISCUSSION

CaP has similar characteristics to the amorphous calcium phosphate complexes secreted from osteoblasts that form inorganic part of bone extracellular matrix (Fig. 1A). Nanoparticles did not show toxic behavior. Cell proliferation regime was dependent on CaP and Li-CaP concentrations (Fig. 1B). The metabolic activity threshold for choosing the appropriate NPs concentrations was set to 80% about the control. When cells were co-cultured with the NPs up to 28 days, they maintained their elongated shape, typical of hMSC cultured *in vitro* (Fig. 1C). Moreover, when osteogenic supplements were provided in culture media, the synergistic effect of regulation of osteogenic markers, such as Runx2 and osteocalcin in Li-CaP (data not shown) and increased evidence of collagen type I was noticed in CaP groups (Fig. 1D). In growth media, angiogenesis was upregulated by Li-CaP nanoparticles and, in osteogenic media, CaP nanoparticle only had a mild effect on angiogenesis, but much less compared to growth media, suggesting that osteo media is inhibiting angiogenesis.

CONCLUSIONS

Altogether, our results show the great potential of CaP and Li-CaP nanoparticles for bone regeneration and inherent angiogenesis.

ACKNOWLEDGEMENTS

Authors would like to thank the financial support from the National Health and Medical Research Council (NHMRC) (GNT1111694 and GNT1141602).

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DEVELOPING AN IN VITRO SYSTEM FOR STUDYING TENDON CELL RESPONSE TO STIFFNESS AND STRUCTURE

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INTRODUCTION

Tendons are a major load bearing tissue in the body, and play a crucial role in locomotion. The major component of tendons is collagen, which is present in a highly organized and aligned structure. The alignment of the collagen matrix provides the mechanical strength for the tendon, and also directional cues for the tendon cells (tenocytes) residing in the matrix, with tenocyte behavior regulated by the matrix biochemistry and biomechanics.

In vitro study of tenocytes exposes the cells to a non-physiological microenvironment, where tenocytes are cultured in plastic tissue culture dishes which have a very high stiffness, and do not provide any architectural cues. In this study we aim to prepare an in vitro model that closely mimics the tendon microenvironment from tendon slices imprinted in PDMS.

PDMS is used in various micro-fabrication methods for preparing biological systems. The stiffness of the PDMS gel can be tuned by altering the cross-linker concentration.

Here, we have prepared tendon imprints using PDMS that mimics the architecture and stiffness of the tendons. The effect of matrix anisotropy on tenocyte morphology and growth rate was explored.

METHODS

Bovine tendons were cut into 10 mm^2 cross-section and 0.3mm thickness slices using a cryo-microtome. The stiffness of the tendon slices were measured by AFM indentation.

PDMS gels were mixed with curing agent in 4 different w/w ratio (5:1, 10:1, 15:1, and 20:1) to alter their stiffness. The stiffness of these gels were measured by AFM indentation to identify appropriate cross-linking ratio to match the PDMS stiffness with the tendon stiffness.

To create imprints of the tendon the different stiffness PDMS/ cross-linker mixtures were poured onto the tendon slices and cured at 80°C for 2 hrs. The PDMS cast the negative imprint of the tendon slice. The positive imprint was achieved by casting the PDMS/cross-linker onto the PVP coated negative tendon imprint. The architecture of the tendon slices and tendon imprints were imaged using SEM and AFM AC-air mode imaging (Figure 1.A).

For cell culture the positive PDMS imprints were coated with collagen-I solution and washed with PBS. Tenocytes were cultured onto these collagen-I coated tendon imprints for 24 and 48hrs and visualised after fluorescent staining of the cells.

RESULTS AND DISCUSSION

The stiffness of the tendon slices were ~1.2MPa. The PDMS gel stiffness increased with increasing crosslinking concentration and varied from 800kPa-3MPa.

AFM indentation results show that the PDMS imprints with a PDMS:cross linker concentration 15:1 have stiffness similar to the tendon stiffness.

AFM scanning and the SEM images show the tendon imprints mimic the highly anisotropic structure of the tendon at the micro-level, however they fail to capture nano-scale features of the tendon slices (Figure 1.B, 1.C).

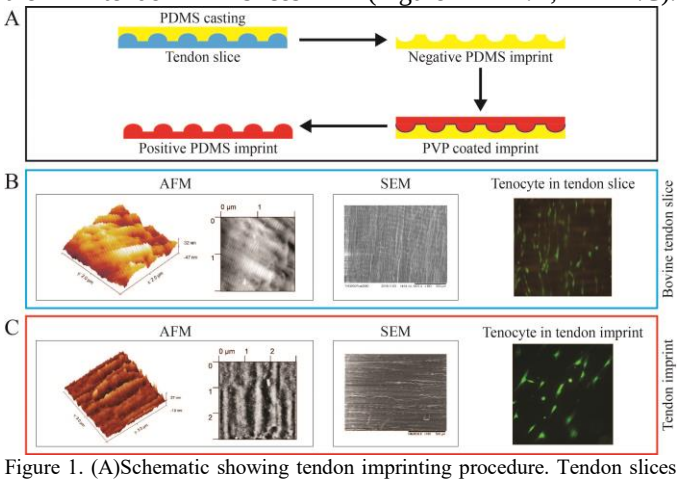

Figure 1. (A)Schematic showing tendon imprinting procedure. Tendon slices are imprinted from bovine tendon slices. The imprints mimic the architecture of the actual tendon. (B), (C) Comparison of AFM and SEM imaging of native tendon slices and negative tendon imprints. Tenocytes on tendon slice and tendon imprints respond to the topography and get aligned. Calcein staining of tenocytes depicting the alignment of tenocytes.

When cultured onto the collagen coated tendon imprints the tenocytes are more elongated and get aligned in the direction of the fibers (Figure 1.B, 1.C). However, on the tissue culture dishes tenocytes orient randomly and the cell shape is dependent upon the cell density.

CONCLUSIONS

The proposed tendon imprints closely mimic the mechanical properties and provides similar directional cues to the native tendon. The versatility of PDMS allows us to explore a wide range of stiffness values by changing the cross-linker concentration, thus allowing us to change the matrix stiffness and architecture independently. During tendinopathy the matrix stiffness increases and become less organized. The effect matrix structure and stiffness on tenocyte behavior will be further studied using this technique.

ACKNOWLEDGEMENTS

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CAN WE PREDICT WHICH PATIENTS ARE NOT FULLY COMPLIANT WITH PATIENT REPORTED OUTCOMES? AN ANALYSIS OF TWO THOUSAND PATIENTS IN CLINICAL PRACTICE

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INTRODUCTION

Patient drop-out and missing data are a common source of bias in longitudinal clinical studies, as they often arise from non-random effects [1,2] Thus closer monitoring of common characteristics associated with patients who return incomplete data may allow researchers to refine their recruitment and data collection procedures to ensure the data is of adequate quality. In particular, there is limited guidance with respect to electronic data capture in private practice and judgements regarding allocation of resources to retrieving patient-reported outcome measures (PROMs) data are often based on stereotypes lacking substantive evidence. The aim of this study was to assess the relationship between patient factors and full compliance for electronic PROMs either in clinic or at home via email.

METHODS

A quality controlled clinical patient registry was planned and implemented into a private clinic, comprising thirteen observational, prospective cohort studies of upper limb pathologies. Patients eligible for intervention were recruited to the registry and asked to complete electronic forms via a link sent by email or at their clinic visit prior to treatment with a tablet. Patients were classified as *Shoulder, Elbow* or *Hand-Wrist* relative to their presenting pathology and those that missed at least one questionnaire were classified as *Missing*. The dataset (N = 1997 patients) was extracted from the registry database (Socrates v3.5, Ortholink Pty Ltd, Aus) and a binary logistic regression model developed to link patient (Age, Gender, Type of presentation, Date of Presentation) and injury factors (side, joint) with the *Missing* classification.

