The UK's largest ever gathering of Biomedical Engineers, Bioengineers and Medical Engineers

MECbioeng14

Medical Engineering Centres Annual Meeting and Bioengineering14

at Imperial College London

10-11 September 2014

mecbioeng.org   **#MECbioeng14**

Contents

FOREWORD FROM CHAIR

Professor Anthony Bull
Chair of MECbioeng14
Head of Department of Bioengineering, Imperial College London
Director of Medical Engineering Solutions in Osteoarthritis Centre of Excellence
Director of the Institute of Biomedical Engineering at Imperial College London

Dear Friends and Colleagues,

It is my delight and pleasure to welcome you to Imperial College London for the fifth annual Medical Engineering Centres meeting and the seventh annual Bioengineering Society meeting.

The merger of these two events reflects so many things that are good about biomedical engineering in the UK: we are well-funded by governments and charities through, for example, the Medical Engineering Initiative; we have a vibrant, strong and growing academic research base that reflects the importance of the discipline to society; and we are keen to collaborate in bringing together the bioengineering discipline together with industry to further our translational research aims as well as to help create a single forum for the discipline.

Such an event doesn't happen on its own and so I would like to thank all those who have worked very hard in the background to make this event the success that I know it will be. The local organising committee led by Dr Jenna Stevens-Smith has worked tirelessly, focusing not only on the operational, but also the strategic level. The wider organising committee with representation from Leeds, Oxford and King's College London has assisted greatly in helping to direct the event and providing excellent collaborative support. We are all very excited about next year's joint event in Leeds.

Our main sponsors are the Wellcome Trust and EPSRC who have graciously supported this event, the previous four MEC Meetings, and we have agreed to support the next four meetings, taking us to 2018. We are indebted to them for their strategic farsightedness in supporting our discipline through the Medical Engineering Initiative.

The Bioengineering Society, led by Professor Peter Weinberg, has worked diligently to help bring together the various groupings in the discipline and our thanks go to them and all our supporters including company sponsors and the medical charities, BHF, ARUK and CRUK who have backed this event.

Finally, my thanks go to you, the delegates. Thank you for coming to Imperial College, thank you for contributing your time and energy to this event. I invite you to participate fully, enjoy our fantastic plenary talks by two great speakers, and take full advantage of the extra-curricular programme. Our conference banquet will an opportunity to make new friends, be entertained and challenged by our after dinner speaker, Dr Michael Mosley, and then cement those new friendships as our late-night entertainment, Gasstrick Band, will keep us on our feet until midnight.

Anthony Bull

Useful Information

Wifi is available for all delegates. If you do not automatically have access to wifi through your Imperial or eduram networks you can pick up your username and password from the registration desk for access for the whole conference.

Blendology badges. The badges enable you to network and share your contact details with others at the conference, like an electronic business card. You can tap with fellow delegates to connect and tap the Blendology boxes outside of each Parallel Session to keep track of your   journey around the conference.
*It is important that the badges are returned to the **Blendology team** at the end of the conference.*

Cloakroom there is a cloakroom located on the Level 2 of Sherfield next to the Great Hall which will be manned during the hours of the conference.

The **Parallel Sessions** will be running in parallel so delegates are able to move between sessions if they wish, please do not disrupt sessions if you are moving between them.

To ensure sessions run in parallel all presenters will be kept **strictly** to time.

About MECbioeng14

This is the UK's largest ever gathering of Biomedical Engineers, Bioengineers and Medical Engineers, with participants from leading academic centres and the MedTech industry.

It is the fifth annual meeting of the Medical Engineering Centres, which were founded by the Wellcome Trust/EPSRC Medical Engineering Initiative, and the seventh annual meeting of the Bioengineering Society, this is the first time these meetings have been combined.

Acknowledgements

Many people and organizations have contributed their time, expertise, funds and energy to ensure the success of the Medical Engineering Centres and Bioengineering14 conference at Imperial College London. We are indebted to your passion and dedication to making this conference one to remember for many years to come. Our goals were to organize a meeting which covered the breadth and depth of bioengineering, the important issues facing the discipline and to bring the growing UK bioengineering community together. Your efforts have made this conference possible!

Professor Peter Weinberg
Co-Chair of MECbioeng14
Chair of the Bioengineering Society

It gives me great pleasure to welcome you to the MEC Annual Meeting and Bioengineering14, and to the Bioengineering Society itself – as in previous years, registration for the meeting automatically includes membership. This is the Society's 7th annual meeting; for the first time it is being held jointly with the annual meeting of the Medical Engineering Centres funded by the Wellcome Trust and EPSRC. I am grateful that the Centres and their funders have agreed to this joint venture. The large number of participants from universities, the NHS and industry demonstrates the phenomenal growth of bioengineering in the UK and the benefits to be gained from bringing together the diverse groups that currently represent the discipline. The MEC meetings will continue for at least another 4 years, at Leeds, Oxford, KCL and Imperial, we look forward to joining forces again for the Leeds meeting in 2015.

When I initiated the Society in 2008, my aim was not only to hold an annual scientific meeting but also to start building an organisation that would represent the interests of bioengineers nationally. Our Oxford and Strathclyde meetings included debates about this, and particularly about the merits of joining forces with the Institution of Mechanical Engineers (IMechE) or the Institute of Physics and Engineering in Medicine (IPEM); there was wide support for the latter. We held positive discussions with both organisations this year. We recommend a merger with IPEM, which has a growing emphasis on bioengineering; combined with the Bioengineering Society, it could become an organisation akin to an Institution of Bioengineering. However, we also want to work with IMechE (and IET and RSM), perhaps by establishing an umbrella organisation to co-ordinate our scientific meetings, accreditation of degrees, etc. These proposals will be presented for debate and approval at the special session on Wednesday.

My term as Chair of the Bioengineering Society finishes at this meeting. I would like to thank my fellow Committee members, especially our Honorary Secretary Professor Peter Brett, for the substantial time and effort they have devoted to running the Society. At the AGM on Thursday, the Committee will propose Professor Alicia El Haj as the next Chair. She is ideally suited to the role by her involvement with the Society and with IPEM and her work in promoting the discipline more widely. We hope you will feel able to support her candidacy.

Finally, I would like to thank the British Heart Foundation, Cancer Research UK and Arthritis Research UK for funding bursaries to help early career researchers attend the meeting, our commercial sponsors, and fellow members of the Local Organising Committee, who have worked tirelessly to make this meeting a success. I look forward to seeing you at MECbioeng15 in Leeds next September.

Peter Weinberg

Sponsors

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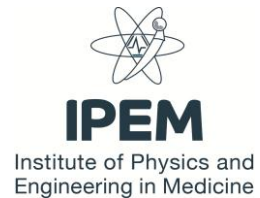
Company sponsors:

Contributors

Local Organising Committee

Professor Anthony Bull
  Chair of MECbioeng14
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  Director of Medical Engineering Solutions in Osteoarthritis Centre of Excellence
  Director of the Institute of Biomedical Engineering, Imperial College London

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Professor Lionel Tarassenko, University of Oxford
Professor Alison Noble, University of Oxford
Sergei Maslau, University of Oxford
Professor John Fisher, University of Leeds
Dr Josephine Dixon-Hardy, University of Leeds

MAPS

Map of Imperial College London, South Kensington campus
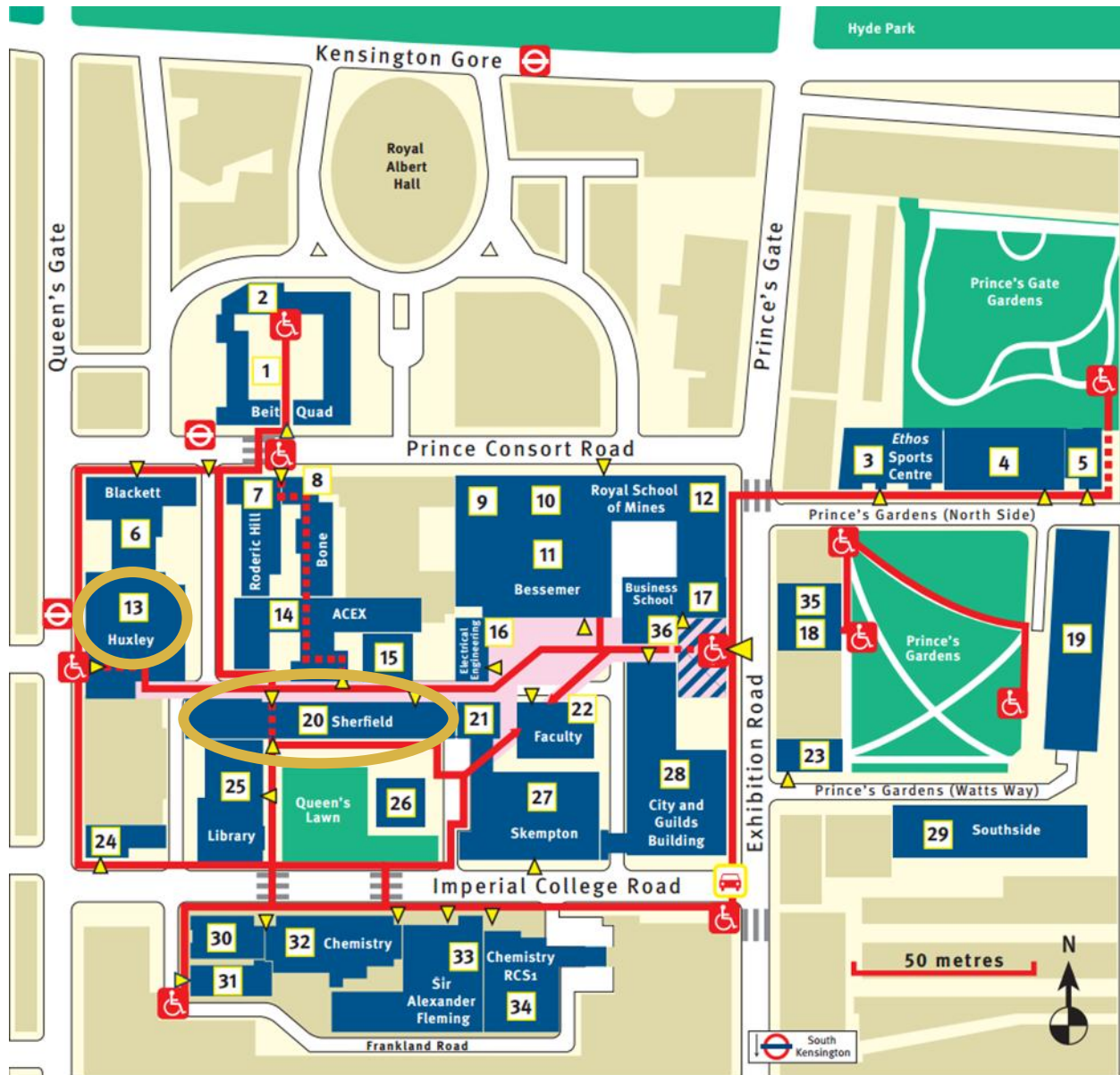
The conference is based in the Sherfield and Huxley buildings, circled on the above map.

Getting to campus

From South Kensington Station, the campus is only a five minute walk. Either follow the subway signposted to the museums or walk north up Exhibition Road. The College is next to the Science Museum. To get to registration walk down Imperial College Road and when you get to the Queen's Tower, turn right and walk around the Queen's Lawn to the main entrance of the Sherfield Building, located next to the Library.

Conference locations

Huxley Building
(Level 1)

Parallel Session Lecture Theatres are located in the Huxley building. This is a short walk from the Great Hall on level two out and along the walkway. Once in the Huxley building follow the signs down to Level 1 where we have Lecture Theatres 130, 140, 144 and 145 on Day 1 and 144 and 145 on Day 2.

Walkway
2nd floor

Sherfield Building

Great Hall

(Level 2)

Main Lecture Theatre where the plenary talks and sessions will be located and on the second day will host one stream of the parallel sessions. Located on Level 2 in the Sherfield building.

Registration is located in the foyer of the Sherfield building outside of the Queens Tower Rooms. This is where you can register for the conference, pick up your bags, programme and first point of call for any MECbioeng14 questions.

Main networking area of the conference. This is where you will find the exhibitor stands, all catering (teas, coffees and lunch) and the poster presentations.

Cloakroom

Stairs

Registration *i*

Queen's Tower Rooms

(Level 1- Ground floor)

Entrance

Conference Schedule at a Glance

Tuesday 9 September		
20:00 to 22:00	**Informal networking and quiz night**	Eastside Restaurant & Bar, Prince's Gardens, London SW7 1LY

Wednesday 10 September		
08:30 to 10:00	Registration	Sherfield Building
10:00 to 10:10	**Welcome and Plenary Introduction**	Great Hall
10:10 to 10:55	**Plenary Talk: Professor Dominque Durand**	Great Hall
10:55 to 11:25	**Plenary Poster Presentation**	Great Hall
11:25 to 11:45	Break and Poster Session	Queen's Tower Rooms
11:45 to 13:15	**Parallel Sessions 1**	
	Biomechatronics and Medical Robotics	Huxley Building 130
	Biomedical Imaging and Image Analysis	Huxley Building 145
	Tissue Engineering and Regenerative Medicine	Huxley Building 144
	Outreach and Careers in Biomedical Engineering	Huxley Building 140
13:15 to 14:00	Lunch	Queen's Tower Rooms
14:00 to 15:30	**Parallel Sessions 2**	
	e-Health	Huxley Building 130
	Orthopaedic Engineering	Huxley Building 145
	Cellular and Molecular Bioengineering	Huxley Building 144
	IP and Translation	Huxley Building 140
15:30 to 16:00	Break	Queen's Tower Rooms
16:00 to 17:30	**Parallel Sessions 3**	
	Bionanotechnology	Huxley Building 130
	Biomedical Electronics, Bioinstrumentation and Medical Devices	Huxley Building 145
	Mechanotransduction	Huxley Building 144
	Taught Courses in Bioengineering	Huxley Building 140
17:30 to 18:30	**Plenary Session: Bioengineering in the UK – Past, Present and Future**	Great Hall
19:00 to 22:00	Drinks Reception, Dinner and After-Dinner Speaker: Dr Michael Mosley	Queen's Tower Rooms
22:00 to 00:00	Followed by musical entertainment until late	

Thursday 11 September

Time	Event	Location
08:00 to 09:00	Registration *(for those attending on Day 2 only)*	Sherfield Building
08:30 to 09:00	**Bioengineering Society Annual General Meeting**	Huxley Building 144
09:00 to 09:45	**Plenary Talk:** Professor Paul Davies	Great Hall
09:45 to 10:15	**Plenary Poster Presentation**	Great Hall
10:15 to 10:45	Coffee Break and Poster Session	Queen's Tower Rooms
10:45 to 12:15	**Parallel Session 4**	
	Cardiovascular and Respiratory 1	Great Hall
	Cancer Engineering and Technologies	Huxley Building 144
	Rehabilitation, Sports And Motion	Huxley Building 145
12:15 to 13:00	Lunch	Queen's Tower Rooms
13:00 to 14:30	**Parallel Session 5**	
	Biomechanics	Great Hall
	Cardiovascular and Respiratory 2	Huxley Building 144
	Biomaterials	Huxley Building 145
14:30 to 15:00	Coffee Break	Queen's Tower Rooms
15:00 to 16:30	**Parallel Session 6**	
	Neurotechnology	Great Hall
	Tissue Mechanics	Huxley Building 144
	Business Pitch Competition and Company Presentations	Huxley Building 145
16:30 to 17:00	Prize Giving	Great Hall
17:00	Close	

DAY 1

Wednesday 10 September	
08:30 to 10:00	Registration — **Sherfield Building**
10:00 to 10:10	**Welcome and Plenary Introduction** — **Great Hall**
10:10 to 10:55	**Plenary Talk: Professor Dominque Durand** — **Great Hall**
10:55 to 11:25	**Plenary Poster Presentation** — **Great Hall**
11:25 to 11:45	Break And Poster Session — **Queen's Tower Rooms**

11:45 to 13:15 Parallel Sessions 1   Huxley Building

Biomechatronics and Medical Robotics   Huxley Building 130

11:45 to 12:00	Keynote: Professor Peter Brett: Discriminating The Real-Time Tissue Working-Environment of Robotic Surgical Devices Using Tactile Information.
12:00 to 12:15	Rashed Karim: Image-Guidance Of An MR-Compatible Catheter Using Combined 2D/3D Models Of The Left Atrium
12:15 to 12:30	Gauthier Gras: A Flexible Robotic Probe for Osteoarthritis Intervention
12:30 to 12:45	Edward Chadwick: Control of a Virtual, Trans-Humeral Myoelectric Prosthesis Using EMG and Kinematic Signals
12:45 to 13:00	Stuart Bowyer: Optimal Tool Pose Control in Active Constraints for Soft Tissue Dissection
13:00 to 13:15	Riccardo Secoli: A Wasp-Inspired 3D Needle Steering System for Soft Tissue Surgery

Biomedical Imaging and Image Analysis   Huxley Building 145

11:45 to 12:05	Meng-Xing Tang: Quantitative Ultrasound Imaging of Arterial Flow, Micro-Circulation and Molecular Targets
12:00 to 12:15	Fabio Alessio Vittoria: Recent Developments and Applications of Edge Illumination X-Ray Phase Contrast Imaging
12:15 to 12:30	Sara Lacerda: New Gd(Iii) Contrast Agents for High-Risk Atherosclerotic Plaques by MRI
12:30 to 12:45	Richard Foster: Activation Energy Mapping in Articular Cartilage
12:45 to 13:00	Thomas Rackham: Fetal Face Segmentation and Contour Characterisation in 3D Ultrasound
13:00 to 13:15	A. N. Cookson: A Physiologically-Realistic Model of Cardiac Magnetic Resonance Perfusion Imaging in the Beating Heart

Tissue Engineering and Regenerative Medicine   Huxley Building 144

11:45 to 12:00	A Abdelgaied: Effect of Decellularisation on the Biomechanical Properties of Porcine Meniscus: Experimental and Computational Study
12:00 to 12:15	Rahul S. Tare: Application of Acoustic Perfusion Bioreactor for Augmentation of Cartilage Tissue Engineering
12:15 to 12:30	Jean-Philippe St-Pierre: Anisotropic Scaffold to Direct Zonally Distinct Articular Cartilage Tissue Regeneration
12:30 to 12:45	Esther Tejeda Montes: Bioactive Membranes for Bone Regeneration
12:45 to 13:00	Yvonne Reinwald: Evaluation of the Growth Environment of a Hydrostatic Force Bioreactor for Preconditioning Tissue-Engineered Constructs for Clinical Application
13:00 to 13:15	Giuseppe Cama: Resorbable Calcium Phosphate Bone Cements Prepared by a Facile Synthetic Method

Outreach and Careers in Biomedical Engineering   Huxley Building 140

11:45 to 12:00	Marlene Mengoni: On Presenting Aspects of Computational Biomechanics to the Non-Specialists
12:00 to 12:15	Rowan Grant: Outreach As a Tool for Growing Company Engagement
12:15 to 12:30	Matthew Tomlinson: Bioengineering Outreach with Schools
12:30 to 13:15	Careers Panel Discussion (Including Representatives from Academia, Industry, and Outreach)
13:15 to 14:00	Lunch — **Queen's Tower Rooms**

14:00 to 15:30 Parallel Sessions 2   Huxley Building

e-Health   Huxley Building 130

14:00 to 14:15	Robert J Dickinson: A Mobile Android-Based Platform for Intelligent Oxygen Therapy
14:15 to 14:30	Thomas Fastl: Towards A Modeling Pipeline for Atrial Electromechanics
14:30 to 14:45	Arvind Raghu: Managing the Burden of Cardiovascular Disease in Resource-Constrained Regions using mHealth
14:45 to 15:00	David A. Clifton: Robust Estimation of Respiratory Rate from Pulse Oximeters
15:00 to 15:15	Luke Moore: Case-Based Reasoning for Antimicrobial Prescribing Decision Support: A Solution for Critical Care?
15:15 to 15:30	Peter Charlton: Electronic Acquisition Of Vital Signs On General Wards

Orthopaedic Engineering   Huxley Building 145

14:00 to 14:15	Joshua W Giles: The Influence of Reverse Shoulder Arthroplasty Implant Variables on Muscle Activation and Joint Load
14:15 to 14:30	Mazen Al-Hajjar: Steep Cup Inclination Can Lead To Severe Edge Loading And Increased Wear Under Surgical Translational Mal-Position Of Hip Replacement Prostheses
14:30 to 14:45	Raelene Cowie: Influence of Lubricant and Temperature on the Wear of UHMWPE Articulating Against Peek Optima
14:45 to 15:00	Richard Abel: 3d Imaging Bone Quality: Bench To Bedside
15:00 to 15:15	Yuxing Wang: Comparison of Stress on Knee Cartilage for Kneeling and Standing by using Finite Element Models
15:15 to 15:30	Gifty Tetteh: Engineering an *in vitro* 3D Bone Model for Implant Testing

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	Cellular and Molecular Bioengineering	**Huxley Building 144**
14:00 to 14:15	Nont Panitchob: Computational Modelling of the Placental Amino Acid Transport System	
14:15 to 14:30	Leila Towhidi: A Novel High-Throughput Platform for Sirna Transfection of Primary Mammalian Cells	
14:30 to 14:45	Suja George: Generation of High Affinity Binders Against Clinically Relevant Cardiovascular Biomarkers and their Potential for the Development of Clinical Diagnostics	
14:45 to 15:00	Stefaan W. Verbruggen: Changes in Bone Cell Stimulation during the Temporal Development of Osteoporosis	
15:00 to 15:15	Kristina Sliogeryte: Stem Cell Differentiation Increases Membrane-Actin Adhesion Regulating Cell Blebability, Migration and Mechanics	
15:15 to 15:30	Sandra Bovens: Large Heterogeneity of KLF2 and KLF4 in Endothelial Cells Covering a Plaque	

	IP and Translation	**Huxley Building 140**
14:00 to 14:15	Tony Hickson, Managing Director Technology Transfer, Imperial Innovations	
14:15 to 14:30	Ceri James Mathews, IP & Licensing Manager, Kings College	
14:30 to 14:45	Dr Richard Holliday, Technology Transfer Team Leader, Isis Innovation Ltd	
14:45 to 15:00	Chris Brown, IP and Commercialisation Manager, Leeds University	
15:00 to 15:15	Trends In Medical Device IP, Sophie Maughan Principal, Scott & York Intellectual Property Law	
15:15 to 15:30	Panel Discussion	
15:30 to 16:00	Break	**Queen's Tower Rooms**

16:00 to 17:30	**Parallel Sessions 3**	**Huxley Building**

	Bionanotechnology	**Huxley Building 130**
16:00 to 16:15	Rafael T. M. De Rosales: Detection of VCAM-1 Expression using Targeted Multimodal Nanoparticles: Towards the Detection of Atherosclerotic Plaque Using Pet-Guided MRI	
16:15 to 16:30	M.G. Katsikogianni: Fluorapatite Coatings are Antibacterial *in vitro* Against Pathogens Implicated In Peri-Implantitis	
16:30 to 16:45	Iraklis Papageorgiou: Structural Alterations In The Dura Mater After Exposure To Clinically Relevant CoCr Nanoparticles. An Organ Culture Simulation With Total Disc Replacement Wear Debris.	
16:45 to 17:00	Rachel Myers: Cavitation Responsive Nanoparticles for the Enhancement of Drug Delivery	
17:00 to 17:15	Christian Coviello: Instigation and Real-Time Mapping of Cavitation from Nanoparticles using a Diagnostic Imaging Platform	
17:15 to 17:30	Fatemeh Mohammdvaligodarzi: Design and Development of Thoracic Aortic Aneurysm (Taa) Stent-Graft using Nanocomposite Material and Shape Memory Alloy	

	Biomedical Electronics, Bioinstrumentation And Medical Devices	**Huxley Building 145**
16:00 to 16:15	Constantinos Gavriel: Smartphone App as Ultra-Low Cost Medical Tricorder For Real-Time Cardiological Measurements Via Ballistocardiography	
16:15 to 16:30	Patrick Carena: A Novel 3D Motion Sensing System for the Early Diagnosis of Huntington's Disease and other Movement Disorders	
16:30 to 16:45	Peter Charlton: Continuous Physiological Monitoring of Ambulatory Patients	
16:45 to 17:00	Stefania Fabbri: Microspray Technology as a Potential Antimicrobial Delivery Method for Dental Plaque Biofilms	
17:00 to 17:15	Katerina Spranger: Methods for Virtual Stent Deployment	
17:15 to 17:30	Hannah Darton: Development of Embedded Piezoelectric Sensors to Determine Implant Loosening	

	Mechanotransduction	**Huxley Building 144**
16:00 to 16:15	Keynote: Professor Martin Knight	
16:15 to 16:30	Oliver Fleck: Employing Synthetic Biology and Shear Stress Sensing to Tackle Atherosclerosis	
16:30 to 16:45	Elisa Budyn: Back To Life: Fresh Osteocytes Spreading their Processes for Optimum Mechanotransduction Near Microdamage in Dead Bone	
16:45 to 17:00	Mario Giorgi: Mechanical Forces Play a Crucial Role During Prenatal Hip Joint Morphogenesis	
17:00 to 17:15	Zahra Mohri: Effect of PECAM-1 on Patterns Of Permeability in the Mouse Aortic Arch	
17:15 to 17:30	Yiannis Ventricos: The Effect of Hemodynamics on Inflammatory Responses in Endothelial Cells	

	Taught Courses In Bioengineering	**Huxley Building 140**
16:00 to 16:30	Discussion and Debate: Bespoke Biomedical Engineering vs. more General Engineering	
16:30 to 16:45	Michael Truong: Augmented Reality for Assisting Learning of Biomedical Engineering Students	
16:45 to 17:00	Value of Accreditation in Biomedical Engineering	
17:00 to 17:15	What is Industry Looking for in a Biomedical Engineering Graduate?	
17:15 to 17:30	Panel Discussion	

17:30 to18:30	**Plenary Session: Bioengineering In The Uk – Past, Present And Future**	**Great Hall**
17:30 to 17:40	Peter Weinberg: Bioengineering in the UK: Past, Present And Future	
17:40 to 17:50	Patrick Finlay: Bioengineering Engineering Institutions in the UK: The Way Forward	
17:50 to 18:00	Anthony Bull: Bioengineering in the UK: Strategy for Translation	
18:00 to 18:30	Panel Discussion (Questions welcomed from the Audience and via Twitter #MECbioeng14)	
	Panel: Anthony Bull (Chair), Peter Weinberg, Patrick Finlay and Representatives from Industry, Academia, Engineering Institutions and Funders.	
19:00 to 22:00	Drinks Reception, Dinner and After-Dinner Speaker: Dr Michael Mosley	**Queen's Tower Rooms**
22:00 to 00:00	Followed by Musical Entertainment until Late	

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DAY 2

Thursday 11 September		
08:00 to 09:00	Registration *(for those attending on Day 2 only)*	**Sherfield Building**
08:30 to 09:00	**Bioengineering Society Annual General Meeting**	**Huxley Building 144**
09:00 to 09:45	**Plenary Talk:** Professor Paul Davies	**Great Hall**
09:45 to 10:15	**Plenary Poster Presentation**	**Great Hall**
10:15 to 10:45	Coffee Break and Poster Session	**Queen's Tower Rooms**
10:45 to 12:15	**Parallel Session 4**	
	Cardiovascular and Respiratory 1	**Great Hall**
10:45 to 11:00	Peressutti D: A Novel Framework For Accurate And Robust Respiratory Motion Compensation In Image-Guided Interventions Using 3D Echocardiography.	
11:00 to 11:15	Junjing Su: Wave Intensity Analysis In The Pulmonary Artery	
11:15 to 11:30	Eleni Bazigou: Unilateral Nephrectomy As A Model Of Altered Blood Flow For The Study Of Arterial Permeability.	
11:30 to 11:45	Henry Chubb: First In Man: Real-Time Magnetic Resonance-Guided Ablation Of Typical Right Atrial Flutter Using Active Catheter Tracking	
11:45 to 12:00	Peter Hoskins: Comparison Of USPIO Uptake And Wall Stress In Abdominal Aortic Aneurysms.	
12:00 to 12:15	Ryan M. Pedrigi: Macrophages Accumulate Preferentially In Local Regions Of Low Shear Stress In A Hypercholesterolemic Porcine Model Of Atherosclerosis	
	Cancer Engineering and Technologies	**Huxley Building 144**
10:45 to 11:00	Gavin AD Metcalf: Sensing And Profiling Of Circulating Cell-Free Nucleic Acids With Fluorogenic PNA Probes: A High-Throughput And Minimally Invasive Approach For Early-Stage Diagnosis And Improved Prognosis Of Cancer	
11:00 to 11:15	Omar S. Al-Kadi: Predicting Tumour Responsiveness To Chemotherapy Treatment In Volumetric Xenograft Images	
11:15 to 11:30	Petros-Pavlos Ypsilantis: Texture Analysis Of 18F-FDG PET Imaging For Prediction Of Neoadjuvant Chemotherapy Response In Oesophageal Cancer	
11:30 to 11:45	Michael Sutcliffe: Calculating Voxel-Based Radiotherapy Dose In Treatment Of Prostate Cancer	
11:45 to 12:00	James Kwan: Nanoparticle Induced Inertial Cavitation For Enhanced Drug Delivery To Tumours	
12:00 to 12:15	Apurva R. Shah: Inertial Cavitation Induced Doxorubicin Release From Nano-Liposomes Exposed To Focused Ultrasound Using Nano-Scale Cavitation Nuclei	
	Rehabilitation, Sports And Motion	**Huxley Building 145**
10:45 to 11:00	Enrica Papi: Wearable Technology In Osteoarthritis: A Qualitative Study Of Patients' Perspectives.	
11:00 to 11:15	Benny Lo: BSN Analytics – A Tool For Pervasive Gait Analysis	
11:15 to 11:30	Angela E Kedgley: Locating The Hip Joint Centre: Functional And Regression Methods Vs. MRI	
11:30 to 11:45	Maximilian M Wdowski: Asymmetry Of Step Characteristics In Acceleration Sprint Running	
11:45 to 12:00	Steven C Abbott: Early Results Of A Method To Measure Short Duration Velocity Fluctuations In Human Motion: A Comparitive Study Between Average Fitness Individuals And Marathon Runners.	
12:00 to 12:15	Tomislav Milekovic: Decoding Activity Of Leg Muscles From Motor Cortex Local Field Potentials In Freely Moving Non-Human Primates	
12:15 to 13:00	Lunch	**Queen's Tower Rooms**
13:00 to 14:30	**Parallel Session 5**	
	Biomechanics	**Great Hall**
13:00 to 13:15	Haoyu Chen: Modelling The Microstructural Adaption Of The Collagen Fabric During Aneurysm Evolution	
13:15 to 13:30	M Keith Sharp: A Mechanism For Perivascular Clearance Of Amyloid-β From The Brain	
13:30 to 13:45	Mohammad Jafarnejad: The Exchange Of Fluid Between Lymph And Blood In Lymph Nodes	
13:45 to 14:00	C. Ross Ethier: Influence Of Lamina Cribrosa Microstructure In Glaucoma	
14:00 to 14:15	Joseph M. Sherwood: A New Approach For Ocular Biomechanics In Mice	
14:15 to 14:30	Martin Stanley: An In Vitro Model To Assess The Biomechanical Function Of Meniscus Repair Methods	
	Cardiovascular And Respiratory 2	**Huxley Building 144**
13:00 to 13:15	Desmond Dillon-Murphy: Multi-Modality Image-Based Analysis Of Hemodynamics In Aortic Dissection	
13:15 to 13:30	Jonathon Bailey: Novel Methods For Computational Simulation Of Complete TAVI Devices And Application.	
13:30 to 13:45	Cesare Corrado: Identification Of Atrial Parameter By Catheter Measurements	
13:45 to 14:00	Yumnah Mohamied: Spatial Correlation Between Atherosclerotic Lesion Frequency, Arterial Wall Permeability And Three Wall Shear Stress Metrics In The Rabbit Aorta.	
14:00 to 14:15	Moshe Brand: Experimental And Numerical Study Of Approaches For Treatment Of Aortic Arch Aneurysm	
14:15 to 14:30	Lionel Tarassenko: Heart Sound Segmentation Using A Logistic Regression-Based Hidden Semi-Markov Model	

	Biomaterials	**Huxley Building 145**
13:00 to 13:15	Keynote: Dr Alvaro Mata	
13:15 to 13:30	Evangelos Liamas: The Effect Of Surface Chemistry On Protein Adsorption – An Experimental And Computational Study	
13:30 to 13:45	Danielle Miles: Design, Characterisation And Evaluation Of Peptide:Glycosaminoglycan Hydrogels For Intervertebral Disc Therapies	
13:45 to 14:00	Mariea A Brady: Development Of A Magnetically Active And Biomimetic Scaffold For Cartilage Tissue Engineering	
14:00 to 14:15	Jonathan Dawson: Clay Gels Localise And Enhance BMP2 Induction Of Osteogenesis	
14:15 to 14:30	Helene Autefage: Effect Of Strontium Incorporation With Bioactive Glasses On Human Mesenchymal Stem Cell Whole Gene Expression	
14:30 to 15:00	Coffee Break	**Queen's Tower Rooms**

15:00 to 16:30	**Parallel Session 6**	
	Neurotechnology	**Great Hall**
15:00 to 15:15	Keynote: Dr Simon J. Archibald: Pathways For Regenerative Medicine In Neurosurgery?	
15:15 to 15:30	Constantinos Gavriel: Next-Generation Medical Diagnostics In Natural Environments Based On Low-Cost Wireless Body Sensor Networks	
15:30 to 15:45	Jiayao Ma: Mechanical Design Of A New Cerebral Flow-Diverter Stent	
15:45 to 16:00	Nada Yousif: A Dynamic Network Model Of Essential Tremor	
16:00 to 16:15	Markus D. Schirmer: Parcellation-Independent Multi-Scale Framework For Brain Network Analysis	
16:15 to 16:30	Jamie A. O'Reilly: Investigating Mismatch Negativity-Like Activity In The MAP2k7 Schizophrenia Model	
	Tissue Mechanics	**Huxley Building 144**
15:00 to 15:15	Mahsa Shahi Avadi: In Vitro Degradation Of Mechanical Properties Of Porcine Femoral Head Bone For Development Of An In Vitro Of Avascular Necrosis	
15:15 to 15:30	Darryl R Overby: Altered Mechanobiology Of Schlemm's Canal Endothelial Cells In Glaucoma	
15:30 to 15:45	Gareth Ward: Design And Development Of A Synthetic Biocompatible Basement Membrane For Use As A Treatment For Age-Related Macular Degeneration.	
15:45 to 16:00	Andrea Fotticchia: Intervertebral Disc Composite Mechanically Stimulated In Bioreactor For Tissue Engineering Of Annulus Fibrosus Artificial Replacement	
16:00 to 16:15	Simon A. Lambert: The Big Impact Of Little Things: Vasculature Bed Can Lead Its Footprint At The Macroscopic Scale Of Magnetic Resonance Elastography Data.	
16:15 to 16:30	Naiara Rodriguez-Florez: The Use Of XFEM To Assess The Influence Of Vascular Canals In Bone Crack Propagation	
	Business Pitch Competition & Company Presentations	**Huxley Building 145**
15:00 to 15:30	Keynote: Professor Colin Caro, in Conversation With Professor James E. Moore Jr	
15:30 to 15:35	Basil Richard Fansa: Developing A Novel Wound Dressing Aiming To Promote Healing In Patients With Chronic Wounds, Namely, Diabetic Ulcers.	
15:35 to 15:40	Karthik Ravichandran: Preventing Breast Cancer Related Lymphedema	
15:40 to 15:45	Sorin Popa: Stent Tek: Enabling Percutanous Creation Of Vascular Access In Dialysis Patients	
15:45 to 15:50	Flavia Tempesti: LOBSTER: Low-Cost Bimanual System For Physical Therapy And Enhanced Rehabilitation	
15:50 to 15:55	Paulo Angeles: Assessment Device To Quantify The Severity Of Parkinson's Symptoms	
16:00 to 16:15	Lars Neumann: 2D, 3D, 4D – Advancing Implant And Device Design (Materialise)	
16:15 to 16:30	Bill Munday: Connecting Conveniently oneTap from Health To Events (Blendology)	
16:30 to 17:00	Prize Giving	**Great Hall**
17:00	Close	

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Professor Dominique Durand

*Elmer Lincoln Lindseth Professor in Biomedical Engineering;
Director, Neural Engineering Center at Case Western Reserve University*

Dr DM Durand is the E.L. Linsedth Professor of Biomedical Engineering Neurosciences, Physiology and Biophysics and Director of the Neural Engineering Center at Case Western Reserve University in Cleveland, Ohio. He received an engineering degree from Ecole Nationale Superieure d'Electronique, Hydrolique, Informatique et Automatique de Toulouse, France in 1973. In 1974, he received a M.S. degree in Biomedical Engineering from Case Reserve University in Cleveland OH., worked several years at the Addiction Research Foundation of Toronto, Canada and in 1982 received a Ph.D. in Electrical Engineering from the University of Toronto in the Institute of Biomedical Engineering. He received an NSF Young Investigator Presidential Award as well as the Diekhoff and Wittke awards for graduate and undergraduate teaching and the Mortar board top-prof awards at Case Western Reserve University. He is an IEEE Fellow and also Fellow of the American Institute for Medical and Biomedical Engineering and Fellow of the Institute of Physics. He serves on five editorial boards of peer-reviewed scientific journals and he is the editor-in-chief and founding editor of the Journal of Neural Engineering. His research interests are in neural engineering and include computational neuroscience, neurophysiology and control of epilepsy, non-linear dynamics of neural systems, neural prostheses and applied magnetic and electrical field interactions with neural tissue. He has obtained funding for his research from the National Science Foundation, the National Institutes of Health and private foundations. He has published over 100 articles and he has consulted for many biotechnology companies and foundations.

Professor Paul Davies

Regents' Professor and Director of the Beyond Center for Fundamental Concepts in Science at Arizona State University

Paul Davies is Director of The Beyond Center for Fundamental Concepts in Science at Arizona State University. He is a theoretical physicist, cosmologist and astrobiologist with research experience ranging from the origin of the universe to the origin of life. He is noted for his work on the theory of quantum fields in curved spacetime, the thermodynamics of black holes, early-universe cosmology, the arrow of time, the nature of the laws of physics and the emergence of life in the universe. He is also Principal Investigator of the Center for Convergence of Physical Science and Cancer Biology.

After Dinner Speaker
Dr Michael Mosley
Science presenter, journalist and executive producer

Michael Mosley is the champion for Food for the Longitude Prize and has recently presented Inside the Human Body and the BAFTA nominated Young Ones for BBC1, as well as the acclaimed Story of Science for BBC2. Michael studied PPE at Oxford University before working in the City. He then trained as a doctor at the Royal Free in London before joining the BBC. He directed films for Newsnight, Tomorrow's World, Horizon. He was Science Editor of QED, Living Proof and Trust Me I'm a Doctor. He made numerous award winning business series – Troubleshooter, Trouble at the Top – as well as some of the biggest international science and history hits of the last decade, including Supervolcano, Krakatoa, Pompeii, Superhuman, Human Face, Superstorm. He is currently making three new series, as well as being a regular science presenter for the BBC's One Show. He has won numerous awards, including being named Medical Journalist of the Year by the British Medical Association and he is the author of the New York Times bestselling 5;2 "Fast Diet", based on a Horizon about intermittent fasting.

Keynote Speakers

Simon J. Archibald, Ph.D., is currently the Chief Scientist for Integra LifeSciences Corporation. He joined Integra in 1997 as Senior Director of Neurological Programs to oversee the clinical and commercial development of the NeuraGen nerve guide system and to explore the development of a neurosurgical product line from the existing Integra collagen wound care business and patent port-folio. In 1997 he initiated the program that resulted in the development of the DuraGen dural graft matrix for which he is a co-inventor. In 1999 he was promoted to Vice President of R&D for the new Integra NeuroSciences business and in 2001 he was promoted to Vice President of R&D & Vice President of Clinical Affairs, in 2005 he was promoted to Chief Scientific Officer, a post he held through to February 2014. Previously Dr. Archibald was Assistant Professor in the Department of Neurosurgery at Duke University Medical Center, to which he was appointed after completing a research Fellowships in Department of Neurosurgery at Duke University Medical Center and in the Department of Neuropathology and Neuroscience at Harvard Medical School. He graduated with a degree in Zoology from the University of Reading in the UK, and has a Ph.D. in Biomedical Engineering from the University of North Staffordshire in the UK. Currently Dr Archibald also serves as an Adjunct Professor in the department of Biomedical Engineering at Drexel University His primary research focus is in peripheral and central nervous system regeneration with a particular emphasis on national and international collaborations for translating discoveries in the basic sciences to clinical practice.

Peter Brett is a Professor of Biomedical Engineering and Theme Leader for Biomedical Engineering and Healthcare Technologies at Brunel University, London. Prof Brett has leading research experience in robotics for surgery and cellular processing, and smart sensing in biomedical applications. His work on robotic surgery commenced in 1989, and he has focused on the real time control of tools in tissues to control interaction, behaviour and state. The novel techniques have been demonstrated successfully in the operating room and work in real time, sensing tool progress relative to flexible, deforming and soft tissues, The techniques are an efficient means for sensing and requiring few sensing elements in contrast to the number of outputs. The new distributive approach to sensing has also been demonstrated successfully in a range of applications from discriminating human motion and behaviour to tactile sense for discriminating contacting conditions on steerable endoscopes and catheters, to discriminating cells and in other defence related applications.

Colin Caro is an Emeritus Professor of Physiological Mechanics and Senior Research Investigator, Department of Bioengineering, Imperial College London he is the Founder and Research Director, Imperial College London Spin-Out Company, HeliSwirl Technologies Limited and Founder and Research Director, Imperial College London Spin-Out Company, Veryan Medical Limited. Professor Caro has qualifications in physiology and medicine and a strong interest in mechanics. His overall objective has been to foster interaction between physiology/medicine and physical science/engineering. In so doing, he has aimed at advancing understanding of the mechanics underlying some normal and disturbed physiological processes and of contributing to the detection/management of medical conditions. Professor Caro was one of the founders of Bioengineering at Imperial in the 1960s through the Physiological Flow Studies Unit.

Martin Knight is a Professor of Mechanobiology. He is also the Programme Director for the Medical Engineering undergraduate degrees and the Director of Public Engagement and Communications for the School of Engineering and Materials Science. Prof Knight is one of the directors of the Institute of Bioengineering and a member of the Biomedical Engineering and Materials research group within the School of Engineering and Materials Science. Prof Knight previously held a prestigious EPSRC Advanced Research Fellowship in cartilage mechanobiology and tissue engineering (2000-2006) and was promoted to Reader in 2009 and Professor in 2012.
Martin Knight has a strong interest in promoting the public understanding of science and has been involved in a wide range of science communication activities. He has participated in many public events including National Science week and Big Bang and has also held an EPSRC Partnership for Public Awareness grant.

Alvaro Mata was born in San José, Costa Rica and holds a Bachelor's Degree from the University of Kansas, USA, a Master's Degree from the University of Strathclyde, UK, and a Doctor of Engineering Degree from Cleveland State University, USA. During his doctorate he worked at The Cleveland Clinic Foundation under the direction of Prof. Shuvo Roy. From 2005-2008 he worked as a Postdoctoral Fellow with Prof. Samuel I. Stupp at Northwestern University in Chicago, developing self-assembling materials for regenerative medicine. From 2008-2013 he was Head of the Nanotechnology Platform at Parc Científic Barcelona in Spain and is currently Reader in Biomedical Engineering and Biomaterials and Associate Director of Strategic Partnerships of the Institute of Bioengineering at Queen Mary, University of London. He received the 2005 Clodomiro Picado Twight Technology Award from the Government of Costa Rica, the 2006 Baxter Early Career Award in Bioengineering, and a Ramón y Cajal Award from the Government of Spain in 2009, and an ERC Starting Grant in 2012.

Oral Presenter Biographies

Steven Abbott has a PhD in Medical Physics (2009), a first degree in geology (1995) and an MSc in oceanography (1998) obtained from the National Oceanographic Centre in Southampton. He specialises in the use of artificial intelligence approaches to account for variability in digital signals, and since gaining his masters, has a research and development background encompassing roles in industry, (GIS data processing), third sector (Assistive Technology for disabled IT users), and academic, (Human and animal motion analysis). He is currently attached to the Sports and Exercise Science Research Group at Anglia Ruskin University in Cambridge, UK.

Omar Sultan Al-Kadi received the B.Sc. degree from Cairo University in 2001, the M.Sc. degree from the University of Canberra in 2003, and the DPhil degree in biomedical engineering from the University of Sussex in 2009. Then he was appointed as an assistant professor at the University of Jordan, and in 2011 was a visiting researcher at the biomedical imaging group within the centre for vision, speech and signal processing at the University of Surrey. Since 2013 he is a research fellow at the biomedical image analysis laboratory within the Biomedical Engineering Institute at the University of Oxford.

Paolo Angeles completed a four year Master's degree at Imperial College in Mechanical Engineering. Having seen the wonders of the medical technology during his final year project, which involved controlling a bionic hand and has been accepted as part of a conference paper, he has opted to venture further into the medical device space by pursuing a Master's in Research degree in Medical Device Design & Entrepreneurship. After being accepted for an Imperial College Brain Science and Engineering Fellowship, Paolo has looked specifically at problems associated with quantifying symptoms of Parkinson's Disease.

Mahsa Shahi Avadi is a PhD doctoral researcher at the Institute of Medical and Biological Engineering (IMBE), University of Leeds. Her research involves creating a better understanding of mechanical properties of the bone following avascular necrosis of the femoral head, and developing a mechanical model of this disease in vitro. She previously worked in industry at DePuy-Synthes as a test engineer involving experimental and theoretical aspects of orthopaedic engineering. She successfully completed her undergraduate degree in Medical Engineering at Queen Mary, University of London.

Daniel C. Baeriswyl holds a M.Sc. in Mechanical Engineering from the Swiss Federal Institute of Technology Zurich. He is currently a postgraduate researcher at the Institute of Biomedical Engineering at University College London, U.K. His research interests include cardiovascular mechanics, cell biology, transport phenomena, drug delivery and novel medical devices.

Eleni Bazigou is a postdoctoral researcher in the department of Bioengineering at Imperial College London. Her research interests lie in the field of mechanobiology and network remodelling. She has previously worked on both neuronal and vascular remodelling while her current project focuses on factors responsible for the development of atherosclerosis. Using a multidisciplinary approach, she examines arterial tissue remodelling, membrane dynamics and changes in wall permeability in an *in vivo* model of altered blood flow. In parallel, she uses blood flow simulations to causally link hemodynamic forces with the development of atheroprone areas.

Sandra Bovens got her masters in cardiovascular diseases from VU in Amsterdam. During this masters her internship took place at the experimental cardiology department in the University Medical Centre Utrecht, the Netherlands, where she subsequently started her PhD project entitled Cardiovascular applications of Magnetic Resonance Imaging. Topics included development and in vivo testing of new targeted contrast agents, MRI for diastolic heart failure and in vivo human atherosclerotic plaque imaging with 7 Tesla MRI. After finishing her PhD in 2012 she started as a postdoc in the group of Rob Krams within the Bioengineering department of Imperial College London.

Giuseppe Cama is a Research Associate at the King's College London Dental Institute's Department of Tissue Engineering and Biophotonics (formerly known as the Department of Biomaterials). He graduated in Biomedcal Engineering at the University of Genoa (Italy) in 2005. At the end of his University study he worked independently with an Italian Company (SAIF S.r.L) on a project concerning energy saving. In 2007 he started his PhD in Chemical and Materials Engineering at the University of Genoa (Italy). A ten month section of the work was carried out in the Dept. of Biomaterials at the KCL Dental Institute where he is currently employed. Since 2010 he has been working as a researcher in the development of improved synthetic bone substitutes.

Patrick Carena Bsc Hons, MEIT, CEng, MIPEM, State Register Clinical Scientist.
For the past 21 years has been working in the Department Of Medical Physics, Ninewells Hospital. Currently Deputy Head of the Instrumentation Section and Manager of the R&D Section and Support Services Sections. Supervisor for a number of UK and international MSc and PhD Students assigned to the Department. The R&D work undertaken by the R&D section is varied from mechanical tools to LED arrays used in determining skin reaction to visible and UV light. These R&D projects are carried out in conjunction with clinician, medical, academic staff and industrial partners.

Ed Chadwick's research interests are in the application of biomechanical modelling and simulation to the study of upper limb function and rehabilitation. He has a particular interest in the use of functional electrical stimulation (FES) for the restoration of function and in the development of assistive devices. He completed his PhD in Bioengineering at Strathclyde University in 1999, and spent a numbers of years as a Senior Research Associate at Case Western Reserve University in Cleveland, Ohio, and at the Delft University of Technology in the Netherlands. He is currently with the Institute for Science and Technology at Keele University.

Peter Charlton has been a Biomedical Engineer in Guy's and St Thomas' NHS Foundation Trust, and a Research Assistant at King's College London since being educated at Oxford. His current research focuses on physiological monitoring of hospital patients. Firstly, he is investigating the effectiveness of technologies for the acquisition of continuous and intermittent physiological measurements in ambulatory and intensive care settings (NCT01549717). Secondly, he is evaluating and developing signal processing techniques for estimation of variables from physiological signals (NCT01472133). Finally, he is developing techniques to transform continuous monitoring data into measurements which are appropriate for real-time alerting of patient deteriorations.

Haoyu Chen is currently a biomedical engineering Ph.D. student at University of Oxford where he aims to graduate in December 2014. His graduate research is focused on applying continuum mechanics and mathematical modelling to develop patient-specific models of vascular diseases, particularly aneurysmal diseases. Starting from January 2015, Mr. Chen will start a one-year postdoctoral position at the Interdisciplinary Mechanics Laboratory at the University of Connecticut. His research interests lie in computational solid/fluid mechanics and mathematical modelling of human biological systems, especially the integration of the two, such as *in-silico* modelling of the biomechanics and mechanobiology of cardiovascular and musculoskeletal systems.

Henry Chubb is currently working towards a PhD in Cardiac Electrophysiology and Magnetic Resonance Imaging at King's College London. Prior to starting his PhD in late 2013, Henry was working as a Paediatric Cardiology trainee at Evelina London Children's Hospital. He obtained a First Class degree in undergraduate medicine at Cambridge before graduating in clinical medicine with Distinction from University College London. His initial postgraduate training was in adult medicine in London and Oxford, before moving back to London to work in Paediatrics then Paediatric Cardiology. His interests include the integration of imaging techniques with electrophysiology, particularly complex arrhythmias in congenital heart disease.

David Clifton is a tenure-track member of faculty in the Department of Engineering Science of the University of Oxford, and a Governing Body fellow of Balliol College, Oxford. He is a Research Fellow of the Royal Academy of Engineering. A graduate of the Department of Engineering Science, Dr Clifton trained in information engineering and started the Computational Health Informatics (CHI) lab when we was appointed to the faculty in 2013. His research includes "big data" and mobile health projects, in the NHS and in China.

Jonathan Dawson has a five-year personal fellowship from the EPSRC to develop his research group exploring the application of clay nanoparticles for regenerative medicine. He has worked as a postdoctoral research fellow within the field of stem cell biology and published in journals such as Stem Cells, Advanced Materials, Bone and Biomaterials. He has also worked closely with clinicians engaged in translational stem cell research and in 2010 was awarded The Engineer Award for collaboration with industry and clinicians developing an intra-operative bone marrow stem cell concentration method.

Robert Dickinson graduated with a degree in physics from Cambridge University, and then obtained a PhD in Biophysics from the University of London, in ultrasound signal processing. Dr Dickinson has extensive experience in medical imaging, in both hospital and industrial environments. He has CE marked a number of medical devices currently in clinical use. He is currently senior lecturer in the Department of Bioengineering at Imperial College London. Dr Dickinson's research interests include interventional imaging, electrosurgical devices and medical devices for oxygen therapy.

Desmond Dillon-Murphy has a BEng in Mechanical Engineering from Dublin Institute of Technology, 2004, a First place MSc in Bioengineering from Trinity College Dublin, 2007 and began his PhD in Blood Flow Modelling with a focus on aortic dissection, Kings College London in 2012. Previously he was a Software Design Engineer MCS ltd, Galway 2005-2006, Consulting Design Engineer, Homan O'Brien Associates, Dublin 2006-2009 and Haematology Lab Aide, Mater Hospital, Dublin 2009-2012.

Ross Ethier holds the Lawrence L. Gellerstedt, Jr. Chair in Bioengineering in the Wallace H. Coulter Department of Biomedical Engineering at Georgia Tech/Emory. Prior to joining Georgia Tech he was HoD Bioengineering at Imperial College. His research is in the biomechanics of cells and whole organs. He has published more than 130 refereed journal articles, and received both Steacie and Humboldt Fellowships. He is a Fellow of the: American Society of Mechanical Engineers; American Institute for Medical and Biological Engineering; International Academy for Medical and Biological Engineering; Association for Research in Vision and Ophthalmology; The City and Guilds Institute.

Stefania Fabbri obtained her BSc degree in Biomedical Engineering at the University of Genoa (Italy) in December 2009, followed by a MSc degree in Bioengineering in March 2012. During her MSc studies, she developed a strong interest in the field in biofluidodynamic and biomaterials. Her MSc thesis concerned the mechanical characterisation and characteristics of perfusion of explanted rat livers. In November 2012, she started the PhD at the University of Southampton, under supervision of Dr P.Stoodley. Her PhD project, funded by Philips Oral Healthcare, aims to assess microspray technology as a potential delivery method for dentifrices into the remaining biofilm.

Basil Fansa has spent six years at medical school, having obtained an intercalated BSc in Biomaterials, prior to entering the exciting world of Bio-Engineering and Medical Devices.
Coming from a medical background has given Basil the opportunity to interact with patients, witnessing first-hand, the genuine medical needs and suffering patients have to endure. He is also aware of the current limitations of existing medical technology and pharmaceuticals in several fields, and therefore would like to make a positive contribution to address these. Owing to the microvascular and macrovascular complications that diabetes presents, this has motivated him to take on this project.

Thomas E. Fastl received his bachelor's degree in Biomedical Engineering with specialization in Bioimaging and Bioinstrumentation and his master's degree in Mechanical Engineering focusing on Biomechanics from Graz University of Technology. He has been associated with the Institute of Biophysics at the Medical University of Graz before starting as a research student at the Department of Biomedical Engineering at King's College London working on personalized computational models of atrial electromechanics. Thomas E. Fastl's research interests focus on the theory, development, and application of computational methods to clinically relevant problems in cardiology.

Andrea Fotticchia received a master degree from Politecnico of Milan in biomedical engineering, in 2009, with a thesis on elastin-like recombinant protein-based hydrogel. Subsequent years were spent in industry working with the electrospinning technology to develop filters. At the end of 2011 he started a PhD programme at Loughborough University where he worked on a tissue engineering project focused on the development of an artificial replacement for the annulus fibrosus. His interests span from manufacturing processes to cell culture, biological characterization and imaging techniques.

Suja Elizabeth George is a WELMEC postdoctoral research fellow in the School of Molecular and Cellular Biology, University of Leeds. She graduated with an MSc in Biochemical Engineering from the University of Birmingham in 2005. She completed her PhD in pre-clinical evaluation of novel anti-psoriatics from the Sunderland Pharmacy School, in 2008. She subsequently did postdoctoral research in antibody production, diagnostics and assay development in Queen's University, Belfast. She joined University of Leeds in 2012, where she is working on the development of Point of Care diagnostics for musculoskeletal and cardiovascular diseases. Her research interests include understanding the role of cytokines in the pathogenesis of cardiovascular and autoimmune diseases and novel biologics for treatment of cancer, cardiovascular diseases and chronic inflammatory conditions.

Josh Giles is a Research Associate in the Mechatronics in Medicine and Biomechanics groups at Imperial College. His research, as part of a Wellcome Trust Translational project, focuses on the design of novel surgical techniques and instrumentation for Total Shoulder Replacement. Joshua completed his Doctorate in Biomedical Engineering (Orthopaedic Biomechanics) at the Hand and Upper Limb Centre, Western University, London, Canada. His research focused on the development of systems that enabled the in-vitro investigation of biomechanical questions relating to orthopaedic injuries and surgical treatment options through the replication of the joint's in-vivo environment.

Mario Giorgi is a PhD student in the Department of Bioengineering of Imperial College London, UK. The aim of his PhD project is to understand how mechanical forces influence joint shape development, especially those caused by pre-natal movement during hip joint morphogenesis. Before joining Imperial College Mario worked in the Department of Mechanics of Politecnico di Torino (Italy). From April 2009 to June 2010, Mario worked at the European Centre for Knee Research in Leuven (Belgium). Mario holds a bachelor degree in Mechanical Engineering and a master degree in Biomedical Engineering.

Fatemeh Mohammadvali Godarzi is currently a PhD student at UCL Division of Surgery and Interventional Science, working on the "Design and development of thoracic aortic aneurysm (TAA) stent-graft, using shape memory alloy and nanocomposite material". She obtained her MEng in Chemical Engineering from University of Birmingham.

Peter Hoskins is Professor of Medical Physics & Biomechanics at Edinburgh. He studied Physics at Oxford from 1977-1980. He was an NHS Medical Physicist from 1980-2002, combining research work with hospital service work, and was promoted to Consultant Medical Physicist in 1998. In 2002 he moved to full time University work and gained a personal chair in 2012. His current research involves patient specific modelling, ultrasound imaging and MRE in cardiovascular disease. He is FIPEM (1994), FInstP (2007), FHEA (2013) and was awarded DSc (2009). He sat on BMUS Council (2010-2014) and will be IPEM Vice President Academic from September 2014.

Mohammad Jafarnejad is a PhD student in the Department of Bioengineering at Imperial College London. He has been working in Vascular and Lymphatic Biomechanics Laboratory under the supervision of Professor James Moore. His research examines the role of mechanics and transport in the lymphatic system. He started his research on lymphatic system by looking at the role fluid shear stress on calcium dynamics in lymphatic endothelial cells. Currently, he is focused on mathematical modelling of fluid, molecule and cell transport in the lymph node.

Rashed Karim received his BSc in Computer Science from the University of Toronto and an MSc with Distinction from Queen Mary, University of London. He obtained his PhD in image processing algorithms for cardiac MRI images from Imperial College London. Since 2010, he has been working as a Postdoctoral Research Fellow at King's College London Medical Engineering Centre (MEC). His current research interests include tissue classification in MR, image-guided robotics and left atrial surface parameterization.

Maria G. Katsikogianni gained her PhD in Biomedical Engineering from the University of Patras in 2008. Her PhD project examined the effect of material properties and flow conditions on bacterial adhesion. In 2009 she joined the Surface Engineering Group in University College Dublin as a postdoctoral researcher in the areas of antimicrobial coatings, plasma modification and characterization. Since October 2011 she is a WELMEC research fellow at the University of Leeds preparing ceramics and examining their effects on human mesenchymal stromal cell differentiation and bacterial viability. She has published 18 peer-reviewed papers, 3 book chapters and one patent application.

Angela Kedgley is a Junior Research Fellow in the Department of Bioengineering at Imperial College London. Dr Kedgley obtained her PhD in Mechanical Engineering from the University of Western Ontario in Canada in 2009, during which she developed a fluoroscopic radiostereometric analysis (RSA) system, which was used to measure human joint kinematics. She then obtained a postdoctoral fellowship from the Natural Sciences and Engineering Research Council of Canada, which provided her with the opportunity to work at the Centre for Hip Health and Mobility at the University of British Columbia. In 2011 she moved to the United Kingdom and took up a position as a Research Associate in the Department of Bioengineering with the Medical Engineering Solutions in Osteoarthritis Centre of Excellence at Imperial College London. Angela is a Chartered Engineer and a member of the Institute of Mechanical Engineering.

Sara Lacerda is an imaging chemist with about 10 years' experience in development of multimodal imaging/theranostic (simultaneous diagnostic and therapeutic) agents.
She has received her PhD from the University of Lisboa in 2009, during which she developed and studied *in vitro* and *in vivo* theranostic agents.
She did a postdoc at the Biochemistry Institute of Lübeck, Germany, on Fragment-Based Drug Discovery. 2010-2012 her research focused on new bimodal Magnetic Resonance/Optical Imaging lanthanide-based contrast agents, at Centre de Biophysique Moléculaire, Orléans, France. Since 2013 she is a Research Associate at KCL's Imaging Sciences Division working on new cardiovascular MR contrast agents.

Simon Auguste Lambert graduated from the Ecole Nationale Superieure de Physique de Grenoble (France-2006) and received the Doctorat-es-Sciences degree from Universite Paris Sud, Paris, France, in 2011. His work was focused on the design of superconducting microcoils for high resolution magnetic resonance imaging. He is presently Post-doc both in London, KCL, in the department of biomedical engineering and in Paris, CRI, INSERM U1149 (CNRS). He is working on magnetic resonance elastography and its applications to medicine as a new biomarker. He focused his theoretical researches on the dispersion of shear waves in heterogeneous media.

Evangelos Liamas is from Stavros in Thessaloniki, Greece. He completed his BSc in materials science and technology from the University of Crete in Greece. His final year thesis was on "Designing novel biocompatible and biodegradable giant amphiphiles for drug delivery". He received his MSc in Nanomaterials for Nanoengineering with high merit from the Universities of Sheffield and Leeds. His passion for science led him to Glasgow where he is doing his PhD on biomaterials in the Chemical and Process Engineering Department. He is in the soft matter team under the supervision of Dr. Zhenyu Zhang.

Benny Lo is a Lecturer at the Hamlyn Centre, Imperial College London. He also acts as the Programmer Manager of the EPSRC funded ESPRIT Programme. His research interests include Body Sensor Networks, Pervasive Computing, Machine Learning, Microelectornics, and Biomedical Engineering. His work mainly focuses on developing technologies for healthcare, sports and well-being applications.

Marlène Mengoni is a Research Fellow in spine biomechanics at the Institute of Medical and Biological Engineering (University of Leeds). She is interested in mutli-scale aspects of tissue biomechanics with a fundamental computational engineering approach. She holds a PhD in Computational Biomechanics from the University of Liège (Belgium) and an MSc in Physical Engineering. Her current work examines the micromechanical aspects of the intervertebral disc and was selected as finalist of the ESB Clinical Biomechanics award. She is actively engaged in public outreach. She has developed activities demonstrating computational aspects of biomedical engineering research with support of the Wellcome Trust.

Gavin Metcalf is a Cancer-Bioengineering Ph.D. student at Imperial College London. He graduated with a B.Sc. in Biosciences in 2012, and then obtained his M.Res in Cancer Biology in 2013 while based at Imperial College's Cancer Research UK Centre where he explored selected RSK kinases involved in chemoresistance and metastasis of non-small cell lung cancer. His doctoral research focuses upon the design and development of novel fluorogenic peptide nucleic acid (PNA) biosensors for early stage cancer diagnosis and improved prognosis, via the sensing of circulating cell-free nucleic acids, particularly microRNAs, in biofluids sourced by minimally invasive means.

Tomislav Milekovic Undertook his PhD studies in the group of Dr. Carsten Mehring at University of Freiburg and Imperial College London, where he worked on developing brain-machine interfaces based on human electrocorticography. In April 2012, he began his first postdoc at the BrainGate group, supervised by Drs. John Donoghue and Leigh Hochberg, at Brown University. There he worked on developing intracortical brain-machine interfaces for people with tetraplegia. In May 2014, he began his second postdoc in the group of Dr. Gregoire Coutine at EPFL, where he works on development of brain-spinal neuroprostheses aimed to alleviate symptoms of neurological injuries and disorders.

Danielle Miles graduated with a first class MChem degree with industrial experience in 2008. She stayed at Leeds for her PhD working on self-assembling *de novo* peptides in physiological conditions, under the supervision of Dr Amalia Aggeli and Prof Ruth Wilcox. During her PhD Danielle won numerous prizes including the University of Leeds postgraduate researcher of the year 2010. She is now a research fellow based within the School of Chemistry and a member of the Institute of Medical and Biological Engineering at the University of Leeds. Her current work concerns the development of peptide hybrid hydrogels for intervertebral disc therapies.

Yumnah Mohamied is a third year PhD student at Imperial College London. After completing a MEng in Aeronautical Engineering in 2012 at Imperial College, she returned on a 3-year inter-disciplinary PhD studentship awarded by the BHF CRE, in the Aeronautics and Bioengineering departments. She is co-supervised by Spencer Sherwin and Peter Weinberg. Her research interest is focused on the role played by multi-directional blood flow dynamics in the initiation of the cardiovascular disease atherosclerosis.

Luke Moore read medicine at the University of Leeds, graduating in 2003, and subsequently trained in internal medicine for 4 years. In 2007 he studied for the Diploma in Tropical Medicine, before spending a further year at the Hospital for Tropical Diseases. In 2008 he began specialist clinical training in Infectious Diseases & Medical Microbiology, achieving two sequential Masters degrees with distinctions, as well as Membership of the Royal College of Physicians and Fellowship of the Royal College of Pathologists. In April 2013 he was awarded an NIHR Clinical Research Fellowship to investigate the impact of rapid infection diagnostics in critical care.

Rachel Myers graduated from Downing College, University of Cambridge in 2009 with a Master's degree in chemical engineering (MEng). After graduating she worked as a process engineer at Davy Process Technology for a year.
Rachel joined University of Oxford in 2010 and subsequently the biomedical ultrasonics, biotherapy and biopharmaceuticals laboratory (BUBBL) in 2011. Her PhD has concentrated on the formulation of nanoparticles capable of acting as cavitation nuclei when exposed to ultrasound. This has led her to look at the ability of these particles to enhance drug delivery of cancer therapies.

Lars Neumann is a global business development manager at Materialise NV, Belgium with specific focus on software for biomedical engineering. Lars is an experimental physicist with research experience in photonics, nanotechnology and optical imaging. After his doctoral degree, Lars engaged in the creation of R&D project and process management in the automobile industry. At Materialise, Lars focusses on the principle of "*Engineering on Anatomy"* within the *Mimics Innovation Suite* and its applications in patient-specific biomedical engineering. He is responsible for the academic users of the Mimics Innovation Suite worldwide and Materialise's developing educational programme in *Engineering on Anatomy*.

Darryl Overby is senior lecturer in the Department of Bioengineering at Imperial College London. Research interests include cell and tissue biomechanics and mechanobiology with an emphasis on endothelial transport and the mechanisms of intraocular pressure regulation in glaucoma. Teaching interests include biotransport phenomena, heat and mass transport, and cellular biomechanics. Darryl serves as the Director of Postgraduate Studies (taught) and is a recent recipient of the President's Award for Excellence in Teaching 2014.

Nont Panitchob is currently a fourth-year Ph.D. student in bioengineering at University of Southampton. His research focuses on mathematical modelling of membrane kinetics to represent placental amino acid transport system. Previously, Panitchob received a M.Sc. degree in Medical Physics and Bioengineering from University College London in 2010 and a B.Sc. in Electrical Engineering from Purdue University, USA in 2009.

Iraklis Papageorgiou is an experienced biology researcher. After graduating from the University of Leeds (2000) with a BSc in Human Genetics, he was offered the opportunity to study for a PhD in the field of Orthopaedic Surgery (University of Bristol) studying the biological effects of orthopaedic wear particles in the periprosthetic tissue of the hip joint.
Since 2009, he has been employed within the Institute of Medical and Biological Engineering (IMBE) as NIH Research Fellow to study the biological effects of wear particles produced from total disc replacement devices on the cells of the dura mater of meninges.
He is currently working on a research project in collaboration with University of Iowa investigating the size and type of 3rd body wear particles that are present in tissues or fluid surrounding an implant.

Ryan Pedrigi is a Research Associate in Bioengineering at Imperial College London. Before joining Imperial College in 2009, he earned a Ph.D. in Biomedical Engineering from Texas A&M University, under the direction of Prof. Jay Humphrey, and a B.S. in Mechanical Engineering from Kansas State University.
Dr Pedrigi's research employs experimental and computational methods to quantify how perturbed tissue mechanics promotes pathological cellular behaviours and tissue remodelling. The goal is to translate an understanding of mechanobiological mechanisms of disease to identify new pharmaceutical targets and improve implantable medical devices in ophthalmology and cardiovascular medicine.

Devis Peressutti is currently an Associate Researcher with the Division of Imaging Sciences and Biomedical Engineering at King's College London. He received a Ph.D in Biomedical Engineering from the same University in April 2014.
His research focuses primarily on the estimation and analysis of motion. During his Ph.D., he developed methods for the estimation and modelling of the respiratory motion of the heart for image-guided interventions. In his current project, Dr Peressutti is interested in analysing motion-based biomarkers for the stratification of patients with cardiac arrhythmias.

Arvind Raghu is currently pursuing a DPhil from the Institute of Biomedical Engineering, University of Oxford. Working alongside clinicians from Australia, India, and Oxford, Arvind's research is focused on the collaborative development of novel telemedicine systems for remote monitoring and clinical decision support in resource-constrained environments. He was a recipient of the Indian Academy of Sciences research fellowships, and has worked in the areas of computational biology (at the Indian Institute of Science) and neuroscience (at the National Centre for Biological Sciences, India). Arvind holds an MSc (with Distinction) in Biomedical Engineering from the University of Oxford.

Naiara Rodriguez-Florez's research explores multiscale biomechanics in cortical bone. Naiara graduated in Mechanical Engineering at Tecnun, University of Navarra (Spain) with first-class honours. In 2011, she joined the Bioengineering Department at Imperial College London to conduct her PhD in the field of Bone Biomechanics with Dr. Sandra Shefelbine. Now being about to graduate, Naiara has characterised cortical bone at the micro- and nano-scale using experimental and computational techniques applied to various mouse models of disease and aging. Part of her work has been published in relevant journals.

Apurva R. Shah is a postdoctoral researcher in Department of Oncology and The Institute of Biomedical Engineering (IBME) at the University of Oxford. At University of Oxford, he is developing ultrasound triggered liposomal drug delivery systems for targeted cancer therapy and nanosized polymeric cavitation nuclei for theranostic use. The project is supervised by Prof. Leonard Seymour (Department of Oncology), Prof. Constantin C. Coussios (IBME) and Prof. Robert Carlisle (IBME) and funded by EPSRC and Wellcome trust. His major research interests are developing smart formulations that release drugs "on demand", understanding its biophysics, pharmacokinetics and pharmacodynamics implications and translational research.

M. Keith Sharp, Professor, Department of Mechanical Engineering, University of Louisville, received his B.S. degree from the University of Cincinnati in 1976, M.S. from Colorado State University in 1978 and Sc.D. from M.I.T. in 1987, all in Mechanical Engineering. He has been at the University of Louisville for 14 years, and is the Director of both the Biofluid Mechanics Laboratory and the Renewable Energy Applications Laboratory. Current research interests are in fluid mechanics and transport phenomena, including shear-induced hemolysis, blood rheology, cerebral flow and transport, and modeling of cardiovascular and ocular responses to microgravity in astronauts.

Joseph M. Sherwood originally studied Mechanical Engineering at King's College London. For his PhD he moved from fundamental fluid mechanics research into the world of bioengineering, using particle image velocimetry, image processing and microfluidic fabrication and flow control to analyse the characteristics of microhaemodynamics. Joseph finished his PhD studies at UCL, before moving to Imperial College London, to work on a biomimetic microfluidic device to analyse the permeability of cultured endothelial cell monolayers. In Dr Darryl Overby's lab at Imperial College London, he also became involved in the design and development of systems for ocular perfusion studies, and continue research in all three fields.

Kristina Sliogeryte Completed her Bachelor degree in chemistry from Vilnius University, Lithuania in 2006. In 2008 she received master degree in biophysics from Vilnius University, Lithuania. She worked as a researcher on single cell mechanics at Katholieke Universiteit Leuven, Belgium. Most recently she is doing her Ph.D. in Biomedical Engineering at Queen Mary University of London, UK. Her research interests are single cell mechanics, cytoskeleton dynamics, membrane-actin cortex interaction.

Martin Stanley obtained his PhD at Durham University investigating new solutions for total knee replacement. He moved to Leeds University in 2011 and has been investigating solutions to meniscus repair. Outside of work he enjoys cycling, computer games, and electronic music.

Jean-Philippe St-Pierre is a Research Associate with Professor Molly Stevens at Imperial College London, where he focuses his research on scaffold design for regenerative medicine applications, directed stem cell differentiation and biomineralization. Dr St-Pierre is currently working to develop anisotropic osteochondral constructs for the treatment of osteoarthritis. He completed his Ph.D. in Biomedical Engineering at the University of Toronto (2011), where he specialized in cartilage tissue engineering. Dr St-Pierre holds a MEng in Biomedical Engineering from McGill University (2004), as well as a BASc in Chemical Engineering (2002) and a B.Sc. in Biochemistry (2002) from the University of Ottawa.
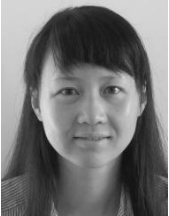
Junjing Su achieved her Master's Degree in Medicine from Aarhus University, Denmark, in 2012. After completing her basic clinical training, she commenced her PhD programme at the Department of Biomedicine, Aarhus University. Her main interest lies in the field of pulmonary hemodynamics. As a part of her PhD programme, she is currently undertaking a one year research fellowship at Imperial College London, where she is involved in a study applying wave intensity analysis in the pulmonary artery.

Michael Sutcliffe is a Reader in Mechanics of Materials at Cambridge University Engineering Department, where he has been a faculty member since 1992. Since completing a PhD in metal working tribology in 1988 he has been active researching both in the areas of engineering composites and bioengineering. His current research interests include diseased artery material characterisation and modelling of material deformation in neurosurgery and radiotherapy treatment.
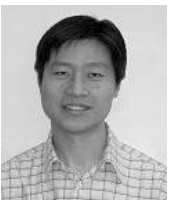
Mengxing Tang joined the Department of Bioengineering, Imperial College as a Lecturer in 2006 and became a Senior Lecturer in 2011. Before moving to London, he was a Departmental Lecturer in the Department of Engineering Science, University of Oxford. Dr Tang's current research mainly focuses on developing new imaging and image analysis methodologies using ultrasound and its allied techniques for quantifying physiological flow, tissue perfusion, tissue mechanical properties and molecular information and their applications in cardiovascular diseases and cancer. Dr Tang has authored more than 50 peer reviewed journal papers.

Lionel Tarassenko gained the degrees of BA in Engineering Science in 1978, and DPhil in Medical Electronics in 1985, both from the University of Oxford. He has been the holder of the Chair in Electrical Engineering at Oxford University since October 1997. His main research interests lie in developing signal analysis and data fusion techniques, principally for patient monitoring. He was awarded the 2001 Rolls-Royce Chairman's Award for Technical Innovation and the 2006 Silver Medal of the Royal Academy of Engineering for his contribution to British engineering. He was the founding Director of the Oxford Institute of Biomedical Engineering in 2008, and he has been the Director of the Centre of Excellence in Medical Engineering funded by the Wellcome Trust and EPSRC since 2009. He was made a CBE for services to engineering in the 2012 New Year Honours List. He has founded four spin-out companies, is a director of Isis Innovation, the University's Technology Transfer company, and is now the Head of the Department of Engineering Science.

Rahul Tare is a Lecturer in Musculoskeletal Science and Bioengineering, in the faculties of Medicine and Engineering & the Environment, at the University of Southampton. Rahul is the recipient of the Career Track Fellowship by the University of Southampton (2008) and Career Establishment Award by the European Calcified Tissue Society (2011).

Esther Tejeda-Montes obtained a BSc in Chemistry (2008), an MSc in Biomedicine (2009), and a PhD in Biomedicine (2013) from the University of Barcelona, Spain. Her PhD project consisted on the design, fabrication, and validation of bioactive membrane scaffolds based on elastin-like polymers to be used as periosteal grafts for bone regeneration applications. She is currently a Postdoctoral Research Assistant working with Dr Alvaro Mata in the School of Engineering and Materials Science (SEMS) at Queen Mary University of London. Her research project combines the areas of biomaterials, peptide synthesis, nano/biofabrication, molecular self-assembly, regenerative medicine and tissue engineering. Esther is Treasurer (2013-2016) for Student and Young Investigator Section (SYIS) of the Tissue Engineering and Regenerative Medicine International Society (TERMIS).

Gifty Tetteh is a second year PhD student at the University of Sheffield. Prior to Sheffield, she pursued an undergraduate degree in Biomedical Engineering at the University of Ghana and was the first female to receive the Overall Best Student Award from the Department of Biomedical Engineering, and the Overall Best Student Award from the Faculty of Engineering Science. Her current research at the Department of Materials Science & Engineering involves studying how tissue-engineered bones grow around orthopaedic implants, by designing a biomimetic construct that can be used to test these implants. Gifty is also actively involved in STEM outreach activities and volunteered for the Discover STEM for Girls event, the Harry Kroto Buckyball Workshop, the 'Sticky Bacteria' outreach sessions and the Labs to Africa Outreach Programme.

Yiannis Ventikos holds the Kennedy Chair at University College London, U.K., where he is also the Head of the Department of Mechanical Engineering. His research interests include transport phenomena, (bio)fluid mechanics, clinical computing, minimally invasive interventional devices design and optimization, and biocomplexity. He has received the M.Eng. in Naval Architecture and Marine Engineering and the Ph.D. in Hydrodynamics and Fluid Mechanics from National Technical University of Athens.

Stefaan Verbruggen has recently joined the Developmental Biomechanics Lab at Imperial College London as a Research Associate. He received his Ph.D. in Biomedical Engineering from the National University of Ireland Galway in 2013, where his research focused on the biomechanics and mechanobiology of bone cells in both health and disease. This research was recognised with multiple national and international awards, including Best Paper at the 21st Annual Symposium on Computational Methods in Orthopaedic Biomechanics, Third Prize at the American Society of Mechanical Engineers (ASME) Bioengineering Conference 2012, First Prize at the Mimics Innovation Awards 2013 and the prestigious Engineers Ireland Biomedical Research Medal.

Fabio Alessio Vittoria is a Ph.D. student in the x-ray phase contrast imaging group of the Medical Physics and Biomedical Engineering Department at University College London. He received a bachelor's degree in physics in 2008, and a master degree in solid state physics in 2012 from Università degli Studi di Bari, Italy. His research interests are in x-ray phase sensitive imaging methods, and in the theory of inverse problems applied to deconvolution and phase retrieval.
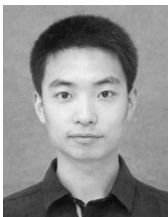
Yuxing Wang is a PhD student in Beihang University, Beijing, China, who is currently in an exchange program to University of Glasgow. He achieved his bachelor's degree of Engineering Mechanics in Tianjin University. He is interested in the mechanical analysis of musculoskeletal system and its responses to mechanical stimulus.

Gareth Ward is a 2nd year PhD student at the University of Southampton who is undertaking research under the supervision of Professor Andrew Lotery and Dr Martin Grossel.
He graduated in Chemistry from the University of Southampton in 2012, and his current research interest is in the development of biocompatible polymers to mimic the Bruch's membrane found in the macular of the eye, spending most of his time trying to create a suitable synthetic replacement to Bruch's membrane, taking into account the porosity, strength and adhesive properties of the original Bruch's membrane and mimicking these in the synthetic polymer.

Maximilian M Wdowski is the musculoskeletal biomechanics research coordinator in the Department of Bioengineering at Imperial College London. His role involves the management of the motion capture and tissue testing laboratories as well as assisting in musculoskeletal biomechanics research projects throughout the Department. Prior to beginning this role he completed his PhD in Biomechanics at Cardiff Metropolitan University in a project with Cardiff University where he investigated sprint running in field sports.

Nada Yousif is a Research Associate in the Division of Brain Sciences at Imperial College London. Nada first studied physics and then obtained her PhD in 2006, with a thesis on computational models of thalamocortical networks. Since then she has been working on understanding the mechanisms of Deep Brain Stimulation (DBS). Nada's work combines finite element, biophysical and network models to obtain a multi-scale view of how DBS impacts on the human brain, which she combines with electrophysiological data. Nada has previously been funded by an MRC fellowship and is currently funded by a research grant from the Bupa Foundation.

Petros-Pavlos Ypsilantis is a first year doctoral student in the department of Biomedical Engineering, King's College London. Petros-Pavlos graduated from National Technical University of Athens department of Applied Mathematics and Physical Sciences in 2012. Before enrolling at King's College, he completed a postgraduate programme: MS in Statistics at Imperial College London (2012-2013). His work focuses on algorithms development for Computer-Aided Detection systems (CAD) to support clinicians in their daily activities. More explicitly, he works on state-of-art machine learning techniques such as deep learning in order to exploit and identify medical imaging patterns and associations of unprecedented clinical value.

ORAL ABSTRACTS

Oral Abstracts are listed in alphabetical order by theme name, and then presentation order within session themes.

Keynote: Dr Alvaro Mata, Queen Mary, University of London

The effect of surface chemistry on protein adsorption - an experimental and computational study

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Department of Chemical and Process Engineering, University of Strathclyde

One of the most important aspects for biomaterial design is the interaction with living tissue, which can cause a foreign body reaction and ultimately rejection of the implant. Proteins play a key role in this process because they can adsorb on the biomaterial surface and act as anchors for subsequent cell binding. Two main factors that determine protein adsorption, and thus cell binding, are the chemistry and the topography of the biomaterial surface. In this project we use a fibronectin fragment to investigate its adsorption on a variety of surfaces. The fragment consists of the modules 8 to 10 of the type III fibronectin ([8-10]FNIII) and contains the cell-binding and synergy sites that mediate the protein-cell interaction through integrins on the surface of the cell. The surfaces that will be used include silica and self-assembled monolayers in order to cover a range of different properties regarding their charge and hydrophilicity. Molecular simulations will be performed using NAMD code on a supercomputer that will allow us to use explicit solvent model for a more realistic representation. Experimental techniques such as single molecule force spectroscopy and quartz crystal microbalance will be used to reproduce the results. Our initial modelling system indicates protein adsorption on positively charged surfaces that depends on the ions concentration of the solvent, while the fragment maintained its ability for subsequent cell binding. This novel approach that incorporates both computational and experimental techniques will allow us to advance the current understanding of protein adsorption. The next stage is to investigate the effect of surface topography on protein adsorption. Using the results that reveal how surface chemistry and topography affect protein adsorption, the final goal will be the organization of endothelial cells into a network of capillaries and their reconnection with the native vasculature.

Design, characterisation and evaluation of peptide: glycosaminoglycan hydrogels for intervertebral disc therapies

Danielle E Miles, *Elizabeth Mitchell, Sami Tarsuslugil, Nik Kapur, Paul Beales, Ruth K Wilcox*
University of Leeds

Introduction: Low back pain is strongly associated with intervertebral disc degeneration. Current surgical treatments for disc degeneration are highly invasive and have relatively low long term success rates. In 2005 the FDA proposed that the introduction of less invasive surgical procedures earlier in the lumbar degenerative disease cascade could defer the need for fusion or disc replacements. This work focuses on developing a minimally invasive therapy for nucleus replacement without the need for surgical incision using synthetic peptides based on natural amino acids. These patented materials harness the intrinsic ability of peptides to self-assemble into micron-sized aggregates, which establish a nanostructured network and cause gelation of physiological solutions. The peptide material properties were further optimised by mixing with glycosaminoglycans (GAGs) that are naturally found in the disc. **Methods:** During this study the self-assembly behaviour of β-sheet tape forming peptides in physiological-like conditions was investigated using NMR, CD UV, FTIR and TEM. Systematic mixing studies with GAGs were carried out to optimize the peptide systems further, and evaluated using NMR, TEM and rheometry. The best candidate gels were injected into a de-nucleated bovine caudal model and evaluated under compressive loading and for GAG leakage using a DMMB assay. **Results and Discussion:** It was found that systematic changes in peptide structure led to aggregates with different morphologies, self-assembly profiles and mechanical properties. An exciting finding was strong evidence that the mechanical properties of these gels could be controlled by peptide design and GAG ratio, allowing up to a 10,000 fold variation in the stiffness. The presence of the peptide greatly reduced the leakage of injected GAG and a de-nucleated disc repaired with a peptide: GAG gel was found to restore the mechanical behaviour to that of a disc with a healthy nucleus intact. In summary a material has been developed that can form a stable hydrogel in physiological solution conditions and mimic the mechanical function of the natural tissue. In addition it imitates the bio-functionality of the disc by providing a charged environment that could potentially lead to the disc swelling pressure and osmotic pumping action being restored. Finally it is injectable i.e. spontaneously transforms from a fluid to a gel *in situ*. The work presented here is the first step to the development of an improved nucleus augmentation treatment. If successful, it could improve the quality of life for patients and reduce the economic burden of disc degeneration.

Development of a Magnetically Active and Biomimetic Scaffold for Cartilage Tissue Engineering

Mariea A Brady, Lucien Talvard, C. Ross Ethier
Imperial College London, Georgia Institute of Technology & Emory University School of Medicine

The permanent loss of articular cartilage is a significant clinical problem and tissue engineering (TE) strategies present an attractive alternative to conventional surgical approaches. The creation of biomimetic scaffolds, which imitate the zonal architecture and depth-dependent mechanical properties of native tissue, may be a key aspect in the creation of functional neocartilage. We have developed a unique tri-laminar ferrogel consisting of magnetic nanoparticles (MNPs) embedded in agarose gel. By varying the concentration of agarose in each zone, a depth-dependent stiffness gradient was achieved. Further, by varying the density of MNPs in each zone, depth-dependent strains could be induced in the presence of an external magnetic field (0.4-0.6T), important for stimulating an appropriate mechanobiological response of local chondrocytes. A theoretical mechanics model of the tri-laminar magnetic scaffold was first used to determine the number of MNPs required in each zone for a physiologically relevant strain. Experimentally, the calculated number of MNPs were incorporated into the respective layers of the ferrogel. Finally, bovine chondrocytes were seeded in the ferrogel to evaluate cell survival. Results showed a homogenous distribution of MNPs within each zone of the agarose gel as observed by 3D microscopy (Histocutter). The material properties of each layer of the ferrogel were determined using a standard materials testing machine (Instron 5866); results showed a depth-dependent stiffness gradient. Finally, LIVE/DEAD® staining indicated good cell viability after 3 days in culture. This magnetically active and biomimetic scaffold developed provides a unique environment to control zone-specific mechanical signals to embedded cells. This could potentially induce zone-specific differentiation and maturation of mesenchymal stem cells/chondrocytes to create functional neocartilage for the treatment of osteoarthritis. Acknowledgements: Funding from the Wellcome Trust, EPSRC (088844/Z/09/Z)

Clay gels localise and enhance BMP2 induction of osteogenesis

Jonathan Dawson, David Gibbs, Cameron Black, Stuart Lanham, Edoardo Scarpa, Richard Oreffo
University of Southampton

Introduction: Bone Morphogenic Protein (BMP) is a licensed therapy to enhance bone repair, however delivered BMP rapidly diffuses and degrades requiring supra-physiological doses for efficacy. The synthetic clay Laponite, is non-toxic with a 25 year history of use in cosmetics. We have shown its potential to form hydrogels able to localise biological molecules to induce regenerative responses[1,2]. Here we demonstrate the utility of this approach to localise BMP2 to enhance bone graft osteo-induction. **Methods:** Clay gels were formed using hydrous suspensions of the synthetic clay Laponite (Rockwood ltd.). The effect of clay gels on BMP-2 localisation and activity was explored *in vitro* using C2C12 cells and staining for alkaline phosphatase activity (APA). Clay gels were spotted on tissue culture plastic (TCP) and BMP-2 added to the media before or at the time of cell seeding. After 72 hours staining and image analysis for APA was performed. Effect of BMP-2, serum, seeding density and BMP-2 incubation time was assessed. *In vivo*, a Laponite-BMP-2 mix perfused into DBG was subcutaneously implanted in mice. New bone formation versus controls was assessed at 28 days using micro-computed tomography (μCT). **Results:** Induction of APA was significantly (p<0.001) enhanced on clay gel surfaces over tissue culture plastic in a BMP-2 dose-dependent manner. Enhanced response was localised to clay gels, independent of local cell density and attenuated by increased serum concentration. While μCT analysis failed to confirm a significant increase in bone volume between variables after 28 days, histological analysis revealed areas of cartilage formation, hypertrophy and new osteoid indicative of endochondral bone only in graft perfused with BMP2 + clay. **Conclusions:** These studies provide *in vitro* and *in vivo* evidence for the utility of Laponite gels to enhance induction of osteogenic responses via the localisation of BMP2. **References:** 1. JI Dawson et al (2011) Advanced Materials 23: 3304-8. 2. JI Dawson & ROC Oreffo (2013) Advanced Materials 25: 4069-86. **Acknowledgements:** We gratefully acknowledge EU (FP7) Biodesign, Rosetrees Trust and the EPSRC (EP/L010259/1) for funding this work.

Effect of strontium incorporation with bioactive glasses on human mesenchymal stem cell whole gene expression

Hélène Autefage, Eileen Gentleman, Elena Littmann, Martin Hedegaard, Thomas Von Erlach, Matthew O'Donnell, Dave Winkler, Molly M. Stevens
Imperial College London, King's College London, Commonwealth Scientific and Industrial Research Organisation

Upon implantation, resorbable inorganic bone substitutes interact with biological fluids and undergo steps of dissolution/reprecipitation. These reactions trigger changes in the ionic microenvironment at the vicinity of the implanted biomaterial that are expected to play an important role in the cell response. To take advantage of these physiological phenomena, we have developed bioactive glasses (BG) which partial dissolution allows the local delivery of strontium (Sr), an anti-osteoporotic ion, within bone or osteochondral defects. It has been shown that Sr favours osteoconduction when incorporated within bone substitute materials, but the mechanism of how strontium addition improves the functional outcome and influences the global cell behaviour of osteoprogenitor cells has yet to be elucidated. Herein, we evaluated how modifying the ionic microenvironment by incorporating Sr within BG (SrBG) affects the whole gene expression profile of human mesenchymal stem cells (hMSC). Objective microarray analyses revealed significant modifications of hMSC global response at the gene level with respect to Sr addition within BG. Interestingly, this study highlighted that SrBG treatment strongly upregulated metabolic pathways responsible for the biosynthesis of sterol and steroid metabolites rather than directly triggering the expression of osteogenic genes. In-cell Western blotting, high resolution Raman spectroscopy and total internal fluorescence microscopy analyses demonstrated that these differences in mRNA expression were further translated to the protein and cell levels, as characterised by increases in cell sterol metabolites and membrane cholesterol and lipid raft contents, in SrBG-treated cells. These unexpected findings are of significant interest as cholesterol and lipid rafts are important cell signalling regulators involved in numerous activities and demonstrate the potency of using unsupervised screening technologies towards a deeper understanding of the cell response to materials.

Modelling the microstructural adaption of the collagen fabric during aneurysm evolution

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University of Oxford, University of Pittsburgh, University of Sheffield

An intracranial aneurysm (IA) is a balloon-like out-pouching of the arterial wall. The prevalence rate is estimated between 0.4% and 6%. The fatality rate can be as high as 50% if rupture occurs; however, most remain asymptomatic. Models of IA evolution may help understand the aetiology of the disease and may assist in distinguishing between those aneurysms that stabilise and those aneurysms that are likely to rupture. A common approach to simulate the evolving tissue structure of an IA is to assume that collagen fibres are continuously remodelling and being configured to the artery in a state of stretch (the attachment stretch) relative to the loaded configuration. In all studies to date, the attachment stretch has been assumed to be a constant value. However, experimental observations demonstrate that collagen fibres are physiologically distributed with a range of waviness relative to unloaded tissue. This implies that there must be a distribution of attachment stretches in the loaded configuration. Furthermore, theoretical considerations demonstrate that the attachment stretch distribution must adapt over time. Hence we propose a novel constitutive model to represent the collagen attachment stretch distribution and, moreover, its adaption during IA evolution. We model the artery as non-linear elastic cylindrical membrane. The medial and adventitial layers are modelled as fibre-reinforced composites consisting of elastin and collagen. The attachment stretch distributions for collagen are defined using triangular distribution functions. Collagen fibres are represented with a neo-Hookean model. Integration of the mechanical response over the distribution of fibres gives rise to the nonlinear mechanical response. The medial layer of the artery is prescribed to degrade and the adventitial adapts to maintain load bearing of the arterial wall. We examine the influence of temporal adaption of the collagen distribution on IA evolution using a conceptual 1D mathematical model [1] and, subsequently, illustrate application of our modelling approach to patient specific geometries of human IAs [2] and rabbit IAs using a 3D multi-physics computational framework for simulating the mechanobiology of vascular disease. [1] Watton et al (2009) Modelling the Growth and Stabilisation of Cerebral Aneurysms, *Mathematical Medicine and Biology,* 26:133-164. [2] Aparicio et al Modelling the Influence of Endothelial Heterogeneity on the Progression of Vascular Disease: Application to Abdominal Aortic Aneurysm Evolution, *International Journal for Numerical Methods in Biomedical Engineering,* 30(5):563-586.

A mechanism for perivascular clearance of amyloid-β from the brain

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University of Louisville, University of Southampton

Alzheimer's disease is characterized by accumulation of amyloid-b (Ab) in the walls of cerebral arteries and in brain tissue. The problem is thought to be caused by insufficient clearance of Ab, rather than overproduction. Hypotheses include breakdown of the blood-brain barrier, mutation of amyloid precursor protein leading to a greater proportion of neurotoxic Ab42, and reduced perivascular transport. The focus of this work is to study a possible mechanism for advection of Ab along artery walls. Ab is largely absent around cerebral veins, but forms plaques in basement membranes between arterial smooth muscle cells. Because the endothelial layer on the inside and the media and adventitia on the outside are relatively impermeable to large molecules, a potential point of entry for Ab from the parenchyma is near the capillaries, where the membrane is not surrounded by media and adventitia. It is expected that arterial pressure drives peristaltic flow in the membranes in the same direction as blood flow. Yet to explain the presence of Ab in basement membranes far from the capillaries requires transport of Ab in the direction opposite that of the peristaltic wave. Here we forward the hypothesis that flexible structures within the membrane, if oriented such they present greater resistance to forward than retrograde flow, may cause net reverse flow, advecting Ab along with it. A solution was obtained for peristaltic flow with low Reynolds number, long wavelength compared to channel height and small channel height compared to vessel radius for ranges of peristaltic wave amplitude to channel height ratio and dimensionless structural drag. Results show that for cylindrical structures, with maximum forward to reverse drag ratio of 2.0 and oscillating in orientation out of phase with the peristaltic wave, retrograde flow is promoted by high structural drag and low amplitude ratio. This mechanism can drive large retrograde flow. For instance, for a structural to Poiseuille drag ratio of 0.1 and amplitude ratio of 0.05, retrograde flow is approximately equal to that of the maximum possible forward flow without structure. While the mathematical model confirms that significant retrograde flow can be produced, this mechanism awaits experimental validation of the presence and nature of such structures within the basement membrane.

The Exchange of Fluid between Lymph and Blood in Lymph Nodes

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Boston Children's Hospital, Harvard Medical School, and Imperial College London

Lymph nodes (LN) are positioned in strategic locations throughout the body as crucial elements of the immune system, and are involved in adaptive immunity. They are also important in the spread of cancer, as metastatic cells from tumors often gather in lymph nodes. It is generally thought that lymph drains to the subcapsular sinus (SS) by afferent vessels (Af), passes through medulla (MS), and exits via efferent lymphatic vessel (Ef). The lymphatic system and blood circulatory system closely interact with each other in LN, exchanging fluid and cells. Mature T-cells leave the blood capillaries through specialized high endothelial venules (HEVs) in LN. Despite the importance of lymph nodes in these crucial disease processes, little is known about how immune cells, cancer cells, antigens and lymph move through nodes and interact. Herein, we propose a 3D computational porous media model for lymph transport inside a LN. The model uses an idealized geometry based on recent multi-photon imaging of mouse lymph nodes. Navier-Stokes equations and Brinkman's equation were solved in a 3D geometry containing several distinct fluidic and porous domains. The flow rate of HEVs has been reported as one of the major outputs that can potentially modulate T-cell entry to the node and its motility. In the basal condition, about 10% of the lymph is absorbed by the HEVs. However, during conditions that cause structural changes such as inflammation, this flow rate can reach zero and even reverse. Additionally, lymph can utilize two pathways to reach efferent vessel(s), the central path through follicles and T-cell cortex, and the peripheral path directly from SS to medulla. Our study shows that only 3% of the fluid permeates through the central path, while 97% of the lymph uses the peripheral path to reach efferent vessels. Finally, this model can be further developed to investigate antigen and cell transport in LN. The results of this study can increase our knowledge of lymph and antigen transport in the regulation of immune response in a lymph node, as well as overall fluid balance and transport.

Influence of Lamina Cribrosa Microstructure in Glaucoma

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Georgia Institute of Technology and Imperial College London

The lamina cribrosa (LC) is a mesh-like connective tissue network in the optic nerve head (ONH) where retinal ganglion cell axons traverse the posterior sclera and join to form the optic nerve. Deformation of the LC under the insult of intraocular pressure is thought to be a key trigger for vision loss in glaucoma, the second most common cause of blindness. Consequently the biomechanics of the LC is a topic of great research importance. To perform subject-specific modeling of LC biomechanics, information about LC microarchitecture is essential. Here we describe tools for the acquisition and use of such information. We imaged the LCs of enucleated porcine eyes using high-resolution micro-computed tomography (μCT) in combination with phosphotungstic acid contrast-enhancement, and the LCs of enucleated porcine and human eyes using second harmonic generation microscopy. Spatially-resolved connective tissue microarchitecture was extracted from images using the Frangi filter, which uses second order gradients of image intensity to automatically detect "plate-like" and "tube-like" structures. From such segmented images we deduced local porosity and local connective tissue orientation, which were then used to drive a finite element model of posterior eye biomechanics. The LC was modelled as a Mooney-Rivlin solid matrix with embedded fibers obeying an exponential power law model. Both the μCT and second harmonic generation microscopy produced 3D image sets of excellent quality that were effectively segmented using the Frangi filter. Finite element model results indicated that incorporation of both local porosity and fiber orientation was essential to accurately describe the local LC strain profiles. We conclude that such microarchitectural details of the lamina cribrosa may explain inter-individual susceptibility to vision loss in glaucoma, as well as regional patterns of vision loss in glaucoma patients. Acknowledgements: Funding from the Wellcome Trust, EPSRC (088844/Z/09/Z)

A New Approach for Ocular Biomechanics in Mice

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Intraocular pressure (IOP) is regulated by the balance between the formation of aqueous humour (AH) and its flow across the hydrodynamic resistance of the conventional outflow pathway. In glaucoma, increased outflow resistance can lead to pathologically elevated IOP, which can cause irreversible damage to the retinal ganglion cells. Decreased scleral stiffness may exacerbate the condition, through excessively large strains experienced under elevated IOP. Mouse models are ideal for testing potential candidates for reducing outflow resistance, however, the diminutive size of these eyes necessitates extremely precise measurements, which previous techniques have been unable to provide. In the present study, a new system was developed, utilising a thermal flow meter, a differential pressure transducer and an actuated pressure reservoir to accurately measure the flow rate and pressure in the eye. Through a hydraulic-electrical analogue, the analytical response of the system was derived and thoroughly validated *in vitro* using glass capillaries and compliant tubing to approximate the resistance and compliance of mouse eyes. Perfusions were carried out on paired enucleated eyes from 10-13 week old C57BL/6J mice. The eyes were cannulated and the IOP and flow rate into the eye were recorded for 9 pressure steps, a resolution made possible by the quick response of the system (~5 min or 5 times quicker than prior systems). The pressure-flow relationship revealed a pressure dependent increase in outflow facility, which may be a result of deepening of the anterior chamber. The commonly used linear fit proved to be insufficient and an alternative model was proposed that accurately captures the pressure dependence of the outflow facility. The pressure dependence of the ocular compliance was simultaneously captured, and was observed to decrease with increasing pressure. Additionally, population data on >30 of mice revealed that the facility is log-normally distributed (8.1*/1.7 nl/min/mmHg) and thus statistical analysis on this parameter should account for this. These new measurements provide unique insight into the biomechanics of mouse eyes that cannot be captured with existing measurement methodologies.

An in vitro model to assess the biomechanical function of meniscus repair methods

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The menisci are integral parts of the knee joint, distributing loads, providing shock absorbance and providing stability. Due to the avascular nature of the meniscus, damage to the meniscus often requires surgical intervention. As such there is much interest in developing new devices and techniques to assist in the repair. However, new devices are not often assessed for their restorative biomechanical function prior to animal or clinical trials. An *in vitro* model using both porcine and cadaveric knee joints is proposed in order to allow new devices and/or repair techniques to be functionally assessed to establish their likely performance *in vivo*. Initial investigations focussed on the porcine knee due to its anatomical and geometrical similarity to that of human knee. Specimens were mounted in a custom rig and loaded with a uniaxial compression tester (Instron 3365). Pressure sensors (Tekscan I-scan) were placed between the tibial plateau and the inferior surfaces of the menisci. The knee was loaded with 500N for 1000s and the pressures transmitted to the tibial plateau were recorded. The contact area was also recorded. The aim of this study was to obtain control data to which repair devices and techniques could be compared to assess their restorative biomechanical function. Two control states were identified, a negative control consisting of an intact knee complete with cruciate and collateral ligaments and both menisci, and a positive control consisting of the intact knee with a total medial meniscectomy. A third state of a partial medial meniscectomy was also investigated. Results demonstrated that transmitted pressures were lowest and contact areas highest in the intact knee, with highest contact pressures and lowest contact areas found in the total medial meniscectomy condition. The partial meniscectomy condition showed values between the two control conditions. We have demonstrated that this model can distinguish between these three meniscus conditions and is suitable for use in assessing the restorative biomechanical function of meniscus repair devices.

Keynote: Professor Peter Brett, Director, Brunel Institute for Bioengineering, Brunel University, London, UK

Discriminating the real-time tissue working-environment of robotic surgical devices using tactile information.

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After two and a half decades of research and development, the field of surgical robotics has shown benefit in terms of greater consistency in the outcome of procedures and the ability to operate reliably through difficult minimal access. Building on this impressive achievement, current research is leading to surgical robots that are smaller, some having mechanically flexible links and, in many examples, improved user interfaces to provide greater perception and augment control. These advances are possible with greater real-time machine perception of its own mechanical behaviour and perception of the interaction with tissues. With flexibility of either or both tissues and the device, the tool position relative to the real time position of tissues is important, rather than just relative to preoperative scan data. Determination of the working environment about the tool in the tissue is likely to be complex and solutions need to provide information for the operator that can be interpreted easily, and, for the automated device perception needs to be correlated to appropriate recovery action.

As a contribution toward this goal, this paper describes research on tactile information used to discriminate the nature of the working environment for tools in tissues. Using two examples the approach is illustrated for penetrating tissues and for following a path within a lumen. The approach is both mechanically and computationally efficient, and in one example has been used in theatre to control an autonomous micro-drilling surgical robot.

Image-guidance of an MR-compatible catheter using combined 2D/3D models of the left atrium

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Introduction Minimally-invasive catheter-based interventions are widely used to treat patients with complex cardiac arrhythmias. In this work, we evaluated the guidance of an MR-compatible catheter using a combination of image-derived 3D models of the left atrium (LA) and their respective 2D unfolded maps. **Methods- Catheter steering mechanism:** The MR-compatible catheter has 3 degrees of freedom and is made of multiple segments stacked together to form a long steerable catheter tip. Each segment can be deflected by means of tendons. The tendons run along the length of the catheter and are driven by four stepper motors allowing the catheter to twist in all directions. Linear and rotational drives are also included to allow the catheter to translate and rotate along its long axis. Overall, the catheter has a full 3D workspace and is controllable by a standard PC joystick. **Image guidance using unfolded maps of the heart:** Guidance of the catheter steering was performed using 3D and 2D visualizations of a glass heart phantom. A CT scan of the phantom was obtained and a 3D mesh was extracted. The 2D unfold representation of the 3D LA mesh was computed using a surface parameterization approach. This approach optimized a cost function minimising angle and area distortions. Point correspondence between 3D and 2D was established using the transformation obtained from parameterization. The catheter steering mechanism was setup as a master/slave configuration where the image guidance software sent commands via network TCP/IP to the catheter control unit. This allowed the system to be remotely controlled. The catheter tip was magnetically tracked in physical space using the Aurora^{TM} tracker (NDI, Canada). Registration between physical and virtual co-ordinate systems was achieved using the absolute orientation method. **Results** To evaluate the system, the 2D unfold maps of the LA were used to select target sites. The catheter was steered using the joystick whilst observing its tracked position in real-time on the 3D model until the tip was as close as possible to the selected target point. The final distance of the catheter's tip to the chosen target was measured in mm. A total of fifty target locations were selected on the unfold map. The mean distance to selected targets achieved was 11.0±8.2mm. **Conclusions** The combined use of 2D and 3D models of the LA for planning and guidance of a robotically steerable catheter is feasible. Although accuracy is sub-optimal at present, this approach may provide a more intuitive method for guidance.

A Flexible Robotic Probe for Osteoarthritis Intervention

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Osteoarthritis (OA) is the most common joint disorder worldwide, with over 6 million people in the UK alone affected by painful symptoms in one or both knees [1]. Treatment of severe osteoarthritis can involve surgical procedures such as chondroplasty or partial/total knee replacement. The lack of space in the joint cavity severely limits the dexterity of the surgeon as well as the visual field, thereby making these operations more challenging and dangerous.

The work proposed presents a novel hand-held device with a flexible robotic tip, equipped with both traditional onboard imaging and an endomicroscopic probe. A software framework was also developed for the hand-held instrument, to provide a virtual environment with dynamic tracking, as well as virtual fixtures [2] when the device is docked onto a robotic arm. The key features of the instrument are:

1. A flexible probe actuated with a dual-tendon system working in opposite directions.
2. An onboard camera for conventional surgical imaging.
3. A multi-mode high-resolution endomicroscopic probe using a fibre bundle.
4. A registration platform using an interactive 3D environment.
5. A dynamically-tracked virtual environment.
6. A robot-docking system to provide virtual fixtures through a robotic arm.

The use of a flexible instrument in the surgical treatment of osteoarthritis can provide the surgeon with an increased dexterous workspace, as well as enhanced surgical exploration. Experiments are currently under way to assess the efficacy of the proposed system.

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Control of a virtual, trans-humeral myoelectric prosthesis using EMG and kinematic signals

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There are approximately 5-6000 major limb amputations carried out each year in the UK (National Amputee Statistical Database). Although the proportion of amputees with upper limb amputations is relatively small, they are a population with high functional demands. A myoelectric prosthesis uses electromyographic signals (EMG) generated by muscles within the person's residual limb to control prosthesis movements. For a trans-humeral amputee, those signals are required to control elbow flexion, pronation-supination and hand opening/closing. The aims of this study were to investigate the potential of combined EMG and proximal motion signals to predict distal arm movements, and to test two different prediction models, both offline and during use in a novel virtual reality environment. People over the age of 18 with no history of injury to the upper limbs were asked to participate in the experiment. Arm kinematics (Xsens BV), and EMG from upper arm muscles (Biometrics Ltd), were recorded while the participants performed reaching movements to targets presented in a VR environment (Oculus VR, Inc.). These signals were used to train two models to predict the distal motions of the limb: a time-delayed artificial neural network (ANN) and a non-linear polynomial. The models were then used to control the distal angles of the virtual arm during online testing of target-reaching tasks. Both models fit the training data with a maximum error of 5 degrees for flexion-extension and 10 degrees for pronation-supination. During online use of the models, errors were higher, but users were still able to successfully acquire targets with a median time-to-target of 8.0s for the polynomial and 8.9s for the ANN. Path efficiencies were 36% for the polynomial and 51% for the ANN. The results show that the combination of kinematic signals and EMG can be used to control a (virtual) prosthetic limb, and that online testing is essential to determine controller usability.

Optimal Tool Pose Control in Active Constraints for Soft Tissue Dissection

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Active constraints were conceived in the 1990s as a way in which the complementary skills of surgeons and robots could be combined by sharing control of the surgical instruments between them. Within an active constraint system, the surgeon has primary control over the motion of the instruments; however, at certain times the robot modulates the motion in order to guide the surgeon along pre-planned pathways or to protect anatomical regions. Historically, active constraints have operated under the assumption that the anatomical environment can be simplified to be rigid throughout a procedure, and this has been well exploited within the field of orthopaedic surgery. Research is currently being undertaken to apply active constraints to soft tissue surgeries in which the constrained pathways and regions change intraoperatively due to physiological effects and tool-tissue interaction. Specifically, active constraints can now be implemented to protect soft tissue structures that are being dissected, allowing for narrower surgical margins and less damage to delicate, healthy tissue structures. To apply active constraints it is necessary to compute a target pose for the surgical instruments that follows the pose of the actual surgical tool, while not penetrating the constrained anatomy. It is this target pose that the robotic system guides the surgeon towards. When the surgical instruments have complex, non-rotationally invariant geometries, computing the target tool pose is not straightforward. It is not sufficient to move the instrument as close to the actual tool as possible because proximity does not have a fixed definition in terms of translation and rotation. To define the optimal pose for a constrained tool, a six-dimensional dynamic proxy simulation is proposed which uses Gauss' principle of least constraint. By defining the constrained acceleration of the target pose based on an efficient consideration of 'close contacts' with the surrounding constraint geometries, the novel proxy method is adapted specifically for deforming environments and avoids the necessity for computationally demanding continuous collision detection. A simulated soft tissue dissection task was implemented and several user experiments showed the efficacy of active constraints by reducing metrics characterising tissue damage.

A Wasp-Inspired 3D Needle Steering System for Soft Tissue Surgery

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Over the last two decades, minimally invasive surgery has become the preferred choice in many surgical specialties due to the reduction in intra- and post-operative risks when compared to open surgical access. Generally rigid needles with straight trocars are employed to reach deep-seated targets within the body. During needle insertion, however, there is a high probability that blood vessels, bile ducts or, in the case of brain surgery, some specific functional areas, will lie on the insertion path. Damaging any of these structures could result in significant complications for the patient. To counteract these issues, needle steering systems have recently attracted significant research interest. Popular approaches include: steering methods through lateral motion of an external base and deformation of the soft tissue; steering control of flexible needles with a fixed-shape bevel tip or a kinked tip; and needle steering by means of nested concentric tubes. Despite significantly advancing the state of the art, practical needle steering remains challenging, especially in the context of delicate surgery within highly deformable tissue, such as the brain. Here, a biologically inspired design, named STING, based on the egg-laying channel of certain ovipositing wasps, is presented, which is able to steer in three dimensions along arbitrary trajectories within a compliant medium. It relies on the relative motion of multiple interlocked segments that, coupled with asymmetric tissue reaction forces generated during insertion, cause the needle to steer in a controlled fashion. Previous work has demonstrated successful planar trajectory following in a gelatine sample, where the strain and deformation at the needle-tissue interface has been measured with unprecedented accuracy and found to be significantly reduced when compared to changes caused by a conventional needle with the same dimensions. A 3D kinematic model of the needle has also recently been published and the present work aims to validate needle performance in 3D by means of controlled experiments in gelatine. Details of a closed-loop curvature controller, coupled with a means to maximise curvature for a given insertion length, will be provided, alongside quantitative results about tracking performance and targeting accuracy under laboratory conditions.

Smartphone app as ultra-low cost medical tricorder for real-time cardiological measurements via ballistocardiography

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Cardiovascular diseases are the major cause of death in the world and they account for more than 30% of all global deaths. By the time these diseases are detected, the underlying cause is usually quite advanced, which delays or complicates treatment procedures and, in many cases, makes even impossible for patients to recover fully. Consequently there is a clear need for detection and proper treatment of cardiovascular problems at a very early stage. We investigated the potential use of smartphones as heart monitoring devices, which can record and analyse heart activity in real time. We placed an iPhone on a subject's chest and using the smartphone app we have developed, exploited the device's inertial sensors in order to capture the subject's chest motion data caused by the heartbeats and breathing. Using an adaptive peak detection algorithm on these data, we are able to accurately capture the heart and breath rate in real time. Additionally, we examined to what extent the collected ballistocardiograph (BCG) signal can be mapped into an electrocardiograph (ECG) signal, which is a standard heart monitoring technique for medical diagnosis. We applied an artefact removal process to reduce the breathing effect on the collected signal and then, using a black-box identification approach, we created a model that maps the BCG into an ECG signal, which can be instantly made available to clinicians for extended analysis and study. Our aim is to provide patients and the general public an easy access to low-cost monitoring and continuous care equipment by simply turning their smartphones into a portable healthcare system that autonomously monitors heart activity. Furthermore, the potential of applying simple machine-learning techniques to learn and identify diseases based on empirical data, can provide medical staff with the biomarkers required for earlier and more accurate detection of heart abnormalities.

A novel 3D motion sensing system for the early diagnosis of Huntington's Disease and other movement disorders

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1. Background, Motivation and Objective Neurodegenerative movement disorders are devastating, late onset diseases that lead to severe disability and early death of patients. The best known and most frequent of them is Huntington's Disease (HD). Typical for these disorders are movement disabilities that, very subtly, start in the early stage of the disease and then become worse with the disease progression. There is no restorative therapy available. Due to the neurodegenerative character of these disorders, any therapeutic strategy that is to be developed must have to diagnose the disease as early as possible. Slight movement and tremor are early symptoms of Huntington's disease. However these slight movements occur randomly and require the patient to be monitored for long periods. The aim of this project is to develop a high sensitive motion sensing system to record the movement of the patient over extended periods and thus become an essential element in the early diagnosis of movement disorders such as HD.**2. Statement of Contribution/Methods** In this project, a wearable motion sensing system incorporating micro-electro-mechanical systems triaxial accelerometer is developed to measure abnormal movement of arm due to HD. The system is robust, compact, lightweight and can be easily worn on the patient's wrist for periods of 48 hours without disrupting the patient's activities. The system is composed by the tri-accelerometer module, control module, SD-card, USB module, Lithium battery and power management module. It is programmed to measure and store data with a sensitivity of 6g ($58.8 m/s^2$) at 200Hz. The vibration data is stored on the SD-card and a dedicated PC based program is used to analyze the recorded data.**3. Results and Conclusions** With the developed system, very slight movements can be detected. From spectral analysis, it can be seen that the frequency and power of the specific movement of patients with HD such as shaking and tremor is different from the movement of healthy people. Initial s results indicate shows that the system is reliable works well and spectral analysis could be helpful to aid physicians to diagnose clearly the Huntington disease at a usefully early stage.

Continuous Physiological Monitoring of Ambulatory Patients

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INTRODUCTION. Clinical deteriorations of hospital patients must be recognised early to maintain patient safety and minimise treatment costs. Routine practice on UK wards is to measure physiological parameters intermittently every 4-6 hours, unless the patient is recognised to be deteriorating. Thus there may be a prolonged period of deterioration prior to recognition. Wireless sensors, combined with risk prediction algorithms, may enable earlier detection of deteriorations by continuously monitoring physiology. However, such systems depend on reliable data acquisition. We assessed the proportion of patient stay for which continuous ECG and pulse oximetry data could be captured using wireless sensors. **METHODS**. A post-surgical cardiac ward was equipped with wireless sensors which transmitted data to a central monitor in real time. 222 patients consented to wear a sensor whilst recovering from cardiac surgery on this ward. **RESULTS**. 196 patients wore a sensor (22 did not stay on the ward, 3 requested not to wear a sensor, and 1 was not given a sensor for clinical reasons). 122 wore a sensor until discharge, 66 requested to stop wearing the sensor early, 6 had the sensor removed for clinical reasons, and 2 were transferred elsewhere. The median length of ward stay was 4.5 (4.9) days (interquantile range). The 196 patients wore sensors for 898 out of 1344 days. ECG and pulse oximetry data were acquired from each patient for 62% (52) and 18% (41) of their stay respectively. **CONCLUSION**. ECG data were acquired for the majority of patient stay, whereas pulse oximetry data were acquired for less than a fifth of the time. Furthermore, over a third of patients requested to stop wearing sensors. Therefore, there is room for improvement to the design of wireless sensors, particularly the pulse oximetry component.

Microspray technology as a potential antimicrobial delivery method for dental plaque biofilms

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Bacteria such as Streptococcus mutans in dental plaque biofilms are responsible for caries development. Dental plaque biofilms are sessile communities of bacteria embedded in an extracellular polysaccharide matrix. This complex structure enhances the resistance to antimicrobial agents by limiting the transport of dentifrices inside the biofilm. However, if the anticaries agent is able to enter inside the biofilm plaque, the biofilm itself could act as a reservoir and prevent the dissolution of the teeth. We assessed the potential for microspray for delivery of dentifrices into the biofilm using fluorescent µbeads. A high velocity (40.9 m/s) microspray of 130 ± 0.03 µL (n=11) made of water and air was generated using a Sonicare AirFloss dental cleaning device (Philips Oral Healthcare, Seattle). 1 µm size carboxylate-modified polystyrene fluorescent beads were incorporated inside the AirFloss at a concentration of 10^9 beads/mL (working solution). *S. mutans* UA159 biofilm colonized slides were shot with the AirFloss positioned perpendicular to the slide. This microspray experiment was compared with an in vitro mouth washing experiment. 2 mL of the beads working solution were poured on biofilm covered slides and then the samples were shacked for 30 seconds at 200 rpm. Confocal images were taken at the edges of the shooting for the microspray experiment. In order to relate the beads position to the biofilm thickness we used the relative depth ratio (RD), which is defined as the ratio between a particles' vertical position and the vertical position of the fluid–biofilm interface at that location. Thus, a RD value of 95–100% corresponded to a bead located in the biofilm substratum, while a relative depth of 0–5% corresponded to a bead located in the near the biofilm surface. The beads and biofilm surface coordinates were measured from confocal images using both Matlab and ImageJ. The AirFloss was able to deliver 279.3 (±19, n=2) microbeads inside the biofilm while the *in vitro* mouth washing allowed only 12 (±5.1, n=3) beads to reach the inner parts of the biofilm. Moreover, the microbeads burst forced the beads up to a RD of 90-100% inside the biofilm. The AirFloss microburst was able to deliver a significant amount of microbeads compared to an in-vitro mouthwashing making the microburst technology a potential antimicrobial delivery device for dental plaque biofilms. Future works will incorporate NaF inside the AirFloss microspray burst in order to study the delivery of fluoride into the biofilm.

Methods for Virtual Stent Deployment

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The effectiveness of intracranial stenting depends on a number of factors such as the released position and shape of the stent, alteration of the vessel haemodynamics, incidence of an arterial injury during the procedure, etc. (Pierot, 2011). However, there is currently no means for a clinician to obtain this vital information prior or during the intervention for a given clinical case. For example, there is no possibility to predict the resulting configuration of the device before the intervention in a clinical setting. Additionally, knowing the accurate configuration of the device, its attachment to the vessel wall, especially the covering of the aneurysmal neck, would enable the subsequent study of the post-interventional haemodynamics of the vessel and possible prevention of such complications as stent migration, endoleakage, etc. Motivated by this clinical need, this study aimed at developing a methodology for modelling the virtual deployment of implantable devices inside patients' vessels, that features fast computational times and can be used in clinical practice. Hence, the methodology had to be general enough to be able to include a broad range of devices, such as stents and flow diverters. With this in mind, we narrowed down the investigated computational techniques to those that are both sufficiently generic and computationally inexpensive. Under these constraints, our attention was drawn to the class of methods called dynamic mesh, in particular, springs analogy methods, that are widely used in many engineering applications (Blom, 2000). Using the idea of a mesh consisting of springs, we have developed algorithms that enable modelling the process of stent expansion and its deployment in vessels. Further, we have compared 3 different spring analogy methods featuring different properties of the springs: (1) lineal spring analogy, (2) semi-torsional spring analogy and (3) torsional spring analogy. The comparison was based on the results of expansion of two different devices – a stent and a flow diverter – in four different scenarios: (1) in the case of free expansion, (2) in the idealised straight vessels, (3) in the idealised bent vessels and (4) in real patient cases. When applied to the stent deployment problem, all three spring analogy methods converged; however, they did so at different rates. The convergence was assessed by different metrics, measuring the displacement and force evolution as well as the evolution of angles between the struts and the struts length. One of the interesting findings entailed the fact that the lineal springs method displays faster convergence rate in all of the four metrics used. Additionally, it produced final results comparable with those obtained by its more sophisticated semi-torsional and torsional counterparts. This was surprising since the lineal method constitutes the base for the other two spring methods and is associated with the simplest implementation. In conclusion, our study demonstrated the overall ability of spring-based methods to model virtual stent expansion in a computationally expedient manner, which constitutes a valuable base for future extensions of the model, with the ultimate goal of enabling predictive simulations of the minimally-invasive methods in a clinical setting. References: Pierot, L. (2011). Flow diverter stents in the treatment of intracranial aneurysms: Where are we? Journal of Neuroradiology, 38:40–46. Blom, F. (2000). Considerations on the spring analogy. International Journal for Numerical Methods in Fluids, 32(6):647–668.

Development of embedded piezoelectric sensors to determine implant loosening

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There is an increasing demand for total knee replacements and subsequently a greater need for revision surgery. One of the most common reasons for revision is implant loosening. However clinically the patient will present complaining of pain, not a loose implant. It would therefore be a useful diagnostic tool to interrogate the implant to ascertain whether it remains well fixed or not, thus either confirming or eliminating this mode of failure and a possible source of pain. For such technology to be adopted by manufacturers, it must be safe, extremely low cost and simple to build into the implant. This research is aimed at developing a sensor that meets these requirements and, whilst embedded in an implant, can provide information on its fixation to the underlying bone. Previous work by the same authors has shown that through interrogating the frequency impedance plots of a small piezoelectric sensor that it is possible to distinguish the time at which the cement bond between Sawbone and tibial analogue cures. The work in this study takes knowledge gained from the aforementioned work; specifically what features of the frequency impedance graphs provide the most relevant information on fixation. It uses these to determine whether it is possible to quantitatively distinguish between the amounts of fixation of an analogue tibial base plate cemented to a block of sawbone. Five categories of cement coverage were investigated: fully cemented, three quarter cemented, half cemented, quarter cemented and no cement. Ten samples of each were tested and a frequency impedance curve was collected for each sample using VIA Brovo Impedance Analyser (AEA technologies). By investigating peak impedances, root mean errors and the mean differential of the trace it has been found to be possible, though the use of support vector machines, to determine the category each sample belongs to with an error of 18.5%. Future work will aim to investigate more bonding situations and optimise the computer's ability to classify the amount of secure fixation.

Quantitative ultrasound imaging of arterial flow, micro-circulation and molecular targets

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Macro and micro blood flow is fundamental to tissue and body function. A wide range of major diseases including coronary heart disease, valvular heart disease, carotid, cerebral and peripheral vascular diseases, cancer and chronic inflammation manifest themselves with abnormalities in macro flow and micro flow (perfusion). The ability to image and accurately quantify flow and perfusion is highly valuable in the detection, diagnosis and staging of these diseases and also in monitoring of progression and treatment response. Ultrasound (US) imaging is non-ionizing, has low cost and excellent accessibility. It operates in real time and is widely used clinically. The advent of contrast enhanced ultrasound (CEUS) with microbubbles has revolutionized the way flow and perfusion can be imaged and quantified using ultrasound. Furthermore CEUS has shown potential of imaging specific molecules using targeted microbubbles. CEUS is gaining increasing acceptance in clinical practice and is an active area of both basic science and clinical research but still face challenges in the areas of imaging SNR, both temporal and spatial resolution and presence of imaging artefacts. We have in this study developed new techniques for imaging of flow and tissue perfusion, taking advantage of recent advances in superfast imaging of up to 20000 frames per second, and contrast enhanced ultrasound. Firstly we explore the application of superfast ultrasound imaging in studying fast arterial blood flows in a model system. The high frame rate enables the visualization and quantification of very fast and time varying flows; Secondly we develop a number of techniques to improve micro-vascular imaging and perfusion quantification by removing various imaging artefacts including attenuation and non-linear artefacts, and by identifying individual specific bubble signals from vasculature for super resolution imaging; Finally ultrasound imaging of molecular targets using functionalized microbubbles will be described.

Recent developments and applications of Edge Illumination x-ray phase contrast imaging

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X-ray imaging plays a central role in a wide range of medical and biological applications, such as mammography, angiography, computed tomography, etc. The relatively low absorption of x-rays in matter, in fact, enables non-destructive analysis and characterisations of several specimens and tissues. However, when materials with very similar or very low absorption properties are imaged, conventional radiography usually provides very low contrast. To overcome this problem several imaging techniques sensitive not only to the absorption, but also to the phase shift of x-rays in matter have been developed. The set of all these techniques are usually referred to as x-ray phase contrast imaging (XPCi). Albeit XPCi has proved to provide increased sensitivity and image quality compared to x-ray absorption imaging, its applicability has primarily been limited to special facilities, such as synchrotrons. This is due to coherence requirements usually needed to exploit phase effects. Recent advances have shown the possibility to adapt some XPCi methods to a compact laboratory set-up, using a standard x-ray source. In particular, Edge illumination (EI) XPCi appears to be an excellent candidate to take XPCi into mainstream applications, since it does not depend on spatial or temporal coherence. EI-XPCi can provide simultaneously low dose, high phase sensitivity and resolution in a laboratory set-up, and can be implemented in a tomographic set-up to obtain three-dimensional maps of the sample phase and absorption. The technique can also be extended to extract the ultra-small-angle scattering signal, which is sensitive to inhomogeneity of the sample at a lower scale than the pixel size. EI-XPCi set-up is relatively simple, requiring only two optical elements, and very flexible. After briefly describing the base principle, this talk will review recent applications in a range of medical and biological applications.

New Gd(III) contrast agents for high-risk atherosclerotic plaques by MRI

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Ruptured atherosclerotic plaques and aortic aneurysms show deposition of tropoelastin (TE), the soluble precursor of cross-linked mature elastin. Tropoelastin is only found in vessel walls with underlying pathologies whereas elastin is endogenously found in normal vessel wall [1,2]. We found increased levels of TE in ruptured compared with stable plaques(41% vs. 18%, P<0.001) in a rabbit model of atherothrombosis. Herein, we present two novel Gd(III)-based MRI contrast agents specific to TE [3]. K(DOTA)-YPDHVQYTHY (**YPDH**) and DOTA-VVGSPSAQDEASPLS (**VVGS**) were designed based on known epitopes which specifically target TE [4]. Binding affinities of Eu(III) complexes were assessed towards Tropoelastin, Elastin, Collagen (types I and III), Fibronectin and Human Serum Albumin. NMRD profiles of Gd(III) complexes were recorded (0.01 – 128 MHz) and the effect of the presence of TE on the relaxivity studied. Eu(III)- and Gd(III)-ESMA (elastin binding agents) and DTPA were also studied for comparison. Both contrast agents show high relaxivities (r_1**YPDH** = 9;r_1**VVGS** = 12 mM^{-1}s^{-1}), high affinity and selectivity towards Tropoelastin (K_D**YPDH** = 7; K_D**VVGS** = 11 μM) particularly when compared to mature Elastin. *In vivo* MRI and PET studies have been done in male apoE$^{-/-}$ mice fed with high-fat diet for 24 weeks. MRI studies (3T, 0.2 mmol/kg) show selective enhancement of the atherosclerotic brachiocephalic but no enhancement of the non-diseased carotid arteries. Immunohistochemistry validated the presence of TE only within the plaque where contrast uptake was observed. Conversely, the non-diseased vessel lacked TE and despite the presence of mature elastin no contrast uptake was observed. PET/CT scans of ^{64}Cu complexes show blood clearance of 1h and mainly renal excretion. We developed new MRI contrast agents that selectively bind to tropoelastin, potentially useful as surrogate markers for the detection of high-risk atherosclerotic plaque.
 References: **1.** Krettek A., et al. *ATVB* 2003, 73:2154 **2.** Akima T., et al. *Circ J* 2009, 23:582. **3.** Phinikaridou A. and Botnar RM, WO2012/107725. **4.** Hinek A., et al. JCB, 1994, 126:563; Finnis ML, et al. 1997, 272:22817.

Activation Energy Mapping in Articular Cartilage

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Magnetic resonance imaging of articular cartilage has, in the past, had a primary focus on clinical, qualitative imaging or quantitative mapping purely using relaxation times (e.g. T_1 and T_2) and the development of phenomenological models to link these to physical properties, such as GAG content. Recent work in the field has looked at more advanced imaging methods, such as dGEMRIC, gagCEST and diffusion tensor imaging in order to attempt to develop a more direct link to physical and biochemical properties of the cartilage. This link is important to further understand the structure and function of cartilage, and here we investigate a novel method to probe the physical and biochemical properties of cartilage tissue. We present a novel method for visualising cartilage using magnetic resonance imaging techniques, which have been developed for probing the structure, mobility and hydration of soft-matter systems. This approach has been used to determine the dynamic activation energy (E_A) of water within articular cartilage. Two related imaging methods have been explored: firstly quantitative mapping of the T_1-relaxation time over a range of temperatures and secondly, quantitative mapping of the apparent diffusion coefficient over a range of temperatures. These are complementary techniques that probe the local tissue environment by extracting the rotational activation energy of the water within articular cartilage from the T_1-relaxation time mapping, and the translational activation energy from the apparent diffusion coefficient mapping. These methods have been shown to provide different information from within the articular cartilage tissue to that seen with other imaging techniques. These quantitative maps can provide a link to biochemical contents or physical properties of articular cartilage tissue and can be interpreted in terms of the known structure and properties of cartilage from other methods.

Fetal face segmentation and contour characterisation in 3D ultrasound

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We present a novel method to automatically segment and characterise fetal face shape from 3D ultrasound (US) images. Following the success of using mid-line profiles to characterise facial dysmorphism in children with genetic conditions, we look at 2D mid-line profiles as a means of representing fetal face shape. The proposed automated method is largely based around the application of the analytic signal and its derivative functions, followed by application of an established approach to constructing a shape model. Segmentation of the fetal profile from 3D-US can be achieved automatically in the following steps; firstly, automatic bone detection is applied using Local Energy and Feature Symmetry to locate high intensity ridges, then the image is aligned based on the detected bone structure. The image is then pruned of small structural details. Finally, a minimum cost path is drawn between extremities of the remaining structure, with costs determined by a combination of Feature Asymmetry and Local Orientation. Once the profile has been segmented, the set of contours are resampled to a standard length, and cropped from below the chin to the top of the head. Through curvature analysis, it is possible to landmark and hence align the shapes automatically. A shape model can then be constructed from the set of densely corresponded contours. By re-expressing the contours as a deviation from the mean facial shape via a set of principal modes of variation, the facial profile can be expressed in a directly comparable way. Contours can be accurately reproduced in this way, and principal differences can be identified by observing variations in the resulting shape vector. Application of the method to fetal ultrasound data shows excellent correlation with manual delineations. Across a set of 17 ultrasound images of fetal faces at approximately 27 weeks gestational age, the mean deviation of our results from manually segmented facial contours is 5.05 ± 5.82 pixels, translating to an average error of around 0.5mm. 90% of the automatically segmented contour pixels lie within 10 pixels of the manually traced contour.

A Physiologically-Realistic Model of Cardiac Magnetic Resonance Perfusion Imaging in the Beating Heart

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Contrast enhanced cardiac magnetic resonance (MR) perfusion imaging provides a non-ionising, non-invasive early indication of the health of the patient's heart, providing direct functional metrics rather than structural surrogates. However, this imaging modality is currently largely confined to research hospitals and remains difficult to optimise due to the large number of acquisition parameters. Computational modelling provides a promising approach to address this issue by expediting the optimisation of the protocols under different conditions, and thereby accelerate its adoption in the clinic. The multi-scale model that is presented consists of three main components. The first is a model of the cardiac perfusion, which uses a 1D Navier-Stokes formulation to represent the larger coronary vessels coupled to a poroelastic medium Darcy model of the myocardium and embedded capillaries. The second component is a coupled system of advection-diffusion-reaction equations that model the transport of the imaging contrast agent through the coronary circulation. Finally, post-processing approximates the MR physics and image acquisition protocols. These equations are discretised using the finite element method and implemented within in-house, parallelised multi-physics modelling software, CHeart. This model, which is the first of its kind, enables the physiologically-realistic simulation of contrast enhanced cardiac MR perfusion imaging in the beating heart. Results are presented that show how the simulated MR images vary with changes in the imaging both acquisition parameters and different contrast agents. We will specifically examine the crucial differences between intravascular and extravascular contrast agents, and the implications that these choices have for the identification of perfusion defects of differing severity and underlying disease type.

Detection of VCAM-1 expression using targeted multimodal nanoparticles: Towards the detection of atherosclerotic plaque using PET-guided MRI

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Vascular cell adhesion molecule (VCAM-1) is expressed on activated endothelial cells [1]. The role of VCAM-1 is to recruit lymphocytes and monocytes during the early stages of inflammation and atherogenesis, leading to plaque formation and making VCAM-1 an attractive target for early imaging and therapy of atherosclerosis. We are interested in developing a bimodal imaging agent that will exploit the synergies of PET-MRI for the detection of VCAM-1 in the vasculature. To achieve this, we have developed a novel PEGylated, ultrasmall superparamagnetic iron oxide nanoparticle (USPIO) platform that combines excellent stability in aqueous solution and prolonged circulation times in vivo with high MR contrast [2]. Exploiting bisphosphonate chemistry allows efficient and tightly controllable modification of the particle surface for PEGylation, attachment of targeting ligands as well as for radiolabelling. For targeting to VCAM-1 expressing tissues, a high affinity anti mouse VCAM-1 single chain antibody fragment (scFv) was site-specifically conjugated to the particles via a bifunctional bisphosphonate-PEG-maleimide linker and an engineered C-terminal cysteine on the scFv. We hypothesised that the bimodal PET-MRI nature of our VCAM-1 targeted USPIOs would be useful to detect the location of lesions on a whole body level, taking advantage of the high sensitivity of PET and to guide MRI with high spatial and temporal resolution to areas in with high VCAM-1 expression. This approach would be particularly useful in areas affected by cardiac/respiratory motion were PET/SPECT suffers from motion blurring effects that complicate the detection of small lesions. Here we report on the design, synthesis and in vitro characterisation of these particles and show efficient and highly selective in vitro binding to VCAM-1 expressing cells. These results highlight the potential of these probes to detect VCAM-1 upregulation associated with atherosclerotic plaques in vivo and warrant further studies using PET-MRI in relevant animal models. [1] Hwang et al. Circulation, 1997, 96, 4219-4225rn[2] Sandiford et al. ACS Nano, 2013, 500 Acknowledgments This work was funded by The Centre of Excellence in Medical Engineering funded by the Wellcome Trust and EPSRC under Grant No. WT 088641/Z/09/Z.

Fluorapatite coatings are antibacterial in vitro against pathogens implicated in peri-implantitis

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Objectives: With increasing concern over the growing antibiotic resistance there is a considerable interest in the preparation of antimicrobial dental implants. One potential solution is the use of a fluorapatite (FA) coating, which is known to induce bone growth. The aim of this study was to explore the antibacterial effectiveness of FA coatings against a number of pathogens implicated in peri-implantitis, an infection commonly associated with implant failure. **Methods:** FA crystal growth on stainless steel (SS) substrates was achieved using the hydrothermal method. Ordered and disordered FA coatings were produced on the under and upper surfaces of the SS discs, respectively. The subsequent coatings were characterized using scanning electron microscopy (SEM), energy dispersive spectroscopy (EDX), non-contact stylus profilometry and x-ray diffraction (XRD), streaming potential and surface energy measurements. The antibacterial activity of the FA coatings against A. actinomycetemcomitans, F. nucleatum and P. gingivalis was assessed in vitro using the colony forming units counting method, confocal and scanning electron microscopies. **Results:** The results showed that the hydrothermal method produced FA coatings with either well aligned and self-assembled crystals or disordered FA coatings that were arranged randomly. XRD confirmed the crystallinity of the FA crystals. Both FA coatings, but mostly the disordered one, presented significantly higher surface roughness, area, fluoride content and surface energy, and lower surface charge in comparison to the SS. In terms of their antimicrobial performance, both FA coatings significantly reduced the growth of all the examined bacterial strains in comparison to the SS. This was attributed to the fact that the FA coatings, and especially the disordered, presented significantly lower surface charge and higher surface roughness and area when compared to the SS, enhancing bacteria –material interactions and therefore bacterial killing by fluoride ions. **Conclusion:** These results show promising signs for FA produced using the hydrothermal method to be used as a dental implant coating due to significant antibacterial activity against bacteria strongly implicated in peri-implantitis.

Structural alterations in the dura mater after exposure to clinically relevant CoCr nanoparticles. An organ culture simulation with total disc replacement wear debris

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INTRODUCTION Total disc replacement is a surgical technique designed to reduce back pain and restore movement in the spine. Many artificial disc prostheses are manufactured using cobalt-chrome alloy popularized by the successful cobalt-chrome alloy artificial hip prostheses. The nanometre sized wear debris generated from such metal prostheses can however lead to adverse tissue reactions [1,2]. We have previously reported that clinically relevant CoCr nanoparticles can have significant biological effects upon cells isolated from the dura mater, a tissue in close proximity to spinal implants [3]. The aim of the current study was to investigate the biological effects of clinically relevant CoCr nanoparticles on the dura mater in an organ culture model. **EXPERIMENTAL METHODS** Dura mater tissue organ-cultures were exposed to physiologically relevant doses of CoCr nanoparticles [5 and 50 μm^3.cell^{-1}] generated using a pin-on-plate tribometer. The resulting biological and structural effects were evaluated using a range of methods including tissue viability (MTT assay), pro-inflammatory cytokine production (ELISA) histology (H&E), immunohistochemistry, and TEM imaging of the CoCr-particle treated tissue compared to control tissue. **RESULTS AND DISCUSSION** There was no loss of tissue viability when the dura-mater was treated with either of the two doses of CoCr nanoparticles over 7 days. However, histological analysis and TEM imaging identified loosening of the epithelial layer of the dura-mater at both doses of nanoparticles. These structural alterations were associated with increased cell and tissue expression of MMP-1, -3, -9, -13 and TIMP-1 in response to both doses of CoCr nanoparticles but the expression varied between epithelial and fibroblast cells as well as between different regions of the extracellular matrix. Significantly increased levels of IL-8, TNF-α, IL-6, IL-33 and tenascin C were released after exposure of the dura mater to CoCr particles. Specifically, IL-8 levels for particle stimulated tissues were persistently higher than for the control tissue for the duration of the treatment (7 days). **CONCLUSION** The exposure of the dura-mater to CoCr-nanoparticle caused histologically detectable structural distortion after 7 days of treatment. This was possibly due to a local inflammatory response as well as the action of matrix metalloproteinases. The results generated from this study contribute to a greater understanding of the potential risks associated with the use of MOM total disc prostheses. **REFERENCES** 1. Berry M I *et al.*, JBJS - *American Volume*2010;92(5):1242-45. 2. Guyer RD *et al.*, *Spine* 2011;36(7):E492-97. 3. Papageorgiou I *et.al.* JBMR-B, 2014.

Cavitation responsive nanoparticles for the enhancement of drug delivery

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Substantial proportions of tumours remain untreated during chemotherapy due to the irregular vasculature and high intratumoural pressure within cancerous tissue. The enhanced permeability and retention (EPR) effect causes drug carriers within the size range of 100-800nm to passively accumulate within tumours, however, the physical barriers of a dense extracellular matrix (ECM) and high interstitial pressure persist leading to the carriers remaining localised around the periphery of the vasculature. Consequently treatment efficacy continues to be limited. Ultrasound-induced cavitation events can stimulate greater drug penetration by microjetting and microstreaming. At present the cavitation nuclei available are an order of magnitude larger than the nano-scale drug carries. *In vivo* this results in spatial separation of the two agents, limiting the capacity for one to impact upon the other. Our group has successfully formulated two different monodisperse suspensions of biocompatible nanoparticles of a size that will permit better co-localisation of cavitation nuclei and therapeutics. A mixture of these nanoparticles and a model drug carrier were passed through a tissue mimicking phantom to provide an *in vitro* simulation of flow through a tumour. The impact of ultrasound on the penetration of drug carrier from the flow channel was compared between both of our ultrasound-responsive particles and the microbubble SonoVue. The cavitation response, circulation kinetics and toxicity profile of our proprietary nanoparticles in tumour bearing murine models was then characterised.

Instigation and Real-Time Mapping of Cavitation from Nanoparticles Using a Diagnostic Imaging Platform

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Inertially cavitating bubbles have been recently shown to enable enhanced extravasation and improved intratumoral distribution during ultrasound-mediated delivery of anti-cancer agents, acting as micropumps to overcome the barriers presented by elevated interstitial pressure and heterogeneous tumor vascularization. . Commonly used nucleation agents, micron-scale ultrasound contrast agents (UCAs), suffer from the inability to accumulate in tumors via the enhanced permeability and retention (EPR) effect due to their size, and their rapid destruction upon exposure, requiring frequent replenishment. Cavitation-inducing nanoparticles (NPs) sized for endothelial gaps in leaky tumor vasculature (100-500 nm) can provide tumor-selective nucleating agents that yield sustained cavitation activity upon ultrasound exposure at intensities achievable by a conventional diagnostic ultrasound scanner. This creates the possibility of a single-low cost ultrasound platform which enables B-mode imaging for treatment guidance, instigation of therapeutic cavitation, and real-time passive acoustic mapping (PAM) of the location and extent of therapeutic delivery. An open-source ultrasound platform (V-1, Verasonics, Inc) using an abdominal diagnostic imaging probe (ATL C4-2, fc=3MHz, 128 elements, 50.2mm aperture) was operated to transmit interlaced therapy and B-mode imaging pulses while PAM was employed to detect and image cavitation in real-time on an overlaid display. To deal with nonlinear propagation, limited probe bandwidth, and removal of transmission pulse, novel PAM algorithms were developed. Therapy pulses were 5 cycles of 2MHz ultrasound in the range 1-5MPa peak negative. Custom polymeric nanocups (NCs) and mesoporous carbon nanoparticