Bone Research Society

British Orthopaedic Research Society

4-6 SEPTEMBER 2019

CARDIFF, UK

FINAL PROGRAMME

BONE RESEARCH SOCIETY

and

BRITISH ORTHOPAEDIC RESEARCH SOCIETY

5TH JOINT MEETING


SIR MARTIN EVANS BUILDING

www.brsoc.org.uk

www.borsoc.org.uk

MAP 4 University and City Centre

Cathays Park Campus (* indicates main site)

Aberconway Building	D5	30
Architecture	E4	6
Biosciences	E4	1, 2
Business		
• Aberconway Building	D5	30
• Julian Hodge Building	D5	29
• Postgraduate Teaching Centre	D5	28
Bute Building	E4	6
Careers and Employability	E4	11
Centre for Professional Legal Studies	E4	4
Chaplaincy	E4	10
Chemistry	E4*, E4	1*, 9
Communications and Marketing	F3	20
Computer Science and Informatics	G3	21
Cardiff University Brain Research Imaging Centre (CUBRIC)	D5	33
Day Care Centre	F4	16
Deri House	F3	19
Development and Alumni Relations	F3	19
Earth and Ocean Sciences	E4	1
Eastgate House	G3	22
Engineering	G3	21
English, Communication and Philosophy	E5	27
Estates	G3	23
Eye Clinic	E5	31
Finance	G3	23
Friary House	F3	20
Geography and Planning	E3	7
Glamorgan Building	E3	7
Global Opportunities Centre	E4	11
Graduate Centre	E4	14
Hadyn Ellis Building	E5	32
Park Place Surgery	F4	16
Healthcare Sciences	G3	22
History, Archaeology and Religion	E5	27
Human Resources	G3	23
International Office	F3	20
IT Services	F4	16
John Percival Building	E5	27
Journalism, Media and Culture	E1	13
Julian Hodge Building	D5	29
Law and Politics	E4*, E4	4*, 8
Main Building	E4	1
Mathematics	F4	18
McKenzie House	G3	23
Modern Languages	E4	8
Music & University Concert Hall	E4, E4*	24, 25
Optometry and Vision Sciences	E5	31
Part-time Courses for Adults	F4	18
Pharmacy and Pharmaceutical Sciences	E4	5
Physics and Astronomy	G3	21
Strategic Planning & Governance	F3	20
Purchasing	G3	23
Psychology	E4*, E4	3*, 9
Queen's Buildings	G3	21
Redwood Building	E4	5
Registry	G3	23
Research, Innovation and Enterprises Services	G3	23
Security Centre	E4	2
Sir Martin Evans Building	E4	2
Social Sciences	E3*, E4 , F4	7*, 11, 17
Southgate House	C6	34
Sports		
• Fitness and Conditioning Centre	E4	15
• Sports Fields	Map 2 (over page)	
• Sports Training Village	C6	34
• Studio 49	E4	11
Student Recruitment	F3	20
Student Support Centre	E4	11
Students' Union	E4	14
Temple of Peace	E4	12
Tower Building	E4	3
Trevithick Building	G3	21
Doctoral Academy	F3	20
Welsh	E5	27

Libraries

Aberconway Building	D5	30
Arts and Social Sciences	E4	26
Biomedical Sciences	E4	2
Brian Cooke Dental	Map 5 (over page)	
Bute and Architecture	E4	6
Health Library	Map 5 (over page)	
Law	E4	26
Music	E4	25
Science	E4	1
Senghennydd	F4	18
Trevithick Building	G3	21

Residences

Aberconway Hall	D5	58
Aberdare Hall	D4	60
Cartwright Court	F6	57
Colum Hall	D5	59
Gordon Hall	F4	64
Hodge Hall	E5	61
Liberty House	D8	50
Roy Jenkins Hall	E6	56
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Additional Information

All Nations Centre	C8	101
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Motorpoint Arena	F2	117
Welsh Government Offices	E4	104
Hospital		
University Hospital	D9	100
Attractions		
Cardiff Castle	E3	111
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St. David's Hall	F2	112
Sport		
Athletic Stadium	Map 2	119
Cardiff Blues RFC	E2	113
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Cardiff RFC	E2	114
Cardiff Tennis Club	E3	110
Sophia Gardens	C4	105
Maindy Pool	C6	102
Principality Stadium	E2	115
Welsh Institute of Sport	D4	106

BRS CLINICAL TRAINING COURSE

OSTEOPOROSIS
& OTHER METABOLIC BONE DISEASES

6-8 APRIL 2020, MERTON COLLEGE, OXFORD, UK

This annual 3-day residential training course provides trainees in medical specialties such as rheumatology, endocrinology, care of the elderly, gastroenterology, orthopaedics, respiratory medicine and clinical chemistry with the knowledge and understanding to manage patients with osteoporosis and other metabolic bone diseases.

The course focuses on practical issues relating to patient management and is strongly recommended for any trainee who foresees that patients with these disorders will form a significant part of their workload in future.

Specialist nurses in osteoporosis and falls will also find this course valuable, as well as newly qualified consultants or others wishing to update their knowledge.

TOPICS INCLUDE:

- Underlying physiology of osteoporosis and other metabolic bone diseases
- Identification of signs and symptoms
- Diagnosis
- Treatment options
- Follow up assessment
- Prevention strategies
- Clinical cases

For more information please visit our website or email ***events@boneresearchsociety.org***

FACULTY AND ORGANISING COMMITTEE

CHAIRS:

Tash Masud *(Nottingham, UK)*

Jon Tobias *(Bristol, UK)*

Bo Abrahamsen *(Holbæk, Denmark)*

Emma Clark *(Bristol, UK)*

Cyrus Cooper *(Southampton/Oxford, UK)*

Adam Darowski *(Oxford, UK)*

Kassim Javaid *(Oxford, UK)*

Richard Keen *(Stanmore, UK)*

Nicola Peel *(Sheffield, UK)*

Mike Stone *(Cardiff, UK)*

David Wilson *(Oxford, UK)*

SOME COMMENTS FROM THOSE WHO ATTENDED PREVIOUS COURSES:

"Fantastic course, probably the best I have ever been on"

"Brilliant course set at the right level, knowledgeable speakers, will definitely recommend it"

"Excellent, relevant course – I have already started recommending it to my peers"

Bone Research Society

British Orthopaedic Research Society

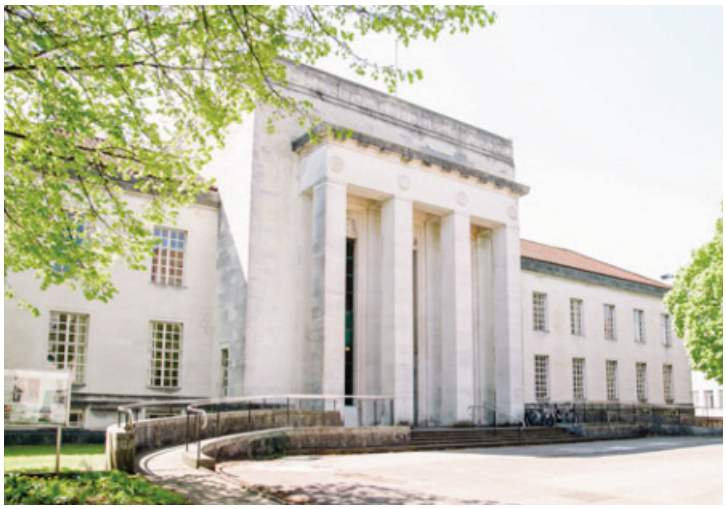
WELCOME

It gives us great pleasure to welcome you to the 5th Joint BRS/BORS Scientific Meeting.

We hope you enjoy the programme of invited talks and free papers, network with fellow musculoskeletal researchers and enjoy the social programme. We also take this opportunity to welcome you to Cardiff.

Our thanks to the joint BRS/BORS organising committee who have been working hard over the last 18 months to put together this meeting.

Bronwen Evans and **Richie Gill**
Co-chairs of organising committee



5TH JOINT MEETING 2019
4-6 SEPTEMBER
CARDIFF, UK

ORGANISING COMMITTEE

Co-Chairs:

Bronwen Evans (Cardiff University)
Richie Gill (University of Bath)
Jim Gallagher (University of Liverpool)
Kassim Javaid (University of Oxford)
Deborah Mason (Cardiff University)
Ines Reichert (Kings College London)
Mike Stone (Cardiff & Vale UHB/University of South Wales)
Mark Wilkinson (University of Sheffield)

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CARDIFF UNIVERSITY
PRIFYSGOL CAERDYDD

AWARDS

NEW INVESTIGATOR AWARDS

New Investigator Awards are awarded prior to the meeting, based on scores achieved during the blind review process of the abstracts

OC2 – Nicholas Fuggle (Southampton, UK)
Which muscle parameters are longitudinally associated with knee osteoarthritis outcomes? Findings from the Hertfordshire Cohort Study.

OC11 – Vee San Cheong (Sheffield, UK)
Predicting cortical bone adaptation in the mouse tibia: a longitudinal study.

OC14 – Lucie Bourne (London, UK)
Understanding the role of L-cysteine and hydrogen sulphide in the beneficial effects of N-acetylcysteine on bone formation and arterial medial calcification.

OC15 – James Fletcher (Bath, UK)
TightRight : augmenting screwdrivers to reduce bone stripping rates and optimise tightness when inserting non-locking screws.

OC18 – Amy Garner (London, UK)
Bi-Unicondylar Arthroplasty preserves healthy gait characteristics and near-normal extensor mechanism efficiency compared to Total Knee Arthroplasty.

OC22 – Alanna Green (Sheffield, UK)
Transforming growth factor (TGF)β inhibition with chemotherapy heals murine myeloma bone disease and improves fracture resistance.

OC28 – Akita Sharma (Southampton, UK)
Molecular imaging modalities reveal pathological matrix disorganisation in whole bone sections and isolated osteoblasts.

PP5 – Hasmik Jasmine Samvelyan (Edinburgh, UK)
Associations between chondrocyte transiency and osteoarthritis pathology.

PP7 – Annie Constable (Exeter, UK)
Determinants of bone mineral content and density in children aged 6-8 years: the PANIC study.

PP17 – Elizabeth Curtis (Southampton, UK)
Higher birthweight is associated with greater limb muscle mass and grip strength in middle age: findings from the UK Biobank Imaging Enhancement.

PP18 – Kartik Logishetty (London, UK)
Measuring Prosthesis Migration using a Novel Ultra-Low Dose CT-Based Method.

PP26 – Scott Dillon (Edinburgh, UK)
A tale of two phosphatases: how do matrix vesicles generate phosphate for bone mineralization?

Bone Research Society and **British Orthopaedic Research Society**
5th Joint Meeting 2019

PROGRAMME OVERVIEW

WEDNESDAY 4 SEPTEMBER

12:00	Registration opens
13:00-15:00	**Mid-Career Development Workshop** *powered by the ORS Ambassadors Program*
15:00-15:30	Refreshment break
15:30-16:45	**Muscle, Tendon and Bone Workshop**
17:00-18:30	**New Investigator Evening**
17:30-18:20	**Public Lecture**
18:45-22:05	**Rare Bone Diseases Workshop and Supper** *supported by Alexion, Kyowa Kirin and Mereo BioPharma*
19:00-21:00	**Biomechanics and Bioengineering Research Centre Versus Arthritis Workshop**

THURSDAY 5 SEPTEMBER

08:30	Registration
09:00-09:15	Welcome and opening remarks
09:15-10:15	**Symposium 1: – Osteoarthritis**
10:15-10:55	**Oral Communications – OA Theme**
10:55-11:55	Coffee and poster viewing (odd numbered posters)
11:55-12:25	**Plenary Lecture**
12:25-12:45	**Poster Pitching**
12:45-13:45	Lunch and Exhibition
13:00	**BRS Annual General Meeting** **BORS Annual General Meeting**
13:45-14:40	**Sponsored Symposium – UCB**
14:45-15:45	**OATech+ Symposium** **Oral communications – Basic**

THURSDAY 5 SEPTEMBER continued

15:45-16:05	Refreshments, Exhibition and Poster viewing
16:05-17:05	**Symposium 2: – Epigenetics** **Symposium 3: – Epidemiology and Health Services Research**
17:05-17:15	Break
17:15-17:45	**Sponsored Symposium – Gedeon Richter**
17:45-18:30	**Debate** *supported by MiLabs*
19:00-00:00	**Conference Dinner** (National Museum Cardiff)

FRIDAY 6 SEPTEMBER

08:00	Registration
08:30-09:30	**Symposium 4: – Cancer and Bone**
09:30-10:00	**Poster Pitching**
10:00-11:00	Refreshments, Exhibition and Poster viewing (even numbered posters)
11:00-12:00	**Oral communications – Clinical** **Oral communications – Basic/Translational**
12:00-12:30	**BRS Dent Lecture** **BORS Presidential Lecture**
12:30-13:30	Lunch and poster viewing
13:30-14:30	**Symposium 5: – Imaging** *supported by ImagingBioPro Network and Scanco* **Symposium 6: – Clinical cases**
14:30-14:40	10 minute break
14:40-15:10	**Plenary Lecture**
15:10-16:10	**Oral Communications**
16:10-16:25	**Awards and closing remarks**

PROGRAMME

5th Joint Conference of the
Bone Research Society (BRS) and **British Orthopaedic Research Society (BORS)**
School of Biosciences, Cardiff University, Cardiff CF10 3AX
4-6 September 2019

WEDNESDAY 4 SEPTEMBER

12:00	*Entrance Foyer, Ground Floor* Registration desk opens
13:00-15:00	*Shared Lecture Theatre, 1st Floor* **Mid-Career Development Workshop *powered* by the ORS Ambassadors Program** Chairs: **Sophie Williams** (Leeds, UK) and **Kassim Javaid** (Oxford, UK)
13:00-13:10	Introduction – **Sophie Williams** (Leeds, UK), **Kassim Javaid** (Oxford, UK) and **Simon Tew** (Liverpool, UK)
13:10-13:20	BRS strategy document – **Kassim Javaid** (Oxford, UK)
13:20-13:50	Life as a mid-career researcher: what happened, what I wish I had known and what I would have changed – **Amy Naylor** (Birmingham, UK)
13:50-14:10	My reflections on what makes a good mid-career researcher – **Tim Arnett** (London, UK)
14:10-14:30	Results of BRS / BORS mid-career survey – **Sophie Williams** (Leeds, UK) and **Kassim Javaid** (Oxford, UK)
14:30-14:50	What is the gap – a discussion
14:50-15:00	Next Steps
15:00-15:30	*Seminar Room E1.22, 1st Floor* Refreshment break
15:30-16:45	*Shared Lecture Theatre, 1st Floor* **Muscle, Tendon and Bone Workshop** Chairs: **Alex Ireland** (Manchester, UK) and **Jolet Mimpen** (Oxford, UK)
15:30-15:55	Tendon Structure, Function and Adaptation in Humans – **Neil Reeves** (Manchester, UK)
15:55-16:20	Making Connections: engineering hard-soft tissue interfaces – **Jennifer Paxton** (Edinburgh, UK)
16:20-16:30	**OC1**, High tibial osteotomy (HTO) and wide stance (WS) gait reduces knee joint loading in individuals with varus knee deformity – **Jake Bowd** (Cardiff, UK)
163:0-16:40	**OC2**, Which muscle parameters are longitudinally associated with knee osteoarthritis outcomes? Findings from the Hertfordshire Cohort Study – **Nicholas Fuggle** (Southampton, UK)
16:40-16:45	General discussion

continued...

WEDNESDAY 4 SEPTEMBER continued

17:00-18:30	*The Lodge, Cardiff University Students' Union, Park Place* **New Investigator Evening –** Round table 'Meet the Expert' Discussions: Organisers: **Elizabeth Curtis** (Southampton, UK), **Hazel Fermor** (Leeds, UK), **Richard van Arkel** (London, UK) and **Dimitris Vlachopoulos** (Exeter, UK) Small project grants Working in industry Clinical academic career Meet the editor/Getting published Bridging the gap Moving abroad for research Improving your online profile Translation pathways (quality management, identifying project partners) Basic science academic career
18:45-22:05	*Temple of Peace, Cardiff CF10 3AP* **Rare Bone Diseases Workshop and Supper** *supported by Alexion, Kyowa Kirin and Mereo BioPharma* Chairs: **Kassim Javaid** (Oxford, UK) and **Ines Reichert** (London, UK)
18:45-19:10	Registration, supper and networking
19:10-19:15	Introduction and setting the scene for rare bone diseases research in the UK – **Kassim Javaid** (Oxford, UK)
19:15-20:00	Rare disease mechanistic insights to therapy – **Brendan Lee** (Houston, USA)
20:00-20:05	**OC3**, Ochronotic pigment distribution in alkaptonuric mice reveals that homogentisic acid deposition in tissues reflects the intensity of mechanical loading – **Juliette Hughes** (Liverpool, UK)
	continued...

17:30-18:20	*Large Chemistry Lecture Theatre, Cardiff University Main Building, Park Place* **Public Lecture** Chairs: **Elaine Dennison** (Southampton, UK) and **Mark Wilkinson** (Sheffield, UK) More than skin deep: how sunlight shapes our bodies and minds – **Linda Geddes** *In conjunction with the BRS Neil MacKenzie Public Engagement award*
19:00-21:00	*Physiology A Lecture Theatre, Ground Floor* **Biomechanics and Bioengineering Research Centre Versus Arthritis Workshop** **'Interdisciplinary research in Osteoarthritis'** Chairs: **Ben Egan** (Cardiff, UK) and **Ilse Jonkers** (Leuven, Belgium)
19:00-19:15	An engineer's perspective – **Gemma Whatling** (Cardiff, UK)
19:15-19:30	A bio-engineer's perspective – **Wayne Ayre** (Cardiff, UK)
19:30-19:45	A biologist's perspective – **Sophie Gilbert** (Cardiff, UK)
19:45-20:00	An orthopaedic registrar's perspective – **Alison Kinghorn** (Cardiff, UK)
20:00-21:00	Light buffet supper and networking

WEDNESDAY 4 SEPTEMBER continued

20:05-20:10	**OC4**, Characterization of Pain in Fibrous Dysplasia – **Tihana Spencer** (Bethesda, USA)
20:10-20:15	**OC5**, Novel use of Burosumab in refractory iron-induced FGF23 mediated hypophosphataemic osteomalacia – **Raj Amarnani** (Oxford, UK)
20:20-20:30	Short break
20:30-21:00	Unanswered orthopaedic issues when treating broken brittle bones – **Fergal Monsell**
21:00-21:30	Rare OI phenotypes: why detailed phenotyping matters – **Meena Balasubramanian**
21:30-22:00	The genetic epidemiology of acquired heterotopic ossification: Prospects for novel treatment strategies? – **Mark Wilkinson** (Sheffield, UK)
22:00-22:05	**LB1**, Imaging Fibrous Dysplasia of bone – **Alan Boyde** (London, UK)

THURSDAY 5 SEPTEMBER

08:30	*Entrance Foyer, Ground Floor* Registration
09:00-09:15	*Shared Lecture Theatre, 1st Floor* Welcome and opening remarks **Bronwen Evans** (Cardiff, UK) and **Richie Gill** (Bath, UK), Chairs of Organising Committee **Professor Andrew Westwell**, Dean of Research and Innovation, College of Biomedical & Life Sciences, Cardiff University
09:15-10:15	*Shared Lecture Theatre, 1st Floor* **Symposium 1: – Osteoarthritis** Chairs: **Bronwen Evans** (Cardiff, UK) and **Richie Gill** (Bath, UK)
09:15-09:45	**IS1**, Comorbidities and Osteoarthritis – **Fiona Watt** (Oxford, UK)
09:45-10:15	**IS2**, Novel strategies in regenerative medicine for musculoskeletal disease – **Andrew McCaskie** (Cambridge, UK)
10:15-10:55	*Shared Lecture Theatre, 1st Floor* **Oral communications – OA theme** Chairs: **Clare Brockett** (Leeds, UK) and **Dimitris Vlachopoulos** (Exeter, UK)
10:15-10:25	**OC6**, Mutations in osteoarthritis susceptibility genes cause functional changes in zebrafish joints that lead to altered load and disease pathology – **Chrissy Hammond** (Bristol, UK)
10:25-10:35	**OC7**, Preclinical diabetes accelerates onset of Osteoarthritis – lessons from model system – **Samuel Joshua Pragasam** (Hyderabad, India)
10:35-10:45	**OC8**, Bi-Unicondylar Arthroplasty preserves the Anterior Cruciate Ligament, retaining near-normal anteroposterior stability in the treatment of medial and lateral tibiofemoral arthrosis – **Oliver Dandridge** (London, UK)
10:45-10:55	**OC9**, Individuals with high bone mass have increased clinical and radiographic progression of knee osteoarthritis independent of fat mass – **April Hartley** (Bristol, UK)
10:55-11:55	*Entrance Foyer area and C0.13, Ground Floor and Seminar room E1.22, 1st Floor* Refreshments, Exhibition and Poster viewing (odd numbered posters)
11:55-12:25	*Shared Lecture Theatre, 1st Floor* **Plenary lecture** Chairs: **Jim Gallagher** (Liverpool, UK) and **Ines Reichert** (London, UK) **IS3**, New therapeutic approaches to OA – **Brendan Lee** (Houston, USA)
12:25-12:45	*Shared Lecture Theatre, 1st Floor* **Poster Pitching** Chairs: **Jim Gallagher** (Liverpool, UK) and **Ines Reichert** (London, UK) **PP1**, High tibial osteotomy (HTO) and wide stance (WS) gait reduces knee joint loading in individuals with varus knee deformity – **Jake Bowd** (Cardiff, UK) **PP2**, Which muscle parameters are longitudinally associated with knee osteoarthritis outcomes? Findings from the Hertfordshire Cohort Study - **Nicholas Fuggle** (Southampton, UK) *continued...*

THURSDAY 5 SEPTEMBER continued

PP3, Ochronotic pigment distribution in alkaptonuric mice reveals that homogentisic acid deposition in tissues reflects the intensity of mechanical loading – **Juliette Hughes** (Liverpool, UK)

PP4, Osteoblast-specific Enpp1 deficiency promotes bone mass whilst worsening the metabolic phenotype – **Fiona Roberts** (Oxford, UK)

PP5, Associations between chondrocyte transiency and osteoarthritis pathology – **Hasmik Jasmine Samvelyan** (Edinburgh, UK)

PP6, Barbara Mawer Travelling fellowship: Associations between endocrine metabolites and bone mineral density in children aged 6-8 years: the PANIC study – **Dimitris Vlachopoulos** (Exeter, UK)

PP7, Determinants of bone mineral content and density in children aged 6-8 years: the PANIC study – **Annie Constable** (Exeter, UK)

PP8, Does screening for high hip fracture risk reduce fractures by modifying falls risk? A post hoc analysis from the SCOOP study – **Eugene McCloskey** (Sheffield, UK)

PP9, The Effect of Bone Quality on the Time Dependant Response of Human Trabecular Bone at Physiological Levels of Strain – **Robert Wallace** (Edinburgh, UK)

PP10, New therapeutic avenues in bone repair: harnessing a novel endogenous molecule to boost bone and prevent bone loss in inflammatory disease – **Jonathan Lewis** (Birmingham, UK)

PP11, Do sex hormones determine sexual dimorphism of the bone vasculature? – **Alice Goring** (Southampton, UK)

12:45-13:45 *Entrance Foyer area, Ground Floor and Seminar room E1.22, 1st Floor*
Lunch and Exhibition

13:00 *Shared Lecture Theatre, 1st Floor*
BRS Annual General Meeting

13:00 *Physiology B Lecture Theatre, Basement*
BORS Annual General Meeting

13:50-14:40 *Shared Lecture Theatre, 1st Floor*
Sponsored Symposium – UCB
Chair: **Mike Stone** (Cardiff, UK)

13:45-13:55 Clinical tools to assist goal-directed therapy for fragility and fracture patients – **Mike Stone** (Cardiff, UK)

13:55-14:15 Mass vs strength: Which measurement can help guide my patients' therapy – **Beth Curtis** (Southampton, UK)

14:15-14:35 How do bone cells translate drug effects into bone strength? – **Jon Tobias** (Bristol, UK)

14:35-14:40 Looking to the future – **Mike Stone**, **Beth Curtis** and **Jon Tobias**

14:45-15:45 *Shared Lecture Theatre, 1st Floor*
OATech+ Symposium
supported by OATech+
Chairs: **Sophie Gilbert** (Cardiff, UK) and **Sabina Gheduzzi** (Bath, UK)

continued...

14:45-15:45 *Physiology B Lecture Theatre, Basement*
Oral communications – Basic
Chairs: **Andrew Chantry** (Sheffield, UK) and **Isabel Orriss** (London, UK)

continued...

THURSDAY 5 SEPTEMBER continued

14:45-15:15	**IS5**, OA – where movement modelling meets biology – **Ilse Jonkers** (Leuven, Belgium)
15:15-15:25	**IS4**, OATech+ EPSRC Network plus funding update – **Cathy Holt** (Cardiff, UK)
15:25-15:45	**IS6**, Imaging OA – technology challenges and opportunities – **David Williams** (Cardiff, UK)

14:45-14:55	**OC10**, Systemic Teriparatide with Locally Injected Mesenchymal Stem Cells Synergistically Enhances Fracture Healing – **Liza Osagie** (London, UK)
14:55-15:05	**OP11**, Predicting cortical bone adaptation in the mouse tibia: a longitudinal study – **Vee San Cheong** (Sheffield, UK)
15:05-15:15	**OC12**, The secretome of mesenchymal stromal cells drives functional heterogeneity – **Andrew Stone** (York, UK)
15:15-15:25	**OC13**, Analysis of osteoclastic resorption in vitro reveals new pathways of bone collagen breakdown and novel markers of bone resorption *in vitro* and *in vivo* – **Brendan Norman** (Liverpool, UK)
15:25-15:35	**OC14**, Understanding the role of L-cysteine and hydrogen sulphide in the beneficial effects of N-acetylcysteine on bone formation and arterial medial calcification – **Lucie Bourne** (London, UK
15:35-15:45	**OC15**, TightRight : augmenting screwdrivers to reduce bone stripping rates and optimise tightness when inserting non-locking screws – **James Fletcher** (Bath, UK)

15:45-16:05 *Entrance Foyer area, Ground Floor and Seminar room E1.22, 1st Floor*
Refreshments, Exhibition and Poster viewing

16:05-17:05 *John Pryde Lecture Theatre, Basement*
Symposium 2: – Epigenetics
Chairs: **Elizabeth Curtis** (Southampton, UK) and **Debbie Mason** (Cardiff, UK)

continued...

16:05-17:05 *Physiology B Lecture Theatre, Basement*
Symposium 3: – Epidemiology and Health Services Research
supported by National Joint Registry for England and Wales
Chairs: **Kassim Javaid** (Oxford, UK) and **Andrew McCaskie** (Cambridge, UK)

continued...

THURSDAY 5 SEPTEMBER continued

16:05-16:35	**IS7**, What has DNA methylation analysis told us about OA? – **Louise Reynard** (Newcastle, UK)	16:05-16:35	**IS9,** Patient reported outcome measures in musculoskeletal disease – How can they inform decision-making? – **Ola Rolfson** (Gothenburg, Sweden)
16:35-17:05	**IS8**, microRNA biomarkers: new diagnostic and prognostic tools for bone diseases – **Matthias Hackl** (Vienna, Austria)	16:35-17:05	**IS10,** A global perspective on adolescent growth and healthy musculoskeletal ageing – **Kate Ward** (Southampton, UK)
17:05-17:15	Break		
17:15-17:45	*This meeting has been sponsored by Gedeon Richter, who have paid exhibition stand fees and speaker fees for the sponsored symposium on 05/09/19 [Professor Mike Stone]. Gedeon Richter has had no involvement in, or influence over, the content of the rest of the meeting.* *Shared Lecture Theatre, 1st Floor* ***Sponsored Symposium – Gedeon Richter*** Building a better future: improving access to eligible bone anabolic therapies for osteoporosis patients – **Mike Stone** (Cardiff, UK) Chairs: **Elaine Dennison** (Southampton, UK) and **Bridget Scammell** (Nottingham, UK)		
17:45-18:30	*Shared Lecture Theatre, 1st Floor* **Debate** *supported by MiLabs* Chairs: **Bronwen Evans** (Cardiff, UK) and **Mark Wilkinson** (Sheffield, UK) This house believes that if it doesn't hurt it isn't a disease: **IS13**, For the motion – **Chris Little** (Sydney, Australia) **IS14**, Against the motion – **Alison Gartland** (Sheffield, UK)		
19:00-00:00	Conference Dinner – National Museum Cardiff		

FRIDAY 6 SEPTEMBER

08:00 *Entrance Foyer, Ground Floor*
Registration

08:30-09:30 *Shared Lecture Theatre, 1st Floor*
Symposium 4: Cancer and Bone
Chairs: **Michelle Lawson** (Sheffield, UK) and **Iain Murray** (Edinburgh, UK)

08:30-09:00 **IS15,** Endogenous production of IL-1B by breast cancer cells drives metastasis and colonisation of the bone microenvironment – **Penny Ottewell** (Sheffield, UK)

09:00-09:30 **IS16**, Bones, Groans and Lumps: Improving Outcomes in Orthopaedic Oncology – **Mike Parry** (Birmingham, UK)

09:30-10:00 *Shared Lecture Theatre, 1st Floor*
Poster pitching x 15 selected from abstract submissions
Chairs: **Michelle Lawson** (Sheffield, UK) and **Iain Murray** (Edinburgh, UK)

PP12, Evaluating strength of 3D printed screw threads for patient-specific osteosynthesis plates – **Alisdair MacLeod** (Bath, UK)

PP13, What is the optimum tightness for non-locking cortical screws, and how can this be predicted prior to insertion? – **James Fletcher** (Bath, UK)

PP14, Genome-wide Expression Analysis of Human Osteoclasts Following Clinically Relevant Cobalt and Chromium Exposure – **Karan Shah** (Sheffield, UK)

PP15, How does body weight influence the risk of vertebral fracture? – **Jin Luo** (London, UK)

PP16, Accelerated osteogenesis in vivo and in vitro achieved through metabolic and secretomic modification in mesenchymal stromal cells – **Alasdair Kay** (York, UK)

PP17, Higher birthweight is associated with greater limb muscle mass and grip strength in middle age: findings from the UK Biobank Imaging Enhancement – **Elizabeth Curtis** (Southampton, UK)

PP18, Measuring prosthesis migration using a novel ultra-kow dose CT-based method – **Kartik Logishetty** (London, UK)

PP19, Pharmacokinetics of parathyroid hormone peptide PTH 1-34 via nasal spray for the treatment of osteoporosis – **Richard Pearson** (Nottingham, UK)

PP20, The influence of the RNA binding protein HuR on skeletal development is not mediated through the control of mesenchymal cell differentiation – **Simon Tew** (Liverpool, UK)

PP21, Investigating the regulation of bone mineralisation through in vitro and in vivo models of chronic kidney disease – **Shun-Neng Hsu** (Edinburgh, UK)

PP22, Changes in gait, knee loading and patient reported outcomes following High Tibial Osteotomy – **Gemma Whatling** (Cardiff, UK)

PP23, An in vitro assessment of knee kinematics following radial tears of the medial meniscus – **Fahd Mahmood** (Glasgow, UK)

PP24, Correlations between Radiographic Classification Systems and Confirmed Cartilage Loss in Severe Knee Osteoarthritis – **Oisin Keenan** (Edinburgh, UK)

PP25, Impact of renal function on response to oral and i.v. bisphosphonate treatment: Real world observational data using linkage to national registers – **Bo Abrahamsen** (Odense, Denmark)

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FRIDAY 6 SEPTEMBER continued

PP26, A tale of two phosphatases: how do matrix vesicles generate phosphate for bone mineralization? – **Scott Dillon** (Edinburgh, UK)

LBPP1, Fleas and bites in bones – **Alan Boyde** (London, UK)

10:00-11:00 *Entrance Foyer area and C0.13, Ground Floor and Seminar room E1.22, 1st Floor*
Refreshments, Exhibition and Poster viewing (even numbered posters)

11:00-12:00	*John Pryde Lecture Theatre, Basement* **Oral communications – Clinical** Chairs: **Elizabeth Curtis** (Southampton, UK) and **Chris Wilson** (Cardiff, UK)	**11:00-12:00**	*Physiology B Lecture Theatre, Basement* **Oral communications – Basic/Translational** Chairs: **Claire Clarkin** (Southampton, UK) and **Andrew Phillips** (London, UK)
11:00-11:10	**OC16**, Targeting Rehabilitation to Improve Outcomes following total knee arthroplasty (TRIO): a randomised controlled trial of physiotherapy interventions – **David Hamilton** (Edinburgh, UK)	11:00-11:10	**OC22**, Transforming growth factor (TGF)β inhibition with chemotherapy heals murine myeloma bone disease and improves fracture resistance – **Alanna Green** (Sheffield, UK)
11:10-11:20	**OC17**, Over-Impaction of Acetabular Cups Can Reduce Fixation Strength: Surgical Technique Is Critical – **Ruben Doyle** (London, UK)	11:10-11:20	**OC23**, Breast cancer metastasis to bone; the effect of LOX and P2X7R inhibition – **Karan Shah** (Sheffield, UK)
11:20-11:30	**OC18**, Bi-Unicondylar Arthroplasty preserves healthy gait characteristics and near-normal extensor mechanism efficiency compared to Total Knee Arthroplasty – **Amy Garner** (London, UK)	11:20-11:30	**OC24**, Sexual dimorphism in both bone geometry and bone strength for a mouse model of Paget's disease of bone (PDB) – **Alisha Sharma** (Southampton, UK)
11:30-11:40	**OC19**, Preoperative Gait Biomechanics and its Relationship to Functional Outcome Following Total Hip Arthroplast – **Cathy Holt** (Cardiff, UK)	11:30-11:40	**OC25**, Is the mechanical function of the meniscus altered in osteoarthritic knees? – **Fahd Mahmood** (Glasgow, UK)
11:40-11:50	**OC20**, Platelet-rich plasma (PRP) for patellar tendinopathy: a randomized controlled trial of leukocyte-rich PRP or leukocyte-poor PRP vs. saline – **Alex Scott** (Vancouver, Canada)	11:40-11:50	**OC26**, Repurposing glutamate receptor antagonists to prevent the onset of post-traumatic osteoarthritis – **Cleo Bonnet** (Cardiff, UK)
11:50-12:00	**OC21**, Charting longitudinal patient function following TKA and evaluating the influence of implant design: 8-year follow-up of a prospective RCT – **David Hamilton** (Edinburgh, UK)	11:50-12:00	**LB3**, Osteoblast interaction with an endothelial cell-specific extracellular matrix protein controls trabecular bone formation rate and patterning – **Georgiana Neag** (Birmingham, UK)
	continued...		*continued...*

FRIDAY 6 SEPTEMBER continued

12:00-12:30	*John Pryde Lecture Theatre, Basement* **BORS Presidential Lecture** **Andrew Amis** (London, UK) Chair: **Richie Gill** (Bath, UK)	12:00-12:30	*Physiology B Lecture Theatre, Basement* **BRS Dent Lecture** **Tim Arnett** (London, UK) Chair: **Jim Gallagher** (Liverpool, UK)
1230-1330	*Entrance Foyer area and C0.13, Ground Floor and Seminar room E1.22, 1st Floor* Lunch, Exhibition and Poster viewing		
13:30-14:30	*John Pryde Lecture Theatre, Basement* **Symposium 5: Imaging** *supported by ImagingBioPro Network and Scanco* Chairs: **Robert Wallace** (Edinburgh, UK) and **Wayne Ayre** (Cardiff, UK)	**13:30-14:30**	*Physiology B Lecture Theatre, Basement* **Symposium 6: Clinical cases** Chairs: **Amy Garner** (London, UK) and **Mike Stone** (Cardiff, UK)
13:30-14:00	**IS17**, Synchrotron imaging for bone research – **Ralph Muller** (Zurich, Switzerland)	13:30-13:45	**OC33**, 6 cases of hypophosphatasia presenting with musculoskeletal symptoms diagnosed in General Rheumatology clinic – **Katie Moss** (London, UK)
14:00-14:30	**IS18**, Making Rainbows: Clinical Applications for Synchrotron Imaging – **Richie Abel** (London, UK)	13:45-14:00	**OC34**, A review of the management of patients found to have syringomyelia: a single centre experience – **Oliver Cottle** (Leicester, UK)
		14:00-14:15	**OC35**, Coming of Age – **Mike Stone** (Cardiff, UK)
		14:15-14:30	**OC36**, Healing of OCD after osteotomy and the effect of tibial slope on knee function – **Chris Wilson** (Cardiff, UK)
14:30-14:40	Break		
14:40-15:10	*Shared Lecture Theatre, 1st Floor* **Plenary Lecture** Chairs: **Bronwen Evans** (Cardiff, UK) and **Richie Gill** (Bath, UK) **IS19**, Mechanistics insights from Combination therapies – opportunities for osteoporosis and fracture healing – **Bente Langdahl** (Aarhus, Denmark)		
15:10-16:10	*Shared Lecture Theatre, 1st Floor* **Oral communications** Chairs: **Bronwen Evans** (Cardiff, UK) and **Richie Gill** (Bath, UK)		
15:10-15:20	**OC28**, Molecular imaging modalities reveal pathological matrix disorganisation in whole bone sections and isolated osteoblasts – **Aikta Sharma** (Southampton, UK)		
15:20-15:30	**OC29**, Can we predict medial knee load during gait for varus osteoarthritc knees using radiographic alignment measures? – **Gemma Whatling** (Cardiff, UK)		

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FRIDAY 6 SEPTEMBER continued

15:30-15:40	**OC30**, Comprehensive evaluation of the morphology and mechanics of the human femoral head – **Mark Wilkinson** (Sheffield, UK)
15:40-15:50	**OC31**, Visualisation and quantification of in situ porcine acetabular soft tissue behaviour: A study of labrum circumferential behaviour – **Jiacheng Yao** (Leeds, UK)
15:50-16:00	**OC32**, AMPA/kainate glutamate receptors regulate inflammatory and degradative markers in 3D loading models of cartilage and bone – **Sophie Gilbert** (Cardiff, UK)
16:00-16:10	**LB4**, Repairing myeloma-induced bone disease using combination bone anabolic and antiresorptive therapy – **Rebecca Andrews** (Sheffield, UK)
16:10-16:25	*Shared Lecture Theatre, 1st Floor* **Awards and closing remarks**

The Scientific Programme has been developed independently by the Organising Committee under no influence from any supporting organisation or their employees.

All parties will make reasonable efforts to present educational subject matter in a scientific, balanced and unbiased way. However, participants must always use their own judgment and professional opinion when considering future application of this information, particularly as it may relate to patient diagnostic or treatment decisions.

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POSTER OVERVIEWS

PP1 High tibial osteotomy (HTO) and wide stance (WS) gait reduces knee joint loading in individuals with varus knee deformity

Jake Bowd[1,2], Paul Biggs[1,2], David Elson[2,3], Andrew Metcalfe[2,4,5], Chris Wilson[2,4], Cathy Holt[1,2], Gemma Whatling[1,2]

[1]Cardiff School of Engineering, College of Physical Sciences, Cardiff University, Cardiff, UK; [2]Biomechanics and Bioengineering Research Centre Versus Arthritis, Cardiff University, Cardiff, UK; [3]Queen Elizabeth Hospital, Gateshead, UK; [4]University Hospital of Wales, Cardiff, UK; [5]Warwick Clinical Trials Unit, Warwick Medical School, University of Warwick, Coventry, UK

PP2 Which muscle parameters are longitudinally associated with knee osteoarthritis outcomes? Findings from the Hertfordshire Cohort Study

Nicholas Fuggle[1], Leo Westbury[1], Karen Jameson[1], Holly Syddall[1], Mark Edwards[2], Kate Ward[1], Elaine Dennison[1], Cyrus Cooper[1]

[1]MRC Lifecourse Epidemiology Unit, University of Southampton, Southampton, UK; [2]Rheumatology, Portsmouth Hospitals NHS Trust, Portsmouth, UK

PP3 Ochronotic pigment distribution in alkaptonuric mice reveals that homogentisic acid deposition in tissues reflects the intensity of mechanical loading

Juliette Hughes[1], Henry Edwards[1], Craig Keenan[1], Hazel Sutherland[1], Lakshminarayan Ranganath[1,2], George Bou-Gharios[1], James Gallagher[1]

[1]Institute of Ageing and Chronic Disease, University of Liverpool, Liverpool, UK; [2]Department of Clinical Biochemistry and Metabolic Medicine, Royal Liverpool and Broadgreen University Hospital Trust, Liverpool, UK

PP4 Osteoblast-specific *Enpp1* deficiency promotes bone mass whilst worsening the metabolic phenotype

Fiona Roberts[1], Nabil Rashdan1, Isabel Orriss[2], Elspeth Milne[1], Nicholas Morton[3], Colin Farquharson[1], Vicky Macrae[1]

[1]Developmental Biology, Roslin Institute, University of Edinburgh, Edinburgh, UK; [2]Department of Comparative Biomedical Sciences, Royal Veterinary College, London, UK; [3]Centre for Cardiovascular Science, Queen's Medical Research Institute, University of Edinburgh, Edinburgh, UK

PP5 Associations between chondrocyte transiency and osteoarthritis pathology

Hasmik Jasmine Samvelyan[1], Anish Amin[2], Colin Farquharson[3], Katherine Staines[1]

[1]School of Applied Sciences, Edinburgh Napier University, Edinburgh, UK; [2]Royal Infirmary of Edinburgh, NHS Lothian, The University of Edinburgh Medical School, Edinburgh, UK; [3]The Roslin Institute, The University of Edinburgh, Edinburgh, UK

PP6 Barbara Mawer Travelling fellowship: Associations between endocrine metabolites and bone mineral density in children aged 6-8 years: the PANIC study

Dimitris Vlachopoulos[1], Alan Barker[1], Annie Constable[1], Eero Haapala[2], Sonja Soininen[3], Timo Lakka[3]

[1]Sport and Health Sciences, University of Exeter, Exeter, UK; [2]Sport and Health Sciences, University of Jyvaskyla, Jyvaskyla, Finland; [3]Institute of Biomedicine, School of Medicine, University of Eastern Finland, Kuopio, Finland

PP7 Determinants of bone mineral content and density in children aged 6-8 years: the PANIC study

Annie Constable[1,2], Dimitris Vlachopoulos[1], Alan R. Barker[1], Eero A. Haapala[2,3], Sonja Soininen[2], Timo A. Lakka[2]

[1]Sport and Health Sciences, University of Exeter, Exeter, UK; [2]Institute of Biomedicine, University of Eastern Finland, Kuopio, Finland; [3]Faculty of Sport and Health Sciences, University of Jyväskylä, Jyväskylä, Finland

PP8 Does screening for high hip fracture risk reduce fractures by modifying falls risk? A post hoc analysis from the SCOOP study

Eugene McCloskey[1], Codrin Condurache[1], Pojchong Chotiyarnwong[1], Sarah Chiu[1], Lee Shepstone[2], Elizabeth Lenaghan[2], Cyrus Cooper[3], Nicholas Harvey[3], John Kanis[4]

[1]Oncology & Metabolism, University of Sheffield, Sheffield, UK; [2]School of Medicine, University of East Anglia, Norwich, UK; [3]MRC Lifecourse Epidemiology Unit, University of Southampton, Southampton, UK; [4]Mary MacKillop Institute for Health Research, Australian Catholic University, Melbourne, Australia

PP9 The Effect of Bone Quality on the Time Dependant Response of Human Trabecular Bone at Physiological Levels of Strain

Robert Wallace, Hamish Simpson

Orthopaedics and Trauma, University of Edinburgh, Edinburgh, UK

PP10 New therapeutic avenues in bone repair: Harnessing a novel endogenous molecule to boost bone and prevent bone loss in inflammatory disease

Jonathan Lewis[1], Amy Naylor[1], James Edwards[2], Helen McGettrick[1]

[1]Rheumatology Research Group, Institute of Inflammation and Ageing, University of Birmingham, Birmingham, UK; [2]Botnar Research Centre, University of Oxford, Oxford, UK

PP11 Do sex hormones determine sexual dimorphism of the bone vasculature?

Alice Goring[1], Aikta Sharma[1], Behzad Javaheri[2], Bjorn R Olsen[3], Andrew A Pitsillides[2], Richard OC Oreffo[4], Philipp Schneider[5], Claire E Clarkin[1]

[1]School of Biological Sciences, University of Southampton, Southampton, UK; [2]Department of Comparative Biomedical Sciences, The Royal Veterinary College, London, UK; [3]Department of Developmental Biology, Harvard School of Dental Medicine, Boston, USA; [4]Centre for Human Development, Stem Cell and Regeneration, University of Southampton, Southampton, UK; [5]Faculty of Engineering and the Environment, University of Southampton, Southampton, UK

PP12 Evaluating strength of 3D printed screw threads for patient-specific osteosynthesis plates

Alisdair MacLeod[1], Michael Patterson[1], Ryan Taylor[2], Alex Harris[2], Alberto Casonato[3], Harinderjit Gill[1]

[1]Mechanical Engineering, University of Bath, Bath, UK; [2]Medical Dental Products Division, Renishaw PLC, Charfield, UK; [3]3D Metal Printing, Bath, UK

PP13 What is the optimum tightness for non-locking cortical screws, and how can this be predicted prior to insertion?

James Fletcher[1,2], Ivan Zderic[2], Boyko Gueorguiev[2], R. Geoff Richards[2], Harinderjit Gill[3], Michael Whitehouse[4,5], Ezio Preatoni[1]

[1]Department for Health, University of Bath, Bath, UK; [2]AO Research Institute Davos, Davos, Switzerland; [3]Department of Mechanical Engineering, University of Bath, Bath, UK; [4]Musculoskeletal Research Unit, Translational Health Sciences, Bristol Medical School 1st Floor Learning and Research Building, Bristol, UK; [5]National Institute for Health Research Bristol Biomedical Research Centre, University Hospitals Bristol NHS Foundation Trust and University of Bristol, Bristol, UK

PP14 Genome-wide Expression Analysis of Human Osteoclasts Following Clinically Relevant Cobalt and Chromium Exposure

Karan M Shah[1], Mark J Dunning[2], J Mark Wilkinson[1], Alison Gartland[1]

[1]The Mellanby Centre for Bone Research, The University of Sheffield, Sheffield, UK; [2]Sheffield Institute for Translational Neuroscience, The University of Sheffield, Sheffield, UK

PP15 How does body weight influence the risk of vertebral fracture?

Jin Luo[1], Raymond Lee[2]

[1]School of Applied Sciences, London South Bank University, London, UK; [2]Faculty of Technology, University of Portsmouth, Portsmouth, UK

PP16 Accelerated osteogenesis *in vivo* and *in vitro* achieved through metabolic and secretomic modification in mesenchymal stromal cells

Alasdair Kay[1], Alice Carstairs[1], Andrew Stone[1], Elizabeth Kapasa[2], Xuebin Yang[2], Emma Rand[1], Paul Genever[1]

[1]Department of Biology, University of York, York, UK; [2]Division of Oral Biology, University of Leeds, Leeds, UK

PP17 Higher birthweight is associated with greater limb muscle mass and grip strength in middle age: findings from the UK Biobank Imaging Enhancement

Elizabeth Curtis[1], Justin Liu[1], Kate Ward[1], Karen Jameson[1], Zahra Raisi-Estabragh[2], Jimmy Bell[3], Steffen Petersen[2], Cyrus Cooper[1,4,5], Nicholas Harvey[1,5]

[1]MRC Lifecourse Epidemiology Unit, University of Southampton, Southampton, UK; [2]NIHR Advanced Imaging, NIHR Barts Biomedical Research Centre, Queen Mary University of London, London, UK; [3]Research Centre for Optimal Health, Department of Life Sciences, University of Westminster, London, UK; [4]NIHR Oxford Biomedical Research Centre, University of Oxford, Oxford, UK; [5]NIHR Southampton Biomedical Research Centre, University of Southampton, Southampton, UK

PP18 Measuring Prosthesis Migration using a Novel Ultra-Low Dose CT-Based Method

Susannah Clarke[1,2], **Kartik Logishetty**[1], Camilla Halewood[2], Justin Cobb[1]

[1]MSk Lab, Imperial College London, London, UK; [2]Embody Orthopaedic, London, UK

PP19 Pharmacokinetics of parathyroid hormone peptide PTH 1-34 via nasal spray for the treatment of osteoporosis

Richard G Pearson[1], Tahir Masud[2], Elaine Blackshaw[3], Andrew Naylor[4], Michael Hinchcliffe[5], Kirk Jeffery[4], Faron Jordan[4], Anjumn Shabir-Ahmed[4], Gareth King[4], Andrew L Lewis[4], Lisbe Illum[6], Alan Perkins[3]

[1]Trauma, Orthopaedics & Sports Medicine, NIHR Nottingham BRC, University of Nottingham, Nottingham, UK; [2]Nottingham University Hospitals NHS Trust, Queen's Medical Centre, Nottingham, UK; [3]Radiological Sciences, University of Nottingham, Nottingham, UK; [4]Critical Pharmaceuticals Ltd, Bio City, Nottingham, UK; [5]Paracelsis Ltd, Bio City, Nottingham, UK; [6]Identity, The Park, Nottingham, UK

PP20 The influence of the RNA binding protein HuR on skeletal development is not mediated through the control of mesenchymal cell differentiation

Johnson Kirsty, Keenan Craig, McDermott Benjamin, Bou-Gharios George, **Tew Simon**

Institute of Ageing and Chronic Disease, University of Liverpool, Liverpool, UK

PP21 Investigating the regulation of bone mineralisation through *in vitro* and *in vivo* models of chronic kidney disease

Shun-Neng Hsu, Vicky MacRae, Amanda Novak, Katherine Staines, Colin Farquharson

Developmental Biology, The Roslin Institute, University of Edinburgh, Edinburgh, UK

PP22 Changes in gait, knee loading and patient reported outcomes following High Tibial Osteotomy

Gemma Whatling[1,2], Paul Biggs[1,2], David W Elson[2,4,3], Andrew Metcalfe[2,4,5], Chris Wilson[2,4], Cathy Holt[1,2]

[1]Cardiff School of Engineering, Cardiff University, Cardiff, UK; [2]Biomechanics and Bioengineering Research Centre Versus Arthritis, Cardiff University, Cardiff, UK; [3]Queen Elizabeth Hospital, Gateshead, UK; [4]University Hospital of Wales, Cardiff, UK; [5]Warwick Clinical Trials Unit, Warwick Medical School, University of Warwick, Coventry, UK

PP23 An *in vitro* assessment of knee kinematics following radial tears of the medial meniscus

Fahd Mahmood[1,2], Jon Clarke[2], Philip Riches[1]

[1]Biomedical Engineering, University of Strathclyde, Glasgow, UK; [2]Department of Orthopaedics, Golden Jubilee National Hospital, Glasgow, UK

PP24 Correlations between Radiographic Classification Systems and Confirmed Cartilage Loss in Severe Knee Osteoarthritis

Oisin Keenan, George Holland, John Keating, Chloe Scott

Trauma and Orthopaedics, Royal Infirmary of Edinburgh, Edinburgh, UK

PP25 Impact of renal function on response to oral and i.v. bisphosphonate treatment: Real world observational data using linkage to national registers

Bo Abrahamsen[1,2,4], Martin T Ernst[1], Mads Nybo[3], Katrine H Rubin[1], Maria Stougaard[1], Daniel Prieto-Alhambra[4], Anne Pernille Hermann[5]

[1]OPEN, Institute of Clinical Research, Univ of Southern Denmark, Odense, Denmark; [2]Medicine, Holbæk Hospital, Holbæk, Denmark; [3]Clinical Biochemistry, Odense University Hospital, Odense, Denmark; [4]NDORMS, University of Oxford, Oxford, UK; [5]Endocrinology, Odense University Hospital, Odense, Denmark

PP26 A tale of two phosphatases: how do matrix vesicles generate phosphate for bone mineralization?

Scott Dillon[1], Fabio Nudelman[2], Colin Farquharson[1]

[1]The Roslin Institute, University of Edinburgh, Edinburgh, UK; [2]School of Chemistry, University of Edinburgh, Edinburgh, UK

P27 Do osteoclasts derived from mice with different bone mass exhibit distinct *in vitro* osteoclastogenic potential and sensitivity to stable sulforaphane?

Polymnia Louka[1], Isabel Orriss[1], Stephen Franklin[2], Andrew Pitsillides[1]

[1]Comparative Biomedical Sciences, Royal Veterinary College, University of London, London, UK; [2]Evgen Pharma, Cheshire, UK

P28 Extracellular pH regulates osteoclast fusion

Bethan Davies[1], Timothy Arnett[2], Gill Holdsworth[3], Isabel Orriss[1]

[1]Comparative Biomedical Sciences, Royal Veterinary College, London, UK; [2]Cell and Developmental Biology, University College London, London, UK; [3]Musculoskeletal Research, UCB Pharma Ltd, Slough, UK

P29 Using wearable accelerometers to discriminate between knee rehabilitation exercises

Philippa Jones[1], Samuel Woodgate[1,2], Emer Doheny[3], Paul Biggs[1,4], Cathy Holt[1,4]

[1]School of Engineering, Cardiff University, Cardiff, UK; [2]School of Medicine, Cardiff University, Cardiff, UK; [3]Insight Centre for Data Analytics, University College Dublin, Dublin, Ireland; [4]Biomechanics and Bioengineering Research Centre Versus Arthritis, Cardiff University, Cardiff, UK

P30 Does the size, speed and timing of pubertal growth impact fracture in later life? The 1946 British Birth Cohort

Kate Ward[1], Camille Parsons[1], Diana Kuh[2], Cyrus Cooper[1], Rachel Cooper[3]

[1]MRC Lifecourse Epidemiology, University of Southampton, Southampton, UK; [2]Musculoskeletal Science and Sports Medicine Research Centre, Department of Sport and Exercise Sciences, Faculty of Science and Engineering, Manchester Metropolitan University, Manchester, UK; [3]MRC Lifelong Health and Ageing at University College London, London, UK

P31 Sustained delivery of glutamate receptor antagonists to prevent osteoarthritis

Ben Egan[1,2,3], Charles Heard[2,3], James Birchall[2,3], Deborah Mason[1,3]

[1]School of Bioscience, Cardiff University, Cardiff, UK; [2]School of Pharmacology and Pharmaceutical Sciences, Cardiff University, Cardiff, UK; [3]Biomechanics and Bioengineering Centre Versus Arthritis, Cardiff, UK

P32 2-oxothiazolidine-4-carboxylic acid: a novel inhibitor of vascular calcification

Jessal J Patel[1], Lucie E Bourne[2], Shori Thakur[1], Ken Farrington[1,3], Diana A Gorog[1,3,4], Isabel R Orriss[2], Anwar R Baydoun[1,5]

[1]School of Life and Medical Sciences, University of Hertfordshire, Hatfield, UK; [2]Department of Comparative Biomedical Sciences, Royal Veterinary College, London, UK; [3]East and North Hertfordshire NHS Trust, Hertfordshire, UK; [4]National Heart and Lung Institute, Imperial College, London, UK; [5]Leicester School of Pharmacy, De Montfort University, Leicester, UK

P33 X-linked Hypophosphataemia: prevalence and mortality within the United Kingdom Clinical Practice Research Datalink

Samuel Hawley[1], Nick Shaw[2], Antonella Delmestri[3], Daniel Prieto-Alhambra[1], Cyrus Cooper[4], Rafael Pinedo-Villanueva[1], M Kassim Javaid[1]

[1]NDORMS, University of Oxford, Oxford, UK; [2]Birmingham Children's Hospital NHS Foundation Trust, Birmingham, UK; [3]NDORMS, University of Oxford, Oxford, UK; [4]MRC Lifecourse Epidemiology Unit, University of Southampton, Southampton, UK

P34 Novel chemical sterilisation of decellularised human bone-patellar tendon-bone (hBTB) grafts for anterior cruciate ligament (ACL) repair

Jennifer H Edwards[1], Daniel S Thomas[1], Hazel L Fermor[1], John N Kearney[2], Paul Rooney[2], John Fisher[1], Eileen Ingham[1]

[1]Institute of Medical and Biological Engineering, University of Leeds, Leeds, UK; [2]NHS Blood and Transplant: Tissue and Eye Services, Speke, UK

P35 Patient and service-level predictors of bone treatment recommendation post-fracture: results from the UK national Fracture Liaison Service (FLS) database

Samuel Hawley[1], Naomi Vasilakis[2], Bonnie Wiles[2], Celia Gregson[3], Neil Gittoes[4], Gavin Clunie[5], Clare Cockill[6], Iona Price[2], Andrew Judge[3], Alison Smith[2]

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P36 Mononuclear Phagocytes in Cartilage Repair

Andrew J Hotchen[1,2], Fransceca E Beaton[1], Karim Fekir[1], Tomas Castro-Dopico[2], Karin J Newell[1,3], Frances Henson[1,3], Mark A Birch[1], Menna R Clatworthy[2], Andrew W McCaskie[1]

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P37 Mesenchymal stem cells in talar and tibial subchondral bone of ankle osteoarthritis patients

William Jones[1,2,3], Jehan El-Jawhari[1], Claire Brockett[2], Hazel Fermor[2,3], Elena Jones[1]

[1]Institute of Rheumatology and Musculoskeletal Medicine, University of Leeds, Leeds, UK; [2]Institute of Medical and Biological Engineering, University of Leeds, Leeds, UK; [3]Biomedical Sciences, University of Leeds, Leeds, UK

P38 Experimental reproduction of periprosthetic joint infection: developing a representative animal model

Irene-Isabel Lopez-Torres[1], Sanz-Ruiz Pablo[1,2], Ana-Isabel Fraguas-Sanchez[3], Jose-Manuel Espinosa-Pereiro[1], Victor-Estuardo Leon-Roman[4], Vaquero Javier[1,2]

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P39 Decellularised Porcine Xenograft for Anterior Cruciate Ligament Reconstruction: A Histological Study in Sheep

Adam Hexter[1], Karen Hing[1], Fares Haddad[2], Gordon Blunn[3]

[1]Institute of Orthopaedic and Musculoskeletal sciences, University College London, UK; [2]Department of Orthopaedics, University College Hospital, London, UK; [3]School of Pharmacy and Biomedical Sciences, University of Portsmouth, Portsmouth, UK

P40 Is Demineralised Cortical Bone strong enough to be an Anterior Cruciate Ligament allograft?