Table 1: Logistic regression results for patients missing at least one PROM at pre-treatment consultation

Predictor	Odds Ratio	95% CI	P-value
Joint (vs shoulder)			0.003
Elbow	0.67	(0.48 - 0.94)	
Hand	0.64	(0.47 - 0.88)	
Date of Exam	0.98	(0.96 - 0.99)	<0.001

RESULTS AND DISCUSSION

Logistic regression revealed a significant association between which joint the patient presented for assessment and PROMs compliance, that is, elbow and hand-wrist patients were at lower risk of partial compliance with the PROMs pack compared to shoulder patients. This may be attributed to the lower number of questionnaires in total (between 2 and 3) for these patients compared to the shoulder patients (between 4 and 6). In addition, more recent date of examination was associated with a significant, but small, improvement in compliance independent of other factors, which may reflect the evolution in processes to capture PROMs over time. Nevertheless, the lack of significant association with any other factors indicates that other unknown factors remain to be accounted for in establishing the likelihood of a patient completing a set of PROMs by electronic data capture.

CONCLUSIONS

There remains insufficient information to accurately predict which patients may not be fully compliant with PROMs associated with treatment of upper limb pathologies. The results of the present analysis suggests that the number of questionnaires presented in a pack may have a role in patient compliance and should be investigated further.

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CONFLICT OF INTEREST DECLARATION

In the interests of transparency and to help reviewers assess any potential bias, all authors of original research papers are required to declare any competing commercial interests in relation to the submitted work. Referees are also asked to indicate any potential conflict they might have reviewing a particular paper.

If you have accepted any support such as funds or materials, tangible or intangible, concerned with the research by the commercial party such as companies or investors, choose YES below, and state the relation between you and the commercial party.

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1. The author(s) did receive payments or other benefits or a commitment or agreement to provide such benefits from a commercial entity.

MC, ME, NE and CS are paid employees of EBM Analytics, and were paid by the senior author (HC) for the completion of this work.

PATTERNS IN PATIENT-REPORTED OUTCOMES REVEALED BY MACHINE LEARNING IN PATIENTS PRESENTING WITH ANTERIOR CRUCIATE LIGAMENT RUPTURE

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INTRODUCTION

Selection for anterior cruciate ligament (ACL) reconstruction requires careful consideration of an individual patient's functional demands and lifestyle [1]. Successful treatment is benchmarked by patient reported outcome measures (PROMs) or return to preinjury sports level influenced by a complex interplay of physical, psychological and sociological factors [2]. The advent of online clinical registries allow for the collection of large volumes of data across several patient reported domains [3]. Analysing these registries provides the key to a more comprehensive understanding of how to optimise treatment for ACL rupture [3]. The aim of this study was to identify subgroups of patients based on their responses to multiple PROMs at the time of diagnosis and decision to undergo ACL reconstruction.

METHODS

Patients presenting with ACL rupture and electing to undergo reconstruction under the care of an orthopaedic surgeon at a metropolitan public hospital were enrolled in a quality-controlled clinical registry. The VR-12 physical and mental total scores, Tegner Activity Rating and IKDC total score (%) were extracted from the electronic registry. A machine learning approach (k-means) was used to identify subgroups based on the similarity of questionnaire responses. The average scores in each cluster were compared using ANOVA (Kruskalwallis) and nominal logistic regression was performed to determine the relationship between cluster membership and patient age, gender, BMI and injury to examination delay.

RESULTS AND DISCUSSION

A sample of 107 patients with ACL rupture were extracted, with 84 (79%) available for analysis with complete datasets. Four subgroups (clusters) were identified with distinct patterns of responses to the questionnaires. They ranged from the lowest scores for VR-12 and IKDC (Cluster 1) to the highest scores for VR-12 and IKDC (Cluster 4). In particular, Cluster 4 returned average scores (median 70.1, IQR 59 - 78) that were within 10 points of the patient acceptable symptom state of the IKDC score. Significant ($P<0.05$) differences in average scores between all clusters was observed. However, cluster membership was not significantly ($P>0.05$) associated with patient age, gender, BMI or injury to examination delay.

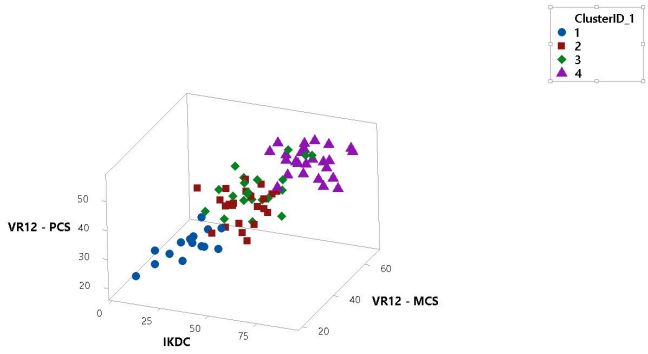

Figure 1: Illustration of patient responses organised by cluster and plotted in three-dimensional space

CONCLUSIONS

Patients undergoing ACL reconstruction do not conform to a homogenous group but instead represent a spectrum of functional deficits, general health and pre-injury activity, which may not lend itself to uniform surgical and rehabilitation protocols. The factors driving these distinct responses to PROMs remain unknown, but are not related to common patient demographic variables.

ACKNOWLEDGEMENTS

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IS SAFE SHORT-STAY TOTAL KNEE REPLACEMENT POSSIBLE IN A REGIONAL HOSPITAL? FACTORS ASSOCIATED WITH HOSPITAL LENGTH OF STAY IN 362 CASES

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INTRODUCTION

Regional hospitals are subject to unique patient demographics and admissions from a wide geographic area [1,2]. Thus, attempts to optimise patient flow through routine arthroplasties should consider the unique characteristics of their patient populations that affect their length of stay (LoS). The aims of this study were to: 1) quantify reduction in hospital LoS for TKA in a regional hospital, 2) identify patient, surgical and management factors associated with hospital LoS, and 3) assess the change in complications incidence and hospital readmission as a function of LoS.

METHODS

A retrospective chart review was conducted on a consecutive series of primary and revision TKAs from January 2012-March 2018. Factors describing patient demographics, and preoperative, intraoperative, surgical and postoperative management were extracted from paper and electronic medical records. Multivariate linear regression assessed the association between these factors and LoS. In total, 362 procedures were included, reduced to 329 admissions with simultaneous bilateral procedures taken into account.

RESULTS AND DISCUSSION

Median LoS reduced significantly (P=0.001) from 6 to 2 days over the reviewed period. Stepwise regression analysis identified patient characteristics (age, gender, comorbidities, discharge barriers), perioperative management (anaesthesia type), surgical (approach, alignment method) and postoperative management (mobilisation timing, postoperative narcotic use, complication prior to discharge) as factors explaining 58.3% of variance in LoS. Re-presentation to emergency and hospital readmission remained low.

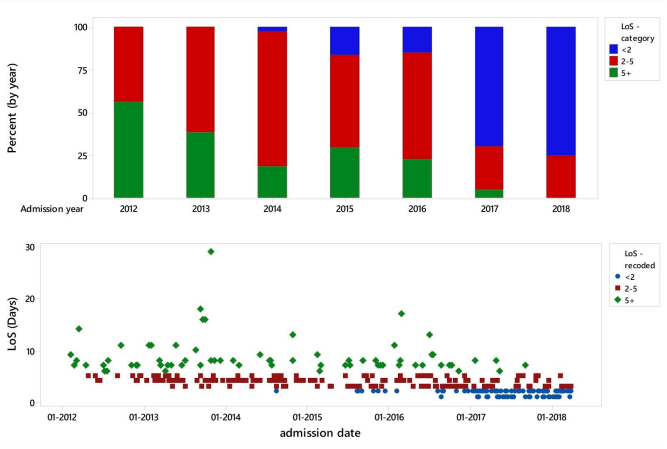

Figure 1: Length of stay categorised over time coded for LoS category as a % of admission for each year of review (top) and over time by category (bottom)

CONCLUSIONS

Efforts to reduce hospital LoS following TKA within a regional setting is achievable over time without significant increases in the rate or severity of complications, or representation to acute care and subsequent readmission. The findings establish the role of patient, surgical and management factors in the context of agreed discharge criteria between care providers.

ACKNOWLEDGEMENTS

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IS SHORT-STAY TOTAL KNEE REPLACEMENT ASSOCIATED WITH SUBJECTIVE AND OBJECTIVE PATIENT FUNCTION? A PROSPECTIVE OBSERVATIONAL SERIES WITH 6 WEEK FOLLOW UP

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INTRODUCTION

The capacity to support shorter hospital stay in elective joint arthroplasty is typically associated with large metropolitan hospitals. However, regional hospitals are subject to unique patient demographics and admissions from a wide geographic area [1,2]. Nevertheless, the relationship between shorter stay and short-term outcomes after total knee arthroplasty (TKA) have yet to be assessed in the regional setting. The aims of this study were to i) establish the change in subjective and objective function after short-stay (average 2 days) TKA and ii) establish the relationship between length of stay and subjective and objective measures of patient function at 6 weeks follow up.

METHODS

A prospective observational cohort study was conducted on a consecutive series TKAs from March -August 2018 to June 2019 within a medium-sized public hospital department. Oxford Knee Score, Timed Up and Go (TUG) and 6 -Minute Walk Test (6MWT) were administered by the physiotherapy department before TKA admission and at the 6-week postoperative clinic. A sample (N = 60, 54% female) were assessed for changes in functional scores using paired t-tests. Univariate (spearman rho) and ordinal logistic regression was used to assess the relationship between length of stay (LoS) and whether patients exceeded the patient acceptable symptom state (PASS) [3] and minimal clinically important difference (MCID) of the TUG [4] and 6MWT [5].

RESULTS AND DISCUSSION

LoS ranged from 1 - 8 days, with a median of 3 (IQR 2 - 4). At 6 week follow up, a significant (P<0.001) increase in OKS (20.4 vs 32.5) was observed with 28% exceeding the OKS PASS. A significant (P<0.01) relationship was observed between LoS and OKS at 6weeks (rho = -0.39, Figure 1). However, LoS was not associated with OKS PASS (P = 0.15), TUG MCID (P = 0.8) or 6MWT MCID (P = 0.22). In addition, Timed Up and Go and 6-Minute Walk Test results were inconclusive, with significant improvements at group and individual level below MCID. Six week followup may be too early to establish conclusive improvements in objective function in generally well functioning patients, whereas the relationship between LoS and TUG has been previously established in a cohort with a wider range of LoS (1-15 days) [6].

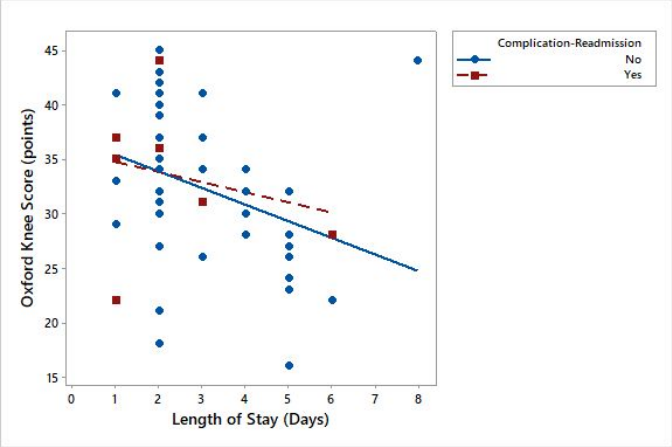

Figure 1: Association between LoS and OKS at 6week follow up, categorised by complication status.

CONCLUSIONS

Reducing LoS within a regional hospital does not lead to adverse early subjective or objective functional postoperative outcomes in patients undergoing TKA.

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EFFECTIVE PLANNING AND STAKEHOLDER ENGAGEMENT KEY TO REGISTRY SUCCESS: LESSONS LEARNED FROM IMPLEMENTATION OF ORTHOPAEDIC REGISTRIES

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INTRODUCTION

Clinical registries are important in monitoring healthcare processes and outcomes, and establishing treatment benchmarks [1]. However, a number of barriers affect the successful implementation of a registry and its quality [2]. This investigation aims to report on the lessons learned from our experience of implementing five orthopaedic registries, and identify key factors affecting registry success and quality.

METHODS

The registries were implemented in three interconnected stages: 1) establishing cohort questions and core datasets, 2) configuration of the systems, audit processes and ethical and governance framework, and 3) documentation of protocols and user training (Figure 1). The performance of the registries to date was reviewed to identify the key inputs required for each stage, and the effect they had on registry quality.

RESULTS AND DISCUSSION

The registries were implemented in a median of 7 months and tracked a median of 7 observational cohorts. Number of cohorts, number of stakeholders and clinical load were important, but not determining factors of registry success. Participating surgeon input was identified as critical to Stage 1, stakeholder (IT and software providers, device companies, staff) engagement was critical to Stage 2, and Stage 3 was wholly dependent on preceding stages and a commitment to registry maintenance and integrity.

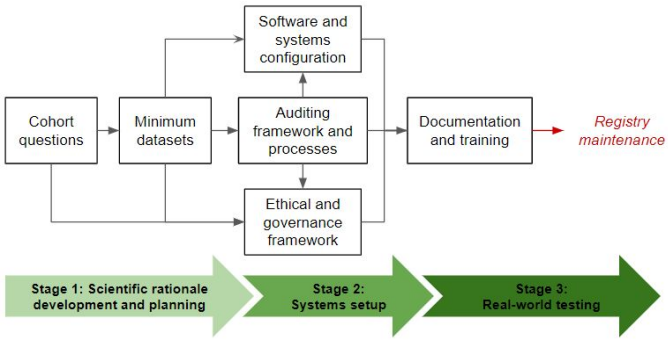

Figure 1: Key stages of implementing a clinical registry

Lack of surgeon input in early stages, particularly for multi-surgeon registries, significantly impacted registry quality. In one registry, compliance for outcome measures and functional tests were on average 11-45% lower for the surgeon who provided less input during planning, compared to the more involved clinician. Even with sound scientific planning, registry systems require ongoing updates and modifications to rectify deficiencies and re-align the registry with clinical interests, with some changes having a knock-on effect on all components (Figure 2). In a 12 month period, the two largest registries required an average of 43 major process modifications.

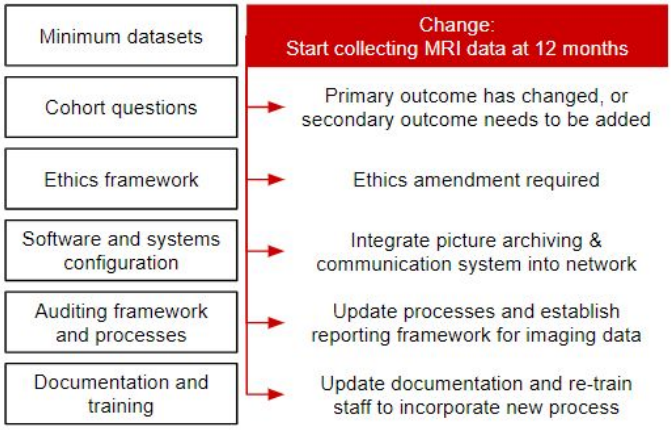

Figure 2: The complexity of technical or process modifications that affect all aspects of the registry

User engagement, feedback and adequate training was critical in the final stage to establish registry quality. In one registry, intraoperative data compliance improved by up to 29% after issues with data entry were identified in the first quarter of operation, and rectified in the second quarter. Compliance in the subsequent quarters remained relatively stable.

CONCLUSIONS

Setting up a clinical orthopaedic registry is a complex process, involving the integration of several moving and often evolving components. Effective planning and active stakeholder and user engagement and feedback are critical to the success of the registry, regardless of its size and complexity.

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A COMPARATIVE STUDY OF COMPONENT POSITIONING IN TOTAL HIP ARTHROPLASTY BY SURGICAL TECHNIQUE, PATIENT POSITIONING AND GUIDANCE MODALITY

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INTRODUCTION

Data regarding the effects of technique evolution on component placement and biomechanics in total hip arthroplasty (THA) are currently lacking [1,2]. The aim of this study was to determine differences in hip joint centre (HJC) location, hip offset (HO) and leg-length (LL) with varying surgical approach (posterior, anterolateral muscle-sparing), patient position (lateral decubitus vs supine) and intraoperative guidance (manual instrumentation, image intensification, patient-specific guides) in primary THA.

METHODS

A retrospective analysis of a prospective, observational cohort (N = 97) was performed on postoperative anteroposterior (AP) pelvic radiographs. THAs where a full-length cemented or cementless femoral component was implanted, were included in the analysis. Patients were categorised into one of three groups based on the combination of approach, position and guidance modality. HJC, HO, and LL were calculated for the operated and contralateral hips and the difference (D) calculated (Figure 1).

RESULTS AND DISCUSSION

No between-group differences were detected for patient characteristics including age, gender, body mass index (BMI), or median between-limb differences, between-patient variability or incidence of outliers exceeding 5mm or 10mm thresholds. Binary logistic stepwise regression revealed that younger age, male gender and increased BMI were significantly ($P<0.05$) associated with an increased risk of LL-D >5mm.

CONCLUSIONS

The ability to accurately position components during THA and match the biomechanics of the contralateral hip may not be primarily driven by surgical factors, but may rather represent an interaction between surgical factors and patient factors. Further work is required to confirm these relationships in a larger, more diverse sample.

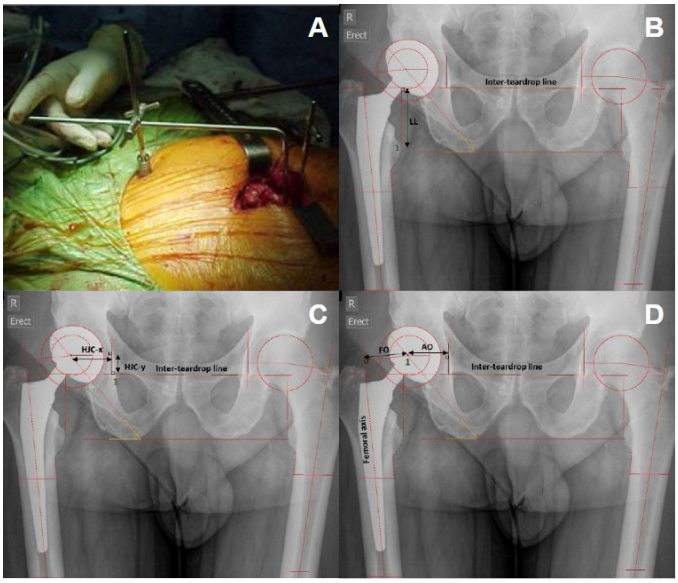

Figure 1: (A) Manual intraoperative LL confirmation; (B) trochanteric method of measurement of LL [3] on radiographs, as well as (C) hip joint centre (D) HO [4]. FO: femoral offset, AO: acetabular offset.

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The authors wish to acknowledge the efforts of Angela Wilbow, Claire Sinclair, Jessica Boh and Nalan Ektas for their efforts with data collection and study administration.

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DO PATIENTS NEED TO BE FOLLOWED UP ANNUALLY AFTER METAL-ON-METAL HIP RESURFACING? AN OBSERVATIONAL COHORT STUDY WITH AN AVERAGE FOLLOW-UP OF 10 YEARS

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INTRODUCTION

The Birmingham Hip Resurfacing (BHR) system is one of a small number of metal-on-metal resurfacing designs still in use to treat hip degenerative disorders. Patient reported outcome measures (PROMs) have been largely positive overall following BHR [1,2], although predictors of poor outcomes have not been examined in detail. There is little guidance regarding the need for long-term clinical follow-up in these patients with respect to length, frequency and domains of interest. In addition, it is not known whether change in patient reported outcomes over time can be predicted by factors present at surgery, or early follow-up. The aim of this study was to identify factors associated with changes in PROMs status between 2-year evaluation and medium-term follow-up.

METHODS

Patients undergoing Birmingham Hip Resurfacing completed the Veteran's Rand 36 (VR-36), modified Harris Hip Score (mHHS), Tegner Activity Score and Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) at 2 years and a minimum of 3 years. Pre-postoperative change was assessed against minimal clinically important difference (MCID) and patient acceptable symptom state (PASS) thresholds [3-5]. Binary logistic regression was used to assess the relationship between patient factors and deterioration in PASS status between follow-ups. The predictive classification accuracy of the model was assessed by calculating the area under the curve (AUC) of the receiver operating characteristic.

RESULTS AND DISCUSSION

Overall, 18% of patients reported reductions in mHHS total score exceeding MCID, and 20.6% reported similar reductions for WOMAC function scores. Nonetheless, almost all patients remained above PASS thresholds for WOMAC function (97.8%) and mHHS (93%). 66% of patients with mHHS scores <PASS at 2 years reported scores >PASS at latest follow-up. Conversely, 5.7% of patients deteriorated from >PASS to <PASS between follow-ups. Multivariate modelling indicated BMI, VR36 PCS, MCS, mHHS at 2 years, female gender and bone graft use predicted these deteriorating patients with 79% accuracy, and AUC of 0.84 (Figure 1).

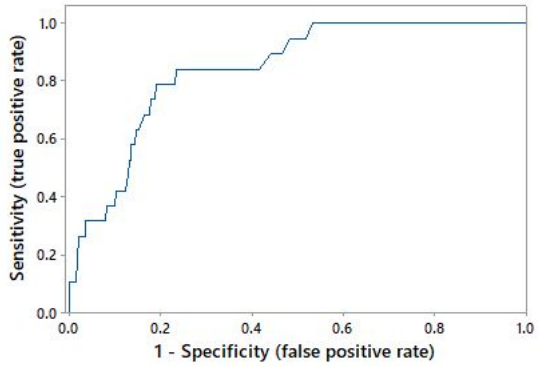

Figure 1: Receiver operator characteristic curve for mHHS PASS status worsening between 2 year and latest follow-up

CONCLUSIONS

Due to largely acceptable results at a later follow-up, extended monitoring of PROMs is not recommended for hip resurfacing patients unless they report borderline or unacceptable hip function at 2 years, are female, are overweight at the time of surgery, or received a bone graft during surgery.

ACKNOWLEDGEMENTS

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A CLINICAL ORTHOPAEDIC REGISTRY FOR MONITORING OUTCOMES WITHIN AN UPPER LIMB CLINIC: A QUALITY ASSESSMENT AND BASELINE REPORT

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INTRODUCTION

Research registries are a valuable source of information for improving patient outcomes [1,2]. However, their efficacy is dependent on the quality of the data contained within [3]. The aim of this study was to assess improvements to data quality over the course of 18 months since the implementation of a patient registry at a multi-surgeon private practice.

METHODS

A quality controlled clinical patient registry was planned and implemented for two surgeons within the same practice, comprising six observational, prospective cohort studies of shoulder and elbow pathologies. Each cohort was defined by a diagnosis, dataset and statistical plan. Data collection procedures were co-developed with clinicians and administrative staff to ensure data was collected in accordance with the relevant dataset and organised into the registry database software (Socrates v3.5, Ortholink Pty Ltd, Aus). Quality controls were implemented to report data completeness and consistency of patients enrolled into the correct cohort. Validation was performed against the clinic practice management system to ensure eligible patients were not missed during consultation lists. Data was extracted at scheduled intervals (3 months) and quality metrics extracted, such as compliance, defined as the ratio .

RESULTS AND DISCUSSION

The first patient was enrolled in July 2017 and the data extracted for analysis in at regular 3-month intervals. Quality auditing revealed that capture into the registry during the prescribed period was between 96.9-100%. Compliance with the predefined datasets for each patient cohort was less accurate, ranging from 9-82.6% and 31.6-88.6% for common preoperative and intraoperative variables respectively. Outlier analysis of continuous variables identified upto 2.8% discrepancies, that were investigated for accuracy. Logic based checks of patient placement into cohort based on diagnosis was also performed with accuracies of 77.6-94.6%. This was investigated further, revealing the major cause to be the use of diagnoses that were not originally included in the audit algorithm.

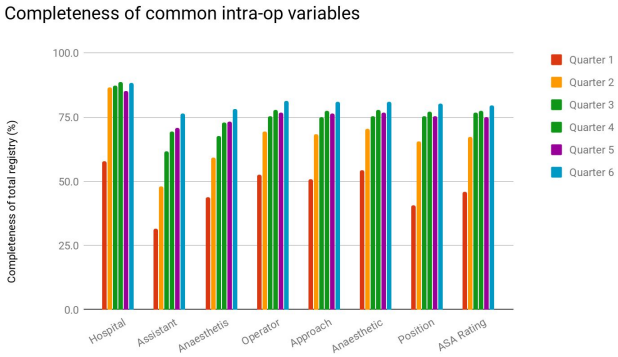

Figure 1: Capture rate of common intraoperative variables across cumulative timepoints

CONCLUSIONS

A quality controlled clinical orthopaedic registry was successfully implemented. Engaging near real-time communication, feedback on quality and targeted process improvements are necessary to achieve quality assurance. Patient registries in an orthopaedic context are powerful tools for care improvement, but should be approached in a holistic and integrated way to ensure that planned analyses are based on quality data.

ACKNOWLEDGEMENTS

The authors acknowledge the assistance of MSEC and EBMA staff, past and present who have assisted with patient recruitment and data collection.

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