Adam Hexter[1], Shirin Shahbazi[1], Tanujan Thangarajah[1], Deepak Kalaskar[1], Fares Haddad[2], Gordon Blunn[3]

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P41 The impact of a Virtual Orthopaedic Triage Clinic Model in Northern Ireland

Raymond McKenna[1], Jim Ballard[2], Aidan Cosgrove[2]

[1]Trauma and Orthopaedics, Royal Belfast Hospital for Sick Children, Belfast, UK; [2]Royal Belfast Hospital for Sick Children, Belfast, UK

P42 Regional variation in functional adaptation and the selection for locomotor efficiency

Bram Mulder[1], Jay Stock[1,2], Jaap Saers[1], Craig Cessford[1], John Robb[1]

[1]Department of Archaeology, University of Cambridge, Cambridge, UK; [2]Department of Anthropology, University of Western Ontario, London, Canada

P43 The paracrine effect of mesenchymal stem cells in healing enhancement in atrophic non-union model

Murtadhah MK Jalal[1], **A Hamish Simpson**[1], **Robert Wallace**[1], Bruno Peault[2]

[1]Orthopaedics and Trauma Surgery, The University of Edinburgh, Edinburgh, UK; [2]Scottish Center for Regenerative Medicine, The University of Edinburgh, Edinburgh, UK

P44 Tissue remodelling changes the stress distribution in additively manufactured porous bone implants

Vee San Cheong[1,2], Paul Fromme[2], Melanie Coathup[1,3], Aadil Mumith[1], Gordon Blunn[1,4]

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P45 Creating an open-source two-phase fluid-structure interaction model of a trabecular bone structure validated against a 3D printed experimental trabecular bone structure specimen

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P46 Using a mouse model of osteochondral injury to understand bone and articular cartilage repair

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P47 Model-based Roentgen stereophotogrammetric analysis (RSA) using a Novel Radiopaque UHMWPE

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P48 Role of Semaphorin-3A in osteoarthritis

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P49 Neural network modeling of mortality and revision risk after hip replacement surgeries

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P50 Novel niclosamide-bisphosphonate vectors as bone-targeted therapy for multiple myeloma

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P51 Characterising the structure of trabecular excrescences found in osteoarthritic and control joint samples

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P52 Validated FE models of vertebral bodies predict displacements and strains from axial impact loading

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P53 Wear Performance of a Mobile Bearing Total Ankle Replacement

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P54 Zebrafish in hypergravity: larval zebrafish experience changes in cartilage material properties after exposure to hypergravity

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P55 Lesser trochanter size could be a novel risk factor for hip osteoarthritis

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P56 Bone mineral response following lumbar stress fracture in elite cricket fast bowlers

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P57 WITHDRAWN.

P58 Dose-response relationship between free-living physical activity and bone health in the middle-aged and elderly

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P59 Microbubbles as oxygen delivery agents for stimulating osteogenesis *in vitro* and *in vivo*

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P60 Pre-operative partial thickness cuff tears do not compromise results of anatomical total shoulder replacement- 5 year follow up

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P61 Performance of TS symmetric cone in revision of total knee arthroplasty

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P62 Effect of an acute bout of high impact exercise on serum sclerostin concentration

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P63 Utilising pressure walkways to modify footwear design to reduce risk of shin splints

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P64 The immunomodulatory activity of mesenchymal stem cells (MSCs) is influenced by their three-dimensional environment *in vitro*

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P65 Incidence of fractures in people with intellectual disabilities

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P66 Dislocation of the mobile bearing in the Lateral Oxford Unicompartmental Knee Replacement (LOUKR): the effect of knee flexion

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P67 WITHDRAWN.

P68 **Leptin remodels tibia trabecular bone volume but not bone mineral density *in vivo* independent of body weight changes**

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P69 **Protein Kinase R activates the NFkB signalling pathway in osteoblast like cells in response to pro-inflammatory cytokines, interleukin-17A and tumour necrosis factor-alpha**

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P70 **Ultrasound applications in knee osteoarthritis**

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P71 **The communication of higher level evidence in Osteoarthritis: are we speaking the same language?**

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P72 **Characterisation of spinal cord injury-induced osteoporosis in a rat model**

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P73 **Jumping Joints: the complex relationship between osteoarthritis and jumping mechanography**

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P74 **Common vitamin D-related genetic variants are associated with bone health in the Hertfordshire Cohort Study**

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P75 **The benefits of regular weight bearing activity throughout the life-course: do men and women reap the same rewards?**

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P76 **A novel 3D loading model for osteoarthritis drug screening**

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P77 WITHDRAWN.

P78 **Knee biomechanics differ between sexes in end-stage knee osteoarthritis**

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P79 **Interleukin-17 is a potential contributor to the inflammatory environment in the osteoarthritic joint**

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P80 **Participation of Wnt signalling pathway on osteogenic potential of titanium with nanotopography**

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P81 WITHDRAWN.

P82 On the SLM and EBM of Ti-6Al-4V ELI alloy for advanced knee arthroplasty

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P83 Cellular behavior of osteoblast on Nanoconvex and Nanoconcave textured titanium surfaces

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P84 Morphological evaluation of subchondral trabecular bone in the talocrural joint

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P85 *Ex vivo* murine metatarsi cultures under quasi-static loading and mTOR/NF-kB treatment modulate endochondral ossification

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P86 The development of a magnetic resonance scoring system for evaluating osteochondral healing in preclinical models – the 'AMOS' score

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P87 The presence of actin-rich cytoplasmic processes of chondrocytes within non-degenerate human femoral head cartilage

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P88 Sonographic Bridging Callus: An early predictor of fracture union

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P89 Correlation between different pain phenotypes and analgesic use: a prospective cohort study of patients suffering from knee osteoarthritis

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P90 Relationship between clinical characteristics and self-declared pain profiling in patients with osteoarthritis undergoing knee replacement surgery

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P91 The most comprehensive tribological assessment to date of PEEK-based materials as potential hip replacement bearing surfaces

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P92 Effects of Matrix Stiffness on Osteoblast Differentiation from Pluripotent Stem Cells

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P93 Disuse does not alter trabecular rod and plate distribution in mouse tibiae

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P94 Investigation of Ankle Fractures, Readmission and Risk Factors

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P95 Identifying multiple adipocyte phenotypes in osteoarthritic and control femoral heads

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P96 Relationship between standardised uptake values, Hounsfield Units and bone density value in the lumbar spine: a study in alkaptonuria subjects using 18 F-NaF PET/CT and DEXA scan

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P97 The prevalence of coronal tibial bowing in a Western population

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P98 Hydroxyapatite surface properties determine mesenchymal stromal cell proliferation via the Wnt signalling pathway

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P99 Preliminary study on the use of 3D printed models in the pre-operative planning of revision ACL reconstruction

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P100 Modelling the effect of bone damage on creep deformation in human vertebrae

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P101 In-Silico Models to Investigate Bone Marrow Lesions

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P102 Self-reported Mobility in Adults with Osteogenesis Imperfecta

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P103 Freeze-thaw cycle enhanced decellularization of osteochondral tissue

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P104 Comparing extracellular vesicles produced by bone marrow mesenchymal stem cells of human, ovine and bovine origin

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P105 Microbiological culture findings of the femoral head as a prognostic factor for infection in primary hip replacement surgery

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P106 The osteogenic potential of weight bearing impact movements in older women

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P107 Bone-targeting glycol chitosan-PLGA nanoparticles for alendronate delivery

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P108 WITHDRAWN.

P109 WITHDRAWN.

P111 Post-Operative Complications in Hip Fracture Surgery for Patients over 90 years old

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P112 WITHDRAWN.

P113 Paradoxical Resistance: A new form of antibiotic resistance explaining recurrent bone and joint infections

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P114 Exploring the patient burden of failed Total Knee Arthoplasty

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P115 Interaction between Collagen and Mineral in human bone tissue in ontogeny

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P116 Manipulation of displaced paediatric limb fracture in Emergency Department is safe and cost effective: a review of a new protocol

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P117 Multicentre Intermediate to Long Term Follow Up of Hintegra Total Ankle Replacements

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P118 Conversion to Combined Partial Knee Arthroplasty for disease progression following Partial Knee Arthroplasty retains a functionally superior gait compared to primary Total Knee Arthroplasty

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P119 Collagen and mineral attributes in Raman spectroscopy correlate with elastic mechanical properties in osteoarthritic subchondral bone

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P120 A retrospective audit of post operative rehabilitation management of quadriceps tendon repair

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P122 Analysis of Reaming Samples Within the T&O Department

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P123 Early outcomes of total knee replacement using a novel technique for proximal tibial alignment

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P124 Is ankle fracture related to low BMD and subsequent fracture? A systematic review

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P125 Effect of gut peptides ghrelin and obestatin on human fetal osteoblasts (hFOB)

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P126 Multiscale subject-specific modelling for the investigation of structural adaptation in the lumbar spine

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P127 The ability of orthopaedic surgeons to assess femoral malrotation post trauma: a questionnaire based audit

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P128 Influence of Poly-beta-amino-esters (PBAE) kinetics and hydrolysis on chlorhexidine release via Layer by Layer (LbL) coated nanoparticles

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P129 Can nerve conduction studies be used as a prognostic indicator of PROMs in carpal tunnel decompression surgery?

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P130 A change of practice in the management of distal radius fractures within a regional T&O Department. Early Mobilisation out of cast at 4 weeks versus 6 weeks

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P131 A novel external fixation method and its impact on wrist distraction in relation to distal radial fracture

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P132 Chemical and Mechanical Regulation of Osteoblast Differentiation from Pluripotent Stem Cells through the Rho/ROCK Pathway

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P133 Ultrasonic attenuation properties of various adhesive couplants for early detection of osteoarthritis by passive monitoring of acoustic emission

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P134 WITHDRAWN.

P135 Should we routinely perform a post-operative haemoglobin check following unicompartmental knee arthroplasty?

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P136 Does virtual reality simulation have a role in training trauma and orthopaedic surgeons?

Raymond McKenna, Dessie Gibson, John Wong-Chung

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P137 Is there an increased risk of peri-operative complication in patients with obstructive sleep apnoea having shoulder surgery?

Parag Raval[1], Megan Scotcher[2], Patrick Musto[3], Radhakant Pandey[1], **Oliver Cottle**[4]

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P138 Stiffness post total knee replacement: a proof of principle study investigating the effect of genetic expression of markers of fibrosis

Charles Mann[1,2], Anne Bradley[1], Eleanor Jones[3], Iain McNamara[1,2], Toby Smith[3], Graham Riley[3]

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P139 Anti-TNF-Alpha Agents: chondroprotective or potentially harmful for articular cartilage?

Emanuele Chisari[1,2], Khaled Yaghmour[1], Wasim Khan[1]

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P140 *In vitro* evaluation of a gelatin/PDMS scaffold seeded with rat bone marrow mesenchymal stem cells for bone fracture repair

Luisa Garcia[1], Elizabeth Gill[2], Matthew Allen[1], Shery Huang[2], Frances Henson[1]

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P141 WITHDRAWN.

P142 WITHDRAWN.

P143 Injection moulding polyimides bone plate and screw design for osteoporosis patients

Jianshu Yu[1,2,3], Ziyu Liu[1,2], Yingying Gu[1,2], Maryam Tamaddon[1,2], Shen-Mao Chen[1,2], Zhongfu Zhou[3], Chaozong Liu[1,2]

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P144 Modelling trabecular bone architecture as a Voronoi network

Andrew Phillips

Structural Biomechanics, Civil and Environmental Engineering, Imperial College London, London, UK

P145 Implementing a disease management program: what works and what doesn't work

Kathy Williams

Clinical Services, Kaiser Permanente, Pasadena, USA

P146 Ex-Vivo Organ Culture of the Porcine Femoral-Tibial Joint in a dynamic loading rig: Work in progress

Natalie Fox[1], Daniel Thomas[1], John Fisher[2], Eileen Ingham[1]

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P147 Bicondylar tibial plateau fractures: A retrospective review of 64 cases

Alexander Matthews[1], Nathan Moore[2], Christoph McAllen[1]

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P148 Muscle activity, joint force and dual-energy X-ray absorptiometry (DXA): generating normative data to facilitate clinical translation

Leanne Sawle, **Jake Bowd**, Zornitza Glavcheva-Laleva, Dionne Shillabeer, Cathy Holt

School of Engineering, Cardiff University, Cardiff, UK

P149 Pilot study on the relationship between patient-reported outcome measures, knee biomechanics, and OARSI suggested performance-based tests in end-stage knee osteoarthritis

Marina De Vecchis[1], Paul Robert Biggs[1], Chris Wilson[1,2], Gemma Marie Whatling[1], Cathy Avril Holt[1]

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P150 Digital volume correlation of bone and biomaterials

Gianluca Tozzi

School of Mechanical and Design Engineering, University of Portsmouth, Portsmouth, UK

P151 Frequency of neck pain among drivers driving during day and night in Lahore: a descriptive cross sectional study

Zahoor Elahi[1], Ayesha Mahmood[1], Muhammad Kamran Hanif Khan[2], Khurram Sohail[3], Waleed Jameel[4]

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P152 Glutamate receptor expression in the tibial subchondral bone changes after medial opening wedge high tibial osteotomy

Alison Kinghorn[1,2], Carole Elford[1], Paul Biggs[1], Chris Wilson[2], Cathy Holt[1], Deborah Mason[1]

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LATE BREAKING POSTERS

LBP1 **Imaging Fibrous Dysplasia of bone**

Alan Boyde[1], Emanuela Spica[2], Alessandro Corsi[2], Mara Riminucci[2]

[1]Dental Physical Sciences, QMUL, London, UK; [2]Department of Molecular Medicine, Sapienza University, Rome, Italy

LBPP1 **Fleas and bites in bones**

Alan Boyde[1], David Mills[1], Agustin Manuel Abba[2], María Cecilia Ezquiaga[2]

[1]Dental Physical Sciences, QMUL, London, UK; [2]Centro de Estudios Parasitológicos y de Vectores (CEPAVE), UNLP-CONICET, La Plata, Argentina

LBP3 **Perlecan Heparan Sulphate Supports Endochondral Ossification by Signalling Fibroblast Growth Factor Receptors and Promotes Cartilage Loss in Osteoarthritis**

Christine Chuang[1], Cindy Shu[2], Susan Smith[2], Margaret Smith[2], Miriam Jackson[2], James Melrose[2], Bruce Caterson, Megan Lord[3], Chris Little[2], **John Whitelock**[3]

[1]Panum Institute, University of Copenhagen, Copenhagen, Denmark; [2]Kolling Institute, University of Sydney/Royal North Shore Hospital, Sydney, Australia; [3]Graduate School of Biomedical Engineering, University of New South Wales, Sydney, Australia; [4]School of Biosciences, Caerdydd University, Cardiff, UK

LBP4 WITHDRAWN.

LBP5 **3D printing for visualisation of bone quality in osteoporosis**

Alexander Jon Cresswell-Boyes, David Mills, Graham Roy Davis, Alan Boyde

Dental Physical Sciences Imaging Unit, Queen Mary University of London, London, UK

LBP6 **Postoperative Blood Testing in Total Hip Replacement, is it needed?**

Vipul Garg, Ian Byrom, Ibrahim Malek, **Mustafa Abdilmalik**

Trauma and Orthopedics, Wrexham General Hospital, Wrexham, Wales

LBP7 WITHDRAWN.

LBP8 **Efficacy of a bone healing stimulator (Exogen) on fracture non-union: a single centre experience**

Muhammad Abuzar Yusuf, Yosef Hamed, Bismah Umerji, Aamir Zubairy

Trauma and Orthopedics, East Lancashire Teaching Hospitals NHS Trust, Blackburn, UK

LBP9 **Re-admission within 28 Day after Elective Total Hip Replacement and Total Knee Replacement in District General Hospital**

Vipul Garag, Raghuvendra Nanjuniah, Ibrahim Malek, **Mustafa Abdilmalik**

Department of Trauma and Orthopedics, Wrexham Maelor Hospital, Wrexham, Wales

LBP10 **An Audit of practice: Use of Anaesthetic in Neck of Femur Fractures**

Vipul Garag, Hayley Lawrence, Yogesh Joshi, **Mustafa Abdilmalik**

Department of Trauma and Orthopedics, Wrexham Maelor Hospital, Wrexham, Wales

LBP11 **Assessment of surgical outcome and complications in cementless Total hip replacements with various femoral stems**

[1]**Kunwar Thakre**, Rama Mohan, Deepu Bhaskar

[1]T&O North Manchester General Hospital, Manchester, UK; [2]ST8 T&O, North Manchester General Hospital, Manchester, UK

LBP12 WITHDRAWN.

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We offer one of the widest ranges of oral contraceptives in the UK, offering high quality products and significant savings for the NHS, complemented by comprehensive support programmes for both medical professionals and patients.

We launched our first Bone Health product in 2014 having identified an unmet need for prescribers and patients to have access to licenced medicines within the vitamin D therapeutic area.

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For more information, please contact us on
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or visit www.mereobiopharma.com

UCB

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As a gold open access journal submission to BJR is free, and no fee is payable unless the article is accepted for publication. All articles published in BJR are completely free to read online and download.

Find out more about submitting a paper or read the latest articles online at:
online.boneandjoint.org.uk/journal/bjr

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IOF

The International Osteoporosis Foundation (IOF) is the world's largest nongovernmental organization dedicated to the prevention, diagnosis and treatment of osteoporosis and related musculoskeletal diseases. IOF members, including committees of scientific researchers as well as more than 246 patient, medical and research societies in 99 locations, work together to make fracture prevention and healthy mobility a worldwide heath care priority. www.iofbonehealth.org

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The purpose of the National Joint Registry for England, Wales, Northern Ireland and the Isle of Man is to collect high quality and relevant data about joint replacement surgery in order to provide an early warning of issues relating to patient safety. The NJR collects data on all hip, knee, ankle, elbow and shoulder joint replacements across the NHS and independent healthcare sector.

In a continuous drive to improve the quality of outcomes and ensure the quality and cost-effectiveness of joint replacement surgery, the NJR will monitor and report on outcomes and support and enable related research.

A wide range of implants can be used in the joint replacement operations. The registry helps to monitor the performance of these implants and the effectiveness of different types of surgery, improving clinical standards and benefiting patients, clinicians and the orthopaedic sector as a whole.

ORS

Orthopaedic Research Society (ORS)
www.ors.org

For over 60 years, the Orthopaedic Research Society (ORS) has been the leading research society supporting engineers, orthopaedic surgeons, veterinarians, biologists, and clinicians in pursuit of a world without musculoskeletal limitations.

The ORS continues to bring together the best researchers and surgeons in the world and gives them a community to share new research findings, discuss new ideas and to collaborate in new and innovative ways. The ORS offers programs that teach, mentor and encourage our members while inspiring them to move the field of orthopaedic research forward.

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Oxford Biosystems, part of the BioVendor Group, has been a supplier of quality products for the investigation of bone and cartilage metabolism for many years.

Our product range includes ELISA kits and reagents for the measurement of biomarkers such as Vitamin D, PTH, Osteocalcin, Ostepontin, TRAP-5, Matrix metalloproteinases, Osteoprotegerin and free soluble RANKL as well as biomarkers of the Wnt signaling pathway such as Periostin, Sclerostin and DKK-1, and osteocyte derived FGF23 (both C-terminal and Intact).

The TAmiRNA osteomiR® kit from Biomedica has been developed to detect and quantify 19 microRNAs in human serum with a known association to bone cell function, bone remodelling and fracture risk. The new miRNA kits from BioVendor offer a novel, immunoassay-based method of miRNA quantification that provides results within 3 hours and is easily automated.

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ROS

The Royal Osteoporosis Society is the only UK-wide charity dedicated to improving the prevention, diagnosis and treatment of osteoporosis. We are committed to supporting people with osteoporosis to live well, research into new treatments and finding a cure. As the UK expert in bone health we provide:

- Accredited training and e-learning for health professionals.
- Patient information and clinical guidelines to promote best practice.
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theros.org.uk/healthcare-professionals

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The concept that drives the Horizon is that it must be future proof with capabilities to meet evolving applications.

Horizon is backed up by Vertec's customer focus which includes skilled applications specialists and service engineers to make sure you get the best from what we supply.

SPEAKER ABSTRACTS

More than skin deep: how sunlight shapes our bodies and minds

Linda Geddes
Journalist, Freelance, Bristol, UK

Our biology is set up to work in partnership with the sun. From our sleep cycles to our immune systems and our mental health, access to sunlight is crucial for living a happy and fulfilling life. New research suggests that our light exposure over a lifetime – even before we were born – may shape our risk of developing a range of different illnesses, from depression to diabetes. Geddes explores the extraordinary significance of sunlight, from ancient solstice celebrations to modern sleep labs, and from the unexpected health benefits of sun exposure to what the Amish know about sleep that the rest of us don't.

Menopause and osteoarthritis: what is the evidence for a link?

Fiona Watt
Kennedy Institute of Rheumatology, University of Oxford, Oxford, UK

Musculoskeletal pain and osteoarthritis are more common in women and their frequency increases with age. Musculoskeletal pain is one of the commonest symptoms reported at the time of the menopause, in up to 50% of women. Estrogen deficiency brings about changes to many joint tissues: muscle, soft tissues, cartilage and bone, as well as changes in pain perception and inflammation, which may predispose to symptomatic osteoarthritis. There is also preclinical evidence implicating the role of sex hormone deficiency in the aetiology of osteoarthritis. There have been few clinical or interventional studies at the time of menopause specifically in musculoskeletal pain or symptomatic OA. The epidemiological and trials evidence for the effects of hormone replacement therapy (HRT) on joint pain or osteoarthritis will be discussed. Most of the randomized control trial (RCT) evidence comes from large HRT clinical trials for typical symptoms of menopause. There is no current evidence to support HRT preventing or delaying the onset of osteoarthritis. Hand osteoarthritis frequently presents around the time of menopause. A new study in post-menopausal women with hand osteoarthritis seeking to test the feasibility of an RCT investigating whether HRT has a therapeutic effect on pain and other symptoms will be discussed. A causal link between hormonal changes at the time of menopause and the pathogenesis of osteoarthritis has not been demonstrated. There remains much still to understand about how we might prevent joint pain and osteoarthritis at the time of the menopause.

New therapeutic approaches for OA including overexpression of lubricin and IL-1Ra

Brendan Lee
Molecular and Human Genetics, Baylor College of Medicine, Houston, USA

Osteoarthritis currently has no approved disease modifying therapies. Gene therapy is a potentially attractive strategy given the closed compartment offered by the targeting of large and small joints. To improve clinical translation of mouse models of OA, we developed high resolution microCt imaging of cartilage to improve objective quantification and throughput of therapeutic evalution of therapies in models of post-traumatic OA. We also adapted the helper-dependent adenoviral vector platform for gene delivery as it shows long duration expression due to reduced immunogenicity as well as having a large cloning capacity of up to 36 kb. By combing in these approaches, we have demonstrated that gene transfer of secreted proteins such as IL1RA and PRG4 can exhibit anti-inflammatory and chondroprotective (anti-catabolic) effects, respectively, in delaying OA progression in multiple mouse models. Morever, we were able to translate this approach into an equine model of post-traumatic OA. These data form the foundation for planned human clinical trials.

A global perspective on adolescent growth and healthy musculoskeletal ageing

Kate Ward
MRC Lifecourse Epidemiology, University of Southampton, Southampton, UK

Sub-Saharan Africa (SSA) already has twice the number of older adults than northern Europe; a figure expected to grow faster than anywhere globally, from 46 million in 2015 to 157 million by 2050. As SSA transitions due to rapid urbanisation, the changing demographics are generating an exponential rise in the burden of non-communicable diseases of ageing (NCD). Musculoskeletal disease is a major, and increasing, contributor to the current global NCD burden, accounting for more years lost due to disability than cancer and cardiac disease. In SSA, there are few data on the prevalence and aetiology of musculoskeletal disease (osteoporosis and sarcopenia), and their impact on health-related quality of life. Both conditions, which represent low bone and muscle mass, muscle function and altered metabolism, are inevitable manifestations of ageing, leading to falls and fragility fractures (from low impact injuries), disability, frailty, morbidity and mortality.

At any one time in the lifecourse internal and external environmental factors may influence musculoskeletal health. Internal environment describes innate factors, such as genotype and consequent phenotype, and external environment are those factors which may

illicit a physiological response and are modifiable such as nutrition. Disentangling the effects of all of these factors is clearly complex, as many are inter-related. Nutritional status is a key determinant of adolescent growth rates, which themselves as determinants of peak bone and muscle mass, are important for future musculoskeletal health. The Gambia and South Africa were both identified in the 2018 Global Nutrition Report to suffer the 'triple burden of malnutrition', i.e. high levels of overweight, anaemia and stunting. These would all impact pubertal timing and growth and also risk of developing NCD's of ageing.

By using the available longitudinal data from cohorts and randomised controlled trials from the UK and SSA, it is possible to investigate how nutrition may influence healthy musculoskeletal growth and ageing. This talk will focus on work from SSA reviewing the importance of adolescent growth for future musculoskeletal health and current knowledge on musculoskeletal ageing.

Endogenous production of IL-1B by breast cancer cells drives metastasis and colonisation of the bone microenvironment

Penelope Ottewell
Oncology and Metabolism, University of Sheffield, Sheffield, UK

Objectives: Breast cancer bone metastases are incurable highlighting the need for new therapeutic targets. We have previously shown that increased IL-1B in primary breast cancers strongly associates with future relapse in bone. The current study investigates: 1) The source of IL-1B in metastatic breast cancers. 2) The mechanism by which IL-1B promotes bone metastasis. 3) Effects of inhibiting this molecule alone and in combination with standard of care drugs on primary tumour growth and bone metastases.

Methods: Tumour/stromal IL-B and IL-1R1 expression was assessed in patient samples and effects of the IL-1R antagonist, Anakinra or the IL-1B antibody Canakinumab on tumour growth and spontaneous metastasis were measured in a humanised mouse model of breast cancer bone metastasis. Syngeneic 4T1 and E0771 mouse models of bone metastasis were used to establish efficacy of Anakinra +/- doxorubicin and zoledronic acid. Effects of tumour cell-derived IL-1B on bone colonisation and parameters associated with metastasis were measured in MDA-MB-231, MCF7 and T47D cells transfected with IL-1B/control.

Results: In tissue samples from >1300 patients with stage II/III breast cancer, IL-1B in tumour cells correlated with relapse in bone (hazard ratio 1.85; 95% CI 1.05-3.26; P=0.02) and other sites (hazard ratio 2.09; 95% CI 1.26-3.48; P=0.0016). In a humanised model of spontaneous breast cancer metastasis to bone, Anakinra or Canakinumab reduced metastasis and reduced the number of tumour cells shed into the circulation. Adding Anakinra to doxorubicin and zoledronic acid significantly reduced primary tumour growth and metastasis in 4T1 and E0771 models: Numbers of mice with E0771 tumours that developed bone metastases reduced from 50% in the placebo to 0% and non-bone metastases from 50% to 16.67%. Production of IL-1B by tumour cells increased EMT, invasion, migration and bone colonisation.

Contact between tumour and osteoblasts or bone marrow cells increased IL-1B secretion from all three-cell types. IL-1B alone, did not stimulate tumour cell proliferation. Instead, IL-1B caused expansion of the bone metastatic niche leading to tumour proliferation.

Conclusion: Pharmacological inhibition of IL-1B has potential as a novel treatment for breast cancer metastasis.

Bone cells: life at the extremes

Tim Arnett
Cell & Developmental Biology, UCL, London, UK

It has long been recognised that the skeleton contains a large reserve of alkaline mineral, hydroxyapatite, which is ultimately available to neutralise metabolic H^+ if acid-base balance is not maintained within narrow limits. With the development of functional cultures of primary bone cells, it became possible to study their direct responses to changes in extracellular pH. Unexpectedly, we discovered that acidosis (pH <7.2) was an obligatory requirement for activation of rodent osteoclasts to form resorption pits in bone and dentine. Less surprisingly, perhaps, we found that acidosis also selectively blocked mineral deposition by osteoblasts. These profound, reciprocal responses to pH could act as a 'fail safe' to maximise the availability of hydroxyapatite-derived OH^- ions in solution for buffering excess H^+. We also investigated the effects of hypoxia (a potential cause of tissue acidosis *in vivo*) on primary bone cells. Hypoxia (pO_2 <5%) robustly blocked the growth and differentiation of osteoblasts, thus preventing bone formation. Interestingly, hypoxia did not acutely affect osteoblast survival, but rather put the cells into a state of reversible quiescence. In contrast, we found that acute hypoxia strongly stimulated osteoclast formation. Equally surprising (for a cell containing abundant mitochondria) was the observation that the resorptive function of osteoclasts was unimpaired in hypoxia, so that large increases in resorption pit formation occurred. Thus, disruption of the blood supply could have multiple negative impacts on bone via the direct actions of reduced oxygen and pH on bone cells. These insights into osteoblast and osteoclast behaviour in extreme environments may shed extra light on the bone disturbances that accompany inflammation, fractures, tumours, anaemias, diabetes, kidney and respiratory disease.

BORS Presidential lecture

Andrew Amis
BORS, London, UK

This lecture will present a range of work which covers the anatomy and function of native human joints and their tissues, then moves into the development of joint prostheses.

The restoration of native joint stability and kinematics is the biomechanical aim when developing treatment methods following sports injuries, the implication being the avoidance of degenerative changes triggered by abnormal articular loading. Our recent work has included a robotic setup capable of moving joints and applying loads akin to clinical examinations. This is able to discern the contributions of individual ligaments and fibre bundles to resisting abnormal joint subluxations under load, thus guiding the surgeon to the primary restraints. A kinematics test rig can then measure joint kinematics across the range of motion, under the influence of joint displacing forces and/or torques. This has had extensive use to evaluate methods of ligament reconstruction, publishing recommendations for surgeons.

The development of a total shoulder prosthesis system will be described, starting from development of a novel minimally-invasive muscle-splitting posterior approach, then analysis of the joint geometry and bone structures, which led to novel configurations for the design of implant fixation features that engage with the strongest bone structure. The resulting component designs were optimised via extensive computer simulations and lab testing. Prototype components in ceramic and polyethylene were supplied by industry for laboratory testing (e.g. a range of impact loading configurations, up to 100 kN impacts). Cadaveric tests of individual components such as fixation interface micromotions under cyclic loads were paralleled by development of novel instruments to enable patient-specific MIS methods, which enable a less-invasive surgery than at present, with greatly reduced hospital stay anticipated. This will lead into some thoughts about the pathway to clinical use, and the impacts of the ever-increasing regulatory hurdles.

Synchrotron imaging for bone research

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Aging is on the verge of a new era. Humans are approaching old age in unprecedented numbers as a result of large baby boom cohorts born in the middle of the 20th century that are approaching traditional retirement ages. Increases in the prevalence of age-related disease, frailty, and disability are visible signs of the potential costs and social burdens arising from this historic demographic shift. Osteoporosis is affected dramatically by this shift with a marked increase in osteoporotic bone fractures. With recent advances in the etiology and treatment of osteoporosis, the development of diagnostic and monitoring tools to image biomechanical bone function is therefore one of the foci in basic and pre-clinical aging research. Biomechanical testing is the gold standard to determine bone function providing detailed information on overall bone mechanical and material properties. Nevertheless, direct testing fails in revealing local failure properties such as local deformations and strains. Incorporation of synchrotron imaging methods in the mechanical setups allows better insight into bone deformation and failure characteristics on various levels of structural organization. As part of the presentation, strategies for advanced hierarchical investigation of bone will be presented, working at different scales of resolution ranging from the whole bone down to its ultrastructure. At the microscopic level, bone microstructure is known to influence bone strength and failure mechanisms significantly. An image-guided failure assessment technique was developed allowing time-lapsed 3D visualization and computation of local displacements and strains for better quantification of fracture initiation and progression. Synchrotron imaging systems allow to uncover fully nondestructively 3D bone micro- and ultrastructure including vascular and cellular structures as well as mineralization and fiber orientation in the extracellular matrix and their effect on the development of damage and local failure. In conclusion, synchrotron-based functional imaging is extremely valuable in studying bone failure mechanisms. Functional investigation of microcrack initiation and propagation using synchrotron light will lead to a better understanding of the relative contribution of bone mass and bone quality in the etiology of osteoporotic fractures and the pharmacological treatment of age-related bone diseases.

Sequential and combination treatment of osteoporosis and fracture healing

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Efficient therapies are available for the treatment of osteoporosis, however, there are still unmet needs. Anti-resorptive therapies only increase bone mineral density to a certain extent and reduce the risk of non-vertebral fractures by 20%, the effect of bone forming and dual-acting treatments wears off over time, and the evidence for combination therapy targeting both resorption and formation is limited. In patients with osteoporosis and severely reduced bone mass and/or recurring fractures antiresorptive therapy may not be the optimal treatment. Two recent clinical trials; ARCH and VERO have compared bone forming treatment with antiresorptive therapy and have demonstrated that bone forming treatment is superior in reducing the fracture risk in patients with severe osteoporosis. These findings suggest

that the future approach to choice of osteoporosis treatment should be individualized taking severity of the disease and urgency of the need for effect into account.

All bone forming agents increase BMD and reduce the fracture risk, however, the effect wears off with time and treatment is therefore only temporary and bone forming therapy should be followed by antiresorptive treatment with a bisphosphonate or denosumab. The sequence of treatment matters as the BMD response to bone forming treatment is reduced in patients previously treated with antiresorptive drugs; however, based on the findings of the VERO trial, the anti-fracture efficacy of bone forming treatment in comparison with antiresorptives seems to be preserved.

The effect of teriparatide in combination with antiresorptive treatment has been investigated in a few studies of limited duration with BMD as the endpoint. The combination with denosumab and to some extent zoledronic acid seems to improve BMD gains but if these translate into increase fracture prevention needs to be demonstrated.

Clinical studies investigating the effect of osteoporosis treatment as monotherapy, sequential therapy or combination therapy on fracture healing are still very limited.

ABSTRACTS

OC1/PP1 High tibial osteotomy (HTO) and wide stance (WS) gait reduces knee joint loading in individuals with varus knee deformity

Jake Bowd[1,2], Paul Biggs[1,2], David Elson[2,3], Andrew Metcalfe[2,4,5], Chris Wilson[2,4], Cathy Holt[1,2], Gemma Whatling1,2

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Objective: Explore the effects of high tibial osteotomy (HTO) and wide stance (WS) gait style on peak external joint moments at the hip, knee and ankle.

Methods: Motion analysis of normal gait (NL) for 20 healthy volunteers (CONT) and 21 (22 knees) HTO patients was performed. HTO participants also performed WS gait and completed the Oxford Knee Score. Peak external moments during the first and second half of stance were analysed for all three planes.

Paired and independent samples t-tests identified changes associated with HTO surgery and WS gait (MATLAB); $p \leq 0.05$ was considered statistically significant.

Results: Oxford Knee Scores increased from 26.10 (9.07) to 37.60 (6.60) 12 months post-surgery, $p<0.001$.

HTO-NL did not significantly change hip, knee or ankle sagittal plane moments. In the frontal plane, HTO significantly reduced first peak (2.91 (0.99) vs. 2.11 (0.94) %BW.h) and second peak (2.43 (1.04) vs. 1.60 (0.77) %BW.h) knee moments. Surgery also significantly reduced the second peak frontal hip moment. There were no significant changes in peak frontal plane ankle moments. Surgery significantly reduced first (0.49 (0.26) %BW.h vs. 0.30 (0.17) %BW.h) and second peak (0.98 (0.48) %BW.h vs. 0.67 (0.38) %BW.h) transverse plane moments at the knee. The second peak transverse moments at both the hip and ankle joints significantly increased.

Post-HTO WS compared to post-HTO NL resulted in significant changes in the first and second peak sagittal plane moments at the hip and knee joints. In the frontal plane there were significant reductions in first and second peak moments at the hip and knee when adopting a WS gait post-surgery. There were significant increases in frontal plane for both ankle moment peaks when adopting WS gait. Post-HTO WS also resulted in transverse plane second peak reducing at the knee, whilst the ankle second peak increased.

Conclusion: HTO reduces peak external frontal plane knee and hip moments to that of CONT. This is further complimented by WS gait, but potentially to the detriment of increased frontal plane ankle moments.

OC2/PP2 Which muscle parameters are longitudinally associated with knee osteoarthritis outcomes? Findings from the Hertfordshire Cohort Study

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Objectives: Osteoarthritis (OA) is the most common joint condition and sarcopenia is defined according to age-related deterioration in muscle parameters. Longitudinal studies examining the relationship between these two conditions are lacking. Thus, we investigated whether muscle strength and body composition was predictive of future knee pain or radiographic knee OA in the Hertfordshire Cohort Study (community-dwelling older adults).

Materials and methods: We recruited 443 older adults (222 males and 221 females). At baseline grip strength was assessed using JAMAR dynamometry. Whole-body dual X-ray absorptiometry (DXA) was used to derive body composition. At follow-up, knee pain was defined as a Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) knee pain score of ≥1 and radiographic OA defined as Kellgren and Lawrence score ≥2. Linear regression was used to assess the relationship between muscle and body composition parameters and knee pain and/or radiographic OA in models adjusted for anthropometric and lifestyle factors, derived from questionnaires.

Results: The mean age of participants was approximately 69 years at baseline and follow-up was 6.5 years. There were no significant sex differences in the prevalence of radiographic OA (males 101 (50.2%), females 118 (58.7%)) or knee pain (males 68 (31.2%), females 82 (37.4%)).

In fully-adjusted analyses, we observed that baseline grip strength (OR 0.56 (0.37, 0.86) z-score $p<0.01$) and conditional change in grip strength (OR 0.69 (0.54, 0.87), $p<0.01$)) were associated with knee pain at follow-up. Total fat mass was associated with the future radiographic OA alone (OR 1.36 (1.03, 1.80) z-score $p<0.03$). Combined knee pain and radiographic OA at follow-up was predicted by baseline grip strength (OR 0.51 (0.28, 0.95) z-score $p<0.04$) but also baseline total fat mass (OR 2.02 (1.28, 3.20) z-score $p<0.01$) and percentage lean mass (OR 0.44 (0.25, 0.78) z-score $p<0.01$)

Conclusions: We observed that muscle mass and body composition were associated with the future development of knee pain and radiographic OA. If our results are replicated elsewhere, individuals with poor grip strength and body composition could

be targeted in order to reduce the risk of future knee pain and radiographic OA.

OC3/PP3 Ochronotic pigment distribution in alkaptonuric mice reveals that homogentisic acid deposition in tissues reflects the intensity of mechanical loading

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Objectives: Musculoskeletal disease is often related to tissue damage from mechanical loading or "wear and tear". Currently there are no good experimental models predicting early tissues changes in response to mechanical damage. In the ultra-rare disease alkaptonuria (AKU) there is failure to metabolise homogentisic acid (HGA). Most HGA is excreted but some is eventually deposited as ochronotic pigment in connective tissues leading to musculoskeletal disorders including tendon ruptures, heart valve stenosis and severe osteoarthritis. Here, the anatomical distribution of ochronotic pigment was investigated in AKU mice to determine potential factors initiating ochronosis.

Methods: Tissues from 1 year AKU mice (Hgd tm1a -/-) were dissected, fixed (10% formalin), hard tissues decalcified (10% EDTA), embedded in paraffin wax and sections stained with Schmorl's stain to detect pigmentation. Pigmented chondrons were quantified in representative whole knee joint sections of mice aged 7-52 weeks.

Results: Pigmentation was first detected at 9 weeks in the calcified cartilage of the knee joint; 2 chondrons/section increasing linearly to 135 chondrons/section at 52 weeks (R^2=0.769, p<0.001). Pigmentation was also found in the calcified cartilage of the hip, shoulder, elbow and ankle joints. In the vertebral column, pigmentation was found in vertebral endplates, but not in bone nor disc. A striking observation was the significantly greater number (mean±SEM) of pigmented chondrons in the more weight bearing thoracic and lumbar vertebrae (56.2±4.1) compared with the tail (1.5±0.4) (p<0.001). Clusters of pigmented chondrons were observed at insertions of tendons and ligaments, such as the Achilles tendon on the calcaneus and the cruciates on the tibia/femur, where more load is transmitted. No pigmentation was observed in the eye, ear, liver, kidney nor notably the heart valves.

Conclusion: Anatomically, the initial sites of ochronosis are in tissues subjected to the most mechanical loading, such as calcified cartilage in weight-bearing joints. Increased stress appears to lead to increased pigmentation; in effect HGA behaves like an endogenous marker of repetitive load-induced matrix damage.

OC4 Characterization of Pain in Fibrous Dysplasia

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Fibrous dysplasia (FD) is a rare disease caused by somatic activating GNAS mutations resulting in replacement of normal bone with fibrous tissue, leading to fractures and disability. Pain in FD is common; however, its mechanisms are poorly understood. Retrospective studies have shown that FD pain responds variably to treatment and does not correlate with skeletal disease burden. The standard treatments offered to patients with FD pain are NSAIDS, opiates and bisphosphonates; typical treatments for nociceptive pain. The contribution of nociceptive versus neuropathic-like pain in FD might explain variabilities in the clinical presentation and response to treatment. There is thus a critical need to characterize the types of pain in patients with FD to develop effective treatment strategies.

Data were analyzed from FD patient registries: the FD Foundation (FDF)(US) and the Rare and Undiagnosed Diseases (RUDY) study (UK). Subjects completed questionnaires to distinguish experienced pain between neuropathic or nociceptive (painDETECT), health-related quality of life (SF-36), sleep quality (Pittsburg Sleep Quality Index)(PSQI) and mental health (Hospital Anxiety and Depression Scale)(HADS). Analyses were performed usingone-way ANOVA, Kruskall-Wallis multiple comparisons, and Chi-squared tests using Graphpad Prism (GraphPad Software.2017.San Diego.CA).

Data from a total of 241 subjects were analyzed: 173 in the FDF registry (mean age 40y, range 18-77, 85% women) and 68 in the RUDY study (mean age 47y, range 18-77, 75% women). Distribution of pain types according to established cutoff values for nociceptive pain (45.2%), unclear pain (23.2%), and neuropathic pain (31.5%) varied by severity of pain. Compared to subjects with nociceptive pain, those with neuropathic pain had scored significantly worse in all SF-36 quality of life scales (p<0.05), more severe anxiety and depression on HADS (p<0.01), and poor sleep quality on PSQI (p<0.01).

These findings demonstrate that pain in FD includes both nociceptive and neuropathic elements, which may contribute to the clinical variability and response to treatment. Compared to patients with FD and nociceptive pain, those with neuropathic pain may be at increased risk for diminished quality of life and mental health. Evaluation of patients with FD should include assessment of neuropathic pain to determine effective management strategies.

OC5 Novel use of Burosumab in refractory iron-induced FGF23 mediated hypophosphataemic osteomalacia

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Background: Refractory iron-induced fibroblast growth factor 23 (FGF23) mediated hypophosphataemic osteomalacia is a rare phenomenon. Treatment in case reports thus far have consisted of iron cessation and phosphate substitution. To our knowledge, we describe the first reported case of FGF23 inhibitor Burosumab being used in this condition.

Presenting Problem: We present a 32-year-old man with a past medical history of complex Crohn's disease and significant iron-deficiency anaemia. Computed tomography (CT) angiogram revealed focal ileocolic venous portal hypertension but after multidisciplinary discussion, a transjugular intrahepatic portosystemic shunt (TIPS) was not considered feasible. This therefore made the patient iron infusion dependent.

The patient subsequently developed severe foot and leg pain and was diagnosed with iron-induced FGF23 mediated hypophosphataemic osteomalacia. He was given oral phosphate and activated vitamin D, and his iron infusions were switched from ferric carboxymaltose to iron isomaltoside. This consequently lowered his FGF23 levels but his profound hypophosphataemia remained. He further developed poor tolerability to oral phosphate supplementation as this worsened his existing diarrhoea from the Crohn's disease.

One year later, he developed a progressive complete left femoral insufficiency fracture after minor trauma. He was therefore started on intravenous phosphate replacement with minimal benefit. Three months later, magnetic resonance imaging (MRI) demonstrated a new atraumatic right femoral head incomplete fracture and multiple pelvic fractures.

Clinical Management: Funding was obtained to start Burosumab (0.3 mg/kg) subcutaneously once a month. After three doses, we found substantial laboratory improvements in his osteomalacia and an increase in patient reported outcome scores such as the EQ5D-5L and the Brief Pain Inventory. Further, subsequent MRI showed complete resolution of the right femoral head fracture and near complete healing of the left femoral and pelvic fractures.

Discussion: We outline the first reported use of Burosumab in refractory iron-induced FGF23 mediated osteomalacia with successful outcomes, resulting in avoidance of orthopaedic surgery. Although the high monetary cost makes routine use of Burosumab difficult, this patient showed good tolerance of the drug with no apparent toxicity. We further discuss the mechanism and applications of this novel treatment and highlight the importance of collaboration between rheumatologists and gastroenterologists.

OC6 Mutations in osteoarthritis susceptibility genes cause functional changes in zebrafish joints that lead to altered load and disease pathology

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Background: Osteoarthritis (OA) is a joint degenerative disease and leading cause of pain and disability worldwide. Genome Wide Association Studies (GWAS) have identified more than 100 genes that are associated with osteoarthritis susceptibility but in vivo systems allowing parallel functional assessment of multiple genes are limited. Zebrafish offer excellent genetic tractability and in vivo imaging.

Objectives: To establish normal osteoarthritis disease course in ageing zebrafish. To test effect of mutation of osteoarthritis susceptibility genes on joint shape and biomechanical function in early development and in adults. To develop screening tools to allow rapid comparative assessment of novel genes on joint physiology.

Methods: We have used confocal microscopy, histology and microCT to capture joint shape and observe cell biology across the mutant lines. We have used CRISPR-cas9 genome editing to generate mutants and analysed both mosaic 'Crispants' and stable mutant lines. We have used high speed video to capture joint motion. We have used a Material Testing Stage (MTS) with microCT to test skeletal performance. We have used Finite Element Analyses to investigate relative influence of shape and material properties on joint strains.

Results: We show that all osteoarthritis susceptibility genes tested *(Col9a1, Col11a2, Wnt16, Gdf5, Mcf2l, Dot1l, Ncoa3, Chsy1, Barx1)* affect joint development in zebrafish, which precede joint pathology. Finite Element analyses of mutant joints reveals changes to the mechanical environment that influence cell behaviour. The mutant phenotypes from the genes tested can be grouped into those affecting different aspects of joint cell behaviour, and spine performance. The changes seen in larvae predict phenotypes seen in the adults.

Conclusions: Taken together our data show that zebrafish can be used to rapidly screen and functionally assess osteoarthritis genes to give insight into how they cause pathological changes in vivo.

OC7 Preclinical diabetes accelerates onset of Osteoarthritis – lessons from model system

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Objective: Osteoarthritis (OA) is the most common joint disorder affecting millions worldwide. Multiple risk factors including obesity, ageing, diabetes, local/systemic inflammation predispose to OA. Metabolic syndrome –– a conglomerate of interrelated metabolic risk factors has been implicated in OA pathogenesis. WNIN/Gr-Ob mutant obese rat strain (Muts) developed indigenously at our institute exhibits preclinical diabetes-like alterations (obesity, insulin resistance, impaired glucose tolerance, higher BMI) with age. We therefore aimed to explore the potential application(s) of these Muts in OA research to study metabolic and structural alterations (knee joints) with age akin to human OA.

Methods: Knee joints were harvested from female Muts aged 3, 6 and 9 months (n = 6 in each group) and evaluated for OA-like changes using radiography, micro-Computed Tomography(CT) and histopathology and compared against their age-matched Wistar controls (WNIN).

Results: Radiographic assessment showed ossification of soft tissues, osteophyte formation (6 months), subchondral sclerosis and bone cyst (9 months) in Muts. Micro-CT studies revealed a significant reduction in tibial subchondral bone plate porosity percentage in Muts when compared to controls (At 6 months: 3.29±1.07 versus 27.36±1.04, $p<0.05$; At 9 months: 1.01±.0.21 versus 23.01±5.60, $p<0.05$) and a significant increase in subchondral trabecular percent bone volume (BV/TV,%) in Muts compared to controls (At 6 months: 77.45±21.31 versus 45.33±3.86, $p<0.05$; At 9 months: 86.98±5.12 versus 48.5±1.91, $p<0.05$) implying subchondral sclerosis. Histopathological evaluation of tibia revealed degenerative changes in cartilage such as fibrillation and erosion in addition to subchondral sclerosis, osteophyte and bone cyst formation in Muts at 6 and 9 months with no abnormalities found in tibia of control rats. These spontaneous pathological alterations (hallmarks of human OA) observed in Muts are novel findings with very few spontaneous rat OA models currently available.

Conclusion: Our findings suggest that the pre-clinical diabetes-like metabolic perturbations in Muts could coalesce to effect OA-like changes in their knee joints advocating for their potential application as a befitting rat model for spontaneously-generating OA en-route the 'natural progression' of the disease, mimicking human OA.

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OC8 Bi-Unicondylar Arthroplasty preserves the Anterior Cruciate Ligament, retaining near-normal anteroposterior stability in the treatment of medial and lateral tibiofemoral arthrosis

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Objectives: The Anterior Cruciate Ligament (ACL) is essential for knee stability and much effort is expended reconstructing it in younger patients. Conversely, the majority of Total Knee Arthroplasty (TKA) systems necessitate ACL resection, resulting in post-operative instability. Bi-Unicondylar Arthroplasty (Bi-UKA) is an ACL-preserving alternative in the treatment of ipsilateral medial and lateral tibiofemoral arthrosis, but little is known of its associated anteroposterior stability compared to posterior-cruciate retaining TKA.

Methods: Eight paired fresh-frozen cadaveric knees were mounted in an validated kinematics rig facilitating optical tracking of tibiofemoral kinematics from 0–90^0 flexion. Anteroposterior stability was defined as change in anterior/posterior translation under 90N of anterior/posterior drawer compared to 0N drawer. The quadriceps, iliotibial band and hamstrings were individually loaded proportional to their physiological cross-sectional area (total 4Kg) ensuring tibiofemoral contact. Knees were tested intact, then following Bi-UKA, then posterior-cruciate-retaining TKA. Data were analysed using two-way repeated measures analyses of variance with post-hoc paired t-tests with Bonferroni correction.

Results: Under anterior drawer, Bi-UKAs were as stable as intact knees from 0 – 70^0 ($p>0.05$) but demonstrated slightly reduced stability at $80^0$and 90^0 ($p<0.02$). Conversely, TKAs were less stable than intact knees at all flexion angles ($p<0.04$) except 20^0 ($p=0.07$). Bi-UKAs were significantly more stable than TKAs at 10^0 ($p=0.02$) and 30-90^0($p<0.019$). Under posterior drawer, Bi-UKAs were as stable as intact knees at all flexion angles ($p>0.05$). Whereas, TKAs were less stable than the intact knees ($p=0.001$) and Bi-UKAs ($p<0.012$) at all flexion angles. The maximum mean anterior translation for the intact knees was 5.1mm compared to 10.8mm for Bi-UKAs and 20.1mm for TKAs. All states translated less posteriorly: maximum mean intact knee -3.9mm, Bi-UKAs -4.1mm, TKAs -8.7mm.

Conclusion: Bi-UKA preserves both cruciate ligaments and results in near normal anteroposterior stability. The resection of the ACL during TKA results in anterior instability. Although the posterior cruciate ligament is preserved during cruciate-retaining TKA, its interaction with the ACL is lost, resulting in a small loss in posterior stability.

The improved stability of Bi-UKA may result in superior post-operative knee function for patients with medial and lateral tibiofemoral arthrosis and warrants further investigation.

OC9 Individuals with high bone mass have increased clinical and radiographic progression of knee osteoarthritis independent of fat mass

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Background: High bone mineral density (BMD) is a risk factor for knee osteoarthritis (OA), yet evidence suggests that higher BMD may protect against OA progression. We performed longitudinal analyses in an adult population with high bone mass (HBM; BMD Z-score≥+3.2) and their unaffected relatives/spouses to determine if HBM is associated with radiographic knee OA sub-phenotype (osteophytes, joint space narrowing [JSN]) progression, and any potential role of total body fat mass (TBFM).

Methods: Bilateral anteroposterior X-rays were performed at baseline and after eight years. OA sub-phenotypes were graded using the OARSI atlas. Medial/lateral tibial/femoral osteophyte and medial/lateral JSN grades were summed and change between timepoints derived (Δosteophytes, ΔJSN). OA progression was determined as Kellgren-Lawrence grade≥2 at baseline with an increase at follow-up. Knee pain was quantified at follow-up using the WOMAC questionnaire. Associations between HBM status and progressive OA sub-phenotypes were determined using multivariable linear and logistic regression with generalized estimating equations accounting for clustering. Analyses were adjusted for age, sex, height, baseline sub-phenotype grade, menopause and education, before further adjustment to determine the mediating effect of TBFM (assessed by DXA at follow-up).

Results: 307 knees from 154 individuals contributed to these analyses. 65% had HBM, 73% were female, mean age at follow-up was 65.8 (SD 12.4) years. Mean(SD) TBFM was 33.3(11.3)kg and 30.2(10.1)kg for those with and without HBM, respectively. HBM was associated with increased Δosteophytes (β=0.50[0.06,0.95],p=0.028) and ΔJSN (β=0.17 [0.03,0.31],p=0.018, β represents the mean difference between individuals with and without HBM). Additional adjustment for TBFM attenuated the associations with Δosteophytes/ΔJSN by 10%. HBM individuals had increased odds of overall OA progression, but confidence intervals were wide (OR=2.66[0.76,9.30],p=0.126). HBM individuals had 8-point higher WOMAC pain scores (β=8.14[2.12,14.16],p=0.008); adjustment for follow-up osteophyte score attenuated this estimate by 45%, follow-up JSN score by 21% and TBFM by 12%.

Conclusions: HBM is associated with clinical/radiographic features of OA progression, which is not explained by higher TBFM. Osteophytes explained an important amount of knee pain in this population. This highlights the utility of OA sub-phenotypes when studying OA progression.

OC10 Systemic Teriparatide with Locally Injected Mesenchymal Stem Cells Synergistically Enhances Fracture Healing

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Objectives: Fracture healing is a successful physiological process in the majority of cases; yet a proportion of fractures (particularly high energy trauma and in the elderly) at risk of developing a non-union or delayed union. As such stem cell therapy and pharmacological adjuncts have been investigated separately as modalities to accelerate and enhance bone healing. The hypothesis of this study was the administration of locally delivered mesenchymal stem cells (MSCs) suspended in fibrin glue, in combination with systemic delivered parathyroid hormone 1-34 (PTH 1-34) treatment, will lead to enhanced healing in a rat femoral non-union fracture model.

Methods: 48 Female juvenile Wistar rats underwent femoral fracture creating a 1.5mm osteotomy critical sized defect, which was stabilised using an external fixator. Animals were treated with intra-fracture injections of 1million cells/kg culture expanded bone marrow MSCs suspended in fibrin, daily subcutaneous injections of high (100mcg/kg) or low (25mcg/kg) dose PTH 1-34, or a combination of PTH and MSCs. A group with an empty gap, served as a control.

Results: Animals treated with high and low dose combination therapies led to increased callus formation compared to controls. In the high dose combination group this callus had significantly greater mineralised tissue volume and increased trabecular parameters compared to controls ($p<0.03$). This translated to significantly improved stiffness ($p<0.05$) and ultimate load to failure ($p<0.04$) in low and high dose combination therapy groups compared to controls. The high dose combination therapy group had the most significant improvement in modified RUST score compared to controls (13.8±1.3 vs. 5.8±0.5), although all groups demonstrated significant increases in radiographic RUST and Allen scores histologically.

Conclusion: We demonstrate the beneficial effect of localised MSC injections on fracture healing, and

the synergistic nature of this effect when combined with low or high dose teriparatide; our results suggest a dose dependency in the efficacy of concomitant PTH treatment. As such, these findings may have implications in the clinical treatment of fractures, especially those that may go onto non- or delayed unions.

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OC11 Predicting cortical bone adaptation in the mouse tibia: a longitudinal study

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The optimisation and personalisation of treatment plans for skeletal diseases requires the understanding of the effect of physiological loading to bone adaptation. This process can be studied with multi-scale computational models. Therefore, this study aims to develop a bone remodelling model to determine the contribution of mechanical loading in a preclinical mouse model and calibrate it with for physiological loading.

The right tibia of 14-week-old female C57BL6/J mice (N=5) were scanned weekly using *in vivo* micro computed tomography (micro-CT, 10.4µm/voxel), until week 22 of age (except week 16). Linear isotropic homogeneous micro-finite element (micro-FE) models were created from the bone mineral density (BMD) calibrated microCT images. The surface elements of bone and adjacent background were permitted to undergo resorption or apposition, based on different local mechanical stimuli (strain energy density, SED, or maximum principal strain, ε_I) by assuming a linear relationship between the change in BMD and the mechanical stimulus. To determine the effect of age, physiological walking load was applied to calibrate the bone remodelling parameters using the images obtained between weeks 14-16 or weeks 20-22. The simulated and experimental spatial patterns of bone apposition, resorption and overlap were compared between experimental and predicted bone at week 22. The Wilcoxon signed-rank test was used to test for any significant difference.

The tuned threshold and rates reflected intra-specimen variation. Periosteal resorption and endosteal apposition were higher between weeks 14-16 than weeks 20-22 but the model was able to achieve a similar degree of overlap for all cases (86%). The spatial match in apposition using week 20 parameters were 59.1 ± 3.3% and 59.3 ± 3.2% for SED and ε_I, respectively. The predicted resorption sites had an accuracy of 47.4 ± 7.0% and 45.7 ± 7.3% for SED and ε_I, respectively. The results obtained using the week 14 calibrated parameters were not significantly different from those obtained with parameters calibrated from week 20 images for both SED and ε_I. The results obtained showed that future bone remodelling simulations in mice can be calibrated from baseline scans and applied throughout the longitudinal study.

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OC12 The secretome of mesenchymal stromal cells drives functional heterogeneity

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Objectives: Mesenchymal stromal cells (MSCs), through their ability to generate bone and cartilage tissues, offer potential regenerative therapies for musculoskeletal disorders. However, MSC heterogeneity is a critical challenge to clinical translation. We identified a biomarker (CD317) that discriminates subpopulations with regenerative properties ($CD317^{neg}$) from those with enhanced pro-inflammatory characteristics ($CD317^{pos}$). Here we demonstrate how secreted outputs (proteins and extracellular vesicle (EV) cargo) of MSC subtypes determines phenotype.

Methods: We generated immortalised clonal lines of $CD317^{neg}$ and $CD317^{pos}$ human MSCs. EVs were isolated by differential ultracentrifugation and characterised by Transmission Electron Microscopy and Nanoparticle Tracking Analysis. LC-MS/MS was used to quantify EV and secreted proteins and a NanoString codeset quantified expression of ~800 EV-related miRNAs. Conditioned media containing secreted proteins and EVs was collected from cells and used in colony-forming assays, which were imaged or lysed for gene-expression analysis. Cell morphometrics were quantified by Phase Focus ptychography and changes in gene expression measured by QPCR.

Result: Of 861 secreted proteins identified across both MSC subtypes, 44 were significantly increased and 129 significantly decreased in $CD317^{neg}$ MSCs compared to $CD317^{pos}$ MSCs ($P<0.05$). Protein abundance was reversed in the EV compartments of $CD317^{neg}$ and $CD317^{pos}$ MSCs with 162 and 14 proteins significantly increased respectively ($P<0.05$). Bioinformatics revealed that the secretome and EVome of the regenerative $CD317^{neg}$ MSC were predominantly linked to migration and cell-matrix interactions. We identified 11 differentially expressed miRNAs in the EVs of $CD317^{neg}$ and $CD317^{pos}$ MSCs

(fold change -2.52-66.25, q<0.001-0.018). Of these, 9 were upregulated in CD317^{neg} MSCs including miRNAs implicated in promoting osteogenesis (miR-125b-5p, let-7i-5p, miR-29a-3p, miR-29b-3p and mir-199a-3p/miR-199b-3p) and negative regulation of inflammation (miR-125b-5p, miR-100-5p, miR-221-3p and miR-21-5p). Growing CD317^{pos} MSCs in conditioned medium from CD317^{neg} cells induced a morphological conversion to a CD317^{neg} phenotype, with significantly reduced cell volume and area, increased length:width ratio and migration, and suppressed expression of hallmark proinflammatory genes.

Conclusion: MSC heterogeneity is reflected in subtype-specific secretomes, which can control function including the interchange of plastic cell states. Appropriate selection of MSC subtypes and/or their secreted products will determine success in clinical applications.

OC13 Analysis of osteoclastic resorption in vitro reveals new pathways of bone collagen breakdown and novel markers of bone resorption in vitro and in vivo

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Objectives: Bone resorption involves dissolution of mineral and enzymic degradation of bone matrix. The primary enzyme is cathepsin K but other proteases including MMPs may be involved. Collagen degradation begins at the ruffled border-bone interface and breakdown products are transcytosed to the osteoclast apical surface for secretion. Some cleavage products of cathepsin K action have been partially identified, including CTX 1, but the pathway of collagen degradation has not been fully elucidated. We aimed to investigate the breakdown of bone collagen during resorption.

Methods: Human osteoclast precursors were cultured on dentine or plastic with MCSF (33ng/ml), plus or minus RANKL (66ng/ml) (n=6 per group). After 19 days medium was harvested and resorption quantified microscopically. Collagen breakdown products were detected by LC-QTOF-MS non-targeted chemical profiling. Profiles of media samples were compared between +RANKL on dentine and three control groups: osteoclast precursors +RANKL on plastic, -RANKL on dentine or –RANKL on plastic. A library was constructed of collagen breakdown products and their presence in mouse and human plasma and urine was investigated. To test correlation with resorption, osteoclast cultures were treated in a subsequent experiment; zoledronate was added to cultures at concentrations of 10^{-14}-10^{-4} M (n=6 per group).

Results: Twenty-eight unique entities were markedly elevated (p<0.001) in +RANKL/+dentine media compared with other groups (mass range 144-1541 Da). These included di- and tri-peptides and entities of greater molecular weight. Zoledronate inhibited resorption with a steep decline between 10^{-8} and 10^{-6} M (p<0.001). Similar dose-response curves were observed for the release of the collagen breakdown products (R^2=0.82). Subsequently, entities identified as glycylprolylhydroxyproline, prolyl-glycine and valyl-glycine were detected in mouse and human serum and urine.

Conclusion: We have identified previously unknown pathways of bone collagen breakdown leading to production of di- and tri-peptides. The release of these correlates with bone resorption and can be used to quantify bone resorption in vitro, simply and reliably. Some of these can be detected in serum and urine thus expanding the range of biomarkers to monitor bone turnover.

OC14 Understanding the role of L-cysteine and hydrogen sulphide in the beneficial effects of N-acetylcysteine on bone formation and arterial medial calcification

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Arterial medial calcification (AMC) reputedly shares similarities with bone mineralisation. However, emerging evidence indicates that these two processes differ in several ways. Understanding these differences is key to finding a treatment that prevents AMC without negatively affecting the skeleton. We have previously shown that N-acetylcysteine (NAC) promotes bone formation by ≤5-fold but inhibits AMC (≤75%). NAC can be deacetylated to L-cysteine, an important component in the intracellular generation of both hydrogen sulphide (H_2S) and glutathione. This study investigated whether L-cysteine and/or H2S mediate the effects of NAC on bone formation and AMC. Human umbilical artery-derived vascular smooth muscle cells (VSMCs) and mouse osteoblasts were cultured in mineralising medium (1mM β-glycerophosphate, 1mM sodium phosphate, 50µg/ml ascorbate) for ≤7 and 21 days, respectively. Cells were treated with NAC (0.5-2.5mM), L-cysteine (0.5-2.5mM) or the H_2S-donor, NaHS (50-300µM) throughout. Effects on cell function, survival and gene expression were investigated using established assays. L-cysteine (≥0.5mM) increased bone formation 3-fold (p<0.05) but inhibited VSMC calcification by ≤70% (p<0.01). In osteoblasts, NAC increases the mRNA and protein expression of osteogenic genes (e.g. osterix, alkaline phosphatase (TNAP), osteocalcin) by ≤6-fold (p<0.05) and stimulated TNAP activity (2.5-fold, p<0.05). Comparable effects were observed

following treatment with L-cysteine (≤3.5-fold, p<0.05). Conversely, NAC and L-cysteine had minimal effects on VSMC gene expression but increased cell survival by 25% (p<0.05). NaHS also increased bone formation (≤1.5 fold, p<0.05) and reduced VSMC calcification by ≤45% (p<0.01) but the effects were less efficacious. Both osteoblasts and VSMCs express mRNA/protein for the enzymes required for endogenous H2S generation, cystathione-γ-lase (CSE) and cystathione β-cynthase (CBS). Pharmacological inhibition of CBS or CSE did not attenuate the effects of NAC or L-cysteine on either bone formation or AMC. Together, these data suggest that the actions of NAC are unlikely to be mediated via H_2S alone but instead involve, at least in part, increased levels of L-cysteine. Our findings also demonstrate that the cellular mechanisms underpinning the functional effects of NAC and L-cysteine differ between osteoblasts and calcifying VSMCs.

OC15 TightRight : augmenting screwdrivers to reduce bone stripping rates and optimise tightness when inserting non-locking screws

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Objectives: Non-locking screws remain one of the most commonly used orthopaedic implants, however they are often poorly inserted. Exceeding the stripping torque for a screw hole reduces pullout strength. The aims of this study were firstly to quantify stripping rates and screw tightness for surgeons and secondly to assess how these change when using a screwdriver that indicates when optimum tightness is reached.

Methods: At the AO Davos Courses 2018 (Davos, Switzerland), 302 orthopaedic surgeons tightened 20 screws in two phases: Phase 1 - screws tightened to the surgeon's perception of optimum tightness. Phase 2 - using an augmented screwdriver that indicated, by audibly alarming and vibrating, when a predetermined optimum tightness was reached (defined as 70% of the maximum stripping torque). Within each phase, 10 partially inserted 3.5 mm non-locking cortical screws were tightened through a 3.5 mm plate into 4 mm thick artificial bone analogue of 0.32 g/cm^3. The stopping torque for each screw was recorded and compared to the stripping torque; if the stopping torque greatly exceeded the stripping torque, tightness values >100% were possible. A confidence value in each screw's purchase was recorded, 1-10. Following tests of normality, Student t-tests were performed to compare different phases and insertion confidences.

Results: For phases 1 and 2 respectively, stripping rates were 58 ±32% and 15 ±25% (p<0.0001) and the tightness for all screws was 190% ±255% (n=3020) and 87 ±49% (n=3020) (p<0.0001). Considering only unstripped insertions, tightness was 81 ±12% (n=1242) and 71 ±12% (n=2579) respectively. In phase 1, confidence was 7 ±2 (out of 10) for screws found to have not unstripped and 6 ±2 for stripped insertions (p=0.441), and 7 ±2 and 7 ±2 (p=0.216) in phase 2 respectively.

Conclusion: With an unaugmented screwdriver (Phase 1), stripping rates were high, though varied greatly amongst surgeons. Using an augmented screwdriver (Phase 2) greatly improved insertion, with optimum tightness being achieving alongside a significantly reduced rate of bone stripping. Further work incorporating these techniques into surgical education and clinical practice are recommended.

OC16 Targeting Rehabilitation to Improve Outcomes following total knee arthroplasty (TRIO): a randomised controlled trial of physiotherapy interventions

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Objectives: Physiotherapy for all patients following TKA is not effective at improving one-year outcomes. The aim of this study was to determine if a therapist-led outpatient intervention offered superior results compared to a home-exercise based protocol when targeting physiotherapy to TKA patients at risk of poor outcomes.

Methods: Parallel-group randomised controlled trial recruited at 13-centres in the UK. Patients were identified as 'potential poor outcome' based on an Oxford Knee Score (OKS) classification at 6-weeks post-surgery and randomised to either therapist-led outpatient rehabilitation or home-exercise based protocols. Evaluation took place following intervention, 6 and 12-months post-surgery. Primary outcome was comparative group OKS at 1-year. Secondary outcomes included, 'worst' and 'average' pain scores, EQ-5D, and satisfaction questionnaire. Health economic analysis was undertaken up to 1-year post-surgery. Incremental cost per Quality Adjusted Life Years (QALYs) were calculated from intervention costs, primary and secondary care usage, and EQ-5D data.

Results: 334 patients were randomised, 8 were lost to follow-up, therapy compliance was >85%. Between group difference in 1-year OKS was 1.91 (95%CI, -0.17-3.99) points favouring the therapist-led arm (p=0.07). Incorporating all time-point data, between group difference in OKS was 2.25 points (95%CI, 0.61-3.90, p=0.008). Small, non-significant reductions in secondary outcomes were observed favouring the therapist-led group. Enhanced satisfaction with pain relief (OR 1.65, p<0.02), ability to perform daily tasks (OR 1.66, p<0.02), and perform heavy tasks (OR 1.6, p=0.04) was reported in the therapist-led group. There was a small non-significant difference of 0.02 points (95%CI -0.02–0.06) between groups in EQ-5D, resulting in a £12,125 cost per QALY of delivering the therapist-led intervention with a 57% chance of being cost-effective at a £20,000 policy threshold.

Conclusions: We evaluated differing post-operative physiotherapy interventions targeted to patients deemed at most risk of poor outcomes following TKA. Differences observed between groups were too small to be clinically relevant, however satisfaction was somewhat higher in those that received greater physiotherapist contact. While cost-per-QALY estimates were below policy threshold, this result is uncertain and insufficient to make accept-decline recommendations.

OC17 Over-Impaction of Acetabular Cups Can Reduce Fixation Strength: Surgical Technique Is Critical

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Cementless acetabular cups rely on press-fit fixation for initial stability, an essential pre-requisite to implant longevity. Impaction is used to seat an oversized implant in a pre-prepared bone cavity, generating bone strain, and a 'grip' on the implant. In certain cases (such as during revision) initial fixation is more difficult to obtain due to poorer bone quality; increasing the chance of loosening and instability. No current study evaluates how a surgeon's impaction technique (mallet mass, mallet velocity and number of strikes) may be adapted to maximise cup fixation and seating. Therefore the objective of this study is to determine an appropriate impaction technique for poor quality bone.

A custom drop tower was used to simulate surgical strikes, seating acetabular cups into a synthetic bone model. Strike velocity (representing surgeon strike level) and drop mass (representing mallet mass) were varied through representative low, medium and high levels. Strain gauge measurements and pushout tests were used to quantify implant fixation. Cup fixation was assessed for two conditions, appropriately seated (moving no more than 0.1mm on the previous strike) and excessively impacted (10 strikes). Repeats (N = 5) were conducted in low and high density bone, a total of 180 tests.

For appropriately seated cups, increasing mallet mass and velocity improved fixation and reduced polar gap. However a phenomenon of bone strain deterioration was identified if an excessive number of strikes were used to seat a cup, resulting in loss of implant fixation. This effect was most severe in low density bone. For the highest energy, each excessive strike halved the measured bone strain (78 ± 7 με/strike). This reduced fixation strength from 630 ± 65 N (optimally seated) to just 49 ± 6 N at 10 strikes.

Extreme caution must be exercised to avoid high velocity strikes in fragile bone for any mallet mass. A high mallet mass with low strike velocity is recommended, resulting in satisfactory fixation (442 ± 38 N) whilst reducing the risk of loosening with excessive impaction.

OC18 Bi-Unicondylar Arthroplasty preserves healthy gait characteristics and near-normal extensor mechanism efficiency compared to Total Knee Arthroplasty

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Objectives: Bi-Unicondylary Arthroplasty (Bi-UKA) refers to the ipsilateral implantation of medial and lateral unicompartmental knee arthroplasty prostheses. Bi-UKA is a bone and anterior-cruciate ligament preserving alternative to Total Knee Arthroplasty (TKA) in the treatment of medial and lateral compartment gonarthrosis. However, little is known of the functional outcomes or biomechanics associated with Bi-UKA.

Methods: Sixteen Bi-UKA subjects were measured on an instrumented treadmill, using standard metrics of gait, at self-selected Top Walking Speeds and compared to age, sex and BMI-matched healthy (n=16) and primary TKA subjects (n=16). Satisfaction was determined using the Oxford Knee Score (OKS) and Quality of Life was assessed using the EuroQol-5D (EQ-5D). Bi-UKA and then TKA were also performed on eight fresh frozen cadaveric knees to investigate knee extensor mechanism efficiency under controlled laboratory conditions using a repeated measures study design.

Results: Bi-UKA walked at higher speeds than TKA patients and exhibited near-normal vertical Ground Reaction Forces, superior to TKA in weight-acceptance, heel-strike and mid-stance (p<0.05). Bi-UKA had longer-stride lengths, contact time and gait cycle time compared to TKA, along with higher OKS and EQ-5D (all p<0.05). In the cadaveric model, Bi-UKA generated the same extensor moment as native knees at flexion angles within a typical gait range of motion, whereas the extensor mechanism following TKA was less efficient than both the

native and Bi-UKA ($p<0.05$). Conversely, at higher flexion angles, the extensor mechanism was found to be marginally more efficient following TKA than Bi-UKA ($p < 0.05$).

Conclusion: The higher function in gait during early stance following Bi-UKA compared to TKA can be explained in part by the improved extensor mechanism efficiency following this procedure. Fewer gait differences were seen at push-off, which is associated with higher flexion angles and minimal quadriceps activity.

This study is the first of its kind to demonstrate a gait advantage of Bi-UKA compared to TKA and to correlate these measurements with in vitro data. Bi-UKA can result in superior function and higher satisfaction than TKA in treatment of medial and lateral tibiofemoral arthrosis and warrants further investigation.

OC19 Preoperative Gait Biomechanics and its Relationship to Functional Outcome Following Total Hip Arthroplast

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Objectives: A recent systematic review concluded that there was strong evidence of a negative association between pre-operative function and short- and long-term functional outcomes following total hip arthroplasty (THA). Of the 17 studies included, only two included an objective measurement of function, one of which found no significant association. Pre-operative gait analysis has been shown to predict functional outcomes following knee arthroplasty using a classification technique called the Cardiff Classifier. This study aimed to explore the relationship between pre-operative gait biomechanics and functional outcome following total hip arthroplasty (THA) using the Cardiff Classifier.

Methods: Twenty-five healthy and 32 subjects with hip osteoarthritis (OA) performed gait analysis and completed the Hip disability and Osteoarthritis Outcome Score (HOOS) before and one year after THA. Perceived functional outcome was measured using the Activities of Daily Living subscale (HOOS-ADL). Lower-limb biomechanics were classified using principal component analysis and Dempster-Shafer theory classification. Eighteen biomechanical features were identified. These features were used to 'train' the classifier to discriminate between hip OA and healthy individuals. This mathematically determines the relationship between biomechanics and the belief in OA (B(OA)), belief in healthy, and uncertainty. The trained classifier was used to quantify the pre-operative B(OA), and change in B(OA) in patients undergoing THA. Pearson's correlation coefficients were used to assess the relationship between pre-operative biomechanics, and perceived and biomechanical outcome following THA. A linear regression was used to test the predictive value of B(OA) in combination with age and BMI.

Results: The gait analysis index, B(OA), at baseline was moderately correlated to post-operative change in HOOS-ADL ($r=0.37$ $p=0.037$) and change in B(OA) ($r=-0.363$, $p=0.041$), but not to absolute post-operative HOOS-ADL ($r=0.17$, $p=0.353$). B(OA) in combination with age and BMI explained 34.8% of the total variance in the change in HOOS-ADL and 30.1% of variance of the change in B(OA) following THA.

Conclusion: Poor pre-operative biomechanics was predictive of a greater biomechanical and patient-reported improvement following THA. Pre-operative biomechanics, however, was not indicative of absolute long-term post-operative functional status, a finding that disagrees with other studies measuring only perceived function.

OC20 Platelet-rich plasma (PRP) for patellar tendinopathy: a randomized controlled trial of leukocyte-rich PRP or leukocyte-poor PRP vs. saline

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Background: A small number of randomized controlled trials have found ultrasound-guided injection of PRP to be no more effective than saline for several tendinopathies; limited information exists for patellar tendinopathy. The purpose of this study was to determine if a single ultrasound-guided PRP injection, either leukocyte-rich (LR-PRP) or leukocyte-poor (LP-PRP), was superior to saline injection, for the treatment of patellar tendinopathy. Our null hypothesis was that no treatment would be superior to another for the treatment of patellar tendinopathy.

Methods: Athletes with patellar tendinopathy for ≥6 months (Blazina stage IIIB) were assessed for eligibility in a multi-site, three-arm, single-blind controlled trial. The three injection arms were LR-PRP, LP-PRP or saline. Patients received a single ultrasound-guided injection, followed by 6 weeks of supervised rehabilitation (heavy slow resistance training, concentric and eccentric, 3 times per week). Outcome measures (VISA-P, pain during

activity, global rating of change) were assessed at 6 and 12 weeks, and 6 and 12 months. VISA-P score at 12 weeks was the primary outcome. Fifty-seven patients (19 in each group) were included in an intention-to-treat analysis. Secondary outcome measures included pain during activity, and patients' global rating of change.

Results: Study retention was 93% at 12 weeks, and 79% after 1 year. There was no significant difference in the average change in VISA score, pain, or global rating of change between the three treatment groups at 12 weeks, or any other time point up. After one year, the outcomes (mean, SD) for the LR-PRP, LP-PRP and saline groups (respectively) were as follows: VISA, 58 (29), 71 (20), 80 (18); pain, 4.0 (2.4), 2.4 (2.3), 2.0 (1.9); global rating of change, 4.7 (1.6), 5.6 (1.0), 5.7 (1.2) ($p > 0.05$ for all outcomes). Of the LR-PRP group, only 35% of the participants improved by at least 13 VISA-P points, compared to 72% (LP-PRP) and 71% (saline) (Chi-square test, df = 2, $p=0.059$).

Conclusions: Combined with an exercise-based rehabilitation program, a single injection of LR-PRP or LP-PRP was no more effective than saline for the improvement of patellar tendinopathy symptoms.

OC21 Charting longituidinal patient function following TKA and evaluating the influence of implant design: 8-year follow-up of a prospective RCT

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Objectives: To chart longer-term functional outcomes following total knee replacement and evaluate any influence of implant design.

Methods: Longitudinal follow-up of a single-centre double blind randomised controlled trial cohort of total knee arthroplasty patients (surgery performed in 2008-9) comparing the (then modern) Triathlon and (then contemporary) Kinemax prostheses (both Stryker). Patients underwent functional tests in an outpatient facility at 8-years matching those performed at earlier trial time points (pre-operation, 6-weeks, 6-months, 1 and 3-year post-operation). Outcomes included the Oxford Knee Score, range of motion (universal goniometry), numerical rating scales (1-10) for 'average daily' and 'worst daily' pain, lower limb power output (Nottingham Rig), timed functional assessment battery and satisfaction survey. New data was linked to that of earlier assessment and analysed with repeated measures ANOVA mixed models, incorporating longitudinal change over all assessment time points. Significance was accepted at $p=0.05$.

Results: 125 patients (59 Kinemax and 66 Triathlon) of the original study cohort of 212 patients were available for analysis at a mean 8.12-years follow-up (7.3-9.4 years). The all-cause revision rate was equivalent between groups at 3.8% (n=4 per group). No differences were seen between groups in baseline outcome or demographic data. There was a notable reduction across the cohort in all assessment parameters at 8-years ($p<0.01$). Over the 8-year period, the modern implant group reported greater range of motion ($p=0.05$), lower limb power output ($p=0.01$), and a lesser report of worst daily pain ($p=0.04$) compared to the contemporary implant group. Small differences in Oxford Knee Score, average daily pain, timed functional assessment and satisfaction score were not significant between groups over time.

Conclusion: This 8-year follow-up of a randomised controlled trial highlights a general reduction of physical function over time following total knee arthroplasty. Although 'implant survival' was high, loss to follow-up of this trial cohort was surprisingly large with many dead or unfit to attend outpatient testing. In surviving patients, modern implant designs may offer enhanced physical outcomes compared to older implant designs.

OC22 Transforming growth factor (TGF)β inhibition with chemotherapy heals murine myeloma bone disease and improves fracture resistance

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Objectives: Multiple myeloma causes a destructive bone disease in ~90% of patients and current therapies do little to repair existing bone damage. We hypothesised that combining a bone anabolic with first-line chemotherapy would improve bone health in a murine model of myeloma. Therefore, we aimed to determine if bone anabolic therapy improves bone recovery.

Methods: Human U266-GFP-luc myeloma cells were i.v. injected into NSG mice (n=7/group). After tumour and osteolytic lesion development, mice were administered first-line chemotherapeutics (bortezomib + lenalidomide) ± a bone anabolic (SD208; transforming growth factor (TGF)β receptor I kinase inhibitor) or vehicles for 2 weeks. Tumour and bone lesions were monitored *in vivo* by bioluminescent imaging, serum paraprotein and µCT. Flow cytometry, histomorphometry, µCT, bone turnover ELISAs, QPCR, Raman spectroscopy and 3-point bending were performed at endpoint.

Myeloma and healthy patient bone marrow stromal cells (BMSCs) were treated with TGFβ±SD-208 in osteogenic media, osteogenic differentiation was assessed by alkaline phosphatase staining and QPCR.

Results: Osteolytic lesions developed 8 weeks after tumour inoculation. Vehicle-treated mice exhibited progressive lesion development and virtually no trabecular bone at endpoint. Total lesion area was unchanged after 1 week of chemotherapy, but after 2 weeks lesions began to repair, with reduced TRAP+ osteoclasts and increased osteoblasts ($p<0.05$). Mice treated with chemotherapy + SD-208 exhibited enhanced repair of bone lesions, with partial repair of perforating lesions within 1 week and complete repair within 2 weeks, with improvement over chemotherapy alone ($p<0.05$). SD-208 significantly increased trabecular bone volume after 2 weeks ($p<0.05$). Lesion repair was identified to occur similarly to intramembranous fracture healing and involved increased *Vegfa*. Analysis of bone material and mechanical properties found enhanced matrix maturation and fracture resistance with SD-208 ($p<0.05$). SD-208 promoted osteoblastic differentiation of healthy and myeloma patient BMSCs.

Conclusions: SD-208 enhanced healing of myeloma bone disease and fracture resistance when administered with first-line chemotherapeutics and promoted osteoblastic differentiation of patient BMSCs, providing incentive for clinical translation to improve patient bone outcomes.

OC23 Breast cancer metastasis to bone; the effect of LOX and P2X7R inhibition

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We have previously demonstrated that lysyl oxidase (LOX), a copper-dependent amine-oxidase is highly expressed in metastatic breast cancer cells and prepares the bone micro-environment for colonisation. Purinergic signalling via the P2X7 receptor (P2X7R) in primary tumour microenvironment has been implicated in tumour survival and progression. This pathway also regulates bone homeostasis, and has been shown to interact with LOX. In this study, we have exciting data showing that combined targeting of LOX and P2X7R reduces pre-metastatic bone lesions.

Murine E0771-luciferase breast cancer cells were injected into mammary ducts of 9-week old C57BL/6 mice (n=5/group). 24hours post-inoculation, mice were randomised and treated daily with vehicle, 100mg/kg LOX inhibitor (B-aminopropionitrile (BAPN)), 10mg/kg P2X7R inhibitor (A740003) or a combination of both. Primary tumour growth was monitored via calliper measurements and IVIS imaging. Mice were euthanized 4 weeks following tumour inoculation, and the tibias were scanned using micro-computed tomography (SkyScan1172, Bruker). Trabecular and cortical morphometry were analysed using CTAnalyser and osteolytic lesions quantified with Osteolytica.

There were no differences in growth of primary tumours between any of the treatment groups, and no overt bone metastases were observed. Consistent with previous results, cortical bone volume (CtBV) and trabecular thickness (TbTh) were lower in tibias of vehicle treated tumour-bearing mice compared to no-tumour age-matched controls (AMC, $P<0.05$). There was with no differences observed between treatment groups for CtBV, TbTh, Trabecular bone volume, number or separation. However, the number of osteolytic lesions and percentage lesion area were higher for vehicle treated tumour-bearing mice compared to AMCs ($P<0.01$ and $P<0.05$ respectively) which were significantly reduced by 48% and 60% respectively with the combined treatment ($P<0.01$).

Combined targeting of LOX and P2X7R to reduce pre-metastatic bone lesions may have implications for breast cancer metastases to bone and is currently being investigated further.

OC24 Sexual dimorphism in both bone geometry and bone strength for a mouse model of Paget's disease of bone (PDB)

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Objectives: Within PDB, poor bone quality accounts for several complications of the disease. Fracture is a predominant impediment, yet treatment and prevention remains a significant challenge. Numerous clinical studies have demonstrated limitations of bone mineral density measurements in assessing fracture risk and thus attention has focused on a broader array of factors that influence skeletal fragility, including the influence of bone geometry and microstructure on bone strength. The aim of this study was to examine murine bone geometry and identify whether geometrical changes could link to fracture occurrence in PDB.

Methods: A mouse model mimicking the Sequestosome-1 mutation present in many PDB patients was used (P394L+/+; Daroszewska et al 2011) with skull and long bones of 8-month-old animals imaged by micro-computed tomography (µCT) at a voxel size of 12-18 µm (using SkyScan 1176, Bruker).

Results: Cranial length (mm), frontal length (mm) and bitemporal distance (mm) were shown to be significantly increased ($p<0.05$, n=4) in the skulls of male P394L +/+ mice *vs.* WT. No significant differences in tibial geometry were observed in either male or female P394L+/+ vs. WT. In contrast, in the femur, cortical thickness (P394L+/+ 0.3195 + 0.4 mm *vs.* WT 0.4625 + 0.06 mm) and polar moment of inertia (P394L+/+ 0.396 + 0.096 mm^4 versus WT 1.725 + 0.485 mm4) was decreased within the distal region of female P394L+/+ versus WT. Four-point bending tests revealed female P394L+/+ femora were significantly weaker than WTs ($p=0.026$, n=5). Interestingly, no biomechanical alterations were identified in male P394L+/+ *vs.* WT (n=7). Whilst fracture acquisition appeared random in WT femurs, fractures were isolated to the distal region in P394L+/+ male and female mice.

Conclusion: In summary, our study reveals sexual dimorphism in bone geometry and bone strength. Our results suggest the distal region of P394L+/+ femurs as a principle fracture site. We will combine these data with image-based finite element analyses in attempt to link bone geometrical changes and bone strength for fracture prediction.

References:
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OC25 Is the mechanical function of the meniscus altered in osteoarthritic knees?

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Deteriorating meniscal function is thought to play a role in the development of knee osteoarthritis. Proteoglycans in the meniscus aid in maintaining mechanical stiffness of the tissue through electrostatic effects. This study aimed to investigate whether mechanical properties of the healthy meniscus change in osteoarthritic knees.

Following ethical approval, discs of lateral meniscal tissue two millimetres thick and of five millimetres diameter were obtained from patients with severe osteoarthritis and from cadaveric donors <65 years of age, with no history of osteoarthritis or meniscal injury. Each disc was placed within a custom confined compression chamber and bathed in isotonic 0.14M PBS, hypotonic deionised water or hypertonic 3M PBS. The apparatus was mounted within a materials testing machine and 0.3N preload was applied. At equilibrium, a 10% ramp compressive strain followed by a 7200 second hold phase were applied. Resultant stress relaxation curves were fitted to a nonlinear poroviscoelastic model with strain dependent permeability using finite element modelling. Goodness of fit (R^2) was assessed using a coefficient of determination. All samples were assayed for proteoglycan content. Comparison of resultant mechanical parameters was undertaken using multivariate ANOVA with Bonferroni correction.

Thirty samples from osteoarthritic knees and 18 samples from healthy donors were tested. No significant differences in mechanical parameters were observed between samples sourced from osteoarthritic knees compared to healthy donors across all solutions. Young's modulus was significantly greater in samples tested in deionised water compared to samples tested in 0.14M or 3M PBS (both $p<0.05$). The zero-strain permeability was significantly decreased in samples tested in deionised water compared to samples in 0.14M and 3M PBS (both $p<0.05$). The mean R2 value was 0.78, indicating a good fit and did not differ significantly with solution or sample source. Proteoglycan content was not found to differ significantly with sample source.

Mechanical parameters and proteoglycan content of the meniscus in osteoarthritic knees are similar to those found in healthy knees. Whilst macroscopic tears in the meniscal ultrastructure may result in accelerated osteoarthritis, mechanical parameters of the intact meniscus are unchanged in osteoarthritic knees.

OC26 Repurposing glutamate receptor antagonists to prevent the onset of post-traumatic osteoarthritis

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Objectives: We previously found that AMPA and kainate glutamate receptors (GluRs) localise to osteoarthritic bone, cartilage and synovium. NBQX (AMPA/kainate GluR antagonist) reduced knee swelling, gait abnormalities and joint destruction in inflammatory and post-traumatic osteoarthritis rodent models. Since NBQX is not approved for human use, we have tested 4 AMPA/kainate GluR antagonists (A-D, passed Phase-1 clinical trials), and compared these to current approved treatments (hyaluronic acid (HA), steroid intra-articular injections) in a mouse ACL-rupture model.

Methods: For ACL rupture, 12N load (ElectroForce® 3200, BOSE) is applied to anaesthetised C57Bl6J mice. A single 10µl intra-articular injection of drug A (n=4), B (n=3), C (n=3), D (n=4), HA (n=8, Durolane, 8mg/kg), steroid (n=7, Depo-medrone, 10mg/kg) or vehicle (100mM NaOH: drug A, n=4; DMSO: drugs B-D, n=4; saline: HA, steroid, n=7) was administered immediately following rupture. Over 21 days, lameness and knee swelling were recorded. Animals were culled (day 21) and knees scored for inflammation and degradation (OARSI).

Results: Swelling: Drugs A and C reduced swelling by day 2 (~50% and ~40%) and did not differ significantly from day 0 measurements, whereas swelling remained increased until day 7 in vehicle

(A: p<0.01, C: p<0.05, general-linear model (GLM)). Drug B did not reduce swelling until day 14. On day 1, steroid significantly reduced swelling (~50%) compared to vehicle (p<0.001, GLM) but this was short-lived with no reductions from day 2. HA had no effect. **Lameness:** Scores were reduced by drugs A-D, with significant reductions compared to vehicle on day 3 by drug B (p<0.001, GLM ~50%), C and D (p<0.05, GLM, ~45%, C&D). HA and steroid had no effect. **Inflammation and degradation:** Drug A reduced inflammation (~60%, p<0.001, ANOVA) and degradation (~40%) scores at day 21; steroid increased inflammation (~30%) and degradation (~50%, p<0.05, ANOVA). Drugs B-D and HA had no effect.

Conclusion: This study shows that AMPA/kainate GluR antagonists, already approved for human use, relieve inflammation, lameness and joint degradation in post-traumatic osteoarthritis. GluR antagonists exceeded anti-nociceptive, anti-inflammatory and anti-degradation effects of HA and steroids. Surprisingly, HA had no effects whereas steroids substantially increased degeneration.

OC28 Molecular imaging modalities reveal pathological matrix disorganisation in whole bone sections and isolated osteoblasts

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Objectives: Vascular endothelial growth factor (VEGF) is crucial for angiogenic-osteogenic coupling with reductions in circulating levels implicated in osteoporosis and fracture risk. How osteoblast (OB)-derived VEGF influences the matrix components of bone remains poorly understood. Raman spectroscopy (RS) and second harmonic generation (SHG) imaging are label-free modalities that allow compositional and structural characterisation of bone, and were used herein to assess the influence of VEGF deletion on collagen species and matrix organisation of whole bones and isolated OBs.

Methods: OB-derived VEGF was conditionally deleted in 16-week old male and female mice expressing floxed alleles of VEGF ($Vegf^{fl/fl}$) and Cre-recombinase controlled by the osteocalcin promoter (OBVEGFKO). Bones were embedded in PMMA and tibiofibular junction sections were used for RS and SHG imaging (n=75 spectra and n=9 regions from 3 bone sections/sex/genotype). VEGF was deleted *in vitro* in OBs from male and female $Vegf^{fl/fl}$ mice using a Cre-recombinase expressing adenovirus. Cells were fixed for RS (n=50 spectra from 10 cells/group).

Results: RS highlighted reductions in carbonate in female OBVEGFKO bone sections (-2.79-fold; p<0.0001) whereas +1.21-fold elevations were observed in male OBVEGFKOs (p=0.002) against WT. Collagen-specific proline was higher exclusively in male OBVEGFKO bone (+1.21-fold; p=0.0001) however the stability of the collagen intra-strand links were -3.17-fold (p<0.0001) lower than the OBVEGFKO versus WT. SHG further revealed reductions in collagen fibre length in OBVEGFKO males and females (-1.06; p=0.0395, -1.08-fold; p=0.0462 respectively), with fibre widths reduced only in female OBVEGFKO bone (-1.11-fold; p=0.0395) compared to WT. *In vitro*, RS identified +1.31-fold elevations collagen-specific proline in female OBVEGFKO cells (p<0.0001) which was reduced in male OBVEGFKO cells versus WT (-1.15-fold; p<0.0001). In contrast, collagen intra-strand stability was reduced in female OBVEGFKO cells (-2.26-fold; p<0.0001) but increased in male OBVEGFKO cells (+1.19-fold; p<0.001) versus WT.

Conclusions: RS and SHG imaging have revealed alterations in matrix signatures and collagen organisation in OBVEGFKO bone sections which appeared sexually dimorphic. Similar sexual divergence in matrix composition was detected by RS *in vitro* thus directly links disruptive VEGF signalling by OBs to altered bone composition.

OC29 Can we predict medial knee load during gait for varus osteoarthritc knees using radiographic alignment measures?

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Objectives: Identify correlations between radiographically defined knee alignment and medial compartment loading during gait, estimated by the external knee adduction moment (EKAM) and knee adduction angular impulse (KAAI). Investigate the feasibility of predicting medial knee load from knee angulation measures.

Methods: Twenty-nine patients listed for opening wedge high tibial osteotomy were assessed performing level gait using three-dimensional motion analysis (Qualisys, Sweden and Bertec Corp., USA). Approval was granted from the Research Ethics Committee for Wales and Cardiff and Vale University Health Board. Joint biomechanics were calculated within Visual 3D (C-Motion, USA). Mechanical tibio femoral angle (mTFA) (8.47 ± 3.94º), lateral distal tibial angle (LDTA) (87± 4.91º) and the Mikulicz point (14.68 ± 14.26% tibial width) were defined from

weight bearing long-leg radiographs. Osteoarthritis (OA) grade was determined using the Kellgren-Lawrence (KL) score (*n*= 6 KL2; 17 KL3; 6 KL4). Pearson's and Spearman's correlations were performed along with linear regression and step-wise linear regression (SPSS Inc., USA). Adjusted R^2 values are presented, providing conservative estimates of predictive power for the regression models.

Results: mTFA correlated significantly with peak EKAM (r=0.538, p=0.003) and KAAI (r=0.634, p<0.001). Mikulicz point correlated with peak EKAM (r=-0.522, p=0.004) and KAAI (r=-0.531, p=0.003). In both cases, the correlations were stronger when considering KL2 subjects in isolation.

Linear regression revealed that the variance in KAAI is best explained by mTFA (R^2=38%), whereas peak EKAM is best explained by the Mikulicz point (R^2=28%). Step-wise regression revealed that in combination the Mikulicz point and LDTA angle could explain 60% variance in peak EKAM. This increased to 77% when including frontal plane trunk range of motion and knee abduction velocity. In combination, mTFA and LDTA could explain 61% variance in KAAI. This increased to 68% when including knee abduction velocity.

Conclusion: Although correlations exist between frontal plane knee loading during gait and clinical measures of alignment, they are not perfect. The ability to estimate the level of knee loading using clinically accessible measures, would provide a useful tool. Including compensatory gait measures improved the predictive model.

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OC30 Comprehensive evaluation of the morphology and mechanics of the human femoral head

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Objectives: Osteoarthritis (OA) affects the properties of subchondral bone; however, it is not known if these changes are localised to discrete regions, and how this complex structure deforms under loading. The goal of this study was to develop an approach to comprehensively evaluate regional bone micro-architectural and mechanical properties in the whole human femoral head.

Methods: Whole femoral heads from osteoarthritic (OA, n=5) and healthy controls (HC, n=5) underwent micro-computed tomography (microCT) imaging (voxel size 39µm). The superior subchondral cortical bone plate was isolated from each image and the mean and standard deviation of plate thickness and plate porosity were computed. The morphometric properties of the trabecular bone were evaluated in 5 volumes of interest (VOI) spatially distributed within the femoral head. Within each trabecular VOI, bone volume fraction, trabecular thickness, trabecular separation, trabecular number, and connectivity density were determined. The OA femoral heads were then step-wise mechanically compressed in a custom jig that fits the microCT scanner. The Digital Volume Correlation (DVC) approach was used to evaluate strain distribution in the elastic range and post yield[(1)]. Repeated scans for each OA specimen were used to evaluate the DVC precision.

Results: OA specimens exhibited a more heterogeneous micro-architecture with trends towards thicker subchondral bone plate (p=0.14) and higher bone volume fraction (p=0.047), trabecular thickness (p=0.047) and connectivity density (p =0.047) in the superior subchondral bone compared with the HC group. Precision of the DVC approach was between 250µε and 350µε. DVC results showed a very heterogeneous strain pattern post yield.

Conclusions: This approach allowed, for the first time, a comprehensive evaluation of: the heterogeneous micro-architectural properties of OA femoral heads, highlighting the effects of the disease in the superior subchondral cortical and trabecular bone; the heterogeneous normal and shear strain distribution in the OA femoral head, highlighting the complex deformation of this complex structure.

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OC31 Visualisation and quantification of in situ porcine acetabular soft tissue behaviour: A study of labrum circumferential behaviour

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Acetabular soft tissue damage in particular labral tears can be a consequence of femoroacetabular impingement (FAI) as a result of abnormal loading conditions. The investigation oftissue behaviour *in situ* provide a better understanding of tissue properties and response to loading. The aim of this study was to investigate the mechanical role of the circumferential properties of the labrum through computed tomography (CT) scans by assessing labrum deformation under different loading scenarios.

Six porcine hip joints were disarticulated and placed into a bespoke loading rig. The femoral head was positioned to provide a contact patch with the acetabulum coincident with the superior edge, on

the cartilage-labral boundary. CT scans (XtremeCT, Scano Medical) with resolution of 82 µm were performed on the porcine hip joints when the head and acetabulum were in contact, loaded, and loaded with a radial cut through the labrum approximately 40 degrees from the superior region. The ilium was used as the reference for rigid registration of the hip joint images (ScanIP 7.0, Synopsys). The labrum was reconstructed by capturing the apex points using a bespoke script (MATLAB R2018a, MathWorks). One unsuccessfully aligned specimen was excluded from the analysis.

A low force was recorded (0-5 N) when the head and acetabulum were in contact. A displacement of 4.3±0.3 mm was applied to each specimen (reaction force of 215.7±55.5 N). The reaction force range under similar displacements demonstrated the variation in response of the *in situ* tissue structure between specimens. The circumferential tension in the labrum was evident by a gap at the cut site of 2.71±0.6 mm when the samples were loaded. The labral apex position in 3D was recorded and compared between the intact labrum and the cut labrum. The pattern of labrum shape change remained similar when the labrum was cut, however the apex was deformed further at the contact region in the cut samples (four out of five samples).

This study provides additional information when using porcine hips in the study of the *in situ* labrum.

OC32 AMPA/kainate glutamate receptors regulate inflammatory and degradative markers in 3D loading models of cartilage and bone

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Objectives: Abnormal joint mechanics are a major osteoarthritis risk factor. Glutamate receptors (GluRs), are expressed in bone cells, mechanically regulated and their activation influences cell phenotype. Synovial fluid glutamate concentrations increase in arthritis and intra-articular injection of NBQX (AMPA/kainate GluR antagonist) prevents pain and pathology in rodent arthritis models. This study assesses the role of glutamate receptors in an *in vitro* 3D loading model of osteocytes.

Methods: Human MSC cells (Y201) were differentiated into osteocytes in 3D type I collagen gels for 7-days. Osteocyte phenotype was confirmed by immunostaining (sclerostin and DMP-1). Cells were subjected to a single physiological (500 µstrain) or pathophysiological (5000 µstrain) load (10Hz, 3000 cycles; TE Instruments) ± NBQX (200µM). Media were analysed for osteoprotegerin (OPG), glutamate and cytokines (23-plex Merck Milliplex multiplex panel). Data analysed by GLM ANOVA and Fisher's post-hoc (Minitab, n=3/treatment).

Results: Dendritic Y201 cells expressed sclerostin and DMP-1 proteins. After 1hr, physiological (1.7-fold, p=0.07) and pathophysiological (3.8-fold, p=0.005) loading reduced OPG release, although OPG release was increased after loading 24hrs later (phys 7-fold, p=0.004; pathophys 2.6-fold, p=0.05). Glutamate release was not affected 1hr after loading, but was reduced by 50% under both loading regimes after 24hrs (p<0.001). Both loading regimes abolished release of GM-CSF and RANTES and reduced release of MCP-1, IL-6 and IP-10 (p=0.05).

NBQX abolished load-induced changes in OPG release (1hr p=0.019; 24hr p=0.05), increased physiological load-induced glutamate release (p=0.027) and mimicked some of the physiological load-induced effects on cytokines, reducing IL-6, IL-8, IP-10, MCP-1 and RANTES release in unloaded cultures.

Conclusion: Human Y201 cells were differentiated to osteocyte-like cells in 3D and reduced OPG and cytokine release in response to load. Antagonising AMPA/kainate GluRs prevented load-induced reduction in OPG, and mimicked the effect of physiological load on pro-inflammatory cytokine release in the absence of load. These mechanisms are consistent with the protective effect of NBQX in rodent models of osteoarthritis, where bone remodelling and inflammation is reduced.

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OC33 6 cases of hypophosphatasia presenting with musculoskeletal symptoms diagnosed in General Rheumatology clinic

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Background: Hypophosphatasia (HPP) is a rare metabolic bone disease caused by loss-of-function mutations in the gene encoding tissue-nonspecific alkaline phosphatase (TNS-ALP).

A hallmark of the disease is a persistently low serum alkaline phosphatase (ALP) level, although this often goes unnoticed for many years prior to diagnosis[1].

HPP is under-diagnosed in adults, in whom there is an estimated prevalence of 1/6370 in Europe[2]. Disease phenotype in adults is heterogeneous. It is well recognised that HPP can present in adults with low bone density and fractures, mainly metatarsal and atypical fractures. However, it is less well known that women with HPP can present with joint pain and calcium pyrophosphate deposition disease (CPPD)[3].

Methods: I present 6 cases of HPP that presented to a general rheumatology clinic over the last decade with musculoskeletal symptoms. Other causes were excluded. All patients had persistently low ALP levels in the absence of other causes. A diagnosis of HPP was confirmed by elevated vitamin B6 levels. 5 patients had pathogenic mutations of the TNS-ALP gene identified.

Results: Mean age at diagnosis of HPP was 50 years. All 6 patients were women. 2 patient presented with fracture (atypical femoral and wrist fractures). All patients had normal bone density on DXA scanning. 4 cases presented with axial and large joint pain, bursitis, acute CPPD and long bone pain. 4 patients had symptom onset before age 18. 4 patients had a relevant dental history and 4 patients had a significant family history of dental disease.

Mean delay from first musculoskeletal symptom to the diagnosis of HPP was 18.3 years. This was despite having a documented low ALP level for a mean of 11.2 years prior to the diagnosis of HPP being made.

Conclusion: Adults with undiagnosed hypophosphatasia can present to rheumatology clinic. Investigation of persistently low ALP levels, as well as taking a thorough dental and family history can help to make the diagnosis.

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OC34 A review of the management of patients found to have syringomyelia: a single centre experience

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Objective: Management of syringomyelia or syrinx is sparse in the literature. The main concern is that a small proportion of these, often, incidental findings can be malignant. Our objective was to review the patient cohort within our trust with findings of a syrinx and how often these are related to a malignancy. Currently there are no clear guidelines for the management of such syrinx findings.

Method: A search of spinal MRI scans within our trust over a 1-year period was carried out using keywords; “syrinx” and “syringomyelia”. Of those who had a confirmed syrinx on MRI, these patient records were then reviewed to determine the outcome, follow up and associated further imaging were recorded.

Results: Incidence of syrinxes found on MRI was 0.52%. 56 MRI found to have positive finding of syrinx in our time period. 40 (71%) of which were incidental. 19 were referred on for further specialty input following the scan; 6 to neurology only, 8 to neurosurgery only, 2 to both neurology and neurosurgery and 2 only to paediatrics. The remaining 18 had unknown or no follow up. 12 had follow up scans. 4(10%) of the incidental findings were related to malignancy.

Conclusion: Our findings show the incidence of these syrinx to be 0.52%, this is 10 times more than in current literature. This could be related to reporting or indeed a reflection of the patient cohort served by our trust. The findings reflect a much higher finding. Nearly half of patients are referred to an appropriate speciality following finding of incidental syrinx. Although the MRIs were performed largely based on neurological symptoms, those too could also be a reason for referral.

10% of the incidental findings were found to be related to malignancy and tumour. This cohort are clearly the patient group that should not be missed.

Our findings show that syrinx management requires more conformation and may well be increasing in incidence and reporting. We should think about appropriate referral and follow up scanning to ensure comprehensive management for this patient population.

OC35 Coming of Age

Mike Stone (Cardiff, UK)

OC36 Healing of OCD after osteotomy and the effect of tibial slope on knee function

Chris Wilson (Cardiff, UK)

PP4 Osteoblast-specific Enpp1 deficiency promotes bone mass whilst worsening the metabolic phenotype

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Ectonucleotide pyrophosphatase/phosphodiesterase-1 (ENPP1) inhibits bone mineralisation by generating pyrophosphate (PPi) and is also recognised as a factor predisposing to insulin resistance. Global ENPP1 knockout mice (*Enpp1*$^{-/-}$) exhibit depressed serum PPi, soft tissue/joint calcification and reduced trabecular bone mass. Enpp1-/- mice also display metabolic protection following chronic high-fat diet (HFD) feeding. To determine these phenotypes are driven via osteoblast derived ENPP1 we investigated osteoblast-specific Enpp1 ablated mice.

For metabolic analysis, Enpp1f$^{lox/flox}$;Ocn-cre conditional knockout (cKO) and Enpp1$^{flox/flox}$ control male mice were reared to 16-weeks old on a standard diet (6.2% fat) or HFD (58% fat). Bones were collected from control diet fed 6-week old cKO and control mice. Metabolic tests (GTT/ITT), gait, histological and serum analysis were performed.

Micro-CT analysis of 6-week old cKO mice exhibited altered femoral bone mass - increased trabecular volume (145%;P<0.001) and number (140%;P<0.001) compared to control mice. These bone architectural changes did not translate into altered biomechanical properties (tested by 3-point bending) although *in vivo* examination revealed an abnormal gait in the cKO mice. cKO mice had normal PPi serum levels and no pathological joint/soft tissue calcification.

The metabolic phenotype of 16-week old cKO mice fed a standard diet was similar to control mice, evidenced by GTT/ITT, metabolic tissue mass and histology. Intriguingly, the control diet fed cKO mice exhibited increased undercarboxylated osteocalcin (195%; P<0.05). Furthermore, HFD-fed cKO mice were not resistant to obesity, exhibiting reduced glucose tolerance coupled with insulin resistance, increased liver triglyceride (185%;P<0.01) and reduced steatosis compared to controls mice.

To conclude, cKO mice exhibit increased bone mass, yet cannot recapitulate the hypermineralisation of soft tissue/joints seen in global *Enpp1*$^{-/-}$ mice. The cKO mice are not protected from the adverse effects of a HFD and demonstrate notable changes to the liver. These data indicate that protection against diabetes; a characteristic of the global *Enpp1*$^{-/-}$ mouse is likely due to the actions of non-skeletal ENPP1, perhaps via a central role in a novel liver-bone axis. Moreover, osteoblast ENPP1 inhibition results in local skeletal structural changes and unanticipated worsening of metabolic function.

PP5 Associations between chondrocyte transiency and osteoarthritis pathology

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Osteoarthritis (OA) is a progressive musculoskeletal disease affecting over 8 million people in the UK. It is characterised by degradation of articular cartilage (AC), formation of subchondral bone (SCB) osteophytes, synovial proliferation and inflammation. We have previously shown that in spontaneous murine model of OA, STR/Ort mice, AC chondrocytes undergo transformation from inherently stable to transient phenotype revealing associations between growth abnormalities and OA predisposition. Thus, we hypothesised that altered growth dynamics underpin OA predisposition.

8-week-old C57BL/6 male mice underwent either SHAM (placebo) (*n*=3) or DMM (destabilisation of medial meniscus) (*n*=3) surgeries to induce OA-like changes in knee joints. Chondrocyte transiency in AC and growth plate (GP) of tibiae was examined at histological and immunohistochemical levels. In ageing model of OA, subchondral trabecular bone parameters were measured using microCT in tibiae and femora of 62-week-old C57BL/6 male mice (*n*=6) and correlated to GP bridging using a 3-dimentional (3D) quantification method.

Higher expression levels of chondrocyte hypertrophy markers; type X collagen (Col10a1) and MMP13 were observed in tibial AC chondrocytes of DMM mice compared with SHAM. In the tibial GP of mice with surgery induced OA, Col10a1 and MMP13 expressions were greater and widely dispersed in enlarged zone of proliferative and hypertrophic chondrocytes defined with histologically observed large cell volumes. Subchondral trabecular bone volume fraction (BV/TV) was significantly increased in medial compared to the lateral tibiae and femora (32.7+3.1% vs 41.5+2.4%, p<0.001; 15.1+5.3% vs 24.05+1.9%, p<0.01 respectively), and SCB thickness (Tb.Th) was significantly increased by 36% in medial compared to the lateral tibiae in aged mice (p<0.0001). 3D quantification revealed enriched GP bridging in the medial compared to the lateral tibiae and high mean areal bridge densities in aged mice.

Results indicate associations between aberrant GP

chondrocyte hypertrophy marker expression and OA pathology and characteristic thickening of medial tibiae and femora SCB in aged animals. GP bone bridging analysis, indicative of growth cessation, may signify accelerated cartilage-bone transition in GP of OA-prone aged mice. Ongoing experiments will further determine these associations and examine their relevance to human OA.

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PP6 Barbara Mawer Travelling fellowship: Associations between endocrine metabolites and bone mineral density in children aged 6-8 years: the PANIC study

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This study investigated the associations of endocrine metabolites with bone mineral density in children.

A sample of 257 children (117 females) aged 6-8 years with available endocrine data from the baseline measurements of the PANIC study were included. Total body less head (TBLH) bone mineral density (BMD), fat mass and lean mass were assessed by dual-energy X-ray absorptiometry. The following ten metabolites were analysed from fasting blood samples: homeostatic model assessment of insulin resistance, leptin, adiponectin, interleukin 6, haemoglobin, insulin-like growth factor, irisin, 25-hydroxyvitamin D (25(OH)D), testosterone and estradiol. These endocrine metabolites were selected following principal component analysis with TBLH BMD and their contribution was examined by adding the endocrine metabolites simultaneously in a linear regression model. The results were adjusted for model 1: age and height, and for model 2: model 1 and lean mass and fat mass.

In model 1 of females, adiponectin was negatively associated with TBLH BMD ($\beta = -0.139$, $p = 0.036$) and leptin was positively associated with TBLH BMD ($\beta = 0.411$, $p < 0.001$). In model 1 of males, adiponectin was not significantly associated with TBLH BMD ($\beta = -0.110$, $p > 0.05$) and leptin was positively associated with TBLH BMD ($\beta = 0.411$, $p = 0.002$). Additionally, in model 1 of males, 25(OH)D was positively associated with TBLH BMD ($\beta = 0.202$, $p = 0.020$). In model 2 of females and males, no significant associations were observed for adiponectin and leptin with TBLH BMD. However, there was a negative association between estradiol and TBLH BMD in males ($\beta = -0.156$, $p = 0.026$).

Adiponectin is negatively associated with TBLH BMD in females and leptin is positively associated with TBLH BMD in females and males when adjusting for age and height. 25(OH)D was positively associated with TBLH BMD in males when adjusting for age and height. However, these associations disappear in both genders when adjusting for lean and fat mass, while a negative association between estradiol and TBLH BMD appears in males.

PP7 Determinants of bone mineral content and density in children aged 6-8 years: the PANIC study

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Objectives: We explored the contribution of physical activity (PA), nutrition and body composition on bone status in children.

Methods: We studied a population sample of 379 children aged 6-8 years who participated in the baseline examinations of the Physical Activity and Nutrition in Children (PANIC) study. Total body less head (TBLH) bone mineral content (BMC), TBLH bone mineral density (BMD), fat mass (FM) and lean mass (LM) were assessed by dual-energy X-ray absorptiometry. Sedentary time (ST), light PA (LPA), and moderate-to-vigorous PA (MVPA) were assessed using combined heart rate and movement sensing. Total PA (TPA) was assessed using questionnaire. Nutritional intakes were assessed from 4-day food records. Serum 25-hydroxyvitamin D [(25(OH)D] was assessed from blood samples. The associations of sex, age, height, LM, FM, ST, LPA, MVPA, TPA, serum 25(OH)D, and calcium and protein intake with BMC and BMD were examined using multiple linear regression. Variables were entered in the model simultaneously using forced entry.

Results: Girls had higher BMC ($\beta = -0.072$, $p = 0.010$) and BMD ($\beta = -0.111$, $p = 0.015$) than boys. LM and FM were positively associated with BMC and BMD ($\beta = 0.420$-0.474, $p < 0.001$).TPA was positively associated with BMC ($\beta = 0.060$, $p = 0.010$) and BMD ($\beta = 0.086$, $p = 0.023$), but LPA (BMC: $\beta = 0.008$, $p = 0.718$; BMD: $\beta = -0.003$, $p = 0.934$) or MVPA (BMC: $\beta = 0.030$, $p = 0.222$; BMD: $\beta = 0.065$, $p = 0.109$) was not associated with either of them. Serum 25(OH)D, calcium intake or protein intake was not associated with BMC ($\beta = 0.024$, $p = 0.287$; $\beta = -0.029$, $p = 0.421$; $\beta = 0.033$, $p = 0.353$)or BMD ($\beta = 0.052$, $p = 0.156$; $\beta = -0.031$, $p = 0.584$; $\beta = 0.077$, $p = 0.186$).

Conclusion: LM and FM were the strongest determinants of BMC and BMD confirming previous evidence. However, objectively-measured PA and nutrition were not associated with BMC or BMD, suggesting that body composition should be considered when investigating the influence of PA and nutrition on bone status in children.

PP8 Does screening for high hip fracture risk reduce fractures by modifying falls risk? A post hoc analysis from the SCOOP study

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SCOOP was a randomised control trial comparing a hip fracture risk screening programme, using FRAX® with or without dual X-ray absorptiometry (DXA), with usual GP management. Screening reduced the incidence of hip fractures by 28%, an effect likely mediated by osteoporosis treatment in high risk patients. An alternative explanation, that knowledge of fracture risk might modify falls risk, was tested in this analysis.

SCOOP recruited 12483 women aged 70-85 years from 100 English GP practices, who were randomly assigned to the intervention arm (n=6233) or control (n=6250). We analysed fall risk factors at entry, including any potential differences between the groups. We then determined whether there were differences in falls risk between the randomisation groups, especially in those identified at high fracture risk.

Several risk factors for incident falls were identified. As expected, women sustaining one or more falls were slightly but statistically significantly older at baseline than those remaining fall free during follow up (75.8 ± 4.2 vs 75.1± 4.0, $p<0.001$). Higher BMI, prior fracture, glucocorticoid use, secondary osteoporosis, and a fall in the year prior to entry were consistently associated with an increased risk of falling. In addition, a higher FRAX 10 year probability of hip fracture was also associated with increased likelihood of falling with increases in risk of 1-2% for every 1% increase in hip fracture probability. However, the risk factors were well balanced between the study arms and, importantly, there were no statistically significant differences in the incidence of falls between the two study groups. In particular, there was no significant interaction ($p=0.18$) between screening and falls risk when compared across the range of baseline FRAX hip fracture probabilities.

Screening for 10-year fracture risk does not modulate fall risk, supporting the conclusion that the reduction in hip fracture is mediated by anti-osteoporosis therapy.

PP9 The Effect of Bone Quality on the Time Dependant Response of Human Trabecular Bone at Physiological Levels of Strain

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Objectives: Trabecular bone is a multiscale hierarchical composite material that is known to display time-dependant properties. However, most biomechanical models treat this material as time independent. Time dependant properties, such as creep and relaxation, are thought to play an important role in many clinically relevant orthopaedic issues; implant loosening, vertebral collapse, and non-traumatic fractures. In our study, we aim to determine if creep and relaxation of human trabecular bone is influenced by bone microarchitecture at low levels of physiological strain.

Methods: Central cores were extracted from 15 female femoral heads and scanned by microCT to determine bone volume fraction (BVF). Mechanical testing using a compressive creep-relaxation protocol was implemented at five levels of target strain (2000με, 4000με, 6000με, 8000με and 10000με).

Time independent analysis determined Young's modulus. Time dependent analysis revealed; instantaneous strain, creep strain, unloading strain, and recovered strain.

Results: Time independent analysis revealed BVF and stiffness are correlated: the higher the BVF, the higher the stiffness and this relationship did was true for all strain levels tested.

Time dependent analysis showed creep strain depended on the instantaneous strain and BVF. In low BVF samples low instantaneous strain gave increased creep strain (R^2=0.524), this was not apparent at higher instantaneous strain (R^2=0.058).

Residual strain was found to also depend on the applied instantaneous strain and the BVF. At low levels of strain, residual strain was similar for all BVF. At high levels of strain, residual strain was greater in low BVF samples.

Conclusion: This research demonstrates that even at loads below recognised yield levels, time dependence affects the mechanical response. In cases of low BVF the amount of deflection due to creep, and the increased amount of irrecoverable strain, could have clinically relevant consequences.

The results could show the mechanisms behind implant loosening and vertebral collapse: low loads over a long duration lead to greater creep and more irrecoverable damage. These results provide time dependant human mechanical properties that could be incorporated in finite element modelling to better predict implant loosening in lower quality bone.

PP10 New therapeutic avenues in bone repair: Harnessing a novel endogenous molecule to boost bone and prevent bone loss in inflammatory disease

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Background: Treating the destructive effects of excessive osteolysis and impaired bone formation associated with age-related bone loss and inflammatory disorders remains challenging. Manipulating the capacity of endogenous proteins to arrest disproportionate or pathological resorption, whilst simultaneously stimulating periods of healthy bone formation, offers the potential to better target and manage the devastating impact of bone disease.

Objectives: We investigated the effect of a novel compound (Pro-B1X) on the bone microenvironment in normal and pathological conditions.

Methods: *In vivo:* Normal 6-week (M, C57Bl/6J, n=>5) mice were given daily intraperitoneal injections of Pro-B1X or control (PBS) for two weeks, or therapeutically during an inflammatory bone loss model. Cortical and trabecular parameters were analysed in long bones and vertebrae (L1-5) by micro-CT, 3-point bend testing was performed, and TRAP staining was done to determine osteoclast number.

In vitro: Primary murine calvarial osteoblasts and the MC3T3-E1 cell line were cultured in differentiation media with and without Pro-B1X. Analyses of osteoblast activity was characterised by alizarin red staining.

Results: In normal mice, Pro-B1X significantly increased BV/TV (12.7 ± 0.3 to 15.5 ± 0.6% (mean ± SEM), n=5, P=0.025), compared to control (n=11). Trabecular number and trabecular thickness were also significantly increased by 20% and 8% respectively (means, p<0.05). No differences were observed in cortical bone parameters over this time-period. However, increases in stiffness and failure load were seen in Pro-B1X bones.

Importantly, Pro-B1X caused a 54% reduction in mean bone erosion scores and a 53% reduction in osteoclast number per section in mice with inflammation induced bone loss, compared to control-treated animals (n=3).

In vitro, Pro-B1X promoted mineralisation of both MC3T3-E1 and primary osteoblasts, after 12 days in culture which persisted through to day 21.

Conclusion: Our data shows that Pro-B1X is able to enhance trabecular bone growth under normal conditions and decrease bone damage during inflammation induced bone loss. Excitingly, this suggests that Pro-B1X is a potential novel treatment to simultaneously block excessive osteoclast resorption and stimulate osteoblast numbers and activity to more effectively repair damaged bone.

PP11 Do sex hormones determine sexual dimorphism of the bone vasculature?

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Objective: Oestrogens and androgens are essential for maintenance of bone health and imbalances are associated with skeletal pathologies. Hormone replacement therapies are ineffective in severe osteoporosis, suggesting an involvement of a genetic counterpart. We have identified a sexually divergent role of vascular endothelial growth factor (VEGF) in maintenance of bone integrity. To identify hormonal contributions to this sexual dimorphism, we studied the bone phenotype of 4-week-old animals and deleted VEGF in vitro in primary osteoblasts (OBs).

Methods: 4-week-old mice carrying floxed alleles of VEGF ($Vegf^{fl/fl}$) and expressing Cre recombinase under the control of osteocalcin promoter were used (OBVEGFKO). Synchrotron based computed tomography scans of the tibiofibular junction (0.65µm) interrogated cortical porosity. Entire tibiae were scanned (18µm) for shape analysis. In vitro, OBs were isolated from male and female $Vegf^{fl/fl}$ mice and VEGF deleted using Adenovirus-Cre. Raman spectroscopy facilitated assessment of matrix components. qPCR enabled estrogen (Er) and androgen (Ar) receptor expression analysis.

Results: Separation of cortical porosity into lacunae and vascular canal fractions revealed significant increases in the canal fraction (49.0±4.6% OBVEGFKO vs 35.5±5.1% WT, p<0.05) and reductions in lacunae fraction (48.7±5.2 OBVEGFKO vs 62.3±4.3 WT, p<0.05) in male OBVEGFKO versus WT. Increases in canal volume reached significance in male OBVEGFKO versus WT (79296.9±19376.5µm3 vs 20189.4±4737.3 µm3, p<0.05), suggestive of vascular sexual dimorphism. Whole tibia analysis revealed significant differences in ellipticity and cortical thickness along the tibial length in male OBVEGFKO versus WT. In vitro deletion of VEGF in males resulted in -1.33-fold (p<0.0001) reduction in mineral/matrix due to elevated production of immature mineral components, whereas an increase was observed in OBVEGFKO females versus WT (+11.89-fold; p<0.0001). No alterations in Er or Ar mRNA expression levels were evident in male or female OBs in vitro.

Conclusion: Our data highlights early sexual divergence in bone porosity and shape following OBVEGFKO, which is augmented with age and could be linked to sex hormone levels. As significant

sexual dimorphism is also present in vitro there are likely other environmental, genetic or mechanical influences contributing to the divergence in osteoblast matrix production following VEGF deletion, which should be explored.

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PP12 Evaluating strength of 3D printed screw threads for patient-specific osteosynthesis plates

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Objectives: The angular stability of locking screws has made them ubiquitous in osteosynthesis plates, due to the importance of maintaining the correction during the course of healing. Bespoke and personalised implants have been made possible by advances in additive manufacture using titanium alloy, however, printed threads are a challenging feature to incorporate in additively manufactured parts due to the feature size in comparison to the main part. This study evaluated the potential to print locking screw threads within an osteosynthesis plate.

Methods: Tapered, double-start threaded Ti-6A-4V screws were custom-made to similar dimensions to the most commonly available locking screws on the market: 6.5mm maximum head diameter, 0.5mm pitch threads and 14 degree total taper angle. One hundred and nine corresponding female threaded specimens were additively manufactured (Renishaw PLC, UK) at different build orientations: 0°, 20°, 45° and 90° with different numbers of threads: 3, 4, 5 and 6. An initial power study determined that at least n=8 per group was required for a power of 80%. The main outcome measure was the 'thread capacity' defined as the maximum force recorded during destructive push-out testing of the screw-sample threaded interlock (strain rate according to ISO6892-1:2016). Mann-Whitney statistical test was used to evaluate the differences between the groups.

Results: A steeper orientation of build direction was generally found to increase the thread capacity for any number of threads. A 90° build orientation was found to produce significantly (p=0.029) larger thread capacity than 0° for all thread numbers. The mean capacity of 5 threads was 2886±584N for 0° build orientation compared to 1435±407N for 90°. Increasing thread numbers increased the thread capacity by 202.3±86.7N per thread for 90° orientation.

Conclusion: The build orientation significantly influenced the thread capacity and we found that a vertical build orientation is superior for push-out thread resistance, however, there was a large variability in thread capacity. We examined a worst-case scenario; in reality the threads would be exposed to a combination of shear and bending.

PP13 What is the optimum tightness for non-locking cortical screws, and how can this be predicted prior to insertion?

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Objectives: When operative management is needed z used implant. The currently used insertion techniques are reliant on a surgeon's subjective feeling of the required and applied torques. In experimental testing, approximately 1 in 4 screws have irreparably damaged the surrounding bone whilst being inserted due to an inability to appreciate the stripping limits, increasing the risk of fixation failure . If maximum and optimum torques could be predicted prior to screw insertion, this could reduce failures, expedite operations and strengthen constructs. The aim of this study was to devise a method to quantify and optimise tightness for the insertion of cortical fracture-fixation screws, based on bone characterisation and screw geometry.

Methods: Cortical human diaphyseal tibiae samples (n=20) underwent destructive testing to firstly establish the relationship between cortical thickness and experimental stripping torque (T_{str}) and secondly to calibrate an equation to predict T_{str}. Using the equation's predictions, 3.5 mm screws were inserted (n=66) to targeted torques representing 40 to 100% of T_{str}, with the compression generated during tightening being measured. Once the target torque had been achieved, immediate pullout testing was performed.

Results: Cortical thickness predicted the stripping torque (R^2=0.862, P<0.001) as did an equation based on tensile yield stress, bone-screw friction coefficient and screw geometries (R^2=0.894, P<0.001). Compression increased with screw tightness – calculated as the ratio of targeted/stripping torque - up to 80% of the maximum (R^2=0.495, P<0.001). Beyond 80%, no further tightness generated the same increase in compression. Pullout force did not change with variations in submaximal tightness beyond 40% of T_{str} (R^2=0.014, P=0.175).

Conclusion: Screws tightened to 70 - 80% of the predicted maximum generated optimum compression and pullout forces. Further tightening

did not significantly increase compression, did not improve resistance to pullout and increased the risk of the bone being stripped. Whilst intraoperative methods for accurately and reliably predicting the maximum tightness for a screw are needed, this work justifies controlled insertion considerably below the maximum torque and demonstrates methods to predict the required torque.

PP14 Genome-wide Expression Analysis of Human Osteoclasts Following Clinically Relevant Cobalt and Chromium Exposure

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Systemic cobalt (Co) and chromium (Cr) concentrations maybe elevated in patients with accelerated tribocorrosion at prosthesis bearing surfaces and modular taper-junctions. Several studies have highlighted the detrimental effects of metal exposure on bone cells *in-vitro*, but their mechanisms remain unclear. In this study, we used whole-genome microarrays to assess differential gene expression in primary human osteoclasts following exposure to clinically relevant concentrations of Co and Cr.

Monocytes from peripheral blood of 3 healthy volunteers were differentiated into osteoclasts on dentine-disks using RANKL and M-CSF. Cells were treated post-seeding till onset of resorption, or 24h post onset of resorption to investigate effects on differentiating and mature osteoclasts respectively. Treatments comprised of 5µg/L and 500µg/L Co^{2+}:Cr^{3+} to simulate systemic and periprosthetic concentrations respectively. Subsequently, total RNA was hybridized to Agilent SurePrint-G3 Gene Expression Microarrays.

Probe signals were normalised using 'Limma' package on R-Bioconductor and differential gene expression assessed with empirical Bayes approach ($Log_2FC>1.00$,$P<0.001$). 'maSigPro' package was used to identify gene-clusters that correlated with increasing Co^{2+}:Cr^{3+} concentrations.

For differentiating osteoclasts, 5µg/L Co^{2+}:Cr^{3+} downregulated genes associated with MAPK signalling($P=9.14e^{-3}$) which promotes cell differentiation, including *Elk1*($P=3.1e^{-3}$) and *RasGRF1*($P=1.7e^{-3}$). Exposure to 500µg/L Co^{2+}:Cr^{3+} downregulated genes such as *IL17RD*($P=9.5e^{-3}$), *CTRC*($P=4.3e^{-3}$) and *CALCA*($P=6.3e^{-3}$) which are associated with decreased osteoclast activity, and upregulated *HMGA2*($P=1.5e^{-3}$) and *Wnt5a*($P=3.7e^{-3}$) which promote osteoclast differentiation. 8 gene-clusters correlated with increasing Co^{2+}:Cr^{3+} concentrations, and pathways of calcium signalling($P=9.5e^{-4}$) and focal adhesion($P=4.0e^{-4}$) showed dose-dependent effects.

For mature osteoclasts, 5µg/L Co^{2+}:Cr^{3+} downregulated genes associated with RAS/MAPK signalling(*RASA4B*,$P=6.7e^{-4}$; *EFNA5*,$P=9.1e^{-3}$;and *RGS12*,$P=4.5e^{-4}$), cell-polarity (*ARHGAP24*,$P=2.1e^{-3}$), adhesion(*ADRGRA3*,$P=4.4e^{-4}$) and endocytosis(*ASAP3*,$P=8.3e^{-3}$). Co^{2+}:Cr^{3+} at 500µg/L downregulated osteoblast-osteoclast coupling genes including *BMP-7*($P=6.2e^{-3}$), *SLIT1*($P=6.0e^{-4}$) and *EFNA5*($P=1.6e^{-3}$). Finally, increasing Co^{2+}:Cr^{3+} concentrations associated with 9 gene-clusters, with focal adhesion($P=5.0e^{-2}$) and chemical carcinogenesis($P=3.6e^{-2}$) pathways showing dose-dependent effects.

This study suggests that systemic concentrations of metal exposure may reduce osteoclast differentiation and activity of mature osteoclasts; consistent with our clinical observation of reduced systemic TRAP5b activity and increased total-BMD. Periprosthetic concentrations seem to promote osteoclast differentiation and inhibit genes associated with osteoblast differentiation with implications for osseointegration of prostheses.

PP15 How does body weight influence the risk of vertebral fracture?

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The aim of this study was to utilise UK Biobank data to examine the association between body weight and the risk of vertebral fracture, and whether this association was influenced by gender and the methods of measuring body weight, and to predict the risks of vertebral fractures using various clinical factors as in FRAX.

This cross-sectional study was based on two UK Biobank datasets: Full dataset from 502,543 participants (229,138 men and 273,405 women) recruited and assessed during the period 2006-2010, which was used to examine the incidence of vertebral fractures in participants with different body mass index (BMI) and waist circumference (WC). The second dataset is a subset of this cohort, 5,189 participants (2,473 men and 2,716 women) who also participated in an imaging study (2014 – on going) that provided dual-energy X-ray absorptiometry (DXA) data of the body. The association of the various categories of BMI and waist circumference with incidence of vertebral fracture was examined in the full dataset using chi-square tests. Multivariate logistic regression was then employed to predict the risks of vertebral fractures using various clinical factors as in FRAX. Linear regressions were employed to look at how vertebral bone mineral density (BMD) and geometry were related to trunk fat mass, visceral adipose tissue, and limb fat mass.

There was a significant association between waist circumference and incident vertebral fracture in

male $\chi^2 = 8.51$, $p = 0.014$, but not in female $\chi^2 = 0.71$, $p = 0.701$. There was no significant association between BMI and incident vertebral fracture in male $\chi^2 = 0.94$, $p = 0.625$ or in female $\chi^2 = 4.28$, $p = 0.118$. However, results from multiple logistic regression showed that body weight, BMI, or WC was not significantly related to vertebral fracture risks. Vertebral BMD and geometry showed negative association with visceral adipose tissue (VAT) mass, trunk fat mass and limb fat mass in both males and females ($p<0.05$).

Obesity is associated with inferior vertebral BMD and geometry, but it does not seem to be related to vertebral fracture risks.

PP16 Accelerated osteogenesis in vivo and in vitro achieved through metabolic and secretomic modification in mesenchymal stromal cells

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Objectives: To identify osteogenic mechanisms in mesenchymal stromal cells (MSCs) in a physiologically relevant culture environment unobscured by undefined serum bioactives.

Methods: We engineered an immortalised human clonal MSC line (Y101), then adapted this line from 10% to 0.5% serum (Y101.5) over twelve weeks in culture. We assessed osteogenesis using Alizarin Red staining and performed transcriptomic (RNA-Seq) and proteomic (mass spectrometry) profiling for Y101 versus Y101.5. We tested Y101.5 secretome compartments on osteogenesis of Y101 MSCs. In vivo bone formation was determined by implanting MSC-loaded hydroxyapatite particles into immunocompromised mice, retrieving at 3 and 8 weeks and processing for histological and immunohistochemical analysis.

Results: Y101.5 MSCs demonstrated clear acceleration of osteogenesis in both 0.5% and 10% serum, with 7 day calcium deposition in Alizarin Red elutions equivalent to parental Y101 MSCs at day 21 (absorbance 26.1±1.4, 31.9±1.6, n=3). RNA-Seq identified 510 differentially regulated transcripts with upregulated pathways in Y101.5 related to fatty acid/lipid/cholesterol metabolism. A functional free fatty acid uptake assay demonstrated reduced lipid dependency in Y101.5 MSCs. Cellular component terms enhanced in Y101.5 pointed to a modified secretome. Mass spectrometry identified differences in the secretome (100 down-regulated, 194 up-regulated) and EVome (14 down-regulated, 92 up-regulated) in Y101.5 versus Y101. Accelerated osteogenic differentiation was conveyed to Y101 cells by day 14 when exposed to Y101.5 conditioned medium (CM), compared to Y101 osteogenesis under standard conditions (12.3±2.6, 1.3±0.1, n=3). Testing secretome compartments showed reduced effects with extracellular vesicle (EV)-depleted CM or EVs alone, suggesting that secretome fractions function synergistically. In vivo, Y101.5 implants indicated organized bone formation by week 3 with increased osteonectin and RUNX2 immunostaining compared to Y101 MSCs (n=6), indicating accelerated osteogenesis of Y101.5 MSCs was retained in vivo. By week 8, bone formation and osteogenic markers were identified in both the Y101 and Y101.5 implants.

Conclusions: Our findings demonstrate accelerated osteogenesis is achieved in MSCs through low-serum adaptation. A metabolic switch favouring lipid/cholesterol biosynthesis alters the MSCs secretome which conveys advantageous osteogenic capacity in vitro and in vivo.

PP17 Higher birthweight is associated with greater limb muscle mass and grip strength in middle age: findings from the UK Biobank Imaging Enhancement

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Objectives: A variety of epidemiological studies have demonstrated associations between low birthweight and poorer musculoskeletal health in later life. We investigated relationships between birthweight, and adult grip strength or magnetic resonance imaging (MRI) measures of muscle volume in UK Biobank.

Methods: UK Biobank is a large prospective cohort of men and women aged 40-69 years. A detailed baseline assessment was performed in which birthweight was collected by self-report. A subset underwent MRI examination with the dual-echo Dixon Vibe protocol, from neck to knees. Automated body composition analysis was performed using the AMRA Profiler™ system, to segment and quantify total thigh muscle volume. Grip strength was assessed using a Jamar hydraulic hand dynamometer. Associations between birthweight, and thigh muscle volume or grip strength (expressed as Fisher-Yates z-scores) were investigated using multivariate linear regression analysis. This study was conducted under generic ethics approval (NRES:11/NW/0382).

Results: 3699 participants [1513 men, median (IQR) age 62 (55-67) years and 2186 women, age 61 (54-66) years] were able to recall their birthweight and had their grip strength assessed and underwent

MRI body composition analysis.

In both men and women, higher birthweight was associated with greater thigh muscle volume (adjusted for age and body mass index (BMI)): men, β(95% CI): 0.23 (0.16, 0.30) SD/kg, p<0.001; women, β(95% CI): 0.28 (0.22, 0.35) SD/kg, p<0.001. Higher birthweight was also associated with higher grip strength (adjusted for age and height); men, β(95% CI): 0.12 (0.05,0.20) SD/kg, p=0.001; women, β(95% CI): 0.07 (0.01, 0.13) SD/kg, p=0.031. Apart from the association with grip strength in women, these associations persisted after additional adjustment for current smoking and physical activity.

Conclusion: Birthweight was positively associated with grip strength and MRI measures of thigh muscle volume in a population of middle-aged UK adults. These findings provide novel evidence in support of the developmental programming hypothesis and suggest that interventions to optimise birthweight may help to prevent sarcopenia and reduce the risk of falls in future generations. (UK Biobank Project 3593).

PP18 Measuring Prosthesis Migration using a Novel Ultra-Low Dose CT-Based Method

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Background: Implant migration is a predictor of survival after hip arthroplasty, and thus crucial to introduce and monitor novel prostheses. Roentgen Stereophotogrammetric Analysis (RSA) is the gold standard method, but requires calibrated radiographs using expensive, specialist equipment and significant technical expertise. We aimed to develop an ultra-low dose CT-based spatial analysis (CTSA) method as an alternative.

Materials and Methods: A ceramic hip resurfacing arthroplasty and 20 tantalum beads were implanted into a pelvis model, mounted onto a 6-degree of freedom motion stage. The pelvis was repeatedly scanned with an ultra-low dose CT protocol, with imposed micromovements in translation (T) from 0.1mm to 1mm, and rotation (R) from 0.2° up to 1° in x, y and z axes to enable the accuracy and precision (double measurements) to be determined. Data were interrogated using a bespoke semiautomated 3D CT model-based technique with Materialise Mimics and Mathworks MATLAB software. The algorithm uses Hounsfield units to locate the tantalum bead centres and then applies an Iterative Closest Point algorithm to match segmented implant meshes. The bead centres between the two images are matched and the matrix transformation between the corresponding implant meshes calculated. The matrix transformation is decomposed into translations (T) and rotations (R).

Results: The effective radiation dose <0.15mSv. For the head, the worst accuracy was 0.19mm (T_y) and 0.74°(R_{zz}); for the cup it was 0.13mm (T_y) and 0.62 (R_{xx}) For the head, the worst precision was 0.36mm (T_x) and 0.38°(R_{xx}); for the cup, it was 0.12mm (T_z) and 0.51° (R_{yy}).

Conclusion: This *in vitro* study demonstrates that ultra-low dose CTSA is similar in accuracy to standard-dose (~0.30mSv) RSA. CT is ubiquitous, and this method may be a safer and inexpensive alternative to RSA to longitudinally measure prosthesis migration in multicentre studies and clinical practice. Clinical validation studies are required to estimate the effect of patient variability on accuracy.

PP19 Pharmacokinetics of parathyroid hormone peptide PTH 1-34 via nasal spray for the treatment of osteoporosis

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Objectives: Nasal delivery of large peptides are not well suited to absorption across the nasal mucosa into the bloodstream. Previously, we have published encouraging (78%) bioavailability in a small animal model for a PTH 1-34 liquid nasal spray formulation containing the permeation enhancer polyethylene glycol (15)-hydroxystearate (PEG 15-HS). Here we report translational research in healthy human volunteers receiving the PTH 1-34 liquid nasal spray. In addition, preliminary pharmacokinetics of a dry powder formulation containing PEG 15-HS was investigated in a large animal preclinical model.

Methods: The clinical study was conducted in accordance with the Declaration of Helsinki (NRES 13/LO/1037, IRAS 126447). An open cross-over clinical IMP (investigative medicinal product) study was conducted in 7 consented healthy women aged over 55 years. Participants were dosed with PTH 1-34 liquid nasal spray. Plasma drug concentrations were measured for 6 hours post dose. Tc-99m-DTPA gamma scintigraphy monitored the deposition and clearance of the nasal spray.

An established ovine nasal delivery model was employed in accordance with the Animals (Scientific Procedures) Act 1986 (PPL 40/3552, PCD 40/2406). The study was a four-way randomised cross-over study in four (Mule crossbred) sheep. Post administration of the PTH 1-34 formulations the plasma drug concentration was measured for 4 hours.

Results: PTH 1-34 mean plasma maximum concentrations (Cmax) of 5 pg/ml and 253 pg/ml

were obtained for the liquid nasal spray and subcutaneous injection respectively and relative bioavailability of the nasal spray was approximately 1% in healthy volunteers. Tc-99m-DTPA scintigraphy identified a 50% clearance time of 17.8 minutes (minimum 10.9, maximum 74.3 minutes). In sheep the relative bioavailability of liquid and powder nasal formulations was 1.4% and 1.0% respectively. The absolute bioavailability (mean 77%, range 55-108%) of subcutaneously administered PTH 1-34 was comparable to published human data for teriparatide (up to 95%).

Conclusion: These findings have important implications in the search for alternative routes of administration of peptides for the treatment osteoporosis and in terms of improving translation from animal models to man.

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PP20 The influence of the RNA binding protein HuR on skeletal development is not mediated through the control of mesenchymal cell differentiation

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Objectives: This project aimed to understand how the RNA binding protein HuR influences the development of skeletal structures. Knockout of HuR in the epiblast is known to result in a severe phenotype, affecting multiple organs and including significantly impaired skeletal development. In this project we conditionally knocked out HuR in mouse limb bud mesenchyme using the Prx1-driven cre recombinase.

Methods: Mice harbouring loxP sites flanking exon 2 of HuR ($HuR^{fl/fl}$) were crossed with Prx1-Cre homozygote mice to generate $HuR^{fl/WT}$ $PRX1\text{-}Cre^{+/WT}$ F1 mice. These mice were crossed back into $HuR^{fl/fl}$ and embryos were collected at E13.5 and E16.5. Maternal delivery of Prx1-Cre has been shown to result in germline transmission and was used to induce generalized HuR knockout. Paternal delivery of Prx1-Cre was used to specifically knockout HuR in early limb bud mesenchyme. Embryos were examined histologically and levels of HuR in limb bud knockouts was determined using immunohistochemistry.

Results: In embryos homozygous for floxed HuR, maternal inheritance of Prx1-Cre from the maternal allele led to a severe skeletal phenotype, similar to that previous demonstrated in epiblast knockout. Embryos were smaller, had severely truncated limbs and craniofacial abnormalities. Surprisingly, homozygous floxed embryos with paternal inheritance of Prx1-Cre had no observable phenotype. Differentiation of skeletal elements appeared normal at each of the stages examined, even though immunohistochemistry confirmed absence of HuR protein in skeletal structures within the limbs of these embryos.

Conclusion: Knockout of HuR in the epiblast has previously demonstrated that the absence of this protein has a severe impact on the development of skeletal tissues. Our work has been able to replicate these findings using maternal delivery of Prx1-Cre. The lack of observable phenotype in the limb bud-specific HuR knockouts driven by paternal Prx1-Cre delivery was unexpected and suggests a role for HuR extrinsic to mesenchymal tissues is important. Prx1-Cre conditional knockout does not affect the ectoderm surrounding the limb bud, which is known to have regulatory roles during limb development, potentially indicating a critical function of HuR there.

PP21 Investigating the regulation of bone mineralisation through in vitro and in vivo models of chronic kidney disease

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Objective: Patients with chronic kidney disease (CKD) present with hyperphosphatemia together with elevated fibroblastic growth factor-23 (FGF23), and parathyroid hormone (PTH) levels. These systemic changes likely account for the observed renal osteodystrophy (ROD) which is characterised by abnormal mineralisation and bone fractures. The role of PHOSPHO1 and tissue non-specific alkaline phosphatase (TNAP) in ROD remains unclear and was the focus of this study.

Methods: Primary murine calvarial osteoblasts were cultured and maintained in rhPTH (0.05-50nM), rhFGF23 (1-200ng/ml) and Pi (1-5mM) for 28 days. PHOSPHO1 and TNAP gene and protein expression were assessed by RT-qPCR and western blotting. The adenine-induced CKD mouse model (groups of 8 male mice) was studied to investigate the effects of the metabolic and hormonal disturbances, typical of CKD on PHOSPHO1 and TNAP expression in long bones.

Results: PTH and Pi induced a concentration dependent decrease in both Phospho1 mRNA (50nM PTH, 93.3%, $P<0.0001$; 5mM Pi, 53.7%, $P<0.001$) and PHOSPHO1 protein (50nM PTH: 93.5%, $P<0.0001$; 5mM Pi: 86.3%, $P<0.01$) expression. High concentrations of PTH and Pi also decreased Akp2 mRNA (PTH: 94.2%, $P<0.0001$; Pi: 61.4%, $P<0.001$) and TNAP protein (PTH: 94.1%, $P<0.001$; Pi: 56.1%, $P<0.01$) expression. FGF23 had no effect on any parameter measured.In the CKD mouse model, circulating PTH, Pi, and FGF23 were all increased ($P<0.01$) after 5 weeks on the adenine diet as were bone formation (P1NP) and resorption (αCTx) markers ($P<0.01$). Micro-CT revealed no differences in trabecular BV/TV or trabecular number, but trabecular BMD and pattern factor were lower

(P<0.01) in CKD femurs. Cortical BMD, BV/TV, cross-section area and thickness were lower in CKD femurs (P<0.05). Akp2 gene expression was lower (P<0.0001) whereas Phospho1 mRNA and PHOSPHO1 protein expression were higher (P<0.001) in CKD femurs.

Conclusion: This study reveals that osteoblast PHOSPHO1 and TNAP expression are reduced by PTH and Pi. Whilst the lower expression of Akp2 expression in CKD bone is consistent with the hypomineralisation noted in ROD, the higher PHOSPHO1 expression is not. Further study is required to understand the role of these phosphatases in ROD.

PP22 Changes in gait, knee loading and patient reported outcomes following High Tibial Osteotomy

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Objective: Identify changes in gait, knee loading and patient reported outcomes resulting from opening wedge High Tibial Osteotomy (HTO).

Methods: Three-dimensional motion analysis with a modified Cleveland Clinic marker set was used to assess level gait for 18 participants (19 knees) with medial OA and Varus alignment (mean mTFA 7.95 ± 3.64°) pre and post-HTO, along with 18 controls. Cameras (Qualisys, Sweden) and force platforms (Bertec Corp., USA) captured data at 120 Hz and 1080Hz respectively. Approval was granted by the Research Ethics Committee for Wales and Cardiff and Vale University Health Board. Joint kinematics, kinetics and temporal parameters were calculated within Visual 3D (C-Motion, USA). Statistically significant changes pre to post-HTO and differences to controls were identified (SPSS Inc., USA).

Results: When compared to controls, pre-HTO participants experienced significantly higher frontal plane loading (78% greater knee adduction angular impulse and 46% greater peak external knee adduction moments (EKAM)), larger transverse plane knee loading, reduced gait speed, increased frontal plane trunk sway and decreased hip range of motion (ROM) in the frontal and sagittal planes. At the timings of the first and second EKAM peaks, knee adduction angles were high, and the ankle was everted. Following HTO, these measures returned to normal ranges and the ankle was restored to an inverted posture.

Post-HTO, statistically significant deviations from the control group included a greater percentage of time spent in stance, 9% longer duration to reach peak knee flexion, reduced ROM of 6° for the knee in the sagittal plane, and 2° for the ankle in the transverse plane, 31% and 25% reduction in knee flexion and extension moment peaks respectively.

Oxford Knee Score, Knee Outcome Survey and pain scores improved significantly, whilst remaining significantly different to controls (p<0.001).

Conclusion: Frontal and transverse plane knee loading improved as a result of HTO. Several gait adaptations observed pre-HTO, were not present post-HTO. Gait alterations maintained following HTO included a prolonged stance duration, reduced transverse plane ankle motion and reduced knee loading and motion in the sagittal plane.

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PP23 An in vitro assessment of knee kinematics following radial tears of the medial meniscus

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Objectives: There has been much recent debate over the utility of partial meniscectomy, particularly in the context of degenerate tears. In undertaking partial meniscectomy, it is assumed that the removed tissue is redundant. The literature demonstrates that removal of the posterior horn of the medial meniscus results in altered knee kinematics. Radial tears are thought to defunction the meniscus by interrupting its ability to generate hoop stresses. This study sought to determine whether isolated radial tears of the posterior horn of medial meniscus resulted in altered knee kinematics.

Methods: Five fresh frozen mid-femur to mid-tibia cadaveric specimens from donors <65 years of age, with no history of knee pathology were cemented into a custom jig within a materials testing machine. Loads of 100/250/500 and 1000N were applied at 0/15/30/45 and 60 degrees of flexion. Kinematic data were collected using a motion capture system and changes in flexion/extension, abduction/adduction and internal/external rotation were calculated compared to the unloaded position. Knees were tested sequentially following sham arthroscopy, a 50% depth radial tear and a 100% depth radial tear at the junction of the anterior two thirds and posterior third of the meniscus. Three-way, repeated measures ANOVA with Bonferroni correction was used to analyse joint angles with respect to load, knee angle and injury.

Results: All soft tissue primary stabilising constraints and menisci were found to be intact. No significant difference in knee kinematics following radial tears was evident. A trend towards increasing posterior translation and varus angulation of the tibia with respect to the femur was observed with sequential meniscal injury and increasing load. A number of

native biomechanical phenomena such as screw home rotation of the knee were observed.

Conclusions: Isolated radial tears of the medial meniscus do not result in significantly altered knee kinematics, yet there is evidence that partial meniscectomy can alter such kinematics. This work highlights that this meniscal function remains largely intact following such injuries and hence reinforces the importance of meniscal preservation as opposed to resection in such scenarios.

PP24 Correlations between Radiographic Classification Systems and Confirmed Cartilage Loss in Severe Knee Osteoarthritis

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Objectives: Though knee osteoarthritis (OA) is diagnosed and monitored radiographically, actual full thickness cartilage loss (FTCL) has rarely been correlated with radiographic classification. This study aims to analyse which classification system correlates best with FTCL and to assess their reliability.

Methods: Prospective study of 300 consecutive patients undergoing unilateral total knee arthroplasty for OA (mean age 69±9.5 (range 44 to 91), 178 (59%) female). Two blinded examiners independently graded preoperative radiographs using 5 common systems: Kellgren-Lawrence (KL); International Knee Documentation Committee (IKDC); Fairbank; Brandt; and Ahlback. Interobserver agreement was assessed using the intraclass correlation coefficient (ICC). At surgery, anterior cruciate ligament (ACL) status and the presence of FTCL in 16 regions of interest were recorded. Radiographic classification and FTCL were correlated using the Spearman correlation coefficient.

Results: On average, each knee had 6.8±3.1 regions of FTCL, most common medially. The commonest patterns of FTCL were medial with patellofemoral (48%) and tricompartmental (30%). Medial FTCL +/- patellofemoral with intact ACLs was present in 129/300 (43%) patients. ACL status was associated with pattern of FTCL (p=0.02). All radiographic classification systems demonstrated moderate ICC, but this was highest for the IKDC: whole knee 0.68 (95% CI 0.60-0.74); medial compartment 0.84 (0.80-0.87); and lateral compartment 0.79 (0.73-0.83). Correlation with actual FTCL was strongest for Ahlback (Spearman rho 0.27-0.39) and KL (0.30-0.33) systems, though all systems demonstrated medium correlation. The Ahlback score was the most discriminating in severe knee OA. Osteophyte presence in the medial compartment had high positive predictive value for FTCL, but not in the lateral compartment.

Conclusion: The Ahlback and KL systems had the highest correlation with confirmed cartilage loss at total knee arthroplasty. However, the IKDC system displayed the best interobserver reliability, with favourable correlation with FTCL in medial and lateral compartments, though it was less discriminating in more severe disease.

PP25 Impact of renal function on response to oral and i.v. bisphosphonate treatment: Real world observational data using linkage to national registers

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Background: Bisphosphonates (BP) are contraindicated in patients with severely compromised renal function (C-G crea clearance < 30-35 ml/min). The impact of milder degrees of renal function impairment on BMD gains in a real-world population is however unknown.

Methods: The study population consisted of 4,080 men and women who began oral or i.v. BP treatment following DXA, divided into high adherence (MPR>=80%, N=2,213) and suboptimal adherence (MPR<80%, N=1,867). Annualized femoral neck BMD change was calculated in all patients who had an eGFR measurement and a DXA scan in the last year before initiating treatment, and where a follow-up DXA was available 2 to 3y after the start of treatment (N=1,761). Further, BMD changes against renal function could be similarly tracked in 3,841 untreated persons.

Results: Though femoral neck BMD improvements were smaller in patients with eGFR<60 (stage 3A) and largely absent with eGFR<45 (stage 3B), the negative BMD change seen without treatment or with suboptimal adherence was avoided. In accordance with the contraindication, BP use in persons with baseline eGFR<30 was practically non-existent. The unadjusted increment in FN BMD with optimal adherence was 1.2% (1.1-1.4%), or 0.9%(0.7-1.2) when adjusted for age, sex, prior MOF, GC use and CKD stage. For the BP population as a whole there was no interaction with CKD stage (p=0.365) on BMD change. When stratified by CKD stage, significant BMD increases were only observed at stage 3A or better.

Discussion: In a real world scenario, significant BMD benefits could be demonstrated in patients with CKD stage 3A (eGFR 45-59). We observed no significant interaction with renal function on relative BMD response but effect modification cannot be ruled out given the low number of patients with CKD stage 3B or 4 beginning treatment in the osteoporosis clinic

PP26 A tale of two phosphatases: how do matrix vesicles generate phosphate for bone mineralization?

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Background: Bone mineralisation is orchestrated by osteoblasts which secrete matrix vesicles (MVs) 100-300nm in diameter into a collagenous scaffold. MVs provide a localised concentration of calcium and inorganic phosphate (P_i) ions to facilitate mineral nucleation, however the mechanism by which intravesicular P_i generation is achieved is currently unclear. The phosphatase PHOSPHO1 is a critical effector of this process post-natally however its role during embryonic development, along with its relationship with established phosphatases including tissue non-specific alkaline phosphatase (TNAP), has yet to be fully elucidated.

Methods: C67BL/6 wild-type and knock-out (Phospho1$^{-/-}$) mouse embryos at 14-17 days of development (E14-17) were generated from overnight matings. Embryos were whole-mount stained with Alizarin Red for optical projection tomography (OPT), or regions of interest were dissected from the lower limb and calvaria and processed for downstream analyses.

Results: In wild-type mice skeletal mineralisation began at E15. qPCR revealed a significant upregulation of Phospho1 ($p=0.024$) and Alpl ($p=0.009$) expression over the time-course. Several other mineralisation-related genes were also temporally upregulated including SIBLING proteins Dmp1, Spp1, Ibsp and Mepe. Only a selection of these genes exhibited upregulation in the calvaria. Immunofluorescence staining for PHOSPHO1 and TNAP with confocal microscopy revealed localisation to mineralising surfaces. Co-localisation occurred at distinct patches at the membranes of both hypertrophic chondrocytes and osteoblasts in the lower limb and calvaria, with Manders' coefficients of 0.953±0.01, 0.971±0.01 and 0.976±0.01 at E17 respectively. OPT demonstrated ablation of mineralisation in both calvaria and long bones in early Phospho1$^{-/-}$ mice, while bone volume was reduced at later stages ($p<0.001$). TEM of developing calvaria revealed a polarised osteoblast layer which generated a collagenous matrix at E15. MVs were secreted into this matrix and provided loci for hydroxyapatite mineral nucleation. In early embryos crystals were randomly orientated 1-2nm plates which became progressively elongated in more mature tissue. Phospho1$^{-/-}$ animals exhibited generalised hypomineralisation and an accumulation of mineral-deficient MVs.

Conclusions: PHOSPHO1 is critical for normal bone mineralisation during development, allowing P_i accumulation inside MVs. Future research will establish the biochemical pathway through which PHOSPHO1 substrates are generated intravesicuarly.

P27 Do osteoclasts derived from mice with different bone mass exhibit distinct in vitro osteoclastogenic potential and sensitivity to stable sulforaphane?

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Sulforaphane exerts both anti-oxidant and anti-inflammatory effects, but is unstable. A chemically complexed stable form (sulforaphane/alpha-cyclodextrin, SFX-01) has previously been found to exert beneficial bone effects in a mouse (STR/Ort) model of spontaneous osteoarthritis (OA) and inhibition of osteoclasts derived from C57/BL6 mice[(1)]. As it is known that these mouse strains have markedly divergent bone mass (BM), we explore herein whether in vitro osteoclastogenic potential and sensitivity to SFX-01 is related to bone mass in different mouse strains. Primary osteoclasts were therefore isolated from bone marrow of 6-8 week-old C57/BL6 (low BM), STR/Ort (very high BM and OA-prone) and CBA (high BM and parental control to STR/Ort) mice and subsequently cultured with M-CSF/RANKL to promote differentiation and resorptive function, assessed by TRAP staining and resorptive activity on dentine, respectively. Cultures were additionally supplemented with various SFX-01 concentrations to determine direct effects on differentiation and resorptive function. We found that 100nM SFX-01 was sufficient to exert potent and significant inhibition of osteoclast number ($p<0.05$, 30%) and resorption, indicative of direct effects on osteoclast maturation in vitro. In contrast, CBA-derived osteoclasts showed markedly lower SFX-01 sensitivity, requiring higher concentrations (1uM) to exert similar levels of inhibition ($p<0.01$, 33%) on osteoclastogenesis and resorption. Strikingly, STR/Ort-derived osteoclasts were totally insensitive to SFX-01 (up to 1mM) on osteoclast formation and resorption and demonstrated less robust maturation in response to M-CSF/RANKL in vitro. These data are consistent with the notion that osteoclasts derived from mice with higher BM exhibiting lower in vitro osteoclastogenic potential as well as a correspondingly reduced sensitivity to inhibition by SFX-01. It is tempting to speculate that the bone marrow origin of osteoclasts imparts conserved and inherent differences in osteoclast behaviour that are matched to bone mass and to sensitivity to SFX-01.

Reference:

(1) Javaheri B et al. Bone. 2017; 103: 308–31.

P28 Extracellular pH regulates osteoclast fusion

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It is well known that osteoclasts are extremely sensitive to small changes in extracellular pH. Bone resorption is directly stimulated by acid with a near-maximal effect at pH7.0, whilst above pH7.4 osteoclast resorptive activity is switched off. The aim of this study was to investigate whether pH also regulates osteoclast formation. Mouse bone-marrow derived osteoclasts were cultured (+ 200ng/ml M-CSF, 3ng/ml RANKL) on dentine discs at pH7.4, pH7.2 or pH6.9 for up to 7 days. Osteoclast formation and resorptive activity were measured by image analysis of TRAP stained discs. The effect of pH on gene expression was investigated using real-time quantitative PCR. After 4 days of culture, early osteoclasts were present in all groups with no effect of pH on osteoclast formation. By day 5, mature, multi-nucleate cells which stained strongly for TRAP were evident at each pH. The number of osteoclasts present was unchanged; however, the cells grown at pH7.4 and pH7.2 were noticeably larger (≤250µm in diameter) than those cultured at pH6.9 (≤140µm). By day 7, pH6.9 osteoclasts displayed extensive resorptive activity (0.011mm^2 ± 0.001, per cell); the level of resorption in osteoclasts cultured at pH7.4 was significantly lower (0.005 mm^2 ± 0.004 per cell, $p<0.001$). Osteoclast number was increased by 60% at pH6.9 (756 ± 128) compared to pH7.4 (276 ± 44, $p<0.001$). Furthermore, greater differences in cell size were evident between the extensively resorbing (pH6.9, ≤140µm) and the less active osteoclasts (pH7.4, ≤320µm). mRNA expression of the fusion marker DC-STAMP was 4-fold higher in cells cultured at pH7.4 compared to pH6.9, whilst RANK and c-fms levels were unchanged. Unexpectedly, the pH7.4 osteoclasts had increased (7-fold) cathepsin K mRNA expression compared to the resorbing pH6.9 osteoclasts. Taken together, these data show that culture at pH7.4 results in the formation of larger, less active osteoclasts than pH6.9. However, the observation of increased cathepsin K mRNA expression at pH7.4 (compared to pH6.9) warrants further investigation. Overall, the current work indicates that osteoclast fusion and size are regulated by extracellular pH.

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P29 Using wearable accelerometers to discriminate between knee rehabilitation exercises

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Objective: To explore whether four different knee rehabilitation exercises can be objectively classified using wearable accelerometers to facilitate unobtrusive monitoring and feedback during knee rehabilitation.

Methods: Four healthy volunteers and four with a self-reported history of knee pain/pathology were recruited. Participants wore seven inertial sensors (Xsens, Holland; sampling tri-axial accelerometer data at 60 Hz) on the posterior pelvis and bilateral thigh, shank and feet. Participants performed 12 repetitions on each leg of four exercises commonly prescribed to total knee replacement patients (sit-to-stand, knee flexion, knee extension and weight shifting). For each participant, 63 accelerometer-derived features were generated including time domain (signal mean, max, min, variance skewness and kurtosis) and frequency domain (90th percentile spectral edge frequency) features.

Following feature scaling, univariate feature selection was performed within a cross validation procedure to select the top ranking feature (Model1), and the optimal two features (Model2). These features were used within a linear support vector machine (SVM) to develop models to discriminate between four knee rehabilitation exercises.

The generalised performance of the SVM models were estimated using leave-one-subject-out cross validation (CV). Within each CV-fold, data from one participant was removed from the training data and used to test the model, resulting in 8 CV-folds. Classification performance was assessed using the mean precision, recall and F1-scores across all CV-folds for each model.

Results: The mean X-axis acceleration of the thigh was selected by all CV-folds for inclusion in Model1. When selecting a two features for Model2, Mean X-axis Thigh Acceleration was selected by all CV-folds, mean Z-axis acceleration of the shank in 5 CV-folds, mean Y-axis acceleration of the thigh in 3 CV-folds. Mean precision, recall and F1-score for Model1 were 0.99 ± 0.02. These improved further to 1.00 ± 0.00 for Model2, with all repetitions of each exercise correctly classified.

Conclusion: Signal characteristics derived from accelerometers on the leg (thigh and shank) can discriminate between the four examined knee rehabilitation exercises, representing a first step towards unobtrusive sensor driven home

monitoring/feedback of knee rehabilitation.

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P30 Does the size, speed and timing of pubertal growth impact fracture in later life? The 1946 British Birth Cohort

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The association between pubertal timing and peak bone mass and later bone health is well-described. The aim of this work is to test whether different parameters of pubertal growth were also associated with risk of fractures across adulthood

Data were from 1821 participants (969 women) in the Medical Research Council National Survey of Health and Development. Self-reported fractures, including the anatomical site and mechanism of fracture (low, medium, high impact), across adulthood were captured up to age 68 years. Pubertal growth parameters of size(cm, kg), tempo(years) and velocity(%) were calculated using the Super Imposition Translation and Rotation method from height and weight data collected at multiple times from birth to the end of growth. Differences in all SITAR measures were tested between fracture and non-fracture groups, for low trauma and radius fracture separately. All data were stratified by sex and are presented as B[95% CI].

Low trauma fractures were reported in 159(16%) women and 51(6%) men. Distal radius fractures in 59 women, and 34 men; 7 and 4% respectively. In women, those who reported an adult low-trauma fracture were heavier, taller and grew quicker in adolescence than those who did not: size height (0.85[-0.13, 1.82] p=0.09) velocity height (0.02 [0.005, 0.04] p=0.01) and size weight (0.64[-0.09,1.36)p=0.09), velocity weight (0.04[-0.003,0.09],p=0.07). In men, those with low trauma fracture had peak weight gain later than those who did not (0.03[0.001,0.06]p=0.04). Also in men, those reporting distal radius fractures were heavier at the end of growth (size weight 1.43[0.03,2.83],p=0.05) and gained weight quicker (velocity weight 0.10[0.01,0.18],p=0.03).

In conclusion, the transition through pubertal growth differs in people who report fracture versus those who do not. These data suggest a faster trajectory of weight gain through puberty has a negative impact on fracture risk in adulthood. In women, greater weight and height gain and greater adult weight and height at the end of growth impact low trauma fracture risk.

P31 Sustained delivery of glutamate receptor antagonists to prevent osteoarthritis

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Introduction: Osteoarthritis therapies are limited to symptom management and joint replacement. Synovial fluid (SF) glutamate concentrations increase in arthritis. AMPA/kainate glutamate receptor (GluR) antagonists (NBQX/DNQX, 2.5-20mM) alleviate symptoms and disease in rodent models of osteoarthritis[(1,2)]. We determined whether poly(lactic-co-glycolic) acid (PLGA) nanoparticles and thermoresponsive hydrogels can sustain GluR antagonist release to improve their efficacy.

Methods: The effect of sustained DNQX/NBQX treatment on toxicity (LDH,14 days) and mineralization (Alizarin red, destained in cetylpyridinium chloride solution quantified at 540nm, 10-28days) was assessed on human osteogenically differentiated Y201 MSCs and primary osteoblasts (hOBs). Drug release in PBS (37°C) was measured by HPLC in samples taken from 2.5mM NBQX/DNQX loaded Poly(lactic-co-glycolic acid) (PLGA) nanoparticles, synthesized using double emulsion method, and thermosetting hydrogels synthesised by homogenising Pluronic-F127 (22%/25% w/v) and Carbopol 934 (0.5% w/v) with 2.5mM NBQX/DNQX in dH2O. Data (normal distribution and equal variances) analysis using t-test/ANOVA with Tukeys (SPSS).

Results: Sustained application of NBQX/DNQX (1-200µM) did not affect toxicity and reduced Y201 mineralization (NBQX 200µM, $p<0.05$; DNQX (200µM, $p<0.01$ and 400µM, $p<0.01$; n=6). DNQX (200 and 400µM) also reduced hOB mineralization ($p<0.01$, n=3). 2.5mM DNQX loaded PLGA nanoparticles (18% encapsulation efficiency) released 45% encapsulated drug over 3 hrs followed by sustained release of the remaining drug over 5 weeks (n=3). 2.5mM DNQX loaded thermoresponsive hydrogels released entire drug load over 27 hours (n=3) and was significantly higher ($p<0.05$, n=3, 6 and 27 hours) from 25% pluronic F-127 hydrogels than from 22%.

Discussion: Sustained 200µM DNQX/NBQX were not toxic to human osteoblasts and reduced mineralisation. This is consistent with anti-degenerative effects of NBQX injected as a free drug into the joint in rodent models of osteoarthritis[(1,2)]. PLGA nanoparticles rapid release of DNQX (6.6µM /3 hours), mimics the free drug effective in vivo[(1,2)], but was followed by sustained release over 5 weeks. Thermoresponsive hydrogels released larger amounts (2.5mM DNQX) over a shorter time (27hrs). These delivery vehicles could be tailored to optimise GluR antagonists release profiles and improve disease modifying effects.

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P32 2-oxothiazolidine-4-carboxylic acid: a novel inhibitor of vascular calcification

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Vascular calcification (VC), the deposition of hydroxyapatite in the arteries, is associated with vascular smooth muscle cells (VSMC) gaining osteoblast-like characteristics. Although VC is a known risk factor for cardiovascular events in diabetes, chronic kidney disease and atherosclerosis, there are currently no specific treatments available. Reactive oxygen species (ROS) and oxidative stress are known to play a role in the induction of VC. The antioxidant glutathione (GSH) scavenges free radicals and prevents cellular damage; however, synthesis of GSH can be limited by cysteine levels. Here, we assessed the effects of 2-oxothiazolidine-4-carboxylic acid (OTC), a prodrug of cysteine, on in vitro VC. Human aortic VSMC were cultured in basal or mineralising medium (1mM calcium chloride/sodium phosphate) and treated with OTC (1-5mM) for 7 days. Cell-based assays and western blotting were performed to assess changes in cell differentiation, survival and function. OTC potently inhibited VSMC calcification (≤90% $p<0.001$), compared to calcifying medium alone. This inhibition in calcification was associated with increased VSMC number (<15% $p<0.001$) and reduced alkaline phosphatase (TNAP) activity (<45% $p<0.05$). Runx2 protein expression was up-regulated in calcifying medium, compared to basal medium; OTC (2.5mM) prevented this. GSH levels, assessed colorimetrically, were significantly reduced in VSMC cultured in calcifying medium (<90%, $p<0.001$), compared to basal medium. Treatment of calcifying VSMC with OTC rescued this decline in GSH. In addition to GSH, the Nrf2 (Nuclear factor erythroid 2–related factor 2) pathway plays a key role in cellular defence against oxidative stress. To ascertain whether OTC affects the Nrf2 pathway, the Nrf2 target proteins HO-1 (Heme-oxygenase-1) and NQO1 (NAD(P)H quinone oxidoreductase 1) were examined. Calcifying medium down-regulated both HO-1 and NQO1 expression, compared to basal medium. In contrast, calcifying VSMC treated with OTC (2.5mM) showed higher levels of HO-1 and NQO1, compared to basal VSMC. Taken together, these results suggest that OTC inhibits VC via reductions in cell death and osteoblast-like phenotype changes in VSMC. This may possibly occur via prevention of GSH depletion and enhancement of Nrf2 signalling. These findings raise the possibility that treatment with OTC could benefit patients susceptible to VC.

P33 X-linked Hypophosphataemia: prevalence and mortality within the United Kingdom Clinical Practice Research Datalink

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Objectives: To determine the prevalence of X-Linked Hypophosphataemia (XLH) in children and adults in the UK and compare mortality rates between XLH cases and matched controls.

Material and methods: The Clinical Practice Research Datalink (CPRD) GOLD was used to identify XLH cases (1995-2016) in primary care using Read codes identifying rickets, hypophosphataemia and osteomalacia. Two clinicians with experience in paediatric (NS) and adult XLH (MKJ) independently reviewed potential cases using Read codes, laboratory values including serum phosphate, alkaline phosphatase, timing and duration of prescriptions, and features inconsistent with a diagnosis of XLH. Cases were graded as highly likely, likely, possible or unlikely. Four non-XLH patients of same age, gender and GP practice were matched to each case. Temporal trends in XLH prevalence were estimated using CPRD annual denominator data. Mortality incidence rates were calculated for cases and controls and compared using extended Cox regression. Main analyses included all possible cases, with sensitivity analyses focussing only on highly likely and likely cases.

Results: Weighted kappa between assessors was 0.88. From 522 potential cases, 122 were scored as at least possible XLH (least conservative) while 62 were defined as likely or very likely (most conservative). In main analyses, prevalence [95% CI] increased from 3.0 [1.2-7.2] per million in 1995/6 to 15.6 [12.0-20.4] per million in 2015/6. Corresponding estimates using the most conservative definition were 3.0 [1.2-7.2] to 8.4 [5.9-12.1]. Nine (7.4%) cases died during follow-up (at median age 64 years) at a rate of 12.1/1,000 person-years. Fourteen (2.9%) controls died (at median age 72.5 years) at a rate of 4.8/1,000 person-years. This yielded a hazard ratio of 2.93 [1.24 – 6.91]; $p=0.014$. Under the most conservative analysis, the hazard ratio was 6.65 [1.44 – 30.72]; $p=0.015$.

Conclusions: XLH prevalence estimates have increased in the UK, most likely due to improved coding practice. Adults with XLH appear to have shortened survival. This has implications for how adults are managed by clinicians, including potential use of novel therapies.

P34 Novel chemical sterilisation of decellularised human bone-patellar tendon-bone (hBTB) grafts for anterior cruciate ligament (ACL) repair

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Decellularised tissues provide a promising alternative to standard autografts or allografts, removing the potential for donor site morbidity or an immune response to donor cells. This work investigated the effects of a novel sterilant on decellularised hBTB grafts for ACL repair.

Tissue was provided by NHS Blood & Transplant: Tissue & Eye Services. Decellularisation of hBTB followed a previously reported procedure(1), including antibiotic washes, protease inhibitors, low concentration detergent, nuclease treatment and peracetic acid (PAA; 4h) sterilisation. Enthesis regions of sterile, decellularised hBTB were inoculated with 10^9 *B. subtilis* spores and incubated with combinations of hydrogen peroxide and copper chloride (H_2O_2:$CuCl_2$). Tissue was then macerated, serially diluted and incubated on nutrient agar to determine the number of viable spores remaining (n=6).

Further tendons were decellularised and sterilised, the chosen H_2O_2:$CuCl_2$ condition replacing PAA treatment. Tissue properties were compared to native hBTB and decellularised, PAA treated hBTB. Biological characterisation involved histology and immunohistochemistry, colourimetric assays and differential scanning calorimetry (n=3). Biocompatibility was investigated via contact and extract cytotoxicity assays. Biomechanical properties of bulk grafts, bone pins and tendon strips were investigated (n=6). A bi-linear model(1) was applied to bulk and tendon testing data.

Treatment of hBTB with 2% H_2O_2:1 $mg.L^{-1}$ $CuCl_2$ for 5 or 6h reduced the number of viable *B. subtilis* spores by over 10^6. This translated to 5.5±0.5h treatment for manufacturing; characterisation of hBTB was carried out following 6h treatment.

PAA and H_2O_2:$CuCl_2$ treatment did not affect tissue morphology, hydroxyproline or denatured collagen content, but glycosaminoglycan content and thermal properties were reduced compared with native tissue. Collagen IV and tenascin-C immunostaining was retained following H_2O_2:$CuCl_2$,but not PAA, treatment. No evidence of cytotoxicity was seen for decellularised grafts. Biomechanical performance of bulk grafts, bone and tendon was similar for all groups.

This study demonstrates that decellularised hBTB treated with 2% H_2O_2:1 $mg.L^{-1}$ $CuCl_2$ offer an alternative to standard allografts for ACL repair.

We are grateful to the donors and their families for the tissue used during this study. The study was funded through the Medical Technologies IKC (EPSRC).

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P35 Patient and service-level predictors of bone treatment recommendation post-fracture: results from the UK national Fracture Liaison Service (FLS) database

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Objective: To describe anti-osteoporosis treatment recommendations post-fracture and identify patient and organisational predictors of: decision to treat (including oral bisphosphonate, parenteral therapy or clinical/GP referral for consideration of treatment) versus decision not to treat; and oral bisphosphonate versus parenteral therapy recommendations.

Methods: Patients with fragility fracture diagnosed in England between 01/01/2017-31/12/2017 were identified from the Royal College of Physicians national FLS database. Patients diagnosed within centres achieving <50% case finding or with ≥50% unknown/missing treatment information were excluded. Descriptive statistics outlined treatment recommendations, with stratification by FLS. Patient and FLS-level factors (highest nurse band; nurse & administrator whole time equivalent per 1,000 admissions (</≥ median)) were identified by complete case analysis using multilevel multivariable logistic regression.

Results: Of 22,500 eligible patients (mean age 73 years; 77% female) from 15 FLS centres, 20% were recommended an oral bisphosphonate, 5% denosumab, 4% zoledronic acid, 20% were referred, <1% given a different recommendation, 31% were neither referred nor recommended treatment and 19% had unknown or missing treatment recommendation status. There was marked variation in these outcomes by FLS. Patient-level characteristics and odds ratios (OR [95% CI]) for appropriate treatment recommendation/referral were as follows: age ≥75 years (OR: 4.59 [4.18–5.03]); male gender (OR: 0.61 [0.55–0.67]); hip (OR: 3.02 [2.68–3.40]) or spine (OR: 3.96 [3.26–4.80]) fracture; smoking (OR: 1.55 [1.36–1.78]), living in a residential home (OR: 0.60 [0.49–0.78]), family history of hip fracture (OR: 2.04 [1.77–2.35]), previous fracture (OR: 1.46 [1.33–1.60]) and previous bone treatment

(OR: 2.78 [2.36–3.29]). FLS-level factors were non-predictive. Many of these factors were likewise predictors of a parenteral therapy recommendation (versus oral bisphosphonate), with the number of full-time nurses per 1,000 admissions (above versus below median of 0.46 whole time equivalents) being significantly predictive (OR: 6.50 [1.16–36.48]) at the FLS-level.

Conclusion: Multiple factors are associated with treatment recommendations made post-fracture, including greater intensity of nurse time. These results provide clinicians and service managers with insights towards standardising and improving services.

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P36 Mononuclear Phagocytes in Cartilage Repair

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Objectives: To determine whether mono-nuclear phagocytes (MNPs) are present and become activated during the initial phase of the cartilage repair process in a mouse models of surgically-induced osteochondral injury.

Methods: Mice (10-15 weeks old) either underwent no surgery (control, n=6), sham surgery (n=3) or osteochondral injury (n=3). For osteochondral injury, a controlled depth and diameter osteochondral injury was made in the trochlear groove of the femur using a hollow-bore needle. Sham surgery involved exposure of the trochlear groove by patella dislocation without damage to the articular surface. Osteochondral tissue distal to the femoral physis was processed and analysed using flow cytometry at 10 days following surgery. MNP populations were defined as $CD45^+$ $CD3^-$ $CD19^-$ $Ly6G^-$. These cells were further phenotyped as dendritic cells (DCs) ($F4/80^-$ $CD11c^+$ $MHCII^{+/-}$), mature DCs ($F4/80^-$ $CD11c^+MHCII^+$), macrophages ($CD11b^+$ $F4/80^+$) and inflammatory monocytes ($CD11b^+$ $Ly6C^+$ $MHCII^-$ $F4/80^-$ $CD11c^-$). Absolute cell numbers were obtained using flow cytometry counting beads. The anatomical location of MNPs following osteochondral injury was assessed using confocal microscopy in CD11c-eYFP reporter mice.

Results: We identified DCs ($5.0x10^3$cells, 95% confidence interval [95%CI] 3.6-$6.5x10^3$cells), macrophages ($0.47x10^3$cells, [95%CI 0.20-$0.76x10^3$]) and inflammatory monocytes (8.6 $x10^3$cells, [95%CI 5.9-$11.4x10^3$]) in the osteochondral tissue in normal joints in control mice. At 10 days following osteochondral injury, there was an increase in DC numbers ($40x10^3$cells, $p<0.01$), in macrophages ($6.3x10^3$cells, $p<0.01$) and inflammatory monocytes ($43x10^3$cells, $p<0.01$) compared to the control joints. In comparison to the sham surgery, osteochondral injury resulted in higher numbers of DCs ($p<0.05$). Furthermore, the proportion of mDCs was increased following osteochondral injury to 63.3% ($25.3x10^3$ mDCs) compared with sham surgery (49.1%, $8.8x10^3$mDCs) and control mice (42.4%, $2.2x10^3$mDCs). Confocal imaging confirmed an increased number of CD11c+MNPs that were localised to osteochondral defect and juxtaposing synovium.

Conclusion: MNPs, specifically DCs, are recruited to and activated in the osteochondral defect during the initial stages of the cartilage repair process. These data suggest that MNPs may be involved in the initiation of cartilage repair in joint injury, including surgically induced microfracture and microdrilling, a question being addressed in on-going research.

P37 Mesenchymal stem cells in talar and tibial subchondral bone of ankle osteoarthritis patients

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Ankle osteoarthritis (OA) onsets at a younger age than OA of other joints, due to its post-traumatic nature(1). Surgical treatments, including ankle fusion or total ankle replacement, have short lifetimes and low patient satisfaction(2). Regenerative treatments, including microfracture, show good short-term outcomes, however fibrocartilage formation leads to treatment failure(3). Microfracture targets local, subchondral bone-resident, Mesenchymal Stem Cells (MSCs) for endogenous repair(4). However, MSC behaviour in ankle OA remains unknown. This study investigates talocrural bone-resident MSCs in ankle OA patients.

Osteochondral talocrural specimens excised following ankle fusion(n=6 patients) were decalcified in EDTA and cartilage damage assessed using Safranin O(n=3). Immunohistochemistry of CD271 was performed to analyse resident-MSC and bone area(5). Subchondral bone cells were extracted using collagenase(n=3)(6). MSCs were characterised using colony-forming unit fibroblast assay, flow cytometry and trilineage assays and compared to gold standard iliac-crest MSCs (n=3)(7,8).

OARSI scoring showed similar cartilage damage between tibia and talus (mean(±SD) 15.7±4.4 and 18.3±2.4, respectively). Subchondral bone plate thickness increased with cartilage damage (grade 1: 0.098±0.04mm, grade 5: 0.86±0.22mm), and bone area (grade 3: 28.6%±0.09, grade 5: 40.9%±0.14).

Immunohistochemistry indicated increased CD271+ MSCs in sclerotic bone.

In the tibia and talus, mean MSC frequency of extracted cells was 0.37%±0.02 and 0.32%±0.02 respectively, lower than iliac crest samples (0.75%±0.36). Extracted-cells expressed standard MSC surface-phenotype[8]. Talar MSCs trended higher calcium deposition than tibial MSCs following osteogenic induction, but significantly lower adipogenesis by area coverage (medians 0.61%±0.68 and 5.01%±2.73, respectively, p=0.01). Chondrogenesis was similar between bones (21.4±2.9 µg/ml and 20.5±2.42µg/ml).

This study has proven MSC presence in OA talocrural subchondral bone. However, their topography suggests involvement in sclerotic bone formation over cartilage restoration. Future studies will investigate whether biomechanical stimulation can induce a more chondrogenic phenotype in MSCs for potential development into a novel augmented microfracture treatment procedure.

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P38 Experimental reproduction of periprosthetic joint infection: developing a representative animal model

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Objective: The objective of the present study is to develop an animal model of periprosthetic infection that can serve as a foundation for future research to develop new therapeutic strategies.

Methods: Fifteen New Zealand White rabbits were employed to reproduce periprosthetic infection by intra-articular inoculation of 10^5 CFU/mL of Staphylococcus aureus ATCC® 29213. 3D printing technology was used to design a species-specific implant, whose stability was judged according to the position of the extremity at rest and its mobility. Weight bearing was recorded as discharge, partial weight bearing and full weight bearing. Response to infection was monitored by clinical (weight and temperature), hematological (leukocyte, lymphocyte and platelet counts) and biochemical (erythrocyte sedimentation rate) analyses at the time of inoculation and 7 days thereafter, when microbiological samples for culture from soft tissue, bone and spacer were taken.

Results: All animals recovered from surgery and all displayed full weight-bearing 6 days postoperative. Statistically significant increase was found in the number of platelets and leukocytes, as well as a significant decrease in the percentage of lymphocytes were detected, with p= 0.0001 in all cases. 14 of the 15 tested animals (93.3%) presented positive microbiological cultures.

Conclusions: an experimental model faithfully reproducing the periprosthetic infection environment and achieving a high rate of infection has been designed. These characteristics make it an ideal model to study its pathogenesis and possible therapeutic strategies.

P39 Decellularised Porcine Xenograft for Anterior Cruciate Ligament Reconstruction: A Histological Study in Sheep

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Decellularised xenografts, such as porcine super flexor tendons (pSFT), represent an alternative to autogenic and allogenic tissue in anterior cruciate ligament (ACL) reconstruction. However, the *in vivo* performance of pSFT has not been reported in a large animal model.

Objective: To determine if pSFT xenograft for ACL reconstruction will remodel into a functional ligament-like tissue.

Methods: Twelve adult sheep underwent unilateral ACL reconstruction using pSFT xenograft with two different femoral fixation systems and a soft screw for tibial fixation. Group 1 (n=6) used a suspensory Endobutton CL femoral fixation, and Group 2 (n=6) used a rigid Stratis ST femoral fixation. Functional recovery was assessed by measuring the ground reaction force passing through the operated leg and this was compared to the force in the un-operated leg at weeks 5, 8 and 11. The sheep were sacrificed after 12 weeks and histological analysis performed to evaluate graft healing in the bone tunnels and the remodelling of the intra-articular graft.

Results: The pSFT remodelled into a ligament-like structure displaying crimp and remodelled collagen fibres. An indirect insertion was seen in both the femoral and tibia bone tunnels characterised by Sharpey's fibers. Direct fibrocartilaginous insertion of the ACL was not seen, but chondroid tissue was sometimes present in the femoral tunnel of the Stratis cohort. Bone ingrowth into the graft was more advanced in the tibial tunnels than the femoral tunnels. Reconstruction using the Endobutton had

faster functional recovery and demonstrated superior graft healing. One graft rupture was seen in the Stratis cohort, and at retrieval two further grafts ruptured on gentle palpation.

Conclusion: When used in ovine ACL reconstruction, pSFT xenografts remodel into a functional ligament-like structure at 12 weeks, as evidenced by the formation of a ligamentous structure associated with restoration of functional weight bearing. Different femoral fixation systems influence the graft healing of pSFT. Future research is now required that correlates the histological and biomechanical properties of pSFT at multiple time points in the post-operative period.

Funding: Royal College of Surgeons Research Fellowship.

Conflicts: none.

P40 Is Demineralised Cortical Bone strong enough to be an Anterior Cruciate Ligament allograft?

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Anterior cruciate ligament (ACL) graft choice remains controversial and some grafts fail due to inadequate osteointegration. Demineralised cortical bone (DCB) is an osteoinductive collagen-based scaffold but it is unknown if DCB has sufficient strength to be an ACL allograft.

Objectives:

- To determine the effect of bone type (femur versus tibia) and bone age on the ultimate tensile strength (UTS) of ovine DCB
- To determine the *ex vivo* UTS of ovine ACL reconstruction using DCB allografts fixed using interference screws and sutures tied to posts has sufficient strength to meet the *in vivo* requirement for sheep model of ACL reconstruction (reported as 150N).
- To determine the *ex vivo* UTS of ovine ACL reconstruction using DCB grafts with a tendon control group, ovine superficial digital flexor tendon (SDFT).

Methods: DCB was manufactured from femur and tibia of young (9 month) and old (2-3 years) sheep. Soft tissues were removed, demineralised in 0.6 N hydrochloric acid, washed in PBS, lyophilised and gamma irradiated (25 KGrays). Dog-bone shaped specimens were hydrated, cut and the UTS measured in a Material Testing Machine (Zwick). The UTS of DCB allograft using two fixation systems, interference screws and sutures tied around screw posts, was measured *ex vivo* in an cadaveric ovine ACL reconstruction model. Comparison was made with ovine superficial digital flexor tendon (SDFT) and ACL. Six samples per group per tested.

Results: The UTS in decreasing order was young tibia DCB (67.7±10.6N), adult tibia (39.8±6.7N), adult femur (19.6±6.3N) and young femur (14.7±6.2N). Statistically significant differences were seen between young tibia, adult tibia and adult femur ($P<0.01$). No fixation system using DCB reach the *in vivo* requirement. SDFT fixation with interference screws (308.2±87.3N) did reach the *in vivo* threshold but was significantly less than ovine ACL (871.0±64.2N).

Conclusion: The tensile properties of DCB are influenced by donor age and bone type. DCB due to its inadequate tensile strength and incompatibility with contemporary fixation devices cannot be recommended as an ACL allograft.

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Conflicts: none.

P41 The impact of a Virtual Orthopaedic Triage Clinic Model in Northern Ireland

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Objective: To assess the impact of a 4 year, prospectively managed virtual orthopaedic triage clinic model in Northern Ireland.

Methods: Within Northern Ireland, delivery of the regional Paediatric Orthopaedic service was unsustainable. There were 2600 outpatient referrals and only 1900 new patient appointments in 2013.

The virtual orthopaedic triage clinic was established using Department of Health funding for a consultant led service (2PA's) with secretarial support. Clinicians have access to regional electronic data, remote login and digital dictation. All referrals were triaged weekly and a database generated.

Results: Between July 2014 and November 2018, 9624 referrals received for 8571 patients. 77% were generated from primary practice with a bimodal pattern in month and age; referral peaks in June/September with increased numbers aged 1-2 and 12-14 years of age. Other sources included paediatricians, emergency departments and physiotherapists.

64% required an orthopaedic appointment, 16% received letters of advice and the remainder redirected to other pathways. 2259 were suitable for physiotherapy assessment.

Pre appointment investigations were requested for 207 patients, 2 were admitted acutely and 20 assigned to fracture clinics for rapid assessment. Cost savings were estimated at £60k per year.

Commonly, gait variants, flat feet in infants, 'hearsay' referrals and review of radiological reports are

managed by advice.

Conclusion: The virtual clinic has streamlined our service bringing it closer to capacity, and could be adapted for use in other institutions.

It provides better needs rationing and a safety net for urgent referrals.

Referrers/patients receive timely feedback with enhanced waiting list management. There are few unknowns on the waiting list and it has reduced repeat referrals.

Service needs are now more clearly understood, and unnecessary clinic appointments are significantly reduced. Referring clinicians are now better informed by letter, and it has led to the development of physiotherapy assessment clinics.

P42 Regional variation in functional adaptation and the selection for locomotor efficiency

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The tapered shape of the lower limb has been suggested to result in a more economical locomotion by keeping bone mass close to the axis of rotation. This minimizing of energy expenditure may have posed a selective pressure on bone functional adaptation during human evolution by constraining distal functional adaptation and allowing for greater variation in more proximal regions. We assessed whether the tapering of the lower limb may have resulted from a selection for tissue economy by examining regional variation in the effects of leg preference on bilateral asymmetry throughout the lower limb. As bone adapts to unequal loading that results from leg preference, the constraints on functional adaptation were expected to cause a relatively lower asymmetry.

Both left and right femur and tibia from each of 25 adults from a medieval British population were micro-CT scanned. Trabecular thickness, degree of anisotropy, connectivity density and bone volume fraction were quantified for spherical volumes of interest. Diaphyseal cross-sections were extracted at 1% increments between 20%-80% of bone length and their geometric properties quantified. Asymmetry was defined as the absolute value of left minus right, divided by their average.

Mean asymmetry was higher in proximal compared to distal epiphyses within each bone, but this was not significant. Moreover, asymmetry in the tibia was on average greater than in the femur, but again this was not significant. Asymmetry in cortical area displayed a proximodistal decline in the tibia only, while other parameters did not follow this predicted trend in either the tibia or the femur.

Only along the tibial diaphysis did we find the expected proximodistal reduction in asymmetry, but not in the femur or the trabecular tissue. This implies that constraints on functional adaptation do not increase throughout the lower limb, but potentially do so within each invdividual bone. Since we did not find the expected relationship with asymmetry, the tapering of the lower limb may be the result of other factors than selective pressures, or may follow a pattern that is more complex than the straightforward proximodistal reduction we examined here.

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P43 The paracrine effect of mesenchymal stem cells in healing enhancement in atrophic non-union model

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Objectives: The underlying mechanism of mesenchymal stem cells (MSCs) in enhancing bone regeneration is not yet clear, however, it is believed to be either by cell differentiation to osteoblasts and / or by a paracrine effect. It has been recently reported that circFOXP1 is the gatekeeper for MSCs differentiation by keeping undifferentiated identity of these cells (Cherubini et al., 2019). We evaluated the effect of injecting silenced circFOXP1-RNA, in vivo, on the differentiation properties and bone formation ability of MSCs.

Methods: Silenced cells were imported from our collaborative group in Milan, Italy, (Cherubini et al., 2019) and were locally injected into the fracture site in a clinically relevant rat model of atrophic non-union (group 1, n=6). Ordinary hMSCs were used as controls, (group 2, n=6). Tibiae were osteotomised at the mid-shaft and fracture was fixed by IM nail, a 1 mm non-critical gap was maintained using a spacer. All surgical procedures were approved by the UK Home Office and Local Research Ethics Committee. Fracture status was evaluated throughout the experiment by serial x-rays with a further assessment, at the end of experiment, by micro CT scan, biomechanical testing, and histology.

Results: Radiographical data showed that only two fractures out of six proceeded to union in group 1, one of which revealed sub-optimal healing, whereas five out of six healed with union in the control group, (P-value 0.242, Fisher's exact test). Histological evaluation supported radiological diagnosis, callus formation and new bone bridging were noticed at the fracture gap in tibiae with union, whereas fibrous tissue filled the gap between fracture ends in non-united tibiae with no bridging detected.

Conclusion: Silencing circFOXP1 – RNA induced stem cell differentiation resulting in loss of MSCs

characteristics and loss of their immune-modulatory properties. Thus, it is postulated that these xenogeneic cells were now exposed to the host immune system and rapidly killed losing their ability to stimulate the healing process. In contrast, the ordinary MSCs persisted long enough to act in a paracrine rather than by cell differentiation to stimulate fracture healing.

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P44 Tissue remodelling changes the stress distribution in additively manufactured porous bone implants

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Implant efficacy and safety of additive manufactured porous implant designs is a growing concern as over the last years there have been several high profile recalls of these structures. Critical steps in evaluating the safety of bone implant designs are associated with the assessment of the effects of the mechanical environment (stress and strain) caused by implantation as well as the implant performance due to partial bone ingrowth. A finite element analysis (FEA) model has been developed, using two new algorithms to simulate additive bone ingrowth, and verified against histology results for an ovine condylar critical sized defect model. The implants were manufactured from Ti6Al4V using selective laser sintering with pore sizes of 700 and 1500 µm, corresponding to porosities of 70% and 75% respectively. Peak walking load of sheep was applied to the bone-implant FEA structure and the failure risk of the implant and periprosthetic bone was evaluated by analysing the stress and strain before, during bone remodelling, and at equilibrium. Parametric analysis was conducted by changing the material properties of the implants. Results showed that partial bone formation improves the stress distribution locally by reducing stress concentrations for implants, by at least 20%. As strain energy density is the driver for bone remodelling, excessively high stress is reduced to safe levels (86% of fatigue strength) for one of the implants as bone forms, thus improving the long-term fatigue resistance. The stress concentrations increased slightly in regions without bone growth. Higher bone ingrowth was predicted for implants made from lower modulus Titanium-tantalum alloy. Both the detailed design of the implant and the rehabilitation programme will have a significant influence on the successful bone integration and need to be considered carefully, as a balance between bone formation and structural stiffness is required. This is important because regions of porous implants with limited bone ingrowth due to stress shielding are weak and may fail due to fatigue depending on the loading conditions. This novel strategy of modelling bone ingrowth helps to improve implant design and reduces the need for animal testing.

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P45 Creating an open-source two-phase fluid-structure interaction model of a trabecular bone structure validated against a 3D printed experimental trabecular bone structure specimen

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Several numerical models are demonstrating the large effect of the interaction between trabecular bone and bone marrow(1). However, the most representative validations published to date have used an approximated geometry(2). This study aimed to create a representative open-source fluid-structure interaction (FSI) model validated against data obtained through experiments on the same structure.

The geometry for the mesh of the physiological model was obtained by µ-CT scanning and segmenting the experimental specimen of a trabecular bone structure. The experimental specimen was obtained by µ-CT scanning, segmenting, enlarging and 3D printing a sectioned porcine trabecular bone. The model was set up using the modified fsiFoam solver of the foam-extend-4.0 FSI toolkit. Replicating the experimental testing (20 experiments per fluid, 5 repetitions per experiment), one model was set up using water and one using silicon oil (v = 3.5e- 4 m2/s) for the fluid domain. A two-phase fluid solver was chosen to mimic the free surface of the fluid during testing. The solid domain was subjected to a vertical displacement of -0.5 mm in 0.13 s as done in the experiments. Pressure data were extracted at the location of the equivalent experimental pressure tappings. After validating the model against the experimental data, the model was run using physiological data input for trabecular bone and a power-law rheology model for bone marrow.

The experimental loading of the bone structure resulted in a variation of pressure throughout the structure ranging from 0.01 kPa – 0.025 kPa. The fluid type further influenced this effect. The simulation results for the pressure around the pressure

tappings were compared and demonstrated similar variations. The physiological model showed variation in pressure depending on the structural environment as well.

The current model reflects the importance of taking into account the sophisticated structure of trabecular bone when creating a validated model.

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P46 Using a mouse model of osteochondral injury to understand bone and articular cartilage repair

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Objectives: Procedures for osteochondral repair, such as drilling or microfracture of the subchondral bone, are thought to help restore cartilage by delivering bone marrow cells to the injury site. Unfortunately, the quality of the new tissue formed is sub-optimal. The objective of this study is to improve the understanding of the cellular and molecular mechanisms that limit cartilage restoration by developing and characterising a mouse model of osteochondral injury.

Methods: Osteochondral defects, controlled for diameter and depth (confirmed by histological and CT analysis), were made in the patella groove of 8-week-old C57BL/6 mice (n=4). The temporal and spatial distribution of key cell types was assessed at 24 hours, 1 week and 2 weeks and the repair of articular cartilage and underlying bone at 4- and 8-weeks using histology and immunohistochemistry techniques.

Results: Defects were 729 (± 42.6) µm wide at the articular surface and penetrated 1205 (± 58.6) µm into the distal femur. At 24 hours post-surgery, defect sites were filled with a blood clot within which neutrophils (anti-NIMP) were embedded. After 1 week, these cells were no longer present within the injury whilst macrophages (anti-CD68) had infiltrated the wound site having previously been rarely observed at 24hrs. At 2 weeks post-surgery islands of chondrocytes surrounded by matrix were observed below the articular surface and at the lower boundaries of the defect, cuboidal osteoblasts were identified on isolated bone fragments. By 4 weeks the articular surface was covered with proteoglycan and type II collagen rich matrix demonstrating repair of the cartilage surface.

Conclusion: A controlled model of osteochondral injury and repair has been developed, which is reproducible in terms of physical profile and injury resolution. Evidence suggests that osteochondral defects in mice heal by both endochondral ossification and appositional bone deposition. The establishment of this mouse model allows for future studies using transgenic mice. This approach will further understanding of the contribution of different cell populations to osteochondral repair and provide insight into the mechanisms that underlie the structural organisation of the newly formed tissue.

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P47 Model-based Roentgen stereophotogrammetric analysis (RSA) using a Novel Radiopaque UHMWPE

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Roentgen stereophotogrammetric analysis (RSA) is a technique to assess the position of implants with respect to their surrounding environment with a sub-millimetre accuracy for metallic implants. However, due to the low visibility of polyethylene implants, RSA cannot currently be used for polymeric implants. This study aim was to investigate the use of a novel radiopaque UHMWPE for RSA and its precision level.

To create radiopaque UHMWPE Oxford Unicompartmental knee arthroplasty (OUKA) bearings (n=4, Zimmer-Biomet, UK) were treated with a contrast agent (Lipiodol, Guerbert, France, T= 105°C for 0,12,18, and 24h). A standard RSA set-up (two synchronized X-ray tubes positioned at 1.5 m above the film cassette with an angle of 20°) was used to acquire stereo-radiographs of 10 successive poses. A carbon uniplanar calibration box (Leiden, Netherlands) was positioned underneath the phantom.

Translational and rotational movements in X-, Y- a Z-direction were applied to mimic clinical positioning variation. Zero motion between the markers and the implants was assumed, hence the measured migrations by the RSA software included the experimental errors.

Secondly, a known amount of separation was applied (0.02 to 2 mm, n=5) using a micrometer stage to the phantom by lifting-up the femoral component. The separation distance was calculated using the RSA software and compared with the micrometer measurements.

The results showed radiopaque UHMWPE can be used for RSA analysis with a precision level comparable with the metallic component for any translational movements (mean: Tx= 0.06 mm

Ty=0.03 mm, Tz= 0.06mm), However, this level is marginally higher for any rotational movement (mean: Rx= 0.069°Ry=0.224°, Rz= 0.089°). Kruskal-Wallis tests showed no difference between the different level of radiopacity or the direction of the measurement (p=0.3 and 0.05 respectively). Furthermore, measured lift-up can be calculated with sub-millimetre accuracy (absolute average mean error = 0.01 mm)

In conclusion, this study used a novel type of polyethylene and confirmed the possibility of using this polymer for RSA studies.

P48 Role of Semaphorin-3A in osteoarthritis

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Osteoarthritis (OA) is a common skeletal disease causing chronic pain. Changes in peripheral joint innervation are associated with the development of OA and can contribute to pain. Semaphorin-3A (sema-3A) is a secreted axon guidance molecule, which acts as a chemo-repellent for growth and sprouting of sensory neurons. The aim of this study was to examine its expression and distribution in healthy and osteoarthritic joints in mice.

We used two mouse models of OA, the mechanical joint loading (MJL) model and the STR/ort model, which spontaneously develops OA 20 weeks after birth. For the MJL model, the right knees of male mice (12-week-old, C57BL/6) were loaded at 9N or 11N (40 cycles, three times/week for two weeks). The entire knee joints and serum were collected at week-6 after loading. Joints were fixed, decalcified and paraffin embedded for immunocytochemistry using sema-3A antibody (Abcam). Sema-3A expression in serum was quantified using a specific ELISA (CUSABIO). Sema-3A mRNA expression was quantified in rat articular cartilage and dorsal root ganglia (DRG) and during the mouse chondrogenic cell line ATDC5 differentiation using qPCR.

Our results show that sema-3A is expressed in cruciate ligaments, in the synovial lining and in subchondral bone in healthy joints. In both OA models, the overall expression of sema-3A in these tissues and in osteophytes increased with severe OA. Sema-3A is also present in cartilage, where its expression did not seem to change with OA. There was a significant 25% increase in serum sema-3A levels 6 weeks after joint loading compared to the non-loaded mice. Sema-3A was expressed at all stages of ATDC5 chondrocyte differentiation, with expression peaking during chondrocyte maturation prior to a decline in expression during hypertrophic differentiation when chondrocytes show raised expression of type X collagen. Sema-3A mRNA was also highly expressed in rat articular cartilage with levels more than 10 times higher than in DRG.

Our results demonstrate that Sema-3A expression is upregulated during OA in joint tissues that are highly innervated, suggesting that it may play a role in the changes in peripheral innervation occurring during joint degeneration. Its role in chondrocytes needs to be further elucidated.

P49 Neural network modeling of mortality and revision risk after hip replacement surgeries

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This research studies personalized risk of death and revision after 327,238 hip replacement surgeries. The data was collected from the National Joint Registry for England, Wales, Northern Ireland and the Isle of Man. Nonlinearities were studied by comparing the flexible parametric (FP) model with a neural network (NN) extension of it.

The NN model used in this work extends the Faraggi & Simon model with nonparametric maximum likelihood estimation of the baseline hazard. The NN employed rectified linear units, dropout and Adam optimization. The NN and the FP were compared using the integrated Brier score (IBS) normalized by the period length and the concordance index (CI), both assuming a Kaplan-Meier censoring model. All results were computed for a period of 10 years in the revision model and of 1 year in the mortality model. They are presented within a 95% confidence interval after ten repetitions of five-fold cross validation.

In the mortality model, the IBS was 0.005228 ± 0.000001 for the FP and 0.005254 ± 0.000001 for the NN, and the CI was 76.4% ± 0.00% for the FP and 76.3% ± 0.01% for the NN. In the revision model, the IBS was 0.01708 ± 0.00001 for the FP and 0.01714 ± 0.00001 for the NN, and the CI was 57.8% ± 0.1% for the FP and 57.8% ± 0.2% for the NN. Calibration plots were made dividing the predictions into five quantile groups. The calibration was equivalent for both methods in the revision model, but was a better fit for the NN than for the FP in the mortality model.

The CI results suggest that the FP and the NN represent equally well the influence of the covariates to the survival function. The better calibration obtained by the NN compared to the FP in the mortality model suggests the existence of patterns that cannot be represented by natural cubic splines. Future research will investigate if the NN may capture patterns in the data that are not detected by the current evaluation criteria.

P50 Novel niclosamide-bisphosphonate vectors as bone-targeted therapy for multiple myeloma

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Myeloma remains a largely incurable cancer despite improvements in survival outcomes over the last few years, due to the development of better therapies. However, these therapies are often not suitable for old, frail patients due to significant toxicities. Niclosamide has been identified to have significant anti-myeloma effects *in vitro*. However, adverse effects have been observed using niclosamide in preclinical models of myeloma. In patients, it has been limited due to its poor bioavailability. Therefore, we conjugated niclosamide to 4 different bone-seeking bisphosphonate vectors (ATA-N1 to ATA-N4).

We hypothesised ATA vectors would target the bone and niclosamide would retain its anti-myeloma activity when released.

Objectives: We aimed to test the efficacy of the niclosamide vectors compared to native niclosamide *in vitro* and assess any adverse effects *in vivo.*

Methods: Myeloma cells lines (U266, JJN3 & 5TGM1) were incubated with 1 µM ATA-N1, ATA-N2, ATA-N3, ATA-N4, native niclosamide or vehicles and cell viability was assessed at 24, 48 and 72 hours. 7 week-old C57BL/6 mice were treated intravenously with 30 µmoles/kg of ATA-N1, ATA-N2, ATA-N3 or vehicle. Animals were monitored and culled 3 weeks later. Micro-CT of the long bones were assessed for differences in bone parameters and histological sections assessed for changes in bone marrow.

Results: ATA-N2 and ATA-N4 reduced cell viability at 72 hours in all cell lines. Using hydroxyapatite coated wells ATA-N2 and ATA-N4 reduced viability in 5TGM1, ATA-N2 reduced viability in U266 & JJN3. In non-tumour bearing mice treated with the niclosamide vectors no toxicity was observed throughout the 3 weeks. No significant differences in trabecular or cortical bone volume of tibias and femurs or any detrimental effects on the bone marrow microenvironment were observed in mice treated with niclosamide vectors compared to control.

Conclusions: ATA-N2, ATA-N4 have anti-myeloma activity *in vitro* and show no adverse effects *in vivo*.

P51 Characterising the structure of trabecular excrescences found in osteoarthritic and control joint samples

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The presence of novel bone structures, termed trabecular excrescences, have previously been found in surgical waste tissue samples from patients with osteoarthritis, alkaptonuria and from aged bone samples. A form of trabecular excrescence is found associated with the presence of bone marrow adipocytes and the absence of bone lining cells. We hypothesise that the adipocytes are contributing to the formation of bone like structures. This is inconsistent with the current paradigm of osteoclast-osteoblast coupled remodelling. This study aimed to determine the topographical distribution of trabecular excrescences throughout the trabecular bone in human femoral heads and to further characterise their internal structure.

Femoral heads were obtained as surgical waste, with informed patient consent, from 5 patients with OA (mean age = 75.4) and 5 control patients without OA (mean age = 73.6). Each femoral head was sliced into sagittal sections and each section divided into 6 regions. The sections were decalcified and processed for histology. Unstained sections were viewed under fluorescence microscopy. Sections were stained with haematoxylin and eosin and with immunohistochemical staining for collagen I, collagen VI and osteocalcin

Excrescences were found in the majority of anatomical regions in both control and osteoarthritic samples. When found, the excrescences were often clustered, with several protrusions shown along a region of trabeculae. These results demonstrate that trabecular excrescences are globally distributed throughout the femoral head, and not specific to areas of osteoarthritic change. This suggests the formation of these structures may be linked to ageing rather than disease progression. Immunohistochemical staining demonstrated the presence of collagen VI within the extracellular matrix of the newly formed excrescences. However, we also noted the presence of osteocalcin in 'smoothed over' versions of excrescences.

This study has shown that trabecular excrescences are initially formed by the deposition of collagen VI by adipocytes. However, the presence of osteocalcin suggested that excrescences have the potential to be remodelled through typical osteoblast-osteoclast remodelling. Future treatments for skeletal disorders could look to exploit the scaffold like properties of structures formed by adipocytes.

P52 Validated FE models of vertebral bodies predict displacements and strains from axial impact loading

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Finite Element (FE) method has been extensively applied to understand the behaviour of bone, including vertebral bodies (VBs), subject to loading with most studies so far having focused on quasi-static conditions. Dynamic studies are, however, important as they can provide insights into how injuries arise from high energy collisions, such as those that can be experienced in sport and road traffic accidents.

The aim of this study was to develop and validate a methodology for FE modelling of VBs subject to impact loading.

Seven (n=7) VBs from four different porcine spines were stripped of all soft tissues, cemented into polyoxymethylene pots, µCT-scanned and positioned in an impact cage. An impact was applied to the VBs via a falling mass of 7.4kg at a velocity of 3.1m/s. Surface displacements and strains were acquired from the anterior VB surface via DIC [Photron,UK] and the impact load was monitored with two loadcells, one cranial and one caudal. Specimen-specific FE models were created based on µCT images. Material properties were assigned based on Hounsfield units and the density-Young`s modulus relationship, validated by previous static experiments, was calibrated for the dynamic case using a factor (KImpact). All DOFs of the caudal pot were locked while the cranial pot was free to move vertically, with the experimental cranial load profile being applied to it, matching experimental conditions. Experimental and numerical load-displacement (LxD) curves were compared using Bland-Altman plots, RMSE and Lin's concordance coefficient (CCC).

With KImpact=0.0825, five models presented good agreement with experimental data, with average RMSE and CCC for LxD being, respectively, 0.036mm and 0.889. For peak load, maximum displacements and strains were, on average, 0.4mm and 0.035, respectively and most Bland-Altman plots showed dispersion around zero. The remaining two models showed poor agreement, with average RMSE and CCC for LxD being, respectively, 0.06mm and 0.32. However, overall strains levels, peak strains and peak strain locations were similar between experimental and numerical models.The majority of FE models had good agreement with experiments and, after calibration, they predicted the dynamic behaviour of VBs.

P53 Wear Performance of a Mobile Bearing Total Ankle Replacement

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Total ankle replacement (TAR) is an alternative to ankle fusion, replacing the arthritic joint with a motion-conserving alternative. TAR's have not been subject to the same pre-clinical testing and validation requirements as hip and knee replacements. This study aims to assess the polyethylene wear of a mobile bearing TAR device.

Six 'medium-sized' BOX® (MatOrtho Ltd, UK) TAR's, were tested in a modified 6 station knee simulator for 5 Mc, under kinematics aiming to replicate an ankle gait cycle(1). The simulator had six degrees of freedom of which four were controlled; axial force up to 3150N, dorsiflexion/plantarflexion (30°), internal/external rotation (10.3°), and anterior-posterior displacement (4mm)(1). The lubricant used was 25% bovine serum and 0.04% sodium azide solution to retard bacterial growth. Gravimetric measurements of polyethylene wear were taken every Mc. Unloaded soak controls compensated for the uptake of moisture by the polyethylene. The gravimetric wear measurements were separated into two phases; initial run-in phase (0-2 Mc) and steady-state phase (3-5 Mc)(1).

The overall mean wear rate (± 95% confidence limits) was 11.00 ± 3.06 mm3/Mc. Steady-state phase wear rate measured 4.26 ± 1.50 mm3/Mc and was significantly lower (P = 0.001) than the run-in phase wear (17.60 ± 7.67 mm3/Mc).

The run-in phase was comparable to wear rates of five Corin Zenith (25.80 ± 3.10 mm3/Mc)(1) and four BOX® TARs (18.6 ± 12.8 mm3/Mc) after 2 Mc, respectively(2). The increased run-in wear rates may not only be due to wear, but due to the creep of the polyethylene. Under similar kinematic conditions, the steady-state phase was substantially lower than the Zenith TAR (13.3 ± 2.5 mm3/Mc) after 2Mc(1). The increased wear rate from Smyth et al.(1) may be due to the previous 8 Mc already tested on their implants, under a variety of simulator inputs. Care must be taken when comparing wear rates from this study to different implant designs tested in different simulators. The study provides a useful benchmark for future TAR wear simulations.

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P54 Zebrafish in hypergravity: larval zebrafish experience changes in cartilage material properties after exposure to hypergravity

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Objectives: The relationship between genes, mechanical loading, and osteoarthritis is not fully understood. *col11a2* is a genetic mutation associated with Stickler syndrome and premature osteoarthritis (OA) in human patients and has been previously characterised in larval and adult zebrafish. As hypergravity can be used to simulate mechanical loading, we exposed wildtype and *col11a2* mutant larvae to high gravity conditions to examine the interplay between mechanical loading and genetic mutations.

Methods: Larval zebrafish with the *col11a2* mutation and wildtype zebrafish were exposed to continuous hypergravity for 48 hours from 3 days post fertilisation (dpf) to 5 dpf in the Large Diameter Centrifuge at ESA ESTEC, Noordwijk. Power calculations were used to determine sample size. The zebrafish were spun at 1 g, 3 g, and 6 g and a control group was kept in the lab at 1g with no spinning force. The zebrafish were fixed for analysis post-spin. Alcian blue alizarin red staining and immunostaining were used to identify changes to joint morphology, chondrocyte morphology, extracellular matrix (ECM) composition, mineralisation and musculature in the zebrafish lower jaw following hypergravity exposure. Atomic force microscopy (AFM) was used to determine material properties and the resulting values were used to create finite element analyses (FEA) of the larval zebrafish lower jaws during jaw opening and closing.

Results: Analysis of zebrafish from different gravity levels reveals that lower jaw morphology, mineralization and musculature were not affected. However, the material properties of the lower jaw cartilage were significantly altered in fish from higher gravity conditions, with zebrafish from the 6 g condition showing stiffer cartilage. FEA showed that increased cartilage stiffness caused a reduction in overall strain and movement of the lower jaw, although the morphological pattern of strain remained similar.

Conclusions: Overall, this demonstrates that exposure to hypergravity affects cartilage material properties resulting in modelled changes to jaw movement, but that this level and/or length of hypergravity exposure is not sufficient to cause gross changes to cartilage or muscle morphology in larval zebrafish.

P55 Lesser trochanter size could be a novel risk factor for hip osteoarthritis

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Objective: Previously, 2D hip shape derived from dual x-ray absorptiometry (DXA) scans has been associated with radiographic hip osteoarthritis (RHOA). It is unclear exactly which aspects of joint shape drive these associations. We aimed to identify more precise shape characteristics related to RHOA, by focusing on subregions identified from whole hip shape models and utilise 3D modelling on quantitative computed tomography (QCT) scans to validate the findings.

Methods: Statistical shape modelling was applied to hip DXAs obtained in the Osteoporotic Fractures in Men Study. A composite 2D at-risk-shape for RHOA was formed from related whole hip shape modes (HSMs). Areas of interest highlighted by the at-risk-shape were broken down into subregional HSMs, and the relationships between these and RHOA were examined by logistic regression. The subregional HSMs were further analysed for associations with 3D-HSMs derived from hip QCTs using linear regression.

Results: 4098 participants were identified with hip DXAs and radiographs. The composite at-risk-shape revealed that a larger lesser trochanter and pistol-grip femoral head are the predominant shape features related to RHOA. In subregional models built for these areas, lesser trochanter mode (LTM)1 [OR 0.74; 95%CI 0.63,0.87], representing a larger lesser trochanter, and cam-type mode (CTM)3 [OR 1.27; 1.13,1.42], representing a classic pistol-grip deformity, were associated with RHOA. These relationships between localised aspects of hip shape and RHOA were similar in strength to those observed previously for whole HSMs. 515 participants had hip DXAs and 3D-HSMs derived from hip QCTs. LTM1 was associated with 3D-HSMs also representing a larger 3D lesser trochanter [3D-HSM7 (β -0.23; -0.33,-0.14) and 3D-HSM9 (β 0.36; 0.27,0.45)], and CTM3 with 3D-HSMs also representing a pistol-grip deformity [3D-HSM3 (β-0.16;-0.25,-0.07) and 3D-HSM6 (β 0.19;0.10,0.28)].

Conclusion: Subregional SSM of hip DXA scans suggested a larger lesser trochanter and pistol-grip femoral head deformity underlie associations between overall hip shape and RHOA. 3D hip shape modelling confirmed our subregional HSMs

represent true anatomical variations in hip shape rather than 2D image artefact resulting from positional variation of the hip. Both shape features warrant further investigation to assess whether they are causal risk factors for hip OA.

P56 Bone mineral response following lumbar stress fracture in elite cricket fast bowlers

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Lumbar stress fracture (LSF) is the most serious injury sustained by cricket fast bowlers, with a time-loss in excess of 24 weeks. Following diagnosis of LSF, fast bowlers undergo a rehabilitation programme which aims to ensure healing of bone, enhance strength and endurance of the lumbar spine musculature and provide a gradual graded return to bowling, to prevent recurrence which occurs in 18% of cases. The response of bone mineral following LSF is currently unknown and may contribute to recurrence of LSF. The aim of this study is to quantify the response of bone mineral at the lumbar spine following LSF. Eight male elite cricket fast bowlers (mean ± SD: 19.46 ± 2.13 years; 1.88 ± 0.07 m; 82.75 ± 5.02 kg) sustained an LSF and received an anteroposterior lumbar spine DXA (Lunar iDXA, GE, Madison, WI, USA) scan at diagnosis of LSF and at both 8- and 21-weeks following diagnosis. L1-L4 BMD (g/cm2) and BMC (g) was analysed (Lunar enCore v17.0). One-way repeated measures ANOVA with Bonferroni correction was used to compare between time points of rehabilitation. L1-L4 BMD and BMC were significantly affected by rehabilitation time (BMD: $p < 0.01$, $\eta p2 = 0.56$; BMC: $p < 0.01$, $\eta p2 = 0.63$). Post-hoc Bonferroni demonstrated significant decreases between baseline and 8 week (BMD: -2.35 ± 1.82%, $p = 0.03$, $d = 0.30$; BMC: -2.15 ± 1.19%, $p < 0.01$, $d = 0.18$), and 21 weeks scans (BMD: -2.31 ± 1.88%, $p = 0.03$, $d = 0.27$) ; BMC: -2.33 ± 1.33%, $p < 0.01$, $d = 0.20$), but not between 8 and 21 week scans (BMD: 0.05 ± 1.90%, $p > 0.99$, $d = 0.01$; BMC: -0.17 ± 1.94%, $p > 0.99$, $d = 0.02$). Bone mineral is rapidly lost within 8 weeks following LSF and has not recovered by 21 weeks post injury. This may provide insight into recurrence of LSF in elite cricket fast bowlers and may suggest that current rehabilitation methods are insufficient to restore bone mass by the time many bowlers return to play.

P57 WITHDRAWN.

P58 Dose-response relationship between free-living physical activity and bone health in the middle-aged and elderly

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The aim of this study was to use UK Biobank data to examine dose-response relationship between mechanical loading of physical activity and bone health at hip and spine in the middle-aged and elderly.

This cross-sectional study was based on data from two UK Biobank studies. Imaging study (2014 – on going) provided DXA imaging data on measures of spinal bone health and geometry. Wrist-worn accelerometer study (2013-2015) provided 7-day raw acceleration data of physical activity. Participants (N=2,989, mean age 62 yrs) with data from both studies were included in the analysis. DXA measurements from lumbar spine included L1-L4 BMC, L1-L4 BMD, L1-L4 vertebral area, L1-L4 vertebral height, and L1-L4 vertebral width, while those from femur included femur neck BMD, femur wards BMD, femur trochanter BMD, and femur total BMD. Raw acceleration data were analysed to obtain loading dose at different intensities of physical activities (i.e. very light, light, moderate-to-vigorous). Multiple linear regression analysis was used to examine the association of loading dose parameters with bone health and geometry.

Loading dose of moderate-to-vigorous physical activity (MVPA) was positively associated with BMC at lumbar spine in both men and women ($p<0.05$). Loading dose of MVPA was significantly associated with L1-L4 BMD ($p<0.05$), but not with L1-L4 vertebral size in female ($p>0.05$), suggesting that increase of lumbar spine BMC by MVPA in female was mainly the result of increase in lumbar spine BMD. On the other hand, loading dose of MVPA was significantly associated with L1-L4 vertebral area and vertebral width ($p<0.01$), but not with L1-L4 BMD in male ($p>0.05$), suggesting that increase of lumbar spine BMC by MVPA in male is mainly the result of increase in lumbar vertebral size. Loading dose of MVPA was significantly associated with femur neck, femur wards, femur trochanter, and femur total BMD in female ($p<0.01$), but not in male ($p>0.05$).

A dose response relationship was found between moderate-to-vigorous physical activity and bone health at lumbar spine and femur in a cohort of middle-aged and elderly UK adults.

P59 Microbubbles as oxygen delivery agents for stimulating osteogenesis in vitro and in vivo

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Introduction: Oxygen tension is known to affect bone formation and healing, but the exact mechanisms by which this takes place are unclear. Microbubbles are lipid-stabilized gas bubbles used clinically in ultrasound contrast imaging that can travel systemically throughout the body, and therefore provide a potential delivery vehicle for oxygen to bone tissues or fractures. This study aims to test the hypothesis that oxygen microbubbles promote osteogenic differentiation and to determine if they induce skeletal changes in mice in vivo.

Methods: Microbubbles (MBs) were prepared containing either oxygen or nitrogen gas and a range of lipid combinations. MBs were tested for their stability at 37°C. Optimal MB formulations containing O2 or N2 were then incubated with human bone marrow stromal cells (BMSCs) for 14 days, with and without osteogenic supplements. Differentiation was measured by alkaline phosphatase (ALP) activity and gene expression. Adult MF1 mice were injected twice weekly with MB/gas formulations and effects on the skeleton were measured using micro-CT (36 µm and 9 µm resolution) and by histology. Formulations were analysed for toxicity via body weight measurements, histological sections and serology.

Results: A DBPC/DSPE-PEG (9:1) microbubble formulation was found to be stable for up to 2 hrs. BMSCs showed significantly elevated ALP activity and alizarin red staining when treated with O2 bubbles compared to controls. Inhibition of BMSCs differentiation by hypoxia was reversed on treatment with O2 bubbles. Osteoclast differentiation was reduced in the presence of O2 bubbles compared with controls. In vivo, all mice showed tolerance to multiple doses of MBs over the study period. There were no changes to the skeletal structure during the course of the study with any formulation.

Conclusion: This study demonstrates that MB-delivered oxygen promotes osteoblastogenesis and inhibits osteoclastogenesis in vitro. This suggests that MBs, which are well tolerated and used as ultrasound agents in imaging, may be used as bone anabolic agents. The lack of activity in vivo suggests that concentration and localisation of MBs may require optimisation prior to their clinical use.

We thank EPSRC for funding.

P60 Pre-operative partial thickness cuff tears do not compromise results of anatomical total shoulder replacement- 5 year follow up

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Background: Reverse shoulder arthroplasty (RSA) in elderly patients with primary osteoarthritis (OA) and cuff pathology is increasing, the purpose of our study was to determine the medium term results of anatomic total shoulder athroplasty (TSR) for OA in patients with pre-operative partial thickness (P/T) cuff tears on MRI scans.

Method: We retrospectively reviewed patients who had TSR for OA with a preoperative MRI diagnosis of P/T cuff tear. Patients were assessed with pre and post-operative Oxford Shoulder Score(OSS), range of movements(ROM) and rotator cuff was clinically assessed. AP and Axillary radiographs were taken for proximal humeral migration (using Torchia classification) and evidence of loosening. Lazarus score was used to grade glenoid radiolucencies.

Results: Thirty-six patients (M14:F22), who underwent TSR had a P/T tear on MRI preoperatively, all demonstrated mild to moderate fatty infiltration. The mean age was 79.2(71-88)years; Mean follow-up was 5.1(4.8-7.0)years. Significant improvements in pain, ROM, was reported in all cases. At the final follow-up the OSS was 42(32-46) with minimum 14 points improvement(p=0.001). External rotation(15°vs30°;P=0.001), forward flexion(80°vs130°;P=0.015) abduction(40°vs70°;P=0.015) and internal rotation also improved. Lucencies has been observed in 8 glenoids. Grade1-6, Grade2-2 & none with Grade3. There were no cases of implant loosening. Clinically four patients had cuff weakness but only 2 showed evidence of proximal migration and one of anterior migration of humerus of which one patient with Torchia moderate grade proximal migration was revised for cuff failure; one patient had washout for infection.

Conclusion: There is paucity of literature on whether preoperative partial thickness rotator cuff tear has an adverse affect on the outcome of TSR. Our results show that the presence of P/T cuff tear on preoperative MRI does not significantly effect function after TSR in the medium term. The use of reverse shoulder arthroplasty in these cohorts of patients, therefore, may not be justified.

P61 Performance of TS symmetric cone in revision of total knee arthroplasty

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Objectives: Management of bone defects is crucial

in revision total knee arthroplasty (TKA). A relatively new system of porous titanium metaphyseal cones are being used for revision TKA to provide stability and replace lost bone. The aim of this study is to evaluate the performance of these cones with varying type of defects using a computational approach.

Methods: Tibial baseplate and an optimally sized cone were virtually implanted to a tibia in which various bone defects were included. Defects at four different anatomic locations, with three different widths and two depths were considered, i.e. 24 cases of tibia defects were considered. The gap between cone and baseplate was filled with cement. Four loading cases were considered: knee bend during squatting, standing up, walking and climbing down the stairs.

Results: Micromotions at the bone-implant interface were found to be small for all defects considered in this study. More than 50% of bone-implant interface had micromotion less than 25 µm. In general, micromotion was found to be influenced by both depth and width of the defect but dominated by defect depth for higher micromotion observed in each loading scenario. Anterior and lateral defects do not significantly alternate strain distribution compared with bone without defect. For medial defects, strain distribution is sensitive to defect width; while strain distribution for posterior defects are associated with defect width and depth.

Conclusion: Porous titanium cone is a reliable way to manage bone loss in revision TKA. The cone is effective in transmitting the applied loads and moments even for bone with large defects.

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P62 Effect of an acute bout of high impact exercise on serum sclerostin concentration

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Objectives: High impact exercises have a potent osteogenic effect due to high strain magnitudes and rates possibly by regulating the expression of sclerostin, a regulator of the Wnt/β-catenin pathway and hence bone accrual. We investigated the effect of an acute bout of high impact exercise on serum sclerostin concentration ([sScl]) in healthy young men.

Methods: Participants completed an exercise (EX) and control (CON) trial on separate days one week apart. In EX, 120 maximum effort multi-directional jumps were performed on a force plate separated by rest pauses; countermovement-jump peak vertical ground reaction force (VGF) was recorded. In CON, participants attended at the same time but rested in a supine position. Venous blood samples were taken at baseline and immediately, 0.5 and 24 h post exercise/rest. Repeated measures ANOVA assessed the effect of time, trial and time*trial interaction on mean [sScl] with subsequent paired t-tests to detect which means differed.

Results: Six men participated (mean(SD); age: 22.3(1.9) years; BMI: 23.1(0.8) kg/m^2); 5 providing 24 h samples. Mean peak VGF was 6.9(2.4) times body weight. Baseline (n=6) [sScl] did not differ between EX (133.7(46.7) pg/ml) and CON (144.8(36.1) pg/ml; P = 0.405). There were no effects of time (P = 0.262) or trial (P = 0.193) but a time*trial interaction (P = 0.001) was found. In EX, there was an increase from baseline to immediately (165.3(48.8) pg/ml; P = 0.002) and 0.5 h post (159.0(42.9) pg/ml; P = 0.008) [sScl]. In CON there were no differences between baseline, immediately (121.4(20.1) pg/ml; P = 0.303) or 0.5 h post (127.3(19.3) pg/ml; P = 0.395). Baseline values (n=5) did not differ from 2 4 h in either trial (EX, P = 0.490; CON, P = 0.585).

Conclusion: An acute bout of high impact exercise caused an increase in [sScl] immediately post exercise, remaining elevated 0.5 h later but declining over the subsequent day; with no change in control. This acute increase counters the lower sclerostin that has been reported with exercise training, that may be associated with higher bone formation.

P63 Utilising pressure walkways to modify footwear design to reduce risk of shin splints

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Objectives: To reduce peak pressure within the heel of the foot whilst wearing standard military issued boots under various loads whilst maintaining a balanced medio-lateral distribution.

Methods: Within the standard issues military boot, the internal midsole system is used to create an even distribution of pressure and to provide shock absorption. Mechanical impact and quasi-static tests are standardised methods to quantify shock attenuation in critical regions of a shoe.

Finite element analysis was selected to facilitate the design iteration process. Developed to replicate standardised mechanical impact testing protocols, finite element analysis (FEA) was selected to facilitate the design iteration process. The F-Scan in-shoe pressure system, and Strideway system were used to collect plantar pressure data. The GAITRite Platinum plus classic walkway system was used to collect spatial and temporal gait parameters. Five healthy female participants were recruited from the School of Engineering, Cardiff University (Age: 22 ± 2.74 years old, Body mass: 60.2 ±2.66kg, Height: 164.66 ±3.52cm and BMI: 22.36±1.38). The project was approved by the Cardiff University Ethics committee. To analyse the peak pressure the foot

was separated into 12 regions to assess the overall plantar pressure map and their variance.

Results: Results indicate significant differences for heel plantar pressure when loaded, e.g. for 5kg the heel mean peak plantar pressure decreased from 124.72 (20.33) KPa for the issued boot to 43.12 (39.03) KPa for the modified boot, p = 0.026. Compared to the issued military boot, the modified boot reduced peak heel plantar pressure with added loads of 5kg, 10kg and 15kg.

Conclusions: Normalised heel peak pressure was reduced after modifying the standard issue military boot midsole.

P64 The immunomodulatory activity of mesenchymal stem cells (MSCs) is influenced by their three-dimensional environment *in vitro*

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Objectives: Mesenchymal stromal/stem cells (MSCs) have been suggested as therapy in orthopaedics either to modulate disease or as an adjunct to surgical interventions such as microfracture. Recent work has focused on the ability of MSCs to influence immune cells during disease or tissue repair. The extracellular environment is very dynamic in these situations and consequently, our studies aim to understand how MSCs are modulated by tissue matrix.

Methods: Human MSCs were seeded in three environments: tissue culture plastic, entrapped within 3D matrices or on the surface of these matrix gels. In all conditions, untreated cells were contrasted with those exposed to a mild pro-inflammatory environment (2ng/µl TNFα and 5ng/µl IFNγ). For 3D matrices, Collagen Type I (2.7mg/ml) was used to create a collagen gel and three concentrations of fibrinogen (5 mg/ml, 10 mg/ml and 25mg/ml) with 5U/ml of thrombin were combined for fibrin scaffolds. CXCL10 (IFN-γ inducible protein 10) and TSG-6 (TNF-stimulated gene-6) mRNA levels were determined using quantitative PCR at days 1,2,3 and 6 in fibrin and at 24hrs in collagen. ELISA was used to confirm levels of secreted proteins.

Results: The expression of CXCL10 by human MSCs was rapidly upregulated in response to pro-inflammatory stimuli in all conditions but interestingly it was expressed at significantly higher levels in all 3D environments. While there was a gradual increase in TSG-6 gene expression after TNFα/ IFNγ treatment in monolayer culture, the opposite pattern was observed in all 3D environments with this gene significantly and rapidly induced at day 1 and then steadily decreasing. In fibrin matrices, there was a concomitant increase in the expression levels of both genes with increasing fibrin stiffness. Pre-treating MSCs with Y27632 (Rho-associated protein kinase (ROCK) inhibitor) enhanced the matrix-dependent influence on CXCL10 and TSG-6 expression whilst the cdc42 inhibitor, ZCL-278 had no effect.

Conclusion: From these results, it can be concluded that MSCs exhibit a differential response to inflammatory stimuli in 3D environments compared to conventional monolayer culture. This further illustrates the importance of the tissue environment in shaping cell activity during processes of disease and repair.

P65 Incidence of fractures in people with intellectual disabilities

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Objective: To compare the incidence of fractures between people with intellectual disabilities (ID) and the UK general population.

Methods: We used data from the Clinical Practice Research Datalink (CPRD) over the years 1998-2018. We identified total 81,996 patients with diagnoses consistent with ID aged ≥1 year and 5 randomly selected age and sex matched control subjects per patient, for a total study population of 493,196 people. We examined fracture incidence rates by 5-years age bands in adults and one- year bands in children. Incidence rates [95% CI] are number of fractures per 10,000 person-years (py).

Results: Data on adults (age ≥ 18 years) are presented. People with ID had higher fracture incidence and younger age at fracture than control subjects. Fracture rates started to differ from age 38 years, after which there was a marked increase in the ID group until the late eighties. In the 38-43 year band the fracture rate was 67.7 [60.6-75.5] per 10,000 py in the ID group, a rate which was only seen in the controls in the 53-58 year group. For hip fracture, differences were even more striking. Overall rates were 4.6 [4.1-5.1] in ID vs 2.15 [1.1-2.3] per 10,000 py in control subjects. Significant differences were seen from the age of 23 years, persisting until the late eighties. In the 53-58 year group, hip fracture rate was 9.6 [6.7-13.7] vs 1.0 [0.6-1.6] per 10,000 py in ID vs control subjects.

Conclusion: This study, the largest ever conducted in people with ID, shows that ID adults have higher fracture rates than the general population. Relative risk is particularly high in younger patients.

Fractures in ID people are particularly serious, due to

difficulties in accepting immobilisation, collaborating with rehabilitation, and pre-existing physical disabilities. Anecdotal but consistent evidence shows generalised unawareness by clinicians, patients, carers and health policy makers of the high fracture risk, partly due to lack of previous studies in the UK. Our study should increase awareness of the problem so that appropriate measures for prevention can be implemented.

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P66 Dislocation of the mobile bearing in the Lateral Oxford Unicompartmental Knee Replacement (LOUKR): the effect of knee flexion

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Background: 1-6% of mobile bearings in implanted Lateral Oxford Unicompartmental Knee Replacements will dislocate. Clinical observations suggest that dislocations can occur medially, anteriorly or posteriorly. Medial dislocations, with the bearing lodged above the medial wall of the tibial component, are the most common, and tend to occur early (within 12 months post-op). Some evidence suggests that dislocations occur with the knee unloaded and in flexion. Previous work has shown that dislocations become possible when the distance between the components is increased vertically or laterally, and that relative to the femur, 5° of internal tibial rotation increases dislocations.

Objectives: 1. Characterise bearing dislocation mechanisms and determine the mechanical factors that influence dislocation. 2. Determine whether knee flexion increases the likelihood of dislocation of the mobile bearing.

Methods: A mechanical rig was produced in which the femoral component was moved away from the tibial component until dislocation was possible. At flexion angles of 0°, 90° and 130°, the vertical distraction distance (0-8 m) and medial/lateral translation (0-4 mm) were varied in 0.25 mm increments. Internal and external tibial rotations (10° and 30°) were also assessed. In all 8415 component configurations, dislocation data were recorded.

Results: In neutral position with components perfectly aligned, 4 mm of vertical distraction was required for medial dislocation. Mediolateral translation of 4 mm reduced the vertical distraction required for medial dislocation to 2.5 mm. With components in neutral position, anterior and posterior dislocation were possible at 6 mm or 6.25 mm of vertical distraction, respectively, with no effect from mediolateral translation. For all modes of dislocation, neither flexion nor internal or external rotation had a clinically significant effect on these results.

Conclusion: Medial dislocation required the least amount of vertical distraction for the mobile bearing to dislocate. The amount of distraction required was surprisingly small, given the amount the knee can distract, especially in flexion. It is likely that dislocations occur in flexion due to the increased ligament laxity in the lateral compartment of the knee. The results from this study will inform instrumentation and implant design modifications with the objective of reducing the risk of dislocation.

P67 WITHDRAWN.

P68 Leptin remodels tibia trabecular bone volume but not bone mineral density *in vivo* independent of body weight changes

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Leptin contributes to energy metabolism, acting to reduce appetite and body weight as well as to increase heart rate and blood pressure. However, the effects of leptin on bone metabolism remain contradictory, partly because leptin may have direct as well as indirect effects on bone due to changes in body weight and central nervous system actions. In this study high resolution µCT was used to scan and analyse tibia samples collected from leptin deficient Ob/Ob mice (n=4), which were weight matched with c57 controls (n=4), from 4-22 weeks of age. Bone samples were scanned at a resolution of 4.3µm, 0.7° rotation step and reconstructed using NRecon. Post-reconstruction, CTAn was used to calculate percentage trabecular bone volume (BV/TV), trabecular thickness (Tb.Th.), trabecular number (Tb.N) structural model index (SMI), bone mineral density (BMD) and cortical bone volume (C.BV). Osteoblast and osteoclast activity were also investigated by immunohistochemical analysis, on paraffin embedded sections, using anti-osteopontin and anti-RANKL antibodies. µCT data showed that BV/TV of the Ob/Ob tibias was significantly decreased compared to c57 controls (7.81 ± 0.91 vs. 12.73 ± 0.73 %, respectively). However, tibia trabeculae BMD did not significantly differ between weight-paired Ob/Ob and c57 controls (1.60 ± 0.02 vs. 1.63 ± 0.01 g/cm3, respectively).Compared to c57, Ob/Ob mice tibia had a significant reduction in

trabecular thickness: 0.043 ± 0.001mm vs. 0.037 ± 0.001mm, and number: 3.19 ± 0.21mm^{-1} vs. 2.09 ± 0.22mm^{-1}, respectively. ObOb mice tibia trabeculae showed a significant increase in SMI (2.07 ± 0.07) compared to c57 (1.83 ± 0.09), demonstrating tibia trabeculae were becoming more rod like, indicative of increased osteoclast activity. Cortical BV of the tibia was reduced in Ob/Ob compared to c57 controls (0.72 ± 0.01 to 0.60 ± 0.02mm^3, respectively); however no differences in cortical BMD were observed (1.71 ± 0.01 vs. 1.70 ± 0.01 g/cm^3, respectively). These findings suggest that, independent of body weight, leptin plays a significant role in promoting resorption and/or inhibition of trabecular and cortical bone formation but that bone mineral density remains unchanged.

P69 Protein Kinase R activates the NFkB signalling pathway in osteoblast like cells in response to pro-inflammatory cytokines, interleukin-17A and tumour necrosis factor-alpha

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Objectives: Protein Kinase R (PKR) activates the NF-κB pathway resulting in transcription of pro-inflammatory genes. Over-activation of PKR *in vivo* leads to subchondral bone changes and osteoarthritis. The objective of this study was therefore to investigatePKR-dependantactivation of the NFkB pathway by the pro-inflammatory cytokines, TNF-α and IL-17A in osteoblasts *in vitro*.

Methods: Mouse osteoblasts (MC3T3-E1) were stimulated with TNF-α (1ng/ml) and IL-17A (50ng/ml) ± a small molecule PKR inhibitor (1μM PKRi; Calbiochem) or vehicle control (DMSO 0.002%) for 1 hour. Translocation of the transcription factor, NFkB to the nucleus was detected by immunocytochemistry. Total RNA from cytokine treated cells with PKRi, (n=4) or vehicle (n=6) was isolated, reverse transcribed and cDNAs combined for each treatment prior to analysis on the mouse NFkB signalling pathway RT^2 Profiler PCR Array (QIAGEN; PAMM-025Z). CT values from each group were normalised to 3 reference genes and fold change calculated using the 2^(-delta delta CT) formula (http://www.qiagen.com/geneglobe). Pooling cDNAs precluded statistical analysis.

Results: Translocation of NFkB to the nucleus was induced by cytokine treatment in a PKR dependant manner. Of 84 genes analysed on the array, 5 were upregulated more than 2-fold by PKR inhibition and 18 genes down-regulated. Down-regulated genes included NFkB signalling ligands and receptors (Cd27, Il1a, Nod1, Tnfrsf1b, Tlr2), NFkB responsive genes involved in the immune response (Ccl5, Csf1, Icam1, Lta) and apoptosis (Birc3), transcription factors (Egr1, Smad3), genes downstream of NFkb (Fadd, Irf1, Traf2), and genes involved in the cytoplasmic sequestering/releasing of NFkB (Bcl3). Up-regulated genes included Tnf, Chuk, Ikbkg, Csf2 and Fos.

Conclusion: NFkB is involved in inflammatory responses and is an important regulator of cell fate, such as apoptosis and proliferation. Here we show that pro-inflammatory cytokines implicated in OA, IL-17A and TNF-α, activate NFkB in a PKR dependant manner in osteoblasts. This mechanism may contribute to the severe OA phenotype observed in p58^{IPK} mice, where PKR is constitutively over-activated.

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P70 Ultrasound applications in knee osteoarthritis

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Objectives: Surface Electromyography (sEMG) is employed to study the muscle characteristics in osteoarthritis (OA) research. To locate accurately the sEMG sensors position on muscle belly, Ultrasonography (US) is used. Since locating the muscle belly is a difficult task, especially on overweight people and/or people with weak muscle activity, it is very important to follow a proper protocol for correct muscle belly identification. Due to the lack of imaging protocols, to increase the measurement reproducibility, different approaches have been utilized to measure the thickness from 2D US images of the quadriceps muscles. This preliminary study aimed to demonstrate the robustness of our US imaging protocols and to evaluate the methods used to interpret the information from US images i.e. to measure the individual pennation angles and to define the muscle bellies of the rectus femoris (RF), vastus lateralis (VL) and vastus medialis (VM).

Methods: Ultrasound measurements with high-resolution Samsung RS80A ultrasound scanner have been performed on muscle thickness and pennation angle at the participant's RF, VL, VM muscles of 10 healthy volunteers (8 females, 2 males; aged, 20-24; BMI, 17.5-25.0). US images of the muscle belly of RF, VL and VM were taken in transverse and longitudinal planes. For every muscle, three repetitive measurements were taken in each imaging plane. Pennation angles were acquired three times from longitudinal plane for the RF, VL and VM. Statistical analysis was performed on SPSS 23 (IBM) and Excel (Microsoft) software.

Results and Conclusion: Novel US protocol of adequate quality and repeatability for research purposes were developed. Intra-class correlation coefficients (ICCs) calculated for transverse US images of the VM= 0.925, RF= 0.833 and VL=0.733 indicated that the results have good reproducibility and reliability when our protocol was applied to measure the muscle thickness at the muscle bellies.

Intra and inter-image reliability analysis suggested that measurements taken in transverse plane are better indicators of muscle thickness compared to the longitudinal measurements. ICCs calculated for pennation angles were not satisfactory due to number of factors including intra-image variation. It was concluded that more comprehensive analysis is needed in order to measure confidently the pennation angles.

P71 The communication of higher level evidence in Osteoarthritis:are we speaking the same language?

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Objectives: Guidelines for research conduct and reporting aim to improve quality. However, there is no single gold standard for the communication of higher level evidence and impact in osteoarthritis (OA) research. To determine the consistency between current guidelines, OA journals were reviewed to test the hypothesis that conduct and reporting guidelines are consistent across disciplines.

Methods: Twenty two OA journals were selected to reflect molecular, cellular, animal and human research. The 'author information' for publication was screened for each of the most frequently cited conduct and reporting guidelines. Similarities and differences between these guidelines were identified objectively and systematically using an inductive approach after categorising into 37 subthemes representing the original text. The content of each guideline was reviewed by JD and DM, experienced in human and animal research respectively, assessed by a third reviewer (AG) and the final output agreed by consensus.

Results: Sixty eight percent (15/22) of the OA journals recommended standardised conduct/reporting explicitly (59%) or implicitly (9%) through reference to websites promoting standardised methods (EQUATOR, ICJME or MIBBI), whilst 32% (7/22) did not. The most commonly endorsed guidelines for human, animal and molecular research were the CONSORT (55%), ARRIVE (23%) and MIAME (32%) guidelines respectively. There were no recommendations for cellular research.

CONSORT, ARRIVE and MIAME guidelines were evaluated with reference to 37 subthemes. Whilst guidelines were similar in terms of the description of trial design, interventions and statistical methods, the language used was often different; 'statistical methods used to compare groups' (CONSORT) and 'MAIME indicates preferred detailed specifications of all numerical calculations'. CONSORT was the only guideline to recommend trial registration.

Conclusions: Standardisation of OA journal recommendations is required. Although, higher level evidence is communicated similarly amongst disciplines using CONSORT, ARRIVE and MIAME guidelines, the language used is inconsistent. The lack of a requirement to define protocols or trials in advance of molecular or animal experiments,may limit reporting of negative data. It remains to be seen whether this effects the potential for interdisciplinary OA research impact. These data will inform a survey to assess higher level evidence and impact in interdisciplinary OA research.

P72 Characterisation of spinal cord injury-induced osteoporosis in a rat model

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Structural, densitometric and mechanical changes that occur in the paralysed limbs of a rat model of complete spinal cord injury (SCI) are described. Providing a uniquely-detailed description of the spatiotemporal changes throughout the distal femur (a fracture-prone site in human SCI patients).

Male rats (200-250g) were assigned into eight (n=8) experimental groups. Four-groups sustained transection SCI at thoracic level T9 and were sacrificed at 2, 6, 10 and 16-weeks post-surgery. Each SCI group had an age-matched sham-operated control group. Bone quantity and quality were assessed using microCT for global and site-specific analysis of trabecular (epiphyseal and metaphyseal) and cortical bone (metaphyseal and diaphyseal) morphometry and densitometry. Whole-bone and material-level properties were assessed using three-point bending and torsional testing.

A severe deterioration of metaphyseal trabecular bone was observed, after 2-weeks volume fraction (BV/TV) was 59% lower than controls, resulting in a compromised structure composed of 53% fewer and 15% thinner trabeculae. At later time points post-SCI there were no further reductions in metaphyseal BV/TV, although microstructural changes did occur. In contrast, epiphyseal trabecular bone was more resistant to SCI-induced osteoporosis. There was a 23% lowering of BV/TV at 2-weeks post-SCI compared to control, characterised by 15% thinner trabeculae, suggesting the epiphyseal structure's connectivity was maintained. At later times post-SCI growth-related increases in epiphyseal BV/TV were observed. Rapid changes to cortical bone were also observed. Metaphyseal regions experienced the most severe lowering of cortical area at 2-weeks post-SCI compared to control. The varying degree of change in the amount of trabecular and cortical bone was concomitant with each region's surface-to-volume ratio. Analysis at more chronic times post-SCI highlighted that caution must be exercised when interpreting results from

skeletally-immature rodents, since SCI-induced bone changes were a combination of bone loss and suppressed bone growth. No difference in mineral-density was observed between SCI and control at any time-point, indicating that decreases in whole-bone mechanical properties post-SCI were a result of changes to the distribution of bone, rather than changes to material properties.

Cumulatively, this illustrates that SCI-induced osteoporosis detrimentally affects the spatial distribution of bone site-specifically.

P73 Jumping Joints: the complex relationship between osteoarthritis and jumping mechanography

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Objectives: We investigated the relationship between lower limb osteoarthritis (OA) and muscle strength and power (assessed by jumping mechanography) in UK community dwelling older adults.

Materials and methods: We recruited 249 older adults (144 males, 105 females). OA was assessed clinically at the knee according to ACR criteria and radiographically, at the knee and hip, using Kellgren and Lawrence grading. Two-footed jumping tests were performed using a Leonardo Mechanography Ground Reaction Force Platform to assess maximum muscle force, power and Esslinger Fitness Index. Linear regression was used to assess the relationship between OA and jumping outcomes.

Results: The mean age of participants was 75.2 years (SD 2.6). Males had a significantly higher maximum total power during lift off (mean 25.7 W/kg vs 19.9 W/kg, $p<0.001$) and maximum total force during lift off (mean 21 N/kg vs 19.1 N/kg, $p<0.001$) than females. We found significant associations in males between clinical knee OA and maximum total power (β -6.00 (95% CI -9.05, -2.94) $p<0.001$) and Esslinger fitness index (-19.33 (-28.98, -9.680) $p<0.001$. In females radiographic knee OA was associated with total maximum power (-2.02 (-3.89, -0.14), $p<0.04$) and Esslinger fitness index (-8.17 (-15.91, -0.42) $p<0.04$). No significant associations were observed for maximum total force.

Conclusions: We observed significant negative associations between maximum total power and Esslinger Fitness Index and clinical knee OA in males and radiographic knee OA in females. We have used novel methodology to demonstrate relationships between muscle function and OA in older adults.

P74 Common vitamin D-related genetic variants are associated with bone health in the Hertfordshire Cohort Study

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Objectives: While single-nucleotide polymorphisms (SNPs) in genes related to vitamin D metabolism have been shown to be associated with serum 25-hydroxy vitamin D (25(OH)D) concentration, no previous studies have related these SNPs to musculoskeletal health in late adulthood. Here we consider relationships between SNPs in the vitamin D metabolic pathway, in DHCR7, CYP2R1 and CYP24A1 and GC and (i) bone indices assessed by DXA at the femoral neck and total hip, and ii) grip strength in a cohort of community-dwelling older adults, using participants from the Hertfordshire Cohort Study (HCS).

Methods: Bone mineral content (BMC), bone area and bone mineral density (BMD) were measured by dual energy X-ray absorptiometry (DXA) at the femoral neck and total hip using a Hologic QDR 4500 instrument. Grip strength was assessed using a Jamar dynamometer. SNPs were genotyped by LGC Genomics (Hoddeston, UK).

Results: Data were available for 495 men and 488 women. The mean age (SD) of the participants was 64.3 (2.5) years for men and 65.7 (2.5) years for women. The median Body Mass Index (BMI) of participants in men and women was similar (26.5 kg/m2 (IQR 24.4 – 28.7) and 26.4 kg/m2 (IQR 23.6 – 29.9) respectively). In men, the common allele of a SNP in CYP2R1, rs10741657, was associated with lower femoral neck BMC (β=-0.15; 95% CI, -0.28 to -0.02; p=0.024) and total hip BMC (β=-0.15; 95% CI, -0.28 to -0.02; p=0.023), after adjustment for season of blood sampling. In women, the same SNP was associated with lower total hip BMD (β=-0.13; 95% CI, -0.24 to -0.11; p=0.032), after adjustment for confounders (season of blood collection, vitamin D intake, age, BMI, social class, smoker status, alcohol consumption, activity, calcium intake, years since menopause and HRT use). No significant associations were observed with grip strength.

Conclusion: A SNP in CYP2R1 was associated with poorer hip BMC in men and hip BMD in women in late middle age.

P75 The benefits of regular weight bearing activity throughout the life-course: do men and women reap the same rewards?

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Higher levels of physical activity (PA) has been shown to be beneficial for musculoskeletal health but few studies have considered relationships between reported PA levels at different stages of life, and musculoskeletal outcomes in late adulthood, particularly in men. We considered this in the Hertfordshire Cohort Study (HCS), a cohort of community dwelling men and women born 1931-9.

The study population comprised 128 men and 130 women. Data were collected via a questionnaire asking their participation in weight bearing PA <18 years; aged 18-29 years; aged 30-49 years and >50 years. Responses were coded as none/ once-a-month/ once-a-week/ >once-a-week. Current PA levels were also recorded. Grip strength was assessed using a Jamar dynamometer. Bone mineral density (BMD) was performed at the total femur (Hologic QDR 4500).

The mean age was 75.4 (SD 2.5) years in men and 75.7 (SD 2.6) years in women. Women were currently more physically active than men, recording a median activity of 206 (IQR 146-277) minutes daily, versus 194 (IQR 110-298) minutes daily in males. However, men reported higher levels of past PA, with significant differences seen in <18 years ($p=0.006$) and 18-29 years ($p<0.001$), when only 15.6% of women reported PA >once-a-week compared to 41.6% of men.We observed greater BMD at the total hip in women who reported regular PA at ages 18-29 years (β weekly exercise 0.72, $p=0.02$; β >once-a-week exercise 0.83, $p=0.01$), and 30-49 years (β weekly exercise 0.52, $p=0.04$; β >once-a-week exercise 0.78, $p=0.02$), compared to no reported PA, despite adjustments for age, BMI, social class, smoker status, alcohol consumption, current physical activity and dietary calcium intake. No such relationships were apparent in men, before or after adjustment. No relationships were observed between past PA and grip strength in this sample.

Regular weight bearing activity around the time of peak bone mass acquisition was less common in women than men in this cohort. However, we observe higher hip BMD in women participating in regular PA throughout the life-course, highlighting the need to promote exercise among young women.

P76 A novel 3D loading model for osteoarthritis drug screening

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Objectives: Abnormal joint mechanics are a major risk factor for osteoarthritis. *In vitro* models for osteoarthritis do not incorporate mechanical loading and crosstalk between bone and cartilage. The AMPA/kainate glutamate receptor (GluR) antagonist, NBQX alleviates symptoms and degeneration in mouse arthritis models. We adapted our *in vitro* 3D loading model of bone to incorporate chondrocytes, and determined loading responses, and the effects of NBQX and cross talk from osteocytes on chondrocyte responses.

Methods: Human MSC cells (Y201), differentiated into chondrocytes in 3D agarose hydrogels for 7-days were subjected to physiological (25%/s) or pathophysiological (100%/s) load (10Hz, 3000 cycles; TE Instruments) ±NBQX (200μM) or ± conditioned media from unloaded/5000με loaded osteocytes in 3D. Phenotype was assessed by immunolabelling (Sox9). CTXII and glutamate (ELISA), and cytokines (Merck Milliplex panel) were measured in media 1hr post-load. The effect of osteocyte media on chondrocytes was assessed after 24hr. Data analysed by Minitab (n=3/treatment).

Results: Rounded Y201 cells expressed sox9. ChondrocyteCTXII release was doubled by pathophysiological load ($p=0.009$ vs unloaded; $p=0.002$ vs physiological load) and this was returned to baseline by NBQX ($p=0.02$). Glutamate release was increased following pathophysiological load ($p=0.011$) and was reduced, although not significantly by NBQX ($p=0.089$). Both loading regimes induced MCP-1 and IL-8 release, which was reduced 2-fold and 4-fold respectively, by NBQX. Media from loaded osteocytes reduced IP-10 (3-fold; $p=0.002$), increased IL-6 (1.5-fold; $p=0.014$) release but did not alter CTXII release from chondrocytes when compared to the effect of media from unloaded osteocytes.

Conclusion: Y201 differentiated to chondrocyte-like cells in 3D and produced readouts of cartilage degradation (CTXII), pain (glutamate) and inflammation in response to mechanical loading. NBQX reduced load-induced CTXII, glutamate and cytokine release consistent with its symptom and disease modifying effects *in vivo*. Crosstalk between osteocytes and chondrocytes influenced degradative and inflammatory readouts in a load specific manner. Models incorporating mechanical loading and cross-talk between joint tissues would improve understanding of disease mechanisms underlying osteoarthritis and thus drug screening.

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P77 WITHDRAWN.

P78 Knee biomechanics differ between sexes in end-stage knee osteoarthritis

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Objectives: Most previous literature analysed knee biomechanics in end-stage knee osteoarthritis (KOA) in groups with mixed genders. A few recent studies highlighted that differences exist between men and women's knee biomechanics at this stage. The aim of this study is to determine possible knee kinematic and kinetic inconsistencies between sexes before total knee replacement (TKR) surgery.

Methods: This was an observational, cross-sectional study including 19 healthy women (HW), 11 healthy men (HM), 15 preoperative-TKR (pre-TKR) women and 15 pre-TKR men. Three-dimensional gait analysis was performed using a lower-limb marker set, Qualisys motion capture system and Bertec force platforms with participants walking barefoot, at a self-selected pace. Spatiotemporal parameters, knee kinematics, and knee kinetics were quantified in Visual3D and data from three to six walking trials were averaged for analysis for each participant. One-way ANOVA (Post Hoc Bonferroni) and Kruskal-Wallis tests were utilised to explore significant differences ($p<0.05$) between:

- pre-TKR women and HW
- pre-TKR men and HM
- pre-TKR men and women
- HM and HW.

Results: Both pre-TKR men and women showed significant reduced spatiotemporal values from HM and HW, respectively ($p<0.001$). Peak extension moment, knee Range Of Movement (ROM) were significantly decreased in pre-TKR males and females compared to their respective controls ($p<0.05$). Only pre-TKR men had reduced peak flexion moment compared to HM ($p=0.001$). Only pre-TKR women had a smaller peak flexion angle (swing) compared to HW ($p<0.001$). Both men and women pre-TKR had a greater flexion angle at stance ($p<0.003$) compared to controls. Pre-TKR women displayed 6.6° more knee flexion at the stance and 8° more restricted knee ROM than pre-TKR men. No significant differences were found in spatiotemporal parameters or knee biomechanics between HM and HW.

Conclusion: Even though both sexes pre-TKR display similar knee biomechanical differences from controls, women's knee function seemed to be affected more than men in end-stage KOA. Future studies investigating knee biomechanics in end-stage KOA should analyse men and women separately.

P79 Interleukin-17 is a potential contributor to the inflammatory environment in the osteoarthritic joint

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Osteoarthritis (OA) has been historically viewed as a degenerative 'wear and tear' disease, which is characterised by the loss of articular cartilage. Modern imaging techniques have shown us that OA is a multifactorial disorder affecting multiple tissues in the joint, including the subchondral bone and synovium. Synovitis is now increasingly recognised to be involved in OA pathogenesis, with *in vitro* studies showing production and release of pro-inflammatory cytokines (such as interleukin (IL)-6, IL-8, and IL-17), infiltration of mononuclear cells, and increase angiogenesis. This study aimed to establish whether the pro-inflammatory cytokine IL-17 contributes to the inflammatory environment within the OA joint. We hypothesize that IL-17 can contribute to immune cell recruitment to the OA synovium and that IL-17 responsive stromal cell populations within the OA joint can further drive inflammation.

IL17RA and *IL17RC* mRNA were detected in cultured chondrocytes and synovial fibroblasts from end-stage OA patients. IL-17 receptors, IL-17RA and IL-17RC, were detected by immunohistochemical staining in synovial tissue sections derived from injured and early-stage OA patients. Protein expression of IL-17RA was significantly higher in patients with a high synovitis score compared to a low synovitis score ($p=0.012$). IL-17RA staining showed a trend towards correlation with CD68 ($p=0.07$) and correlated significantly with CD206 staining ($p=0.004$). IL-17RC demonstrated a trend towards significance with CD206 ($p=0.053$). FACS data confirmed the presence of CD206+ macrophages in freshly isolated synovium from end-stage OA patients. RNA-Seq analysis showed that 24h treatment of 10ng/ml rh-IL-17A in cultured synovial fibroblasts and chondrocytes from end-stage OA patients significantly upregulated mRNA expression of several granulocyte-related chemokines such as *CCL2*, *CXCL3*, *CXCL6*, and *CXCL8*.

In conclusion, this study shows that IL-17 may contribute to the inflammatory environment in the joint by acting on synovial fibroblasts and chondrocytes to driving mononuclear cell influx. As IL-17 responsive cells are correlated with macrophage populations, IL-17 may be able to further drive inflammation by acting on these inflammatory cells as well as on synovial fibroblasts and chondrocytes.

P80 Participation of Wnt signalling pathway on osteogenic potential of titanium with nanotopography

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Objectives: The Wnt signal transduction is crucial for cell differentiation and homeostasis of adult tissues, including bone. It is well established that titanium (Ti) with nanotopography favours osteoblastic differentiation by modulating integrin and bone morphogenetic protein signalling pathways. However, few studies have addressed the role of Wnt on osteoblast response to nanoscale topographies. Therefore, we aimed at investigating the participation of Wnt signalling pathway in the osteogenic potential of Ti with nanotopography.

Methods: Ti discs were treated with sulphuric acid/hydrogen peroxide solution to produce nanotopography (Ti-Nano) and discs without treatment were used as control (Ti-Control). MC3T3-E1 cells were cultured on both surfaces to evaluate the effect of Ti-Nano on the expression of genes related to canonical Wnt/β-catenin and non-canonical Wnt/Ca^{2+} signalling pathways. Based on real-time PCR data, the most intensely modulated genes by Ti-Nano, the Wnt/β-catenin pathway-related *Fzd4*and Wnt/Ca^{2+} pathway-related *Fzd6*, were selected and silenced by CRISPR. Then, we investigated the effect of both silencing on osteoblastic differentiation of cells grown on Ti-Nano and Ti-Control. The whole set of experiments were repeated at least twice in triplicate (n=3) and the data were compared by Student's t-test or one-way ANOVA ($p \leq 0.05$).

Results: *Fzd4* gene silencing impaired the osteoblastic genotype and phenotype expression, corresponding to the negative regulation of Wnt/β-catenin targets in cells grown on Ti-Nano on day 5. *Fzd6* silencing also inhibited the osteoblastic genotype and phenotype expression; however, Wnt/Ca^{2+} pathway targets were not changed, but a lower expression of β-catenin protein was detected in cells grown on Ti-Nano on day 3, as wells as a higher expression of phospho-β-catenin protein. It is worth of note that these inhibitory effects on osteoblastic differentiation were more pronounced in cells grown on Ti-Nano compared to Ti-Control.

Conclusion: These results indicate that the higher osteogenic potential of Ti-Nano is, at least in part, due to the activation of Wnt/β-catenin signalling pathway, since *Fdz4* and *Fzd6* gene silencing significantly impaired the osteoblastic differentiation of cells grown on Ti-Nano compared to Ti-Control. These findings shed light on the understanding of intracellular mechanisms triggered by nanoscale surfaces to drive the osteoblast fate to accelerate/enhance the process of implant osseointegration.

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P81 WITHDRAWN.

P82 On the SLM and EBM of Ti-6Al-4V ELI alloy for advanced knee arthroplasty

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Introduction: Total knee joint arthroplasty surgery is very common orthopaedic procedure that treats end-stage degenerative osteoarthritis. The articular surface of a musculoskeletal joint is replaced with metal and plastic components, remodelled, or realigned by osteotomy or some other procedure.

Objectives: Research and development of a novel implant knee design and insertion technology, preservation of original healthy bone, light mass of the implant, prolongation of time for re-operation. Optimisation of technological routines for production of samples made from Ti6Al4V ELI powder suitable for knee implant production, testing of dimensional accuracy, quality, mechanical and fatigue properties, production of implant prototypes.

Methods: Selective Laser Melting (SLM) and Electron Beam Melting (EBM) of the Ti6Al4V ELI alloy, advanced machining, analytical electron microscopy, mechanical, tribological and fatigue testing were used as principal techniques. Two series of solid cylindrical specimens (diameter 14mm, length 120mm; 24 bits) were made for the standard mechanical testing. Several samples of knee implants have been made and tested also.

Results: Both additive technologies proved to be competitive for the knee implant production. The EBM technology allowed a production of very fine structured materials with a low porosity (<0.1%), high mechanical properties of Ti6Al4V (tensile strength more than 1,000 MPa, elongation more than 12%), tumbled glossy surface (Ra<0.03) mm, and better fatigue resistance (tension/thrust mode). A statistically significant low coefficient of friction on high molecular polyethylene ($m<0.03$, $p<0.01$) compared to the standard polishing was found due to smooth surface topography of samples.

Conclusion: The novel design of the knee implant, digital technologies, EBM technology and surface post-processing of Ti6Al4V, allow to reduce the weight of the novel type of the distal femur implant (> 60%) with a higher preservation of the original bone. The EBM samples showed a better combination of tensile strengths, plasticity and fatigue resistance.

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P83 Cellular behavior of osteoblast on Nanoconvex and Nanoconcave textured titanium surfaces

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Objectives: Cells initial attachment to implant surface is vital for osteointegration and in vivo performance of orthopaedic implants(1). However, the problem of cell-material interactions are still largely unresolved(2). The cell attachment process involves biomolecules interactions on implant surface and the morphology of material surfaces also affect proteins adhesion. We have developed novel nano-textured surface with aim to enhance cells attachments.

Methods: Electrochemical anodization method was applied to generate nanoconvex and nanoconcave on titanium surface. SEM and AFM were used to characterise the topography. Human osteoblasts were seeded on both surfaces at cell density of 1000/cm2. After 12 hours culture, the cell spreading area, shape (aspect ratio), filopodia/lamellipodia were examined by SEM. The cytoskeletal proteins such as actin, were observed by confocal. Further, combined with experimental data, Laplace in spherical equation was taken into account to calculative analysis electrostatic attractive force to proteins.

Results: The nanoconvex and nanoconcave, sized in the range of 50 nm to 80 nm in diameter, textured surfaces were successfully generated on Titanium surface, as confirmed by SEM and AFM analysis. It was observed that osteoblasts exhibited different attachment patterns on the two textured surfaces. Significant filopodia formation on nanoconcaved surfaces. The spreading area of cell on nanoconcave were three to five times than area on nanoconvex. However, lamellipodia was spreading more on nanoconvex surface.

Conclusion: The cellular behavior of osteoblasts on these textured surfaces were investigated. The results demonstrated that nanoconvex surface has potential to induce cells migration, while as nanoconcaved surface enhanced cell adhesion and spreading.

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P84 Morphological evaluation of subchondral trabecular bone in the talocrural joint

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Characterising the microarchitecture of subchondral bone provides an insight to bone quality, aiding surgical planning or evaluating the effects of disease. Little literature exists on the morphological properties of subchondral bone in the ankle. Hence, this study characterised the morphology of bone in the distal tibia and talus in non-diseased ankles.

Nineteen cadaveric specimens (REC MEEC 15-020) were imaged using HR-pQCT (XtremeCT, ScanCo, N=16: 123 µm, N=3: 82 µm). Cylindrical volumes (6.5 mm Ø and length) of subchondral trabecular bone were extracted from the talar dome (N=6 per talus: posterior/anterior and medial/central/lateral), and the tibial plafond (N=4 per tibia: posterior/anterior and medial/lateral). Key morphological indices (BV/TV, DA, Tb.Th and Conn.D) were evaluated using BoneJ(1). F-tests and Student's T-tests were employed to establish equality of variances and differences of means in the datasets. A Bonferroni correction was implemented, with a non-adjusted criterion of $\alpha = 0.05$.

Across the talar dome, little variation was observed for BV/TV (0.48 ± 0.02) and Tb.Th (0.46 ± 0.02 mm), with the highest variations observed in DA (0.50 ± 0.09, CoV = 18.01%) and Conn.D (2.36 ± 0.24, CoV = 10.09%). Examining regional differences, significant differences in DA were observed between medial and lateral areas (P=0.0002) and between anterior and posterior areas (P=0.0022). BV/TV (P=0.0002) and Tb.Th (P=0.0040) also varied significantly between anterior and posterior areas. Similarly, significant differences in DA were observed in the tibia between medial and lateral areas (P=0.0017). Across the tibial plafond, morphological values were of similar order to the talus, except for Conn.D (1.45 ± 0.11).

Significant variations to morphology, namely DA, were predominantly observed on the medial talar dome. DA is known to impact variations to bone stiffness in the ankle(2) and may suggest a link between morphology and the formation of osteochondral lesions, commonly observed on the medial aspect of the talus(3). Correlating mechanical properties to morphology may provide an insight to disease progression.

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P85 *Ex vivo* murine metatarsi cultures under quasi-static loading and mTOR/NF-kB treatment modulate endochondral ossification

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Osteoarthritis (OA), a chronic disease characterised by articular cartilage degradation, osteophyte formation and subchondral sclerosis, is the most common cause of pain and disability in adults. Recent research have highlighted the potential involvement of cartilage-to-bone transition in OA development, nonetheless its pathophysiology remains unresolved. Recent data indicate that mTOR and NF-kB pathways regulate cartilage-to-bone transition that is recapitulated in OA. The aim of the study was to determine whether regulators of these pathways interact with mechanical factors to control endochondral ossification (EO) processes that underpin cartilage-to-bone transition.

Metatarsi isolated from E17 mouse embryos (C57BL/6) were cultured for 2 weeks in alpha-MEM medium supplemented with 0.2% BSA, 5 µg/mL L-ascorbic acid phosphate, 0.05 mg/mL gentamicin and 1.25 µg/mL amphotericin-B. Metatarsi (n=10-17) were treated from day 0 of culture with inhibitors/activators of mTOR (100 nM rapamycin and 10 mM leucine) or NF-kB (2.5 µM betulinic acid and 20 µM SC-514). To explore whether mTOR/NF-kB pathway regulation interacts with mechanics to control EO, treated metatarsals were also cultured within a hydrogel to provide quasi-static mechanical loads. Total element length was measured using images collected at the start and end of the 2 week incubation period. Data were statistically analysed using a linear mixed effect model.

Metatarsi grown under control conditions expanded ~2.5 fold following 2 weeks of culture. Treatment with rapamycin/leucine and betulinic acid/SC-514 under aqueous conditions failed to modify length. When metatarsi were cultured in the presence of hydrogel, longitudinal growth was almost completely arrested ($p<0.0001$). However, metatarsi grown in hydrogel revealed a growth-promoting influence for both modulators of the mTOR pathway, which reversed the growth-restricting effects of culture in the presence of quasi-static loading ($p<0.05$).

These data reveal interactions between mechanical factors and mTOR/NF-kB pathways in the control of EO. Therefore, the role for these pathways in OA development requires interpretation in the context of the modifications in mechanical loading conditions that underpin pathological bone-to-cartilage transition.

P86 The development of a magnetic resonance scoring system for evaluating osteochondral healing in preclinical models – the 'AMOS' score

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Purpose: The purpose of this study was to create and assess the reliability of an Animal Magnetic resonance imaging Osteochondral Score (AMOS) to evaluate the healing of experimentally created osteochondral defects in preclinical models.

Materials and Methods: The AMOS score consists of an objective score and four subjective scores (integration, repair tissue surface, infill signal intensity and signal change outside surgical site). The AMOS score was applied to lesions in forty-six sheep using an ovine medial femoral condyle osteochondral defect model as an exemplar. These defects were subsequently evaluated histologically using the modified O'Driscoll score.

Results: The AMOS scores recorded ranged from 35 to 100. The AMOS score had 92.5% inter-rater reliability and 80% intra-rater reliability for the four subjective components. The mean inter-rater-reliability was 85% (+/- >1%) for integration; for intensity of infill, the mean inter-rater reliability was 95% (+/- 0%); the mean intra-reliability was 92.5% (+/- 2.5%) for repair tissue surface; and the mean inter-rater reliability was 97.5% (+/- 2.5%) for signal change outside the operated site. No correlation was found between the AMOS score and the modified O'Driscoll score.

Conclusions: The AMOS score had high inter-rater reliabilities, suggesting that it would be an effective scoring system. The AMOS score is a user-friendly semi-quantitative method of assessing osteochondral defect from magnetic resonance appearance for following ovine defect changes. The lack of correlation between AMOS and histological scorings reflects their different sensitivities to healing, suggesting that the AMOS score is complementary to histological evaluation.

P87 The presence of actin-rich cytoplasmic processes of chondrocytes within non-degenerate human femoral head cartilage

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It is well established that the morphology of articular chondrocytes within normal cartilage varies with depth. At the synovial surface, the chondrocytes are typically elliptical while with cartilage depth, their

morphology becomes spheroidal. However, by fluorescently-labelling *in situ* human femoral head cartilage chondrocytes and observing them using confocal laser scanning microscopy (CLSM), chondrocytes with long fine cytoplasmic processes extending into the extracellular matrix are frequently observed[1]. Here, we have determined whether actin is present in these processes.

Macroscopically non-degenerate human femoral heads from 8 separate patients with femoral head fractures were obtained with ethical permission and patient consent. The cytoplasm of *in situ* chondrocytes was labelled with CellTracker™ Green CMFDA (5-chloromethylfluorescein-diacetate) to determine cell morphology. Cryosections of cartilage were subsequently labelled with fluorescently-conjugated phalloidin, a high-affinity filamentous actin (F-actin) probe, and the cells visualised by CLSM[1]. Phalloidin fluorescence was then quantified in 3D (average fluorescence intensity per pixel; AFI/px) in regions of interest (ROIs) within chondrocytes of normal (rounded) and abnormal morphology (defined as possessing one or more cytoplasmic process).

Total fluorescence intensity of labelled phalloidin in chondrocytes of normal or abnormal morphology was not different (P=0.48; 21 normal cells *vs* 21 abnormal cells). However, there was significantly greater average fluorescence of ROIs within the cytoplasmic processes in abnormal cells compared to ROIs of membrane areas where no cytoplasmic processes were present (92 *vs* 129 AFI/px; P=0.000014; n=27). This suggests that while total F-actin levels were not changed in the abnormal cells, there was an accumulation of this structural protein within the processes.

These results indicate that changes to chondrocyte shape involve the active production of actin-enriched cytoplasmic processes. The resulting fibroblastic morphology is potentially important as there is a strong relationship between chondrocyte phenotype and cartilage matrix metabolism[2]. Chondrocytes with a fibroblastic morphology may produce a fibro-cartilagenous rather than a hyaline-like extracellular matrix, resulting in focal regions of mechanical weakness in otherwise non-degenerate, healthy cartilage.

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P88 Sonographic Bridging Callus: An early predictor of fracture union

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Background and Objectives: Ultrasound has the potential to detect early bridging callus prior to radiographs. This may have clinical application to confirm union or identify those at high risk of nonunion. There is currently a lack of agreed criteria for sonographic assessment of callus and reliability between reviewers.

The primary aim of this study was to determine objective criteria and reviewer agreement for assessment of sonographic bridging callus (SBC) on ultrasound.

Methods: A prospective cohort of conservatively managed displaced midshaft clavicle fractures underwent ultrasound scanning at three-, six- and 12-weeks post-injury. Five nonunions were matched against a control group of 15 unions.

The ultrasound scans were initially interpreted by two blinded reviewers to determine the most clinically relevant sonographic callus features with agreement assessed by weighted kappa. Interpretation at the fracture site was based on the sonographic detection of early fibrocartilaginous material and SBC. A further validation study was undertaken by four blinded reviewers using the intraclass correlation coefficient (ICC) using the most relevant findings of the initial pilot work.

Results: At three weeks post-injury fibrocartilaginous material was present in 80% (16/20) of patients. When detected this was associated with union (sensitivity 93%, specificity 60%, p=0.03) with the inter-observer agreement rated 'fair' on kappa (0.44).

At six weeks only 10% of patients had bridging callus on radiograph but 60% (12/20) had SBC on ultrasound and when present all united. When absent 63% of patients (5/8) developed a nonunion at six months post-injury (sensitivity 80%, specificity 100%, p=0.002). At twelve weeks, bridging callus was present on both radiographs and ultrasound in all patients that united (sensitivity 100%, specificity 100%, p<0.001). The SBC detection rated 'very strong' for intra- (kappa 0.92) and inter-observer agreement (kappa 0.84).

The ICC of six-week SBC detection with multiple blinded reviewers was 0.82 (CI 0.68-0.91).

Conclusions: Ultrasound evaluation of bridging callus at six weeks has excellent accuracy to predict union with strong reviewer agreement. This is the first study to establish time specific ultrasound fracture findings and assess the agreement between blinded reviewers.

P89 Correlation between different pain phenotypes and analgesic use: a prospective cohort study of patients suffering from knee osteoarthritis

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Objectives: Analgesic prescribing in knee osteoarthritis (OA) can be particularly challenging

owing to individuals presenting with different pain phenotypes. It has been suggested that in addition to the stereotypical inflammatory or nociceptive pain, some patients exhibit features of neuropathic pain. Catastrophic thinking has also been shown to impact pain experience. Here, we explored the relationship between different pain phenotypes and analgesic use in a cohort of patients suffering from knee osteoarthritis.

Methods: The Pain Catastrophising Scale (PCS), PainDETECT score and the Knee Injury and Osteoarthritis Outcome Score for Joint Replacement (KOOS, JR), all validated scoring tools in knee arthritis populations, were collected pre-operatively in a prospective cohort of patients undergoing Total Knee Arthroplasty (TKR). Medication prescriptions at the time of surgery were also extracted.

Results: Our analysis encompassed 150 patients undergoing TKR for knee osteoarthritis. Study participants were divided in 3 cohorts based on their emotional (PCS), neuropathic pain symptomatology (PainDETECT) and overall knee health (KOOS, JR) and the distribution of drug classes across each was analysed. The prescription of nonsteroidal anti-inflammatory drugs (NSAIDs), selective serotonin reuptake inhibitors (SSRIs) and anticonvulsants used for neuropathic pain was comparable among all groups. Patients with poor knee health (37.8% vs. 24.4%, p=0.211) and those with catastrophic thinking (44.4% vs. 22.2% p=0.108) showed a non-statistically significant trend towards increased opiate prescription. Acetaminophen was significantly more prevalent in the cohort perceiving their knee health as poor (39.5% vs. 15.8%, p=0.015), however no statistical difference was detected in patients with neuropathic components (39.5% vs. 21.1%, p=0.128) and pain catastrophisation (42.1%, 21.1%, p=0.162).

Conclusion: This study demonstrated the lack of a significant correlational relationship between the type of pain experienced and the analgesic prescribed. Identification of pain phenotypes via questionnaire use may provide better guidance on the type of pain relief required and permit more targeted pain management in individuals with knee osteoarthritis.

P90 Relationship between clinical characteristics and self-declared pain profiling in patients with osteoarthritis undergoing knee replacement surgery

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Objectives: The Pain Catastrophising Scale (PCS) and PainDETECT score are validated tools to assess emotional and neuropathic pain symptomatology, respectively. The Knee Injury and Osteoarthritis Outcome Score for Joint Replacement (KOOS, JR) assesses overall knee health on an inverse scale to the other measures. The aim of this study was to explore the relationship between clinical demographic characteristics in patients with osteoarthritis and different aspects of pain and function, as measured by these questionnaires.

Methods: PCS, PainDETECT and KOOS JR were completed pre-operatively on the day of surgery in 150 men and women undergoing knee replacement for idiopathic osteoarthritis. The relationship between individual scores and clinical characteristics was analysed by regression analysis, and the relationship between individual questionnaire scores by Spearman rank correlation.

Results: Mean age at time of surgery was 70.6 years (95% CI, 69.2 – 72.0) and 72 (48%) were female. The KOOS JR median (IQR) score was 42 (16), and ranged from 0 to 85; the median PainDETECT score was 12 (8, range 1 to 33); and PCS was 30 (35, range 0 to 88). Linear regression analysis found no relationship between age, gender and pain scores. A weak relationship was identified between BMI and PCS score (r^2=0.041, p=0.015) and an inverse relationship between BMI and KOOS JR score (r^2=0.063, p=0.002). Using Spearman's rank test, the correlation coefficient for the PainDETECT and PCS was 0.522 (p<0.001), demonstrating a moderate positive relationship, and for the KOOS JR (a score of knee health) and PainDETECT -0.57 (p<0.001), indicating a moderate negative relationship. The analysis between the PCS and KOOS JR yielded a correlation coefficient of 0.63 (p<0.001), a strong negative relationship.

Conclusion: In this study we found co-existence of neuropathic components and pain catastrophising and highlighted their negative correlation with perceived 'knee health'. We also found a weak relationship between BMI and emotional symptomatology and its inverse relationship with knee health. Further work to confirm these relationships and their mechanisms may help tailor interventions to improve perceived knee health.

P91 The most comprehensive tribological assessment to date of PEEK-based materials as potential hip replacement bearing surfaces

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Background: Optimum hip replacement bearings should be virtually non-wearing, low-friction, generate bio-inert wear particles and tolerate non-optimum surgical positioning (e.g. positioning outside Lewinnek's "safe zone" is now advocated to reduce the dislocation risk in spinal fusion patients).

This study assessed wear, friction and wear particles of PEEK-based materials under normal and non-optimum (adverse) conditions (control: XLPE).

Methods: As per power assessment, 3-4 samples

per combination were tested.

Simple Geometry Wear: Unfilled PEEK, CFR-PEEK (carbon-fibre-reinforced) and XLPE articulating against high carbon (HC) CoCr and Biolox Delta ceramics were wear tested in pin-on-plate machine for one million cycles (MC) at 1.6-8MPa.

Complex Geometry Wear: CFR-PEEK acetabular cups were wear tested against 36mm Biolox Delta heads in ProSim hip simulator in optimal, then in edge loading conditions (6MC in total).

Friction: This was assessed in a POP friction machine at 1.6-8MPa.

Wear Particles: Wear particles were assessed according to ISO 17853 and ASTM F1877.

Results:
Simple Geometry Wear: Unfilled PEEK exhibited high wear and was deemed unsuitable bearing. CFR-PEEK wear factors were extremely low; 0.49, 0.92 and 2.00x10^{-7}mm^3/ Nm when articulating against HCCoCr; and 1.63, 1.29 and 0.82x10^{-7}mm^3/ Nm when articulating against Biolox Delta at 1.6, 4 and 8MPa respectively.

Complex Geometry Wear: CFR-PEEK cups exhibited extremely low wear in optimum and edge loading conditions. Carbon fibre (CF) pull-out was noted; no fatigue fractures were noted on micro-CT.

Friction: Regardless of CF reinforcement, counterface material or contact pressures, PEEK-based bearings had always two to three-fold higher friction coefficient than XLPE (p-values<0.001).

Wear Particles: In the presumed biologically active size range (0.1-1 µm), unfilled PEEK had the highest particle area distribution (62%); followed by XLPE (38%) and CFR-PEEK (32%). XLPE particles were more likely to be smaller than CFR-PEEK (p-value<0.0001).

Conclusion: This is the most comprehensive tribological assessment of PEEK-based hip bearings to date. CFR-PEEK *vs.* Biolox Delta ceramics is a low wearing, high friction combination even under adverse conditions with potentially low bioactivity wear particles. This bearing may accommodate the current demand for non-optimal surgical positioning in certain patient populations.

P92 Effects of Matrix Stiffness on Osteoblast Differentiation from Pluripotent Stem Cells

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Directed differentiation of pluripotent stem cells are promising approaches to generate specific lineages and to facilitate restoration of tissue defects. We have previously developed a step-wise, serum-free differentiation protocol using various recombinant factors to induce mouse embryonic stem cells (ESCs) to somatic mesoderm and bone/cartilage cell lineages, and have explored the role of Rho Kinase (ROCK) signaling. Recent studies showed that stem cells can respond to biophysical cues, whereby they are able to perceive the mechanical properties and stiffness of their substrate and differentiate accordingly. We have investigated the role of substrate stiffness in combination with BMP and ROCK signaling in the commitment of pluripotent mouse ESCs to the osteoblast lineage.

We first used primary mouse calvarial osteoblasts to investigate the effects of matrix stiffness on committed osteogenic precursors. We plated osteoblasts on collagen-coated polyacrylamide (PA) gels with matrix elasticities of 0.5, 2 and 40kPa in the presence or absence of BMP-2 and the ROCK inhibitor Y-27632 and analysed bone nodule formation by alkaline phosphatase and von Kossa staining. In control cultures on a plastic substrate, inhibition of ROCK with Y-27632 promoted nodule formation. This was further enhanced by pre-treatment with BMP2 and this was confirmed by qPCR analysis of the osteogenic markers RUNX2, osteocalcin, BSP and ALP. On PA gels, osteoblasts remained rounded on soft (0.5, 2kPa) substrates and failed to form bone nodules, and the addition of Y-27632 rescued the spreading of osteoblasts but not their ability to form nodules. Notably, BMP2 pre-treated osteoblasts spread well on soft gels (2kPa), although this spreading alone also did not stimulate osteogenesis. However, a combination of both BMP-2 and Y-27632 rescued both spreading and nodule formation at low stiffness (2kPa) and enhanced nodule formation at high stiffness (40kPa). Preliminary experiments using mESC-derived osteoblastic cells has similarly shown that cells remain rounded on soft substrates (2kPa) and that ROCK inhibition rescues cell spreading. We are currently investigating the effects of ROCK and BMP signaling on mESC-derived osteoblast nodule formation to provide further insights into mechanical and biochemical factors control osteoblast differentiation.

P93 Disuse does not alter trabecular rod and plate distribution in mouse tibiae

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SMI is the *de facto* standard for analysis of trabecular rods and plates in osteoporotic bone, despite being biased by the presence of concave surfaces (of which there are many in trabecular bone) strongly correlated with bone volume fraction.

An alternative way to measure rods and plates in trabecular bone is Ellipsoid Factor (EF), an algorithm that classifies foreground voxels in three-dimensional scans of trabecular bone based on the geometric properties of the locally largest ellipsoid in volume. EF assigns a value between -1 and 1 to each

trabecular voxel: the closer to -1, the more plate-like the local geometry, and the closer to 1, the more rod-like the local geometry, with numbers in-between placing trabecular voxels on a spectrum between rods and plates. We aimed to investigate changes in trabecular rods and plates using SMI and EF in a model of disuse osteoporosis.

We scanned murine tibiae *ex vivo* using X-ray microtomography at 4.9 micron voxel size. Separate scans were taken 5, 35, and 65 days after a sciatic neurectomy to the right hindlimb had induced unilateral osteoporosis in the animals. We segmented proximal metaphyseal trabecular bone from left and right tibiae and measured EF distribution, SMI and bone volume fraction (BV/TV) using BoneJ2.

Bone volume fraction measurements confirm severe disuse osteoporosis in the neurectomised limb (BV/TV significantly lower in right limb at all time points, $p<0.05$). SMI consistently increased in the disuse tibia compared to the control tibia ($p<0.05$). Normalised EF distributions do not differ between osteoporotic and healthy limb in the same animal at any time point during disease progression (Kolmogorov Smirnov test, $p>0.7$ in all cases).

All EF distributions are unimodal and approximately centre around EF = 0 (i.e. neither rod nor plate) with no skew, suggesting binary distinctions between rod- and plate-like trabeculae are arbitrary. There is no indication that the trabecular local shape of mouse tibiae changes with osteoporosis progression beyond the loss of bone mass. SMI is a misleading measure of trabecular organisation and should not be used.

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P94 Investigation of Ankle Fractures, Readmission and Risk Factors

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Objectives: To examine the readmission rates for ankle fracture patients focusing on risk factors, overall outcomes, and complications.

Method: This study focuses on patients admitted to the orthopaedic service of Cork University Hospital over a one year period (2014) with a special interest in ankle fracture. After retrieving the sample from a HIPE database search. Statistical analysis and inclusion/exclusion criteria were applied.

Results: Study examined ankle Fracture patients over the 10-year period, there were 1,697 admissions relating to 1,579 unique patients. Seventeen independent variables were included in the model. The full model containing all predictor variables was statistically significant in predicting readmission, $\chi2 = 202.856$ ($p < 0.001$, 17 degrees of freedom, n = 1697). The model correctly classified 87.7% of readmission cases (sensitivity = 10.6%, specificity = 98.5%, positive predictive value = 50.0%, negative predictive value = 88.7%).

Six of the predictor variables made unique statistically significant contributions to the model. Having a primary diagnosis that was not an ankle fracture was the strongest single predictor of readmission (OR = 2.875, 95% CI = 1.370 – 6.035). Cases in which ankle fracture was managed via closed reduction were also significantly related to readmission (OR = 1.852; 95% CI = 1.105 – 3.104), when controlling for other factors in the model. Other factors which uniquely contributed to an increased likelihood of readmission were injury caused by external mechanical forces (OR = 1.806; 95% CI = 1.039 – 3.141) and current tobacco use (OR = 1.684; 95% CI = 1.111 – 2.551).

Conclusions: This study demonstrates the importance of controlling post-operative complications in ankle fracture surgery. Readmission rates can be prevented with identification of high-risk patient groups such as associated with causes of delayed wound healing such as smoking, diabetes, and raised BMI. Ankle Fracture management is dependent on the type of fracture and mechanism of Injury. Readmission profile is essential if strategies are to be developed to reduce cost and surgery time within hospitals.

P95 Identifying multiple adipocyte phenotypes in osteoarthritic and control femoral heads

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Bone marrow adipose tissue (BMAT) constitutes 10% of all adipose tissue found in the human body. There are three known types of adipocyte: white, beige and brown. BMAT has previously been described as a heterogeneous mix of adipocytes, however, this has not been quantified. BMAT in osteoarthritic (OA) patients typically has an increased number of adipocytes, though whether there is a change in the types of adipocyte present has not been demonstrated. This study aimed to identify and quantify the types of adipocyte present in OA BMAT and in the BMAT of patients without OA (control).

Human joint samples from 27 patients (12 control, 14 OA) were obtained with informed consent from patients undergoing joint surgery at University Hospitals of Morecambe Bay NHS Trust. North of Scotland NHS Research Ethics Committee approved this research. Samples were prepared for routine histological analysis and flow cytometry.

Flow cytometric analysis gated cells by size and lipid content. Adipocyte types were identified by using adiponectin (Acrp30), uncoupling protein 1 (UCP1) and myogenic factor 5 (Myf5) as adipocyte

cell markers. The data analysis showed an approximate 9:1 ratio of white to beige adipocytes found within BMAT, with only trace amounts of brown adipocytes identified. ANOVA analysis to account for disease, age and biological sex demonstrated no significant difference in the adipocytes present between control and OA samples. However, male sex and ageing were shown to be significant factors for an increase in beige adipocytes. These results were corroborated with immunohistochemistry of paraffin cut sections to validate the flow cytometric analysis. The anatomical location of the adipocyte type was also recorded. The histological study showed that beige adipocytes were found closer to the bone surface than the centre of the bone marrow adipose tissue.

This research gives a quantitative method of identifying different types of bone marrow adipocytes. Understanding changes in the anatomical composition of BMAT and the role of adipocytes in skeletal health may prove important in understanding the progression of age associated bone disorders.

P96 Relationship between standardised uptake values, Hounsfield Units and bone density value in the lumbar spine: a study in alkaptonuria subjects using 18 F-NaF PET/CT and DEXA scan

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Aim: Alkaptonuria (AKU) is a metabolic bone disease characterised by elevated homogentisic acid (HGA), which causes severe osteoarthropathy. This study aimed to clarify the differences in 18F-NaF uptake and bone attenuation coefficients according to the bone densitometry reports at the lumbar spine levels (L1-L4) using semi-quantitative maximum standardised uptake values (SUVmax) and Hounsfield Units (HU) from PET/CT images.

Methods: We analysed the data of 38 patients with alkaptonuria 50.3 ± 10.9 years old who underwent 18FNaF PET/CT and DEXA scans. To determine HU, ROI was drawn covering the trabecular bone region in the sagittal slice section at three different anatomical locations. The exact ROI was copied to PET images to measure the SUVmax. The average HU and SUVmax for each lumbar level were generated.

Results and discussion: According to the DEXA report, thirty-one patients (75.6%) of the 38 AKU patients had a normal bone mineral density at the average lumbar vertebral body (L1-L4), noting that mean SUVmax value measured from PET was 12.22 ± 38.9 and mean HU measured from CT was 159.1 ± 82.7. Five patients (12.2%) had osteopenia, with measured SUVmax of 11.54 ± 3.9 and mean HU of 99.6 ± 38.9. Only one patient (2.4%) had osteoporosis at lumbar spine with SUVmax 9.99 and mean HU 18.2. There was a moderate correlation between SUVmax and T-score at L1 and L2 ($p < 0.05$), and no clear correlation at L3 and L4 ($p = 0.67$ and 0.63). A strong relationship was noted between HU and T-score ($p < 0.001$). SUVmax at lumbar vertebral bodies proportionally increases at the higher values of vertebral HU. These observations were more significant in L1 and L2 and less so at L3 and L4.

Conclusions: Lower bone mineral density at the lumbar spine was associated with decreased 18F-NaF uptake in PET imags and less bone attenuation coefficients in CT images. Radiographic quantitative methods from 18F-NaF PET/CT can highlight areas of higher bone metabolism and give structural information in AKU patients.

P97 The prevalence of coronal tibial bowing in a Western population

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Objectives: The anatomical and mechanical axes of the tibia in the coronal plane are widely accepted to be equivalent. This philosophy guides the design and placement of orthopaedic implants within the tibia and in both the knee and ankle joints. However, coronal tibial bowing may result in a difference between these axes and cause suboptimal implant placement. Although the prevalence of tibial bowing has been reported in Asian populations, no exploration of this phenomenon in a Western population has been conducted.

Methods: This was a retrospective cohort study using anteroposterior long leg radiographs. Using a technique previously described in the literature, two lines were drawn, each one third of the length of the tibia. The first was drawn between the tibial spines and the centre of the proximal third of the medullary canal. The second was drawn from the midpoint of the talar dome to the centre of the distal third of the tibial medullary canal. The angle subtended by these two lines, if more than two degrees, determined the presence of bowing. The apex of the bow determined whether it was medial or lateral. Ten percent of measurements were repeated by a single observer and two further observers to allow calculation of intraclass correlation coefficients (ICCs).

Results: A total of 975 radiographs were reviewed. 399 (40.9%) tibiae were bowed, 232 (23.8%) were bowed medially and 167 (17.1%) were bowed laterally. The mean bowing angle was 3.51° (s.d. 1.24°) medially and 3.52° (s.d. 1.33°) laterally. The distribution of bowing angles followed a normal distribution, with the maximal angle observed 10.45° medially and

9.74° laterally. An intraobserver ICC of 0.97 and a mean interobserver ICC of 0.77 indicated excellent reliability.

Conclusions: This is the first study reporting the prevalence of tibial bowing in a Western population. In a significant proportion of our sample, there was divergence between the anatomical and mechanical axes of the tibia. Further research is necessary to investigate whether prosthetic implantation based on the mechanical axis in bowed tibias results in suboptimal implant placement and adverse clinical outcomes.

P98 Hydroxyapatite surface properties determine mesenchymal stromal cell proliferation via the Wnt signalling pathway

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Objectives: Plasma-sprayed hydroxyapatite (HA) surfaces are designed to encourage osteointegration of orthopaedic implants, such as those used to treat severe osteoarthritis (OA). However, the biological effects of different HA surfaces on resident mesenchymal stromal cells (MSCs) has not been determined. We use an efficient design of experiments approach to test the effect of plasma sprayer settings on material properties and Wnt-mediated proliferative responses in MSCs.

Methods: HA coatings were created by industry standard plasma spraying on surgical grade titanium discs. Parameters tested were plasma flow, spindle speed, HA powder feed and carrier gas rate, each at low, medium and high levels, resulting in 17 different surfaces, which were characterised by contact profilometry (roughness) and X-ray diffractometry (crystallinity). Wnt responses were determined using an eGFP-Wnt reporter MSC line and a Wnt QPCR array. Proliferation was measured using a RealtimeGlo assay in the presence and absence of Wnt antagonist (XAV939).

Results: HA surfaces could be predictably changed by altering plasma gas flow to produce a range of roughnesses (mean surface roughness: 8.8µm-15.6µm; maximal peak heights: 29.5µm-69.4µm; maximal valley depths: 33.1µm-63.3µm). Higher flow rates increased crystallinity, although powder feed rate dampened this effect. On plastic, Wnt3a caused a 2.5-fold increase in MSC Wnt reporter activity, compared to untreated controls. MSC Wnt3a responses were of the same magnitude on 9 of the 17 HA-coated surfaces, but increased to 5-7.5-fold increase on HA surfaces 1-3 and 9-13; an effect determined by the feed rate and carrier gas flow. By QPCR we identified an upregulation of non-canonical, and downregulation of canonical Wnt-related genes in MSCs on HA surfaces in response to Wnt3a. MSC proliferation was either stimulated or inhibited by XAV939, depending on the surface, demonstrating a link between HA surface properties, Wnt signalling and MSC growth, and these effects were driven by a combination of plasma gas flow, carrier gas glow and powder feed rate.

Conclusions: HA surfaces have a significant, Wnt-mediated effect on MSC proliferation, which we have modelled to plasma spraying parameters, allowing fine-tuning of MSC responses. Parameters that affect proliferative behaviour of MSCs similarly affect HA surface roughness and crystallinity, suggesting a causative link.

P99 Preliminary study on the use of 3D printed models in the pre-operative planning of revision ACL reconstruction

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Revision anterior cruciate ligament (ACL) reconstruction is a technically demanding procedure, reporting poorer outcomes compared to the primary procedure. Identification of the cause of primary failure and a thorough pre-operative evaluation is required to plan the most appropriate surgical approach. 3D printing technology has become increasingly commonplace in the surgical setting. In particular, patient-specific anatomical models can be used to aid pre-operative planning of complicated procedures. We have conducted a qualitative study to gauge the interest amongst orthopaedic knee surgeons in using a 3D-printed model to plan revision ACL reconstructions.

A tibia and femur model was printed from one patient who is a candidate for the procedure. The binder jetting printing technique was performed, using Visijet PXL Core powder. 12 orthopaedic knee surgeons assessed the usefulness of the 3D-printed model compared to conventional CT images on a likert scale. 6 key steps of preoperative planning were assessed, including the size and location of the tunnel defects, the need for notchplasty, and whether a staged revision was required.

We found that surgeons preferred the 3D-printed model to conventional CT images only, and 92% of them would use such a model for both pre-operative simulation, and as an intra-operative reference. However, there were some variation in the perceived usefulness of the model in several areas assessed. This may reflect differences in individual's approach towards planning of the procedure.

Our findings suggest that 3D-printed models could be a versatile pre-operative and intra-operative tool for complicated arthroscopic knee surgery. While 3D printing technology is becoming increasingly accessible and affordable, in-depth cost-effectiveness studies need to be conducted before it can be

integrated into clinical. Further study would be needed to determine the clinical utility and economic cost-effectiveness of the 3D-printed model in revision ACL reconstruction.

P100 Modelling the effect of bone damage on creep deformation in human vertebrae

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Osteoporotic vertebral fractures are common, and some continue to collapse over time, resulting in spinal kyphosis. How to predict such creep deformation of a fractured vertebra, although clinically important, remains unstudied. The purpose of this study was to develop a mathematical model to depict the quantitative relationship between initial bone damage and creep deformation in human vertebra. Based on the Kachanov's creep damage theory, the predicted variable in the model is creep rate after fracture, and the predictor variables are creep rate before fracture and the degree of vertebral bone damage. The model is defined by a parameter that quantifies how bone damage affects creep rate. Two sets of in-vitro mechanical test data, based on 37 vertebral trabeculae samples and 38 motion segments of human spines, respectively, were analysed to obtain creep rate after fracture, creep rate before fracture, and bone damage. These measurements were fed into the model to estimate the model parameter. As vertebral bone damage consists of trabecular bone damage, cortical bone damage, and endplate damage, the modelling process was designed to differentiate how each of them contribute to the model parameter. In the first stage, experimental data on 37 samples of vertebral trabeculae were used to determine the model parameter, which reflected the contribution of trabecular bone damage. In the second stage, experimental data of 38 motion segments were used to determine the model parameter and to further examine how cortical bone damage and endplate damage affect the model parameter. In both stages, model parameters were determined using curve-fitting through regression analysis. The model parameter was estimated to be 1.31 (model $R2 = 0.72$, $p < 0.001$) in the first stage and 2.67 in the second stage (model $R2 = 0.26$, $p = 0.001$). Further analysis showed that cortical bone damage and endplate damage did not have significant moderation effect on the model parameter ($p > 0.05$). The established model can be used to develop a clinical tool to predict whether a patient with vertebral fractures is at risk of progressive vertebral collapse.

P101 In-Silico Models to Investigate Bone Marrow Lesions

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Introduction: Osteoarthritis (OA) affects more than four million people in the UK alone(1). Bone marrow lesions (BMLs) are one feature of subchondral bone involvement in OA. BMLs are radiological features defined on fat-suppressed T2 MRI images as areas of ill-delineated hyper signal intensities in comparison to unaffected areas(2) suggesting a change in material properties in the affected regions. Both bone volume fraction and mineral density within the lesion have been seen to alter(3).

The aim of this study was to develop a finite element (FE) model of the knee joint to enable the mechanical effects of BMLs to be investigated.

Methods: FE models of a right human tibiofemoral joint were created from the Open Knee Generation 1 Specimen 1(4). Each model was manipulated in ScanIP (Synopsys-Simpleware, UK) to incorporate a BML. For this study, a spherical defect with 6mm radius was created in the tibia, initially centred 7mm below the surface of the bone beneath the contact region. Models were tested under a representative physiological load, and the effects of changes in the material properties and location of the defect on the contact pressure were investigated.

Results: For the initial defect location, there was little change in the maximum contact pressure of the defect when the elastic modulus was halved or doubled (<2%). Changes in the location of the defect appeared to have a greater effect, influenced by distance below the bone surface and proximity to the centre of contact.

Conclusion: A finite element model of the tibiofemoral joint was created with the ability to investigate the mechanical effect of size, location, and material properties of bone defects. Preliminary results indicate that the location of the defect is an important factor in governing the effect on the contact mechanics. The model provides the capability to more extensively examine the behaviour across the complex and varying shape of the joint.

Funders: *EPSRC, NIHR.*

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P102 Self-reported Mobility in Adults with Osteogenesis Imperfecta

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Objectives: While fractures are a recognised complication in osteogenesis imperfecta (OI), there is a paucity of data describing the impact of OI on mobility in adulthood. We describe differences in mobility by type of OI in adults and its wider impact on quality of life.

Method: Adults with OI were recruited via the Rare and Undiagnosed Diseases Study (RUDY), a web-based platform for patient recruitment. Participants completed a generic tool for mobility (EQ5D-5L), and other patient reported outcome measures (Pain - PainDetect; Fatigue - FACIT-F; depression and anxiety – HADS). Scores were compared using Kruskal Wallis, Spearman's correlation and by type of OI.

Results: 87 adults with OI completed the questionnaires (38 with Type 1, 11 with Type 3, 10 with Type 4 and 28 without reporting an OI type). 73% were women with a mean age of 44 years (age range 18 to 75 years). Mobility was a severe/extreme problem for 16% of people with type I OI, 67% of Type III, 50% of Type 4 and 41% of an unknown OI type using the EQ5D-5L. Reduced mobility was associated with fatigue (FACIT-F; r=0.444, p=<0.001), and pain (PainDetect; r=0.383, p=0.001), whereas no relationship were found with depressive and anxiety symptoms as measured by HADS. Compared to those with no or light problems, even moderate limitation in mobility was associated with more severe pain (31.6±12.3 vs 17.8±10.5 p=0.032) and fatigue (37±11.9 vs 27±15.4, p=0.001).

Conclusion: As expected, higher rates of mobility restriction were reported by Type III and IV OI. However, severe limitations in mobility were also reported by a minority of patients with Type I OI as well as those unable to classify their OI type. Reduced mobility was associated with a higher level of pain and fatigue but not with emotional distress. Further work is needed to understand the underlying mechanisms, such as recency of fracture, to inform clinical management and development of novel treatment approaches as well as examining the value of a person knowing their type of OI.

P103 Freeze-thaw cycle enhanced decellularization of osteochondral tissue

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Objectives: As a promising technique for osteochondral defects repair, allogeneic osteochondral scaffold (AOS) can be processed to match the defect precisely without risk of immune rejection and disease spreading, with easily available graft sources. However, the current methods of AOS developments are generally complicated (Benders et al., 2013; Crapo et al., 2011). This study aims to develop an efficient method with good in vitro biological performance for decellularization of osteochondral tissues.

Methods: A hollow core drill was used to core a cylindrical osteochondral tissue specimen (10 mm in both height and diameter) out, from specific areas of porcine hind legs. After washing with PBS, those cylinders underwent freeze and thawing cycles followed by a detergent to lyse cell membrane. DNase was used for breaking down the DNA fragments. In the process, the structural integrity of the osteochondral tissue could be maintained by the pH value regulation. Decellularization was confirmed by histological/immunohistological staining. Compressive test, nanoindentation test and Scanning Electron Microscopy (SEM) were used to examine the properties and structure of resultant tissues. Cell viability assay (cell counting kit 8) was used to confirm biocompatibility.

Results: It is revealed that between the H&E staining sections before and after decellularization there are obvious differences, which showed the cells nuclei had been removed from the osteochondral tissue, both cartilage and bone components completely, as confirmed by immunohistochemistry examinations. For mechanical properties, there was no significant difference in the Young's modulus, maximum compression strength and yield strength of AOS, and the structure of matrix could be well preserved as confirmed by SEM examinations. The cell viability assay indicated that the decellularized AOS had good biocompatibility without cell toxicity.

Conclusion: By this developed method, the enhanced decellularized AOS has been successfully produced without using protease inhibitor cocktail and phenylmethylsulfonyl fluoride (PMSF). Preliminary experimental verification has confirmed the cells nuclei in the structure were efficiently removed. This method reduced the interaction from seven days to five days and the cost by 90%. The resultant decellularized AOS has exhibited good biocompatibility and preserved the mechanical integrity of the osteochondral tissue.

P104 Comparing extracellular vesicles produced by bone marrow mesenchymal stem cells of human, ovine and bovine origin

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Objectives: In this study, we aimed to isolate extracellular vesicles (EVs) from bone marrow

Mesenchymal Stem Cells (MSCs) from various species and to characterise their EVs produced to MISEV2018 standards and to demonstrate interspecies EV uptake by chondrocytes.

Methods: MSC isolation and culture: Human bone marrow was collected from bone marrow transfusion washout bags. Bone marrow of ovine and bovine origin was aspirated from the femur. MSCs were expanded to passage 3. **EV Harvest;** Upon reaching 80% confluency, MSCs were cultured in serum free media for 48 hours. This media underwent differential sequential ultracentrifugation at speeds of 10,000g and 100,000g with the media being transferred into fresh centrifuge tubes between centrifugation steps. **Characterising EVs:** Transmission Electron Microscopy and flow cytometry enabled EV surface phenotypes investigations. **Flow cytometry**, EVs were coupled to aldehyde/sulphate latex beads before staining with anti-CD9 and CD63. **Protein:** Total protein was calculated using BCA assays and the presence of flottillin was demonstrated using western blotting. **Investigating EV size/concentration:** Data was gathered using a nanosight NS3000. **EV internalisation:** EVs were stained with PKH67 before co-culture with primary chondrocytes. Chondrocyte membranes were stained with WGA-55 and the nucleus with DAPI. EV uptake was assed via confocal microscopy and Z stack images.

Results: We obtained human, bovine and ovine bone marrow derived MSCs and demonstrated their tri-lineage potential and surface phenotype was in accordance with international standards. EVs derived from these MSCs were characterised to MISEV2018 standards via single and multiple EV analysis. We have shown human, bovine and ovine EVs are all of similar sizes (40nm-300), they have similar internal and external protein markers (CD9, CD63) however our data suggests that total EV protein levels differs between species. Via confocal microscopy, we have ascertained that EVs are readily internalised by chondrocytes regardless of EV species origin.

Conclusion: We have shown no observable differences in the proteomics of EV obtained from MSCs of different species and that EVs are internalised by chondrocytes regardless of species origin indicating that cross-species applications of EV are realistic.

P105 Microbiological culture findings of the femoral head as a prognostic factor for infection in primary hip replacement surgery

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Objectives: Musgrave Park Hospital operates a living donor bone bank, which, utilises femoral heads, harvested during primary total hip replacement surgery. This study examines whether a positive bacteriology culture at harvest predicts a subsequent infection or prosthesis failure in donors.

Methods: 12 year review of prospectively gathered data within regional bone bank, identifying all femoral heads discarded due to positive microbiology culture, in patients with a minimum 3 years follow up from primary surgery. Clinical review of paper and electronic records during perioperative period and subsequent outpatient follow up, including laboratory and radiological investigations. Information compared to ASA comparable hospital deep infection rates over 10-year period.

Results: 65 femoral heads identified (2003-2015), average age 63, ASA 2, 40% cementless implants. Cultured pathogens; 27 % Bacillus, 34% Staphylococcus, 11% Micrococcus, 12% Fungi, 11% unknown. 28% confirmed on repeated cultures (78% in Tryptose at 22C, none at 37 C and 22% in anaerobic Thioglycollate broth), 15% felt to be contaminate, 9% insufficient material for further testing. Samples arrived within 24 hours to labs, average time for full results including confirmation 18 days. Three early superficial wound infections, two required oral antibiotics, one intravenous, with no systemic upset or significant rise in inflammatory markers, total course 1 week. Positive and confirmed microbiology not significant for superficial infection using Chi-Square test P=0.147. No deep infections or revision surgery. Unit deep infection rate for ASA 1/2 THR's 0.43% cohort 10936 patients.

Conclusion: A positive microbiology culture at femoral head harvesting, employing modern aseptic techniques and laboratory testing is not always associated with elevated risks of infection or prosthetic failure after THR. Therefore, such findings cannot be used as a prognostic factor and this would support the limited published literature to date.

P106 The osteogenic potential of weight bearing impact movements in older women

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Moderate to high impact exercise increased femoral neck bone mineral density (FNBMD) and is recommended in bone health guidelines. Currently there is limited reference data to inform on which movements can be considered high, moderate or low impact. Strain magnitudes and rates, the key determinants of osteogenesis, cannot be measured non-invasively but are associated with ground reaction forces (GRF) which are thus used as surrogates for quantifying impact exercise intensity. The aim of this study is to measure the GRF and rate of force application (RFA) of impact movements in a group of older women to inform on which may be suitable for interventions to improve FNBMD.

Healthy women aged >55y were recruited from the

local community and asked to perform 19 movements on a force platform embedded in the floor. Participants were familiarised with each activity and three good trials recorded. Peak GRF of three trials was used in the final analysis. Raw data were normalised to participants' body weight and RFA was calculated by dividing the change in force from the start of the movement to peak GRF, by the time taken to reach peak vertical GRF. Wilcoxon signed-rank test was used to identify differences between the group means of GRF (BW) and RFA (BW/S).

Twenty-eight participants (age:77.0±0.9y BMI: 25.37±0.67kg/m^2) completed the study. One participant could not complete lateral jumps, another could not complete anterior-posterior hops and another could not complete a rocking step, otherwise all movements were completed (number of impacts = 2166). A single leg stamp (4.0±1.0BW) and countermovement jump (CMJ) (3.9±0.7BW) generated the vGRFs that were significantly higher than all other movements. The CMJ had the largest RFA (58.21±25.32BW/s) and was significantly higher than all other movements.

Multidirectional jumps(1) and hops(2) have both resulted in increases in FNBMD. This study found that stomps generated similar GRF and RFA to these movements. Although transmission of forces proximally may be less than in a jump, movements such as a stamp may benefit lower limb bone density in those unable to jump.

P107 Bone-targeting glycol chitosan-PLGA nanoparticles for alendronate delivery

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Osteoporosis is a major health burden. Current therapeutic treatments have disadvantages such as systemic side effect and low bioavailability. Bone-targeting drug delivery system are designed to improve the therapeutic effect of drugs and minimize the potential toxic side effects. We fabricated a novel nanocarrier for bone-targeting alendronate delivery using glycol chitosan (GC)-poly(lactide-co-glycolide) (PLGA) and PLGA-alendronate conjugates.

PLGA is a biocompatible, biodegradable and nontoxic material widely utilized to obtain nano- and microparticle drug delivery systems and has received worldwide marketing approvals. GC is a linear polysaccharide with potential for bone targeting because of positive charge. Alendronate sodium, a commonly used bisphosphonate drug for osteoporosis therapy, is also reported as bone-targeting ligand due to its strong affinity to hydroxyapatite mineral of the bone. Nanoparticles made of GC-PLGA and PLGA-alendronate were prepared using nanoprecipitation method. The size of the nanoparticles was determined by dynamic light scattering (DLS) measurement. The morphology of the GC-PLGA/PLGA-alendronate nanoparticles was examined by scanning electron microscopy (SEM). Drug release profile and cytotoxicity were evaluated *in vitro*. Bone-targeting potential was assessed by hydroxyapatite binding assay and cellular uptake assay.

The conjugation of GC-PLGA and PLGA-alendronate was confirmed by Fourier-transform Infrared Spectroscopy (FTIR) and nuclear magnetic resonance (NMR) analysis. The prepared nanoparticles are highly aqueous dispersible with an average size range from 90 to 130 nm based on various polymer ratio. Morphological characterization (SEM) revealed that the nanoparticles are spherical in shape. *In vitro* tests demonstrated good biocompatibility and sustained release of alendronate. Hydroxyapaptite affinity test and cellular uptake assay comfirmed the bone-targeting potential.

These results demonstrated that the PLGA-GC/PLGA-ALD nanoparticles may be a potential drug delivery system for the treatment of osteoporosis. Further study of hemocompatibility and biodistribution is warranted.

P111 Post-Operative Complications in Hip Fracture Surgery for Patients over 90 years old

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Objective: The geri-orthopaedic population has a high mortality in surgery due to multiple co-morbidities and risk factors, which can all adversely affect their outcomes. Assess patient risk factors in order to reduce mortality and identify causative factors.

Method: This study focuses on patients admitted to the orthopaedic service of Cork University Hospital over a one year period (2014) with a special interest in hip fracture. Patients 90 years of age or older were included in the study. After retrieving the sample from a HIPE database search, evaluation of the data collection sheet of potential parameters was carried out. Statistical analysis and inclusion/exclusion criteria were applied.

Results: Post-operative complications were the most important indicator of patient mortality. Type of fracture and treatment method were not statistically significant predictors for mortality. 69 patients were included in the study (n_{OA}= 69). Following this, seven independent variables were investigated: age, gender, type of treatment, type of anaesthetic, type of fracture, length of hospital stay, and complications post-operatively. The full model containing all predictors was not statistically significant in predicting

death at follow-up, χ^2= 15.622 (p = 0.209, n_{OA}= 69). There was an overall mortality rate of 21.7%. 15 patients in total. Those patients who did not survive, the experience of surgical complications was present in 86.7% of cases.

Conclusions: This study demonstrates the importance of controlling post-operative complications in hip fracture surgery for over 90's. Associations between mortality and age, gender, previous history of hip fracture, the type of injury, are presented. The sub-group of patients who had died at follow-up is very small (nM= 15). New measures and criteria need to be assessed to practically predict mortality on Hip fracture patients over 90 years.

P112 WITHDRAWN.

P113 Paradoxical Resistance: A new form of antibiotic resistance explaining recurrent bone and joint infections

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Paradoxical resistance is a new form of antibiotic resistance seen on antimicrobial biomaterials such as gentamicin bone cement. Gentamicin is released to inhibit growth of the bacteria, yet the same bacteria are able to survive and colonize the bone cement. This has clinical importance as antibiotic loaded bone cement is used to treat bone infections such as osteomyelitis but persistence of bacteria on bone cement often lead to recurrent infections in patients. We aim to investigate the cause of paradoxical resistance and develop strategies to prevent this phenomenon.

Antibiotic loaded bone cement was made manually. Gentamicin and clindamycin were added separately and in combinations to the bone cement. Bone cement cylinders were challenged with MRSA in a serial plate transfer test (SPTT) over 21 days. Any bacteria found growing on the cylinders were identified and antimicrobial susceptibility testing was done.

Paradoxical resistance developed on 66% and 100% of gentamicin and clindamycin bone cement while none was found on bone cement containing both gentamicin + clindamycin. All isolated bacteria developed antibiotic resistance, with a raised minimum inhibitory concentration (MIC) up to 4000-fold.

The use of dual-antibiotic loaded bone cement prevents paradoxical resistance. This suggests that dual-antibiotic loaded bone cement could potentially prevent recurrent infections in patients.

P114 Exploring the patient burden of failed Total Knee Arthoplasty

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Objectives: Surprisingly little is known about the patient burden and experience of living with a failed TKA. The aim of this study was to evaluate the patient experience of a failed TKA.

Methods: Semi-structured qualitative interviews were conducted pre-operatively with 10 patients (7 Females, mean age 70, range 42-77) who were undergoing revision TKA. Interviews were transcribed verbatim and analysed thematically using a phenomenological approach. Codes were generated by a single researcher using NVivo v12 software and independently verified to ensure validity. Themes were derived from these codes and agreed by a panel of 3 reviewers.

Results: Three clear themes were evident. Patients reported significant burdens in terms of pain, physical restrictions, and psychological impact of dealing with the illness burden associated with a failed TKA. A range of reasons for failure of TKA were seen in this group. The pain and physical restriction themes were consistent across all patients, however the psychological impact varied with failure aetiology. This variation was not directly related to mode of failure, but those who experienced a sudden onset of symptoms (eg. septic or traumatic failure) felt a much deeper distress than those with a gradual onset of symptoms.

Conclusions: There is a significant personal burden to the patient with a failed TKA that has not been well reported in the medical literature. Patients consistently reported significant pain, physical restriction, and psychological impact on their quality of life. Surprisingly, there was only variation in the psychological impact dependent on failure aetiology.

P115 Interaction between Collagen and Mineral in human bone tissue in ontogeny

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Objectives: Bone has a composite material nature and it changes in ageing and disease. Variations in its properties are responsible for its fragility and changes in its quality underpin this fragility. Important aspects are the way the organic/mineral phase interaction contributes in bone integrity(1); the way the collagen matrix influences 3-dimensional organisation of apatite crystals; and changes in shape/size/properties of Hap crystals and in relation to bone hydration(2,3). The present study aims to investigate thermal stability of collagen in conjunction

with alterations in mineral crystal geometry and mineral content at the bone tissue level.

Methods: Fresh human cadaveric material (N=44) between 17 and 59 yrs from the 4th sternal end of rins from the Forensic Institute in Tirana, Albania was analysed. Homogenised powder powder (106 µm fine) was produced in a Retsch Mixer miller 2000, 1 min, 60 Hz. Thermal and gravimetric collagen analysis was performed in TGA/DSC3+ (Mettler Toledo®, Indium calibrated), FTIR-ATR (Bruker Optics®, ALPHA T Platinum spectrometer) for ion substitution and collagen content and XRD (PANalytical X'Pert PRO Multi-Purpose Diffractometer by means of a Cu Kα radiation) for coherence length (CL), strain and size of mineral crystals.

Results: Results show significant correlations between (1) the increase in collagen stability at both endothermal and exothermal peak and decrease in coherence length (CL) both 002 and 004 peaks ($P<0.001$); (2) the increase in mineral/collagen ratio & level of hydration with the CL measurements ($P<0.001$); (3) the increase in crystal strain with enthalpy peak responsible for collagen denaturation and hydration level ($P<0.001$).

Conclusions: Our results are in line with various reports in past literature which have linked collagen integrity and crystal growth characteristics, i.e. both collagen quality and content play an important role in mineral growth, geometry and crystal strain and that also hints towards a certain pattern for bone mineralization throughout ontogeny in human bone.

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P116 Manipulation of displaced paediatric limb fracture in Emergency Department is safe and cost effective: a review of a new protocol

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Objectives: An Isolated Deformed Limb Protocol (IDLP) had been designed to establish appropriate management of a deformed paediatric limb in the Children's Emergency Department (CED).

The IDLP aimed to address the suitability of manipulation in the CED, with early treatment intended in the child's best interests to alleviate the pain and distress of the injury.

Key parameters of effectiveness of the protocol included evaluation of the patient and parent experience and reduction in number of interventions required in theatre.

Methods: A retrospective review was performed for all paediatric (age below 16) orthopaedic referrals between August 2018 and March 2019, in children presenting with an isolated limb injury requiring a manipulation. Post-reduction X-rays were evaluated by a blinded orthopaedic consultant.

Parental questionnaire feedback was sought on experience of pain control, explanation of treatment, and whether the manipulation in CED was appropriate. A numerical scale of 1(poor) to 10 (excellent) was utilized.

Exclusion criteria were major trauma injuries and injuries requiring plastic surgery transfer.

Results: Paediatric patients (n=326) were referred to Orthopaedics within the specified time period in a district general hospital. The inclusion criteria were met by (n=84). On presentation (n=66) received a manipulation in CED (forearm (n=56): lower limb (n=8): phalanx (n=2)). Of those manipulated (n=10) were for pain relief before inevitable general anaesthetic and (n=10) required a second manipulation. Of the remaining, (n= 17) were direct to theatre and (n=1) conservatively managed. 46 manipulations were a definitive treatment in CED with no need for further intervention.

Parental feedback responses were gained for (n=23) with pain control management (8.7), explanation of treatment (8.6) and overall experience (9.1). Parental evaluations (n=20) felt manipulation in CED was appropriate.

Conclusion: The established IDLP demonstrates its effectiveness with highly positive patient feedback of their child's pain and fracture management. Furthermore there is value in manipulation in the CED to reduce theatre intervention for the children and overnight admission. The implications of such are greater patient satisfaction and potential reduction in the financial management of these cases.

P117 Multicentre Intermediate to Long Term Follow Up of Hintegra Total Ankle Replacements

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Objectives: Degenerative changes at the tibiotalar joint affect 1% of adults. The optimal management is complex, arthrodesis traditionally is the reference standard. New generation total ankle replacements(TARs) in appropriately selected patients, have reported 10 year survival rates up to 89% from design centres, with good reported outcomes. We report multicentre, intermediate to long-term outcomes, of the Hintegra TAR.

Methods: This study utilised a prospective, nonrandomised observational approach to assess survival and revision rates, in all Hintegra TARs, performed in Musgrave Park and Altnagelvin Hospitals from 2004-2013. All procedures performed, by two fellowship trained foot and ankle consultants.

Review clinics were established in 2018 to update patient history, clinical examination, radiographs, AOFAS hindfoot scores and Charlson Comorbidity Index(CCI). Radiographs were reviewed for evidence of loosening, by two authors who were blinded to clinical outcomes.

Results: Between 30/03/2004-18/01/2013 62 primary TARs were performed on 58 patients. Excluding the deceased (n=9) and those lost to follow up (n=1) our mean follow up was 12 years 3 months, average AOFAS score 78.

During the first 4 years 11/23(48%) required additional surgery; reduced following a modification of the surgical technique. Our 5 and 10 year survival rates are 84% (52/62) and 71% (27/38) respectively.

Risk factors for revision include BMI>30 (Chi-squared P=0.006), smoking history (Chi-Squared P=0.027) and lower ASA scores (One-way ANOVA P=0.034). No association between CCI and revision. Asymptomatic osteophyte formation and polyethylene wear noted after 8-10 years. 6.4% deep infection rate.

Conclusion: The Hintegra TAR is a good alternative in the management of ankle arthritis, providing good function and sustained pain relief in the intermediate to long term.

We would stress the steep learning curve and the importance of achieving correct alignment to maximise longevity. Caution is advised in patients who are obese, smokers/ex and those with a high functional demand.

P118 Conversion to Combined Partial Knee Arthroplasty for disease progression following Partial Knee Arthroplasty retains a functionally superior gait compared to primary Total Knee Arthroplasty

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Objectives: Partial knee arthroplasty (PKA) is associated with more normal gait characteristics than Total Knee Arthroplasty (TKA) but higher revision rates are often cited as a reason to avoid these procedures. Conversion to 'Combined Partial Knee Arthroplasty' (CPKA) through the addition of a PKA to a newly degenerate native compartment in a knee with an existing PKA, is an alternative to revision to TKA, but it is unclear whether there is a functional advantage.

Materials and Methods: Patients converted from PKA to CPKA were measured on the instrumented treadmill, using standard gait metrics and compared to matched primary TKA and healthy subjects at the subject's preferred top walking speed (TWS). Variables were compared using Kruskal-Wallis, Mann-Whitney Tests with Bonferroni Correction (α=0.05).

Results: Sixteen subjects were measured following conversion of PKA to CPKA: medial unicompartmental to bi-unicondylar n=6, medial unicompartmental to medial bicompartmental n=1, lateral unicompartmental to bi-unicondylar n=5, lateral unicompartmental to lateral bicompartmental n=3, patellofemoral to medial bicompartmental n=1. Subjects were compared to age, sex and BMI matched primary TKAs (n=16) and healthy controls (n=16). Mean age 68yrs (p=0.5), BMI 28 (p=0.4); 44% male.

Objectively, all implant states walked slower than healthy controls (TWS healthy 7.3Km/h, CPKA 6.3Km/h, TKA 5.6Km/h CPKA vs TKA p=0.009) but CPKA walked 14% faster than TKA, with 31% of CPKA walking faster than the fastest TKA. At top speeds, CPKA demonstrated an advantage over TKA in terms of Vertical Ground Reaction Force at heel strike (p=0.03), mid-stance (p=0.03) and Weight Acceptance (p= 0.02) and approached significance for functionally advantageous push off force (p=0.05). CPKA median stride length normalised for leg length was 5cm (5%) longer than TKA (Healthy 98, CPKA 90, TKA 85, p=0.03)

Discussion: CPKA is associated with a more-normal, functionally superior gait compared to primary TKA, despite multiple procedures.

Conclusions: Revision of PKA to CPKA preserves healthy bone and functional cruciate ligaments. This small study suggests a compartmental approach to new degeneration following PKA is associated with functionally superior outcomes.

P119 Collagen and mineral attributes in Raman spectroscopy correlate with elastic mechanical properties in osteoarthritic subchondral bone

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Objectives: Osteoarthritis (OA) is the leading cause of pain and disability in adult populations. Subchondral bone has now been accepted as having a key role in the disease initiation and progression. Determining the chemical and mechanical properties of the bone may facilitate real-time characterization for diagnostic purposes. The aim of this study is to investigate how changes in the biochemical fingerprint of collagen and mineral influences the mechanical properties in OA bone.

Methods: A total of three osteoarthritic human knee tibial plateau samples obtained from knee replacement surgery were graded according to OARSI scores. Cylindrical subchondral bone specimens were collected from both of the medial and lateral zones and specimens were subjected to Raman spectroscopy and mechanical compression test.

Results: Severe OA areas from OARSI scores depicted by cartilage degradation and osteophytes were always located at the medial zones of the tibial plateau, which is the main weight-bearing area of the knee. A systematic decrease in relative intensity ratio between the Raman mineral (hydroxyapatite) and collagen (proline/hydroxyproline) peaks was observed in the medial tibia compared to the lateral tibia. The hydroxyapatite peak showed an increase trend of the width in the middle of the peak of the medial tibia compared to the lateral tibia, which suggested less mature of the mineral crystals. The medial zone had a lower elastic modulus than the lateral zone.

Conclusion: In summary, lower mineral to collagen ratio from Raman spectra correlated with lower elastic modulus, which may lead to less capacity for weight bearing and deformation. Our study provides further evidence that subchondral bone chemical properties of collagen and mineral is related to the mechanical properties of OA bone. Provided that the close relationship of Raman spectroscopy with the mechanical properties in OA bone, Raman spectroscopy could contribute to the non-invasive diagnosis of early OA in sub-clinical patients.

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P120 A retrospective audit of post operative rehabilitation management of quadriceps tendon repair

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Objectives: Quadriceps tendon rupture repair has few established protocols for recommended regime of rehabilitation. This audit aimed to evaluate the post-operative rehabilitation management plans of patients who had undergone a repair of a ruptured quadriceps tendon in a UK district general hospital according to six pre-defined criteria.

Methods: A retrospective audit was performed of patient operative notes generated by utilising pathway coding term 'quadriceps tendon repair' in the Trust's theatre patient data system between January 2014- January 2019. The following six parameters were reviewed in the management plans for quadriceps tendon rupture: a recorded plan for range of motion (ROM), initialised time of full weight bearing (FWB) use of hinge knee brace (HKB), duration and requirement of thromboprophylaxis, time and requirement of physiotherapy (PT) input and outpatient (OPD) follow-up schedule.

Exclusion criteria included: tibial spine avulsion injuries, paediatric extensor mechanism injuries and patella fractures.

Results: A total of 34 operative case notes were reviewed for patients who had undergone a repair of quadriceps tendon rupture. All notes (n=34) included a plan for ROM. However, only 21 (62%) indicated the initialised time of FWB, 29 (85%) mentioned use of HKB, 13 (38%) detailed duration and requirement of thromboprophylaxis, 19 (56%) specified time and requirement of PT input and 5 (14%) included OPD follow-up schedule.

Whilst a ROM plan had been fully documented in each operative note, the described plan of allowances and restrictions in ROM demonstrated different recommendations amongst surgeons.

Conclusion: This audit showed that there is significant inter-surgeon variability in the post-operative rehabilitation approach taken for patients with quadriceps tendon rupture repair. This lack of consensus can cause uncertainty amongst clinicians and physiotherapists managing these patients either in the immediate ward setting or subsequent outpatient clinics. Proposal for a single pathway could be beneficial in ensuring an evidence based single post-operative plan for these patients, as is frequently encountered for total hip and knee replacement patients.

P122 Analysis of Reaming Samples Within the T&O Department

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Objectives: Intramedullary nailing is a common operation in suspected, impending and pathological fractures of long bones. Reaming samples obtained during this operation are often sent for histology in the hope that they aid diagnosis and management. The aim of this study is to determine the outcomes of these samples.

Methods: We retrospectively reviewed 51 cases of suspected or confirmed pathological fractures over a one-year period in a large teaching district general hospital.

Results: Forty patients had a history of malignancy, sixteen of which had known metastases (31%). Positive histology results were found in thirteen patients (26%). All positive samples had radiological evidence of metastases at time of presentation. All positive histology matched known primary tumors. In patients without radiological evidence or a history of malignancy all histological samples were negative.

Discussion: Our results suggest in the presence of radiological changes consistent with metastatic deposit reamed histological samples are likely to be positive. In the absence of radiological evidence of metastatic deposit reamed samples are likely to be negative even with a previous history of cancer.

Conclusion: Although of small sample size our study provides evidence that routine use of reamed histology samples in patients with radiological evidence of metastasis are likely to yield positive

histology, which may direct further oncological treatment. In those patients with no radiological evidence of metastases these samples are likely to be negative and the routine sending of samples in patients with no real clinical suspicion of metastases is not justified.

P123 Early outcomes of total knee replacement using a novel technique for proximal tibial alignment

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Conventional instrumentation for total knee replacement (TKR) assumes the anatomical and mechanical axes of the tibia are aligned. Work at our institution using long leg xrays has demonstrated that >40% of tibiae in our population were bowed a mean 3.5°. Conventional TKR techniques in bowed tibiae may result in proximal tibial malalignment with the tibial keel adjacent to cortical bone, risking increased stresses to this region. To minimise this risk, we present early results of a novel surgical technique, in a single surgeon series performed at a high-volume arthroplasty centre, which aims for accurate proximal tibial alignment but accepts greater deviation from the mechanical axis.

Patients with tibial bowing were identified from preoperative long leg xrays. Computer navigation and gap balancing were used, with the tibial cut adjusted depending on the bow; such that a 3° valgus cut would be used for a 3° medial bow. Patients were followed up at 6 weeks and 1 year and data on range of movement, patient reported outcomes, patient satisfaction and complications were collected.

68 knees in 65 patients were identified. The mean tibial bow was 2.45° (-1.28-4.76°), 67 of 68 knees had a medial bow. In keeping with the described technique, 88.2% of patients had coronal implant alignment within 3° of the proximal tibia, but only 70.6% were aligned within 3° of the mechanical axis. Data was available for all patients at 6 weeks and 29 patients at 1 year. At 6 weeks, mean range of movement was 1.7 – 98.1°, this improved to 1.4 – 101.4° at 1 year. Pre-operative, 6 weeks and 1 year Oxford knee scores were 16.2, 29.3 and 9.6 respectively. 92.5% of patients were satisfied or highly satisfied at 6 weeks and

82.7% at 1 year. No patients required revision. One patient underwent manipulation due to stiffness and two suffered superficial wound infections.

Early outcomes using this technique are comparable with those described in the literature for TKR. Recruitment of a larger cohort and extended follow up will establish whether this technique is associated with improved implant survival.

P124 Is ankle fracture related to low BMD and subsequent fracture? A systematic review

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Objectives: Ankle fracture is one of the most common fractures in the elderly; however, its association to osteoporosis remains controversial. This systematic review aims to investigate the relationship between ankle fracture and osteoporosis, which is manifested by (1) bone mineral density (BMD) and (2) subsequent osteoporotic fractures.

Methods: A systematic literature search was conducted in MEDLINE (Pubmed) and Scopus databases from inception to March and April 2019, respectively. Potentially eligible articles were selected by two independent reviewers according to the inclusion criteria: cross-sectional, cohort, or case-control studies examining the BMD or subsequent fracture risk in low-energy ankle fractures patients in comparison with those of normal population. Data extraction was performed by two investigators. Any discrepancies were resolved with the third reviewer for consensus. Quality assessment was conducted using modified Newcastle-Ottawa Scale.

Results: A total of 18 articles were included in our study. On average, the quality of studies scored 74.3%, indicating low-to-moderate risk of bias, mainly due to potential confounders and inadequate follow-up period. Association between BMD and ankle fractures were explored in 12 studies, three of which found lower central BMD in ankle fracture patients compared to normal population, while two studies reported lower peripheral BMD in ankle fracture group. The risk of subsequent fracture was examined in 11 studies with relative risks ranging from 0.7(0.02-4.0) to 4.59(2.45-8.61), five of which found an increased risk of any subsequent fractures, major osteoporotic fractures, other weight-bearing bone fractures, or wrist fractures in postmenopausal women. Two articles suggested a higher risk of subsequent fractures in both genders. One study particularly found a greater risk in men after an incident of ankle fracture.

Conclusion: Without a clear association with BMD, ankle fracture is not considered a typical osteoporotic fracture. However, its contribution to an increased risk of future fracture cannot be overlooked, and awareness of its potential role as an early predictor of future fracture should be raised in order to promote secondary prevention. Further studies with longer follow-up period and stricter control of confounders are recommended.

P125 Effect of gut peptides ghrelin and obestatin on human fetal osteoblasts (hFOB)

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There is increasing evidence of cross talk between the regulatory pathways for bone and fat metabolism. The "hunger hormone" ghrelin has been shown to increase osteoblast number and alkaline phosphatase expression in vitro[1,2,3] but the function of obestatin has been widely disputed. While other studies have considered the effect of these peptides on osteosarcoma cells[4] they lacked testing on non-cancerous bone cells. The aim of this study was to compare the effect of these gut hormones on hFOBs- a cell line immortalised by transfecting temperature sensitive SV40-T antigen.

hFOB 1.19 cells were cultured in standard media (Dulbecco's Modified Eagle Medium Nutrient Mixture F-12 (DMEM/F-12) with 10% FBS, 2mM L-glutamine and 0.1 mM genetecin) treated with ghrelin and obestatin (2.75x10-12 to 3x10-10 mol/ml) at 34°C for 1, 4, 7 and 14 days with 4 repeats per treatment. Outcome measures were cell proliferation (crystal violet assay) and osteoblast differentiation (alkaline phosphatase activity (ALP) which was normalised against total protein measured by bicinchoninic acid assay (BCA). Peptides were dissolved in distilled water therefore 0.1% distilled water in medium was used as control.

At the highest concentrations obestatin treatments produced a significant reduction in crystal violet absorbance, relating to a reduced cell proliferation. Despite this reduction in proliferation none of the obestatin ALP activities saw the same reduction suggesting that the ALP activity per cell was increased with obestatin treatment. Treatment with ghrelin showed no significant difference from the controls in either crystal violet absorbance or ALP activity. All treatments of both ghrelin and obestatin saw no significant change in total protein content in the BCA with every well containing ~250-300 µg/ml of protein each.

Obestatin reduced cell proliferation, it increased ALP activity per cell meaning greater osteoblast differentiation. Ghrelin treatments had no effect on the relatively immature hFOB cells. These results highlight that obestatin may promote osteoblast differentiation and protein production unlike previous studies which did not consider these on an activity per cell scale.

P126 Multiscale subject-specific modelling for the investigation of structural adaptation in the lumbar spine

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Very little is known about the development of common spinal disorders such as scoliosis or low back pain. Studying the mechanical environment of the spine to predict the progression of the condition is of paramount importance, but remains difficult and ethically troublesome in-vivo. Computational approaches are a powerful alternative, as they allow time-dependent hypothesis to be tested without putting the patient at risk. In this study, a computational pipeline combining subject-specific musculoskeletal (MSK) and finite element (FE) models was developed to investigate bone structure adaptation in the spine.

Bone geometry and muscle anatomy for the MSK and FE models were derived from magnetic resonance images of the full body acquired from healthy volunteers with no history of spinal disorders. Body kinematics for a wide range of daily living tasks were acquired from the same volunteer with motion capture technology. Recorded activities involved walking at normal pace, walking up and down the stairs, sit-to-stand and stand-to-sit, and various lifting tasks including twisting movements. For each of these activities, the MSK model computes the muscle and joint contact forces in the lumbar spine. The computed loading envelope is then used as input for the FE model which uses an algorithm[1] to predict how the structural architecture of bone adapts to its mechanical environment.

When using the modelling pipeline for the full range of daily living tasks, the adapted vertebrae show a trabecular structure similar to that observed in healthy bones. Modification of the loading envelope by changing the body kinematics or the properties of the surrounding structures like the intervertebral discs results in alterations in the structural architecture of the vertebra.

The computational pipeline developed in this preliminary study is a powerful tool for predicting bone structure under various mechanical loadings. Applied to pathological scenarios, this modelling approach can give insights on how bone structure will adapt in specific lumbar disorders. It can also help in the development of spinal therapies and treatments.

References:

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P127 The ability of orthopaedic surgeons to assess femoral malrotation post trauma: a questionnaire based audit

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Objective: Post traumatic iatrogenic femoral malrotation has an incidence of 8%-28%. Literature repeatedly states that malrotation is difficult to asess, however, with many rotational assessment techniques published, the ability of surgeons to assess rotation has yet to be established. Whilst malrotation can be compensated for in gait, between 15°-30° of malrotation leads to osteoarthritis. A 30° malrotation can result in patients having difficulty climbing stairs and walking, requiring further surgery. This study aimed to assess orthopaedic surgeons' ability to estimate degrees of malrotation using radiological imaging.

Methods: Radiographs were taken of a transversely fractured femoral sawbone with the distal fragment rotated at 10°, 20° and 30° of internal and external rotation. Full length anteroposterior femoral radiographs and image intensifier radiographs were acquired emulating preoperative, and intraoperative imaging respectively. Imaging was repeated post intramedullary nail fixation. Radiographs were exported into a questionnaire. 14 orthopaedic surgeons, 2 consultants, 9 speciality trainees and 3 core trainees were asked to identify the degree and orientation of malrotation apparent on the radiograph. Participants were asked how they assessed the malrotation and their awareness of alternative assessment techniques.

Results: Questionnaire average score: 2.8/12. Median: 3, (range 1/12 to 7/12). Adjusted for orientation, internal rotation was identified 38.1% correctly and external rotation 47.6% correct. 57.1% of responses identified orientation incorrectly with IR mistaken for ER and vice versa. Degree of angulation was recognised 41.7% correctly across the 12 radiographic questions.

Conclusion(s): The current radiographic techniques used in routine femoral fracture fixation and the assessment methods employed by surgeons are insufficient to identify and avoid iatrogenic malrotation.

P128 Influence of Poly-beta-amino-esters (PBAE) kinetics and hydrolysis on chlorhexidine release via Layer by Layer (LbL) coated nanoparticles

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Total joint replacement is the last choice for the treatment of end-stage joint diseases. Prosthetic joint infections are an undesirable event that are currently treated via impregnation of bone cement with antibiotics. These drugs produce a short-term burst release and are gradually losing efficacy due to bacterial resistance. Therefore, the development of novel antimicrobial approaches is required.This work aims to determine the optimal nanocarrier construct, to provide prolonged chlorhexidine release as alternative strategy of prophylaxis for orthopaedic infections.

Diacrylates A and F have been co-polymerized with three amines to form six poly-beta-amino-esters (PBAE) polymers, characterized by ^{1}H and ^{13}C NMR spectroscopy, Gel Permeation Chromatography (GPC) and zeta potential. Six nanocoating systems have been obtained, via Layer by Layer technique (LbL), and the drug release has been monitored over weeks in buffers at pH 5 and pH 7.4.

Zeta potential and thermogravimetric analysis examined the binding among drug, PBAEs and nanoparticles. The chlorhexidine has been released for a period between 45 and 60 days showing that lower electrostatic interactions of the polyelectrolytes at pH 7.4 increased the release kinetics, while the opposite occurred at pH 5. These results were consistent to the pH degradation profiles of the six PBAEs: the polymers hydrolysed more slowly at pH 5 than pH 7.4.

LbL is a suitable technique that can control chlorhexidine release by diffusion of the drug through the layers and the possible delamination of the coating from silica nanoparticles for several days. The choice of the monomers employed in the polymerization is crucial and it greatly influences the physicochemical properties of PBAEs, including molecular weight and charge, as well as, the release of the bioactive compound embedded onto the surface of the nanoparticles. Future applications on bone cement of these coating systems will be pursued.

P129 Can nerve conduction studies be used as a prognostic indicator of PROMs in carpal tunnel decompression surgery?

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Background: Carpal tunnel decompression (CTD) surgery is frequently performed and now appears on lists of procedures of limited clinical value. Therefore, evidence to support clinical benefit and tools to improve patient selection are increasingly valuable.

Aim: This study aimed to prospectively assess whether nerve conduction study can predict improvement in Patient Reported Outcome Measures (PROMs) following CTD.

Method: This pilot study recruited 20 patients clinically diagnosed with carpal tunnel syndrome.

Subjects underwent pre-operative NCS, stratified as per the Canterbury Grading Scale and grouped: Grade 0-1= normal to very mild, Grade 2-4 = mild to moderate, Grade 5-6 = severe to extremely severe. Patients were blinded to their Canterbury grading. Subjects had baseline PROMs data collected in the form of the Patient Outcomes of Surgery Hand/Arm Questionnaire, which has 3 key domains providing an indicative scores for: Symptom, Activity and Psychology. The questionnaire was repeated following decompression surgery.

Results: Patient spread was as follows: Canterbury Grade Group 0-1: n=6, Group 2-4: n=9, Group 5-6: n=5. Mean follow-up was 12 weeks. For the whole patient group there was a significant improvement in Symptom ($p< 0.001$) and Psychology Score ($p=0.009$) post operatively. There was no difference in baseline score Symptoms, Activity and Psychology score between Canterbury graded groups. Canterbury grade did not predict differences in improvement of Symptoms or Psychology score post operatively. The moderate Canterbury grade group was the only subsection of patients who demonstrated a significant improvement in Activity score post operatively ($p< 0.05$).

Conclusions: This data shows that CTD significantly improves PROMs score in Symptom and Psychology domains regardless of NCS grading. NCS can add value in predicting improvement in Activity score, seen only in the moderate Canterbury grade group. These results could aid selection of surgical candidates, informs the consent process and highlights when Canterbury graded NCS have utility.

P130 A change of practice in the management of distal radius fractures within a regional T&O Department. Early Mobilisation out of cast at 4 weeks versus 6 weeks

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Objectives: Distal radius fractures(DRFs) are a common injury, reviewed in the fracture clinic. Stable fractures were traditionally treated with immobilisation for 6 weeks. The new BOAST guidelines implemented in December 2017 recommend mobilisation at 4 weeks. The emphasis is based on functional outcome over radiological features.

Methods: We performed a local study involving a single consultant practice of patients managed prior to and post implementation of guidelines. We used electronic care records to perform a retrospective analysis of the pre guideline arm of the study and a prospective approach following implementation of guidelines.

Results: Group 1 (n=23) pre implementation had on average 1.9 clinic appointments, 2.7 radiographs performed, and 56% had a radiograph on cast removal. Group 2 (n=17) had 1.77 clinic appointments, 2.11 radiographs performed with 29% on cast removal. No patient in the post implementation group has had an adverse outcome (clinically or radiologically) or represented to the fracture service on 1 year follow up.

Conclusion: Currently the evidence is poor for the inclusion of this guideline to the management for DRF. By adhering to the recommendation, we reduced the number of clinic appointments, radiographs and patients were successfully mobilised sooner with no adverse outcomes.

This guideline changes the course for the majority of conservatively managed distal radius fractures improving patient care and fracture clinic flow.

P131 A novel external fixation method and its impact on wrist distraction in relation to distal radial fracture

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Distal radial fractures are one of the most common fractures in the world. Indirect reduction using external fixation is a commonly used treatment option for these fractures. ligamentotaxosis is utilised to realign and heal fractures. Uneven distraction forces can lead to radial/ulnar deviation and radial shortening. A common after-effect of this is wrist stiffness. Novel therapeutic options harnessing a modified method to achieve an even distraction forces across the wrist can lead to improved outcomes for these patients. Aim of this study is to test if modified Aberdeen method is superior to standard method by testing the ligament length changes caused by both methods and to find a safe pin insertion point for Aberdeen method. Formalin fixed cadaveric specimens (N=8) were dissected to optimise application of Aberdeen method (N=2). Tantalum markers were inserted into bone/ligaments near ligament endpoints. Radiosteriometric Analysis (RSA) was then used to measure change of ligament length (before and after applying distraction) by two different methods to determine which method achieve better wrist distraction. Average relative ligament change (RLC) was analysed (N=6) using GraphPad Prism. The Aberdeen method could be applied, damage free, to all wrists (N=6) on the 4rth metacarpal bone. The Dorsal Radiocarpal Ligament (DRL, average RLC, Aberdeen=0.048, Standard=0.030), the Radial Collateral (RC, average RLC, Aberdeen=0.112, Standard=0.105) Ligament and the Ulnar Collateral (UC, average RLC, Aberdeen=0.079, Standard=0.068) Ligament were

described and measured. Initial results of the Aberdeen method demonstrated increased ligament length compared to the Standard method (Mann-Whitney test; P=non-significant). With a reverse order of the frame application, this data was not reproducible. However, we believe this is due to limitation of formalin fixed cadaveric specimens which led to alteration of the ligaments by the traction from the first run. This novel cadaveric study demonstrates that the fourth metacarpal bone is a safe place to apply the Aberdeen frame. Initial results showed the Aberdeen method to be superior than the standard method. The Aberdeen method has emerged as a promising treatment option for distal radial fracture, but larger studies must now be conducted.

P132 Chemical and Mechanical Regulation of Osteoblast Differentiation from Pluripotent Stem Cells through the Rho/ROCK Pathway

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It is well-established that the commitment and differentiation of stem cells can be influenced by both chemical as well as mechanical signals provided by the niche and the extracellular environment that they interact with. It has been established recently that matrix stiffness plays a key role in regulating osteoblast differentiation from mesenchymal stem cells. However, the regulation of osteogenic differentiation from pluripotent stem cells by defined growth factors and matrices of different stiffnesses requires further investigation.

In this study, I have used the *in vitro* differentiation of pluripotent mouse Embryonic Stem Cells (mESCs) to osteoblasts and chondrocytes, to investigate the interplay between BMP signalling, matrix stiffness and Rho/ROCK signalling on chondro-osteo differentiation. Specifically, differentiation of mESCs through a step-wise protocol involving primitive streak/mesoderm specification and FGF-2-dependent mesoderm enrichment, yields a population of precursors that have both chondrogenic and osteogenic potentials when cultured in specific media.

Our current studies now show that addition of BMP-4 during a small interval, designated the mesoderm-enrichment phase of differentiation, induces the osteoblast lineage over the chondrocyte lineage, as determined by histochemical staining and molecular marker gene expression for lineage-specific markers. The addition of a ROCK inhibitor enhanced the BMP-4 effect, suggesting an important additional role of cell spreading and cell-matrix interactions. To test this, mESC differentiation was carried out on polyacrylamide gel substrates of low (2KPa) and high (50KPa) stiffness. It appears that matrix stiffness regulates both osteoblast and chondrocyte lineages, however, BMP-4 dominates over the effects of matrix stiffness by inducing bone and reducing cartilage differentiation. The findings also suggest that inhibition of ROCK reverses the cell rounding phenotype induced by seeding on 2KPa substrates, therefore subsequent effects on differentiation are related to cell spreading, as ROCK inhibition increases cell spreading on soft substrates as well as induces osteogenic differentiation. These results suggest that although mESC-derived chondro-osteo lineage commitment is regulated by both chemical and mechanical signals, there is a greater dependence for differentiation on chemical/biological signals over mechanical ones.

P133 Ultrasonic attenuation properties of various adhesive couplants for early detection of osteoarthritis by passive monitoring of acoustic emission

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In the later stages of Osteoarthritis (OA) joints can produce audible grating or clicking noises during regular movement. This is indicative of friction between bone and cartilage (crepitus) and could be present when it is too late to slow disease development. It has been shown that joints and bones with earlier onset of the disease also emit noise; however, this is typically confined to higher, inaudible frequencies. These higher frequency sounds coincide with those used in the field of Acoustic Emission (AE), a non-destructive testing technique which is widely used in civil and mechanical engineering applications.

In this current study to develop AE in the early detection of OA, a key challenge is to identify a suitable couplant that can bond the AE sensor to soft tissue around the knee joint. The criteria for selecting a suitable couplant were; 1) does not attenuate ultrasonic emissions in the frequency range of 50kHz to 150kHz, 2) will not cause irritation to skin, including sensitive skin, and 3) will remain adhesive and experience no change in acoustic properties for the session duration, up to 3 hours.

The adhesive couplant was tested in comparison to silicone grease which is one of the standard couplants in AE research. Five PZT AE sensors were used during testing in order to eliminate any sensor effect, these sensors were mounted in turn to a block of aluminium using the 10 adhesives available. Three frequencies, 50, 100 and 150 kHz were pulsed into the aluminium using a signal generator.

Preliminary results suggest that there are several suitable couplants which fulfil the criteria set out above, some couplants which had been selected

have been ruled out due to their recorded attenuation properties. Further work is to be undertaken to understand which adhesive has the optimal properties for application in a clinical setting; where time and cost will determine clinical uptake of the new sensing technology.

This research was supported by the Engineering and Physical Sciences Research Council (EPSRC) doctoral training grant (EP/R513003/1).

P134 WITHDRAWN.

P135 Should we routinely perform a post-operative haemoglobin check following unicompartmental knee arthroplasty?

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Aims: To study the importance of post-operative hemoglobin and hematocrit check following Uni Compartmental Knee Replacement.

Setting: Single center. Multiple surgeons.

Material and Methods: Following institutional approval a retrospective analysis of all patients undergoing UKA at our level one academic university hospital was conducted. Imperial College Healthcare in London offers elective Orthopaedic services at Charing Cross Hospital. Operative records of all patients undergoing primary UKA were reviewed between March 2016 to March 2019. Patients pre-operative hemoglobin and hematocrit, weight, height, BMI, co-morbidities, application of tourniquet, tourniquet time, administration of Tranexamic Acid, hospital length of stay, complications and re-admission were all recorded. Total amount of blood loss and percentage of blood loss were estimated using the post- operative hematocrit.

Results: We found a total number of 155 patients operated for UKR during the study period. There were 70 females (45%) and 81 men (55%). The mean age was 66±10. Median pre-op blood volume was 4700(IQR; 4200-5100). Median blood loss was 600 ml (IQR; 400-830). Mean pre-op Hemoglobin was 135±14 and mean post-op Hemoglobin was 122±13. No patient had post-op Hemoglobin under 80 (Range 93-154). No patient in our study need transfusion.

Conclusion: The results of our study did show that pre-operative group and save and post-operative hemoglobin and hematocrit check could be avoided in all of our patients. We conclude that routine post UKR check of hemoglobin and hematocrit can be avoided and be saved for special circumstances depending on patient's physiology.

P136 Does virtual reality simulation have a role in training trauma and orthopaedic surgeons?

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Objectives: Surgical simulation has become increasingly prevalent and is relevant for orthopaedic trainees. The traditional method for arthroscopic training relies on appropriate clinical cases, costs particularly with operative time and has implications for patient safety. The Virtamed ArthroS was released in December 2017 and is the world's first high-fidelity simulator for ankle arthroscopy. The primary aim of this study was to determine the utility of this arthroscopic simulator for training based on level of training and experience.

Methods: Volunteers were recruited from each training level; medical students through to consultants. They performed five arthroscopic procedures under control conditions. A 10-minute demonstration on the setup and operation of the simulator was given prior to testing. Performance was evaluated by obtaining predefined metrics for each procedure within the simulator with photo and video acquisition. A questionnaire was administered to evaluate previous arthroscopic and video gaming experience, levels of stress, usefulness and authenticity.

Results: Each arm consisted of a minimum of 5 participants from medical students, foundation level, core trainees, orthopaedic registrars and consultants. All groups demonstrated an improvement in time, economy and safety with 20 minutes exposure, reporting high levels of satisfaction and usefulness. All participants recommended simulated training prior to patient exposure. Significant reductions in camera and hook path distance alongside articular cartilage damage particularly within more junior trainees and those with no prior arthroscopic experience was demonstrated.

Conclusion: The Virtamed ArthroS ankle module provides an authentic simulated experience for all levels of training with demonstrable improvements in performance, anatomy knowledge and reductions in adverse events. In the current climate of reduced working times and increased indicative arthroscopy numbers for completion of training the real-world benefits for orthopaedic trainees is promising.

Further work is required to validate this simulator with respect to the transferability of acquired skills into clinical practice.

P137 Is there an increased risk of peri-operative complication in patients with obstructive sleep apnoea having shoulder surgery?

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Background: With the rise of obesity the incidence of obstructive sleep apnoea is increasing. This condition often worries anaesthetists and surgeons alike especially in patients who have shoulder surgery in a beach chair position.

Methods: We prospectively followed up 26 patients undergoing shoulder surgery with a diagnosis of obstructive sleep apnoea. All patients were on continuous positive airway pressure (CPAP) and had no other significant comorbidity. Arthroscopic procedures were performed in the lateral position and open procedures were performed in beach chair position.

We looked at intra and post-operative complications, use of high dependency unit (HDU) bed, increased recovery time, increased hospital stay. We also looked at 30-day mortality and morbidity.

Results: There were six women and twenty men; age range was 44 to 68. Ten patients had their procedure done as a day case and 16 patients as an inpatient. Five patients had awake interscalene block only, the rest had general anaesthesia with an interscalene block with little or no opioids.

4 patients had shoulder arthroplasty, 8 patients had arthroscopic subacromial decompression +/- acromio-clavicular joint excision, 14 patients had cuff repair. 15 patients had arthroscopic surgery. All patients had CPAP treatment post surgery.

In our study, no patients had any significant perioperative mortality or morbidity in the first 24 hours or in the first 30 days following surgery. Our study did not show any increase in the inpatient stay or increased time in the recovery, no patient required a HDU bed

Conclusion: Our study shows that patients with obstructive sleep apnoea can safely have shoulder surgery without any significant increase in the perioperative morbidity and mortality. In our opinion, this is largely because of awake interscalene block anaesthesia and general anaesthesia with interscalene block, which reduces or eliminates the use of opioids. Use of CPAP post-operatively also helped and many of our patients could be done as a Day case. Surgery can be performed in a beach chair position or in the lateral position without significant increase in risks.

P138 Stiffness post total knee replacement: a proof of principle study investigating the effect of genetic expression of markers of fibrosis

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Background: To establish proof of principle of a link between phenotypic expression and stiffness after TKR.

Methods: From 100 patients, genetic expression of markers of fibrosis were performed for 15 synovial samples from patients categorised as 'best post-operative range of movement (ROM)' and 15 samples from patients with 'worst ROM'. These markers included Matrix Metalloproteinases (MMPs), A Disintegrin and Metalloproteinases with Thrombospondin (ADAMTs) and Tissue Inhibitors of Matrix Metalloproteinases (TIMPs). Genetic marker data were compared to Oxford Knee Scores (OKS) and Pain Catastrophizing Scores (PCS).

Results: Quantitative markers for gene expression demonstrated more outliers in stiff compared to non-stiff knees, suggesting a greater imbalance in pro- and anti-fibrotic makers in stiff knees. Whilst there was a significant difference in the range of post-operative knee flexion ($p=0.001$) and extension ($p=0.001$), there was no statistically significant difference between stiff and non-stiff knees in pre-operative or post-operative OKS ($p\geq0.06$). There was no difference in the individual components of the individual PCS score items nor the PCS total scores when stiff and non-stiff knees were compared ($p>0.05$).

Conclusion: There is proof of principle that biological factors may contribute towards post-TKR stiffness. This now warrants further investigation to better understand this relationship.

Level of Evidence: Level 3.

Keywords: knee arthroplasty; limited range; arthrofibrosis; gene expression; case-control.

P139 Anti-TNF-Alpha Agents: Chondroprotective Or Potentially Harmful For Articular Cartilage?

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Human cartilage is a unique avascular, aneural and alymphatic tissue with limited cellular mitotic activity. In many autoimmune and inflammatory diseases involving the cartilage, cytokines including Tumour Necrosis Factor (TNF) are released as part of the pathophysiologic response. TNF is known to signal chondrocyte apoptosis, inhibit the ability of

mesenchymal stem cells (MSCs) to differentiate into chondroblasts, promotes the release of matrix metalloproteinases (MMPs) resulting in cartilage destruction, and inhibits chondrogenesis. We discuss the effect of anti-TNF-alpha agents on articular cartilage.

A systematic review was performed by searching PubMed, Embase and Cochrane Library databases. Inclusion criteria were studies of any level of evidence published in peer-reviewed journals reporting clinical or preclinical results. Relative data were extracted and critically analysed. PRISMA guidelines were applied, and risk of bias was assessed as well as the methodological quality of the included studies.

Four studies investigating *in vivo* effects of anti-TNF drugs on animal osteoarthritis (OA) models concluded that inhibiting TNF has substantial chondroprotective effect. TNF inhibition reduced degenerative changes, demonstrated significantly ($p<0.05$) improved histological and macroscopic outcomes, and considerably reduced MMP expression. Despite the chondroprotective effects, these subset of drugs still exhibit a degree of chondrotoxicity.

TNF-alpha is one of the proinflammatory cytokines involved in inflammatory reactions occurring in cartilage tissue due to trauma and systemic diseases. Biologic therapy is able to inhibit and counteract its effects in cartilage with possible benefit for OA patients. Some concerns regarding their chondrotoxicity exist, however, there is good quality evidence to support its positive effects both in *in vitro* and *in vivo* studies of OA, cartilage repair and autoimmune diseases models. Overall, anti-TNF-alpha drugs show promising outcomes in cartilage repair and should be evaluated in randomized clinical trial in human.

P140 In vitro evaluation of a gelatin/PDMS scaffold seeded with rat bone marrow mesenchymal stem cells for bone fracture repair

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Objectives: In this study we evaluated, in vitro, the potential of an electrospun gelatin poly(dimethylsiloxane) (PDMS) scaffold for bone repair by assessing the ability of the scaffold to support the growth and differentiation of rat bone marrow mesenchymal stem cells (BM-MSCs).

Methods: BM-MSCs were isolated from femora and tibiae of adult male Sprague-Dawley rats (9-12 weeks) and cultured to passage 3 (P3). BM-MSCs P3 were characterised by flow cytometry and trilineage assay. The PDMS supplied as a two-part kit consisting of pre-polymer (base) and cross-linker (curing agent) was prepared following manufacturer's instructions. An electrospinning solution (3% v/v) composed of a gelatin mix was printed by an Aether 1 Bioprinter on top of the PDMS. Cells were seeded onto scaffolds and scanning electron microscopy (SEM) was performed in order to visualise cell morphology and attachment to scaffold. MTT (Thiazolyl Blue Tetrazolium Bromide) viability assay was carried out at 2, 7 and 15 days. Cells' ability to produce a bone-like mineralized extracellular matrix (ECM) was assessed by Alizarin Red staining (AR-S) at 14 and 21 days.

Results: Flow cytometric analysis revealed cells were positive for CD90 and CD29 and negative for CD45 (hematopoietic marker). Trilineage differentiation assays demonstrated multipotential ability. SEM demonstrated cell attachment to scaffolds three days after seeding. At 21d AR-S showed cell mineralisation capability and cell proliferation; some scaffolds presented marked gelatin fibre disintegration, even in the absence of cells, and in those scaffolds that disintegrated cell viability was reduced.

Conclusions: Rat BM-MSC can be readily used for tissue engineering scaffold investigations. This study showed that an electrospun gelatin/PDMS scaffold holds promise as a biological scaffold as it supports cell growth and differentiation. However, further optimization in the fabrication of the scaffold is necessary due to a lack of scaffold integrity in vitro.

P141 WITHDRAWN.

P142 WITHDRAWN.

P143 Injection moulding polyimides bone plate and screw design for osteoporosis patients

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Objectives: More than 50% of women and 30-45% of men over 50 years of age suffer from osteoporosis. For osteoporosis patients, losing critical skeletal interconnection and lack internal support from trabecular bone would cause comminuted fractures easily. Lack of sufficient mechanical strength of cortical bone and trabecular bone will lead to failure of surgery for those patients. In that case, finding a new material and design for bone screws and bone plate with stronger mechanical fixation with loose bones is very promising. Polyimide is an incredibly powerful synthetic polymer with amazing heat and chemical resistance. The mechanical properties of polyimide are very similar to those of bone which could support enough strength for fixing the bone

and could also avoid stress shielding.

Methods: Polyimides usually take one of two forms. The first of these structures is a heterocyclic structure where the imide group is part of a cyclic unit in the polymer chain. The second is a linear structure where the atoms of the imide group are part of a linear chain. The strong intermolecular forces between the polymer chains, which involve polar interactions, aromatic stacking and most important here, charge transfer complexation, give the polyimides these great properties. Injection moulding is used to manufacture the bone plate.

Results: The mechanical properties of polyimides are similar with bones, which reveal the potential in bone repair without changing the stress in surrounding tissues. Through Antibacterial experiment, polyimide has good biocompatibility and good biological activity. Moreover, Polyimide has minimal cytotoxicity and hemolysis.

Conclusion: Polyimide is a very compatible material for bone plate and screws as it has minimal cytotoxicity and hemolysis and also has very similar mechanical properties as cortical bones. Stress shielding and mechanical fixation could all be solved by using this novel material. And new polyhedron structure could further increase the fixation through injection moudling. Moreover, different porous polyimide membranes have different effects on new bone formation. Polyimide can improve its biological activity by surface modification, which is beneficial to the attachment and growth of bone cells.

P144 Modelling trabecular bone architecture as a Voronoi network

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Structural finite element models of trabecular bone adaptation within the femur[1] and pelvis[2] used randomized networks of truss elements with strain due to axial force used as a driver for adaptation of trabeculae cross-sectional areas. At the macro-scale the adapted models successfully highlighted trabecular trajectories and were used to predict fracture initiation and progression, in the femoral neck[3]. The use of a truss network requires a high nodal connectivity (NC) defined as the number of structural elements representing trabeculae connecting to each node, in order to maintain structural and computational stability. A minimum NC of 6 results from the orthotropic nature of the principal stress directions that bone is believed to form trajectories along, while higher NCs are required to resist multiple load cases that introduce shear due to off axis loading compared to the principal stress directions obtained when adaptation is carried out for a single load case.

Recent micro-CT studies characterising the structural architecture of trabecular bone[4] contradict the trajectory hypothesis indicating frequent NC values of 3 and 4 with nodes having common structural arrangements or motifs. A Voronoi network is a structural form that provides an abundance of nodes with a NC of 4. The Voronoi method of partitioning space around control points is implemented in Rhino using the Grasshopper parametric design tool to create a network as a collection of node and element definitions. The Abaqus finite element solver is used to analyse this network using beam elements with strains developed due to axial force, biaxial bending and torsion moments. An extended bone adaptation approach is used to adapt the cross-sectional properties at multiple points along the length of each trabeculae.

Initial results suggest using a Voronoi network is a promising approach to model trabecular bone adaptation and fatigue micro-fracture. Ongoing work will investigate the iterative placement of the control points used to construct the Voronoi network.

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P145 Implementing a disease management program: what works and what doesn't work

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Objectives: The aim of this study was to identify and determine the extent to which effective steps for change were/and were not present in the implementation of the Kaiser Permanente Southern California Healthy Bones Model of Care as perceived by physician champions and Healthy Bones Care Managers.

Methods: The subjects in the study included 20 physician champions and 35 Healthy Bones Care Managers employed in the Kaiser Permanente Southern California Healthy Bones Model of Care. 25 have been employed in their current role since the implementation of the program. Of those, 16 agreed to participate. The instrument for interviewing was an email interview.

Results: Each participant was asked to respond to a set of nine standard questions. Examination of qualitative data resulted in eight major findings. Among the findings were the following: nine effective and six ineffective themes were identified and as a result ten best practices for creating change efforts when implementing disease management programs emerged.

1. Relentlessly informing, advocating, and networking.
2. Balancing the merits of consistency gained by centralized control, with the merits of creativity and innovation, guided by autonomous flexibility.

3. Creating strong multi-disciplinary champions.
4. Providing hands-on monitoring and management of change.
5. Creating inclusive feedback systems.
6. Leveraging external forces and available data to support change.
7. Rewarding meritorious or noteworthy behaviors, innovations, and ideas.
8. Personalizing interactions with potential change agents.
9. Providing adequate resources and administrative support.
10. Providing adequate short-term plans and goals.

Conclusions: This combination will greatly increase the likelihood of success and long-lasting sustainability of a disease management program. The results of this study support effective guides for healthcare reform initiatives at the national, corporative, and medical center levels. At this time there are many opportunities for the incorporation of disease management programs in many avenues. Proponents of improvements to any healthcare system can use recommendations from this study to remove obstacles and barriers to change and foster supportive participation from involved health care professionals.

P146 Ex-Vivo Organ Culture of the Porcine Femoral-Tibial Joint in a dynamic loading rig: Work in progress

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The ability to pre-clinically evaluate novel cartilage substitution therapies in viable physiological biotribological models, would be advantageous. Methods for the organ culture of whole femoral condylar and tibial osteochondral ("whole joint") tissue under static conditions have previously been developed. The aim of this study was to extend these methods and develop a novel natural knee joint simulator culturing whole femoral condylar and tibial tissues under dynamically loaded conditions contacting opposing joint surfaces.

Porcine femoral condyles and tibial plateaus were aseptically dissected. The majority of cancellous bone removed leaving intact cartilage and a layer of cortical bone. These were fixed into a bespoke natural knee loading rig under aseptic conditions. The condyle and plateau were aligned allowing dynamic loading between the opposing surfaces. These were cultured in defined medium, initially under static conditions and the viability of the cartilage at day 0 and 9 of static culture was assessed by XTT assay and LIVE/DEAD staining and glycosaminoglycan (GAG) levels determined by Dimethylmethylene Blue (DMMB) assay.

"Whole joint" tissue was successfully secured and aligned into the loading rig and sterility maintained over 9 days of static culture (n=3). There was no significant reduction in the XTT conversion levels by cartilage (with exception of peripheral tibial cartilage) between days 0 and 9. LIVE/DEAD staining showed the majority of cells remained alive in the mid and deep cartilage zones. There was a band of mainly dead cells in the surface zone, from day 0. GAG levels were maintained between day 0 and 9 of static culture (DMMB).

Results demonstrate that the loading rig supported whole joint organ culture for extended periods of time. Surface zone chondrocytes rapidly lost membrane integrity ex-vivo whereas mid- and deep zone chondrocytes remained viable. It is hypothesised that the application of physiological loading in the novel natural knee loading rig will improve chondrocyte viability and this will be the focus of future studies.

P147 Bicondylar tibial plateau fractures: A retrospective review of 64 cases

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Bicondylar tibial plateau fractures are complex injuries without a clear standard of optimal treatment. We examined the outcomes of such fractures managed with peri-articular locking plates in the largest single centre consecutive series to date.

Between October 2011 and August 2018 a total of 64 fractures in 63 patients were treated by fixation using periarticular locking plates. A retrospective review of medical records, plain radiographs and CT scans was performed. Patient reported outcome measures using the WOMAC index, Short Form 36 and Oxford knee score were obtained at a minimum follow up period of eight months.

We achieved good clinical and radiological outcomes with a similar early complication rate to that shown in the literature. Our deep infection rate was 7%. Only two patients experienced loss of fixation and collapse of the joint of >4mm. Nine patients (14%) underwent subsequent removal of symptomatic metalwork and one amputation occurred.Our study supports the use of locking plates as safe and effective way to treat these fractures.

P148 Muscle activity, joint force and dual-energy X-ray absorptiometry (DXA): generating normative data to facilitate clinical translation

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Objectives: To investigate the repeatability of:

- developing a standardised approach to

integrating quadriceps surface electromyography (sEMG) and isokinetic dynamometry in healthy and knee pain volunteers.
- establishing bone densitometry (hip and spine) precision data for the Hologic Discovery (Delphi-A) DXA scanner in healthy participants

Methods: 30 volunteers recruited through Cardiff University, Summer 2019

DXA scan: Bone densitometry (hip and spine) scans are undertaken in a randomised order, following standardised positions.

Isokinetic dynamometry and sEMG:

The Surface Electromyography for the Non-Invasive Assessment of Muscles (SENIAM) project protocol for the placement of quadriceps electrodes are followed.

Following a familiarisation session and warm-up, trials of various maximum voluntary contraction (MVC) percentages (isometric quadriceps contractions) are undertaken at selected knee joint angles, in a randomised order.

Two measurement sessions undertaken; 7 days apart

Results: Following reliability analyses to establish repeatability of procedures, results on the linearity of the muscle activity to force generation relationship will be compared to existing literature. DXA bone densitometry precision data, will provide the necessary foundation for establishing a normative database for future clinical work.

Conclusions: A standardised approach to sEMG integration and isokinetic dynamometry during isometric quadriceps contractions (using in early stages of rehabilitation), and the potential linear relationship linked with vastus lateralis may translate the use of sEMG into clinics as a more convenient measure for those with knee pathology.

If repeatable, assessing bone densitometry through DXA scanning may offer an additional tool for providing greater insight into knee pathology research.

Longitudinal work is proposed to use these tools to monitor strength deficits that may be linked with future ACL injury in female athletes. The effectiveness of clinical interventions on a potential ACL and subsequent early stage osteoarthritis (OA) risk factors may be objectively measured. These tools may also offer an insight into OA progression in this population.

Ethics: Approval given through a Cardiff University Local Ethics Board

Funding: *These projects are funded through Cardiff University (CUROP and CITER).*

P149 Pilot study on the relationship between patient-reported outcome measures, knee biomechanics, and OARSI suggested performance-based tests in end-stage knee osteoarthritis

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Objectives: Recent evidence suggests patient-reported outcomes (PROs) fail to capture changes in performance-based measures following total knee replacement (TKR) surgery. A recent study, however, identified a strong relationship between improvements in lower-limb biomechanics and PROs using a global measure of biomechanical function – the Cardiff Classifier. The aim is to explore this finding further by assessing the relationship between PROs, biomechanical classification, and the set of performance-based tests (PBTs) recommended by OARSI. A secondary aim is to assess how each of these outcome measures is affected by the presence of comorbidities.

Methods: A pilot, observational, cross-sectional study will be carried out on ten participants with end-stage knee osteoarthritis (KOA), waiting to undergo TKR surgery. Qualisys motion capture system will be utilised to collect kinematic data during level ground walking, sit-to-stand and stair-climbing. The Cardiff Classifier will be used to assess the lower-limb biomechanics and quantify the belief of osteoarthritic function (BOA) for each subject. Additionally, subjects will be asked to perform 30s Chair-Stand Test, 40m Fast-paced Walk Test, Stair-Climb Test, and Timed-up&go Test. Outcome measures will include scores from the Charlson Comorbidity Index (CCI) and the following PROs: The Western Ontario and McMaster Universities Osteoarthritis Index, Knee Injury and Osteoarthritis Outcome Score, Oxford Knee Score, Brief Pain Inventory and EQ-5D-5L. Pearson correlation coefficient will explore correlations between PROs, PBTs, BOA, and CCI.

Results: Based on previous literature, we expect to find a weak to moderate correlation between PROs and PBTs. Based on our recent findings, we expect to find a stronger relationship between PROs and BOA. We hypothesised a weaker relationship between CCI and PROs than between CCI and PBTs.

Conclusion: This pilot study will help us further understand which is the most appropriate objective functional outcome measure for end-stage KOA before TKR.

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P150 Digital volume correlation of bone and biomaterials

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Introduction: With the rapid progress of *in situ* biomechanical imaging (i.e. via micromechanics and X-ray computed tomography), digital volume correlation (DVC) has become a powerful tool to measure 3D full-field deformation in bone(1) and biomaterials(2). Research at the University of Portsmouth is at the forefront of this technique for musculoskeletal research. This talk is intended to report recent advances of DVC application in this area and to foresee future scenarios in its development.

Recent Advances:

1) **Measurement of accuracy/precision in different imaging conditions (i.e. lab microCT vs SRmicroCT).** In this area a lot of work has been done and 'zero-strain' testing for the determination of DVC uncertainties was fully established for bone and bone-biomaterial systems from organ to tissue level(3,4).
2) **Bone tissue integrity during SRmicroCT imaging.** This area emerged as a necessity to provide reliable protocols for in situ SRmicroCT experiments, where high dose is known to affect bone tissue and therefore alter its mechanics. Some very important indications were provided by DVC in this field(5,6).
3) **DVC-informed FE modelling.** This area is in continuous evolution and proposed DVC strategies to validate microCT-based models of vertebrae(7).
4) **Bone-biomaterial systems.** In this field DVC work has been done at apparent(8) and organ level(9), characterising bone-cement interfaces. More recently, bone-biomaterial integration ex vivo at tissue level was investigated(10).

Future directions: Although a number of important improvements have been achieved in recent years, DVC applied to bone and biomaterials still needs to address some fundamental aspects such as:

- Sub-volume meshing to enhance geometrical fidelity and spatial resolution.
- Alternative strain computation strategies.
- Hybrid local-global approaches.
- Improved use of the technique with clinical images.
- Analysis of soft-hard interfaces (i.e. cartilage-bone).
- Full-field strain in correlative imaging.

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P152 Glutamate receptor expression in the tibial subchondral bone changes after medial opening wedge high tibial osteotomy

Alison Kinghorn[1,2], Carole Elford[1], Paul Biggs[1], Chris Wilson[2], Cathy Holt[1], Deborah Mason[1]

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Objectives: Osteoarthritis of the knee affects 18.2% of adults over 45 in England, causing significant pain and disability. Although knee replacement surgery is very successful, there remains a significant treatment gap for younger, active patients in whom replacement is poorly tolerated and preservation of function is essential. For those with isolated medial compartment disease, valgus high tibial osteotomies (HTO) aim to slow, halt or even reverse progression of osteoarthritis. Clinical research shows HTO can improve pain and function whilst regeneration of damaged cartilage has been observed in the off-loaded compartments. However the underlying mechanism remains unclear.

Glutamate is present in increased levels in osteoarthritic joints and is involved in the inflammatory process. In animal models the glutamate signalling pathway has been shown to be mechanically regulated; driving pain, inflammation and cartilage degradation. We hypothesised realignment of the weightbearing axis of the knee via valgus HTO would cause down-regulation of glutamate receptor expression within the off-loaded medial compartment.

Methods: Twenty-one patients, recruited as part of the Arthritis Research UK Biomechanics and Bioengineering Centre HTO study, underwent valgus (medial opening wedge) HTO. Subchondral bone samples were taken from four quadrants of the proximal tibia at time of surgery (pre-HTO) and at plate removal approximately 12 months later (post-HTO). Glutamate receptors, NR2D and GRIK4, mRNAs were measured using quantitative reverse transcription polymerase chain reaction (RT-qPCR). The expression within each quadrant as a proportion of whole joint expression was compared longitudinally between pre and post samples and a paired sample t-test performed.

Results: Expression of NR2D and GRIK4 was significantly reduced within the posteromedial quadrant as a proportion of whole joint expression following medial opening wedge HTO. Mean NR2D expression (n=18) decreased by 15.5% (p=0.025), whereas mean GRIK4 expression (n=16) decreased by 17.9% (p=0.002) in the posteromedial subchondral

bone post-HTO.

Conclusions: These results suggest that expression of NR2D and GRIK4 receptors may be mechanically regulated in human subchondral bone. This supports the hypothesis that altering knee biomechanics via HTO causes changes in subchondral bone biology which are related to the progression of knee osteoarthritis.

P154 Frequency of neck pain among drivers driving during day and night in Lahore: a descriptive cross sectional study

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Objective: The purpose of this study is to find out frequency of neck pain among the two shifts of bus drivers in Lahore, Pakistan and to compare that which group is on greater risk of developing neck pain.

Methodology: it was an observational, descriptive study. A total of 80 individuals were selected randomly from the different bus stations of Lahore and included in this study after passing the inclusion and exclusion criteria to collect data by use of self-made questionnaire. The data was collected and treated statistically by SPSS 20 software and results were calculated.

Result: A total of 80 subjects were involved, in which 43(53.75%) were working in morning shift and 37 (46.25%) were working in night shift. Through this data, it was concluded that neck pain is the common disorders that was found in 22(27.5%) participants among bus drivers where drivers driving during night shift were on greater risk 12(15%) and drivers driving during day shift 10(12.5%) developed neck pain.

Conclusion: The current study concludes that frequency of neck pain is more among drivers driving during night shift as compared to the drivers driving during morning shift.

LATE BREAKING ABSTRACTS

LBP1 Imaging Fibrous Dysplasia of bone

Alan Boyde[1], Emanuela Spica[2], Alessandro Corsi[2], Mara Riminucci[2]

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We have studied routine decalcified human histopathology sections from Fibrous Dysplasia (FD) using unstained, H&E and picrosirius-red stained sections with a new polarised light microscopy (PLM) method.

In normal PLM we see collagen fibres parallel with the section plane in the 45° and 135° sectors, those parallel with the polarising filters appearing black, as all fibres perpendicular to the plane of the section. The problem can be overcome by using circularly polarised light (CPL) when the local image brightness is governed by the extent to which the collagen lies in the section plane (dip). Such images are monochrome, but dip can be scaled using pseudocolour.

We have recently developed a new automated method of PLM where we record multiple images between rotating, crossed plain-plane-polarising filters, then post-processing the image sets with ImageJ software. A typical routine is to assign one of six 15° interval sets to Red, the next Yellow, then Green, Cyan, Blue and Magenta in the colour circle sequence. The merged, pseudo-coloured image shows all elements with same orientation in the same colour, but all elements in all orientations are seen simultaneously. As with CPL, brightness equates with dip.

The structure of bone tissue and bone marrow in FD lesions is complex at all size scales. Large diameter collagen bundles in very fibrous marrow insert into seemingly randomly ordered bone trabeculae as penetrating, extrinsic, Sharpey fibres. The bright elements cross at right angles and appear like the warp and the woof of a woven fabric, but this is an imaging delusion. However, cancellous FD bone consists largely of extrinsic fibres, which, possibly because of the small gauge of the bone trabeculae, cross each other at large angles. That there is such a high proportion of the extrinsic fibre component has the corollary that FD bone has very little matrix made by osteoblasts. How little or how much has yet to be determined. The large proportion of penetrating fibres in normal bone tissue would be interpreted as indicative of load applied to the bone. Is this abnormal FD bone tissue loaded by the marrow?

LB3 Osteoblast interaction with an endothelial cell-specific extracellular matrix protein controls trabecular bone formation rate and patterning

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Objectives: Recent identification of a specific subtype of blood vessels (type H) that support osteoblast activity(1) has sparked renewed interest in the role of endothelial cells in controlling bone formation during health and disease.

Previously, we reported that genetic deletion of the transmembrane receptor CD248 in mice causes a dense bone phenotype(2). CD248 is expressed on osteoblasts and complexes with the endothelial-specific transmembrane receptor CLEC14A via their shared extracellular ligand, Multimerin 2 (MMRN2)(3). Here we explored the effect of inhibiting the endothelial-specific portion of this complex, the CLEC14A:MMRN2 interaction.

Methods: Mice: Male C57Bl/6J wildtype (WT), $CD248^{-/-}$ or $CLEC14A^{-/-}$ mice (n=5). Immunofluorescence and z-stack confocal of H-vessel markers (CD31, Endomucin) and for MMRN2. MicroCT analysis (Bruker 1172) was performed on tibiae. WT mice were given anti-CLEC14A monoclonal antibodies twice-weekly for 2 weeks that either block or do not block CLEC14A:MMRN2 binding(4) (n=4). Statistical analysis by unpaired t-test.

Results: Increased deposition of MMRN2 was seen around H-vessels compared to other bone vessels in WT mice, whilst $CLEC14A^{-/-}$ animals showed disrupted and disorganised H-vessel morphology. Genetic deletion of CD248 (expressed on osteoblasts) or CLEC14A (endothelial cell-specific) increased trabecular parameters; 4 week old $CLEC14A^{-/-}$ mice showed a 120% increase in BV/TV vs WT [Mean WT=3.9%; CLEC14A-/-=8.6%; P=0.001] and a corresponding 112% increase in trabecular number [Mean WT=0.81/mm-1; $CLEC14A^{-/-}$=1.72/mm^{-1}]. Strikingly, both $CD248^{-/-}$ and $CLEC14A^{-/-}$ had extensive trabecular bone in the diaphysis, quantified as distance from the metaphyseal growthplate to the most distal site trabeculae (mean: WT = 1.8mm; CLEC14A = 2.8mm; P=0.01). No differences were observed in cortical bone parameters. Phenotypes were maintained at 8, 12 and 32 weeks. WT mice treated for 2 weeks with CLEC14A-MMRN2 blocking antibody had 20% increased trabecular extent compared to control.

Conclusion: Our findings demonstrate that blocking binding of either the osteoblast-specific or endothelial-specific receptor to their common endothelial cell-specific extracellular ligand results in more extensive trabecularisation. This suggests a novel, and druggable, pathway for accelerating bone formation.

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LB4 Repairing myeloma-induced bone disease using combination bone anabolic and antiresorptive therapy

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Multiple myeloma is a haematological malignancy, where ~90% of patients develop devastating myeloma-induced bone disease (MBD) resulting in osteolytic lesions, increased fracture risk, chronic pain and reduced quality of life. Antiresorptives are the current standard of care, which prevent further MBD but do not repair it. Recently, inhibitors of TGF-β have been shown to have bone anabolic effects and repair MBD. Therefore, we hypothesised that combination antiresorptive and bone anabolic therapies would repair MBD significantly more than either therapy alone.

NSG female mice were inoculated intravenously with 10^6 U266-GFP-Luc human myeloma cells. Tumour burden was monitored by bioluminescence imaging (BLI) and MBD by *in vivo* microCT. When MBD was established, mice were randomised into 5 treatment groups (n=8/group); 1) vehicle, 2) dual chemotherapy with Bortezomib (B) and Lenalidomide (L), 3) B/L and SD208 (a TGF-β receptor I kinase inhibitor), 4) B/L and the anti-resorptive Zoledronic acid (ZA) and 5) B/L/ZA/SD208, receiving 4 weeks of treatment before sacrifice.

Tumour burden was significantly reduced from 1 week post-treatment in all B/L treated groups compared to vehicle as demonstrated by BLI ($p<0.01$); and at end-point by flow cytometry ($p<0.01$) and by serum IgE levels ($p<0.01$). Total bone volume (TBV) was presented as percentage change from baseline (week 0 of treatment), with increases demonstrated with B/L as early as week 2. At week 4, percentage increase in TBV was 48% for B/L ($p<0.01$), 58% for B/L/SD208 ($p<0.01$), 117% for B/L/ZA ($p<0.01$) and 129% for B/L/ZA/SD208 ($p<0.01$). Vehicle had a further decrease in TBV of 20%. In groups receiving ZA, dense cancellous bone was observed below the growth plate, likely accounting for the higher TBV.

In conclusion, the addition of SD208 has no tumorigenic effects. The bone anabolic and antiresorptive combined treatment demonstrated the most significant increase in TBV. Morphological differences in trabecular structure were observed between antiresoprtive and anabolic treatment

groups, requiring further exploration. Analysis to determine bone quality and lesion repair is ongoing to determine the role of combination therapy.

LBPP1 Fleas and bites in bones

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Armadillos are bitten by several species of flea. Females of the genus *Tunga* penetrate the epidermis and when in place are fertilised by males, after which the abdomen increases in size by up to ten times to form a 'neosome'. Within the *penetrans* group of *Tunga*, a new species, *T. perforans*, discovered by Ezquiaga et al (Medical and Veterinary Entomology 2015 29, 196–204) perforates the bones within the integument of its host. We hypothesised that the cavities eaten into the bone might be generated by recruitment of the host's osteoclasts and that they would resemble Howship's lacunae, being formed of multiples of small resorption pits.

We studied bones from two species, *Chaetophractus villosus* [greater hairy armadillo] and *Tolypeutes matacus* [southern three-banded armadillo, a species capable of rolling into a complete ball in self- defence] which showed the characteristic 2 to 3 mm diameter 'flea bite' holes in the external surfaces of the osteoderms. For backscattered electron scanning electron microscopy [BSE SEM: Zeiss EVO-MA10] samples were studied after treatment with sodium hypochlorite bleach to remove residual adherent soft tissue and contaminant soil or dust particles, washed, dried and imaged uncoated at 20kV, 50Pa chamber pressure. For x-ray microtomography (XMT: QMUL MuCat2 system, 90kV), larger samples consisting of many adherent osteoderms were cut to isolate regions containing the bony lesions and imaged at 10 micron voxel resolution. 3D rendering was performed using Drishti software.

3D BSE-SEM of the deepest lesions showed resorption pit complexes characteristic of those made by osteoclasts. Many lesions were centred on the syndesmoses between adjacent bones, but some on the centres of bones. Shallower lesions showed evident signs of repair by deposition of new bone. XMT showed extra non-bone space tunnels converging on the lesions, analogous to the micro-anatomy of overload arthrosis lesions in equine fetlock joints which we have studied extensively.

We conclude that the *Tunga* neosome creates a local host response which causes bone resorption, creating the space in which it can grow. Owing to the superficial location of the lesions, we speculate whether this might constitute a useful experimental model in the future.

LBP3 Perlecan Heparan Sulphate Supports Endochondral Ossification by Signalling Fibroblast Growth Factor Receptors and Promotes Cartilage Loss in Osteoarthritis

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Perlecan, the ubiquitous heparan sulphate proteoglycan (HSPG) of basement membranes, is important for skeletal formation as perlecan deficient mice suffered from achondroplasia and skeletal dysplasia. The objective of this study was to investigate the roles of perlecan and its HS chains in binding and controlling the activity of the fibroblast growth factors (FGF) 2 and 18.

Perlecan, FGF2, FGF18 and FGF receptors 1 and 3 were localised to the peri-chondral regions of chondrocytes in areas of endochondral ossification in developing foetal human joints. Chondrocyte-derived perlecan was decorated with both heparan and chondroitin sulphate and bound both FGF2 and FGF18 and formed ternary complexes with FGF receptors 1 or 3, in an heparan sulphate dependent fashion. Baf32 cell-based assays demonstrated that chondrocyte-derived perlecan promoted the signalling of FGF18 and FGFR3 but not FGF2 with either FGFR1 or 3 suggesting specificity of signalling. This activity was inhibited by heparanase digestion suggesting that it provided a negative feedback loop to the cell signalling. These results support the hypothesis that endochondral ossification and long bone formation require correct spatio-temporal signalling of growth factors, which suffers when perlecan and its HS are absent leading to a lack of FGF signalling and chondrodysplasias.

Mice deficient in the exon encoding the HS attachment sites synthesised perlecan lacking HS. Osteoarthritis was induced in these and wildtype mice via surgical meniscectomy and expression of FGF2, 18, FGFR1 and 3 were examined by immunohistology at weeks 4 and 8 after surgery. The perlecan HS deficient mice suffered less cartilage erosion than controls and showed a decrease in FGF18 and FGFR3 expression at 4 weeks, in a similar fashion to control animals, which was reversed significantly by 8 weeks. This suggested that the both the growth factor and receptor were not being turned over and that there was decreased signalling. This supports our in vitro studies and suggested that preventing the signalling of FGFR3 by FGF18 by removing the HS protects the cartilage from the erosive effects of osteoarthritis.

LBP4 WITHDRAWN.

LBP5 3D printing for visualisation of bone quality in osteoporosis

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Second lumbar vertebral body specimens (32 female, 27 male, ages 24-92) from the European Union BIOMED I study 'Assessment of Bone Quality in Osteoporosis' had been used to study variations in density of the calcified tissues using quantitative backscattered electron imaging. In a continuation of this study, samples were imaged using X-ray microtomography (XMT) for 3D visualisation and the XMT datasets converted and edited for 3D printing and Virtual Reality (VR).

The parasagittal bone slices were embedded in PMMA and block surfaces micro-milled and carbon coated. In this study, samples were imaged with 30 µm resolution using the QMUL MuCAT2 system, scans lasting approximately 72 hours. The 3D XMT datasets were rendered using Drishti software to produce static and movie images. The data sets were exported from Drishti to Meshlab modelling software, where they were converted to stereolithography files for 3D printing and polygon file format for VR. 3D models were printed at 100 µm resolution using fused-deposition modelling techniques with a wood-polymer composite, taking around 26 hours per print. The same data was also uploaded to the open-source Sketchfab site [https://skfb.ly/6GpVo] for 3D viewing, VR and augmented reality, allowing for full representation where the 3D printing process could not cope.

The female cases selected for 3D printing and VR represented the youngest, oldest, best and worst preservation of structure in the post-menopause, and as showing anterior and central compression fractures and anterior collapse with fusion to L3. A good proportion of elderly samples showed excellent bone architecture, but with retention of fewer but more massive load-bearing trabeculae. Male cases were selected for their good structure or for showing major lesions, including healed fractures and end-plate implosions.

The most porotic cases were also the most difficult to reconstruct with the 3D printing technique we used. This mimics the situation in the living bone, where bone cannot be added to non-existent scaffolding.

The ability to visualise a 3D representation of bone quality at a larger scale allows a true representation of changes in bone volume fraction and trabecular connectivity in osteoporosis.

LBP6 Postoperative Blood Testing in Total Hip Replacement, is it needed?

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Intro-Demand for Total Hip replacement (THR) is set to rise significantly due to increase in prevalence of osteoarthritis. In many institutions post-operative blood investigation in the form of Haemoglobin (Hb) and renal function (U&E) for patients underwent elective THR is routine management protocol. We observe postoperative blood derangement to be rare in THR and question the clinical value of these tests.

Methods: Patients underwent elective THR from Jan 2014 to Aug 2018 were included in a retrospective observational study looking into their pre and post-operative haemoglobin (Hb) levels as well as post-operative electrolytes.

The Hb and electrolytes were assessed and compared against other variables including Gender, Age, Approach, ASA grade. Subsequently data was collected in a spreadsheet for statistical analysis.

Results: Over period of 4 years 353 patients underwent elective THR. Mean age of patients were 70 years (range 42-90). There were 203 Male and 150 Female.

Mean pre-operative Hb was 134.7g/l. Mean drop in Hb post operatively was 22.3g/l.

6.4% of patients (n= 18) with an ASA of 1-2 had postoperative blood results requiring intervention compared to 17.8% of patients (n= 13) with ASA 3-4.

Overall none of the patient in ASA grade 1 and 2 with age less than or equal to 70 need blood transfusion post operatively and only 1.2% of patient had deranged renal function that need clinical intervention.

Conclusion: For patients undergoing elective THR routine post-operative bloods may not be required for young and healthy patients.

LBP7 WITHDRAWN.

LBP8 Efficacy of a bone healing stimulator (Exogen) on fracture non-union: a single centre experience

Muhammad Abuzar Yusuf, Yosef Hamed, Bismah Umerji, Aamir Zubairy

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Objectives: Exogen treatment for fracture non-union has been practiced in our institute since 2015. According to the manufacturer, the healing rate following the use of Exogen is 86%. We conducted a study to assess the success rate and cost efficacy following the usage of Exogen for fracture non-union.

Methods: 30 patients with fracture non-union were provided with Exogen treatment at our institute since 2015. We reviewed the radiographs during the course treatment to assess for radiographic evidence of fracture healing. Patients were also assessed clinically on a regular basis.

Results: The median age of the patients was 52. 63% were female and 37% were male patients. Nearly 10% were diabetics, over 10% were on long term NSAID's and just over a third were smokers. The majority, apart from two, had a closed fracture. 50% of patients had initial surgical fixation, In these patients Exogen treatment was started after a median of 7 months with a success rate of 72.2%, and the device was used for a median of 6 months in these patients. On the other hand, 50 % were started on the non-surgical treatment which continued for a median of 5 months, at which point Exogen treatment was commenced and 53.3% then united, with the median length of treatment 6 months. The Exogen device is marketed at £2562 for each case which provides 8 months of treatment. This includes a performance guarantee enforced through 90% compliance and a minimum usage of 4 months in stable fractures. However, the treatment course does not include the fracture clinic visits cost.

Conclusion: Our union rate following the use of Exogen was 63.63%. Median length of treatment was 6 months in the union cases. Cases in which treatment failed the median treatment time was also 6 months. Our healing rate is lower than the published healing rate. This could be due to comorbidities and compliance. Overall, Exogen is a good treatment modality when other options fail. Further comparative study is required against non-union fractures managed conservatively.

LBP9 Re-admission within 28 Day after Elective Total Hip Replacement and Total Knee Replacement in District General Hospital

Mustafa Abdilmalik, Raghuvendra Nanjuniah, Ibrahim Malek

Department of Trauma and Orthopedics, Wrexham Maelor Hospital, Wrexham, UK

Background: Readmission after elective Total Hip and Total Knee arthroplasty places a huge burden on the health care delivery system. Enhanced recovery program (ERP) was implemented to optimize the hospital stay in Joint Arthroplasty patients. We sought to identify common Orthopaedic reasons for 28-day hospital readmissions following Elective Total Hip and Total Knee Arthroplasty after introduction of Enhanced Recovery Pathway in our department in last nine years.

Methods: National Joint Registry database was utilised to extract the number of patients who underwent Elective Total Hip and Total Knee arthroplasty from January 2010 onwards till April 2019 in our hospital. From that data we found out the patients who got readmitted within 28days of discharge using the Clinical information electronic portal. We then sought to identify common orthopaedic reasons for readmission.

Results: Between January 2010 to April 4733 patients underwent Elective Total Hip and Total Knee arthroplasty. We had 157 out of 4733 patients (3.31%) who got readmitted within 28 days discharge. Of the 157 readmissions sixty nine patients had underwent Total hip arthroplasty and Eight eight has underwent total knee arthroplasty.

Among all the reasons identified, 53 patients were readmitted secondary to orthopaedic issues. Most common Reason among them was leg swelling (16, 0.3%) to rule out DVT, followed by dislocated hip joint (9, 0.19%). Other reason were pain (8, 0.16%), joint swelling (8, 0.16%), periprosthetic fracture (5), wound infection (2), and a single case of wound dehiscence, pseudo aneurysm, IVC filter removal each.

Conclusion: The number of patients getting readmitted after an elective total Hip and Total Knee arthroplasty due to orthopaedic reason was 53(1.12%) which is minimal and shows that the Enhanced recovery pathway has worked well in Elective Total Hip and Total Knee arthroplasty patients. We found the most common orthopaedic reason for readmission being leg swelling to rule out DVT.

LBP10 An Audit of practice: Use of Anaesthetic in Neck of Femur Fractures

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Introduction: Recent published literature has shown no statistically significant difference for Neck of Femur Fracture surgery. Current guidelines recommend offering patients both options of a spinal or general anaesthetic. At local level we attempt to ensure whether similar outcome is reflected in our practice. The aim of this study was to demonstrate difference in Morbidity (duration of stay) and Mortality (30 days and 120 days) for patients receiving either a general or spinal anaesthetic that have undergone surgery for NOF.

Methods: Data from spreadsheet maintained for NHFD was used to identify patients with Neck of Femur Fracture (NOF) in 2018.Mortality data was retrieved from the Welsh Clinical Portal. Data was organised according to the type of anaesthetic received. Outcome measures for Morbidity (length of stay in hospital) and Mortality (at both 30 days and 120 days) following surgery, were then inputted for these patients. Statistical analysis was performed using SPSS software. A Mann Whitney U Test was performed for length of stay and Kaplan-Meier Estimates for survival at 30 and 120 days. Log Rank (Mantel Cox) Hypothesis Test is used to compare mortality.

Results: We reviewed 203 patients elderly hip fracture with mean age of 83 (range 60-99), there were 142 Female and 61 males.4 patients were treated none operatively, and 2 patients had no data available .146 patient received GA and 46 received spinal anaesthesia. Hemiarthropasty and DHS are commonest procedure in both groups. On applying Mann Whitney U-test there is no statistical difference between the length of stay there is no statistical difference between the length of stay for SA and GA Patients. (p = 0.483). For SA and GA Patients (p = 0.483). On APPLYING Log Rank (Mantel-Cox) Analysis there is no statically difference in mortality at 30 days and 120 days with p value 0.087 and 0.397 respectively.

Conclusion: In summary, this audit remains in line with current literature, that there is not a significant difference between the length of stay, survival at 30 days and at 120 days between the two different groups.

LBP11 Assessment of surgical outcome and complications in cementless Total hip replacements with various femoral stems

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Objectives: The primary aim of this study was to compare the complications like infection, dislocation, periprosthetic fractures, aseptic loosening and any revision surgery after cementless total hip replacements (THR) in taperloc, triloc and Fiber metal taper (FMT) femoral stems. The secondary aim of the study was to assess the orientation of the THR complex focussing on various parameters like the acetabular version, acetabular inclination, limb length discrepancy, femoral and global offset and centre of rotation.

Methods: It was a retrospective study and the data was retrieved from the logbook of a senior consultant who specialises in revision THR in the trust, with permission. Radiographs of 450 patients were analysed by two surgeons. The inclusion criteria were all those who underwent cementless THR for traumatic or atraumatic causes, had a follow up for at least one year, had taperloc or triloc or FMT stems, all surgeries through posterior approach. The exclusion criteria were all those who had revision surgeries, had follow up of less than one year.

Results: around 5 patients had periprosthetic fractures in FMT stems and one patient with triloc stem. These fractures were more common in Dorr type C femurs. About 5 patients had dislocation and underwent relocation procedure and one had revision surgery. Around 4 patients had revision surgeries for infection.

Conclusion: The cementless stems are very popular stems in THR surgeries. The tapered stems are better at preserving the bone substance and hence are recommended for younger population.

LBP12 WITHDRAWN.

NOTES

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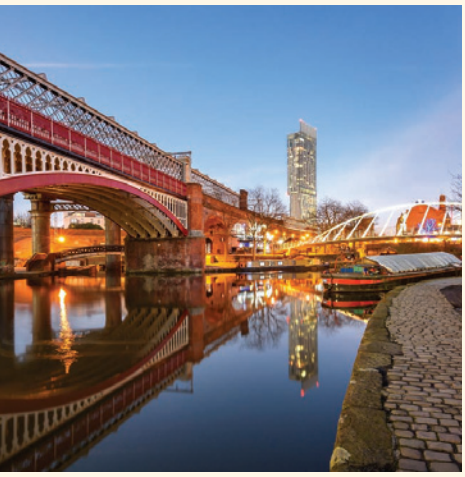

PROGRAMME HIGHLIGHTS INCLUDE:

SYMPOSIA AND OTHER SESSIONS:

- Bone Mechanoadaptation
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- Nutrition and the Gut
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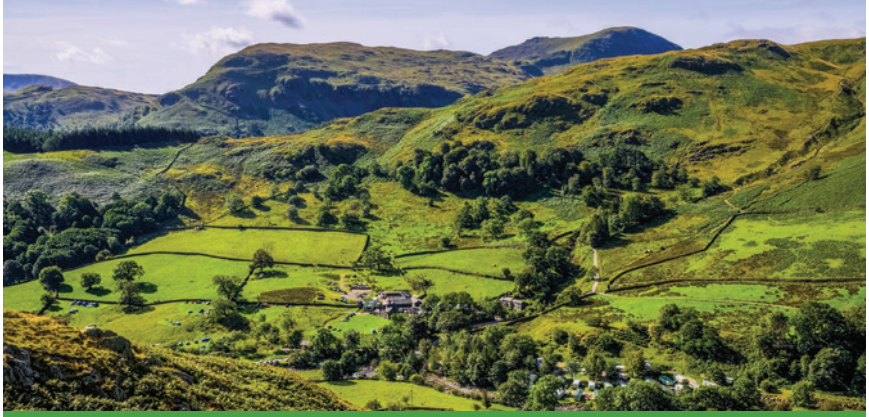

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Bone Research Society

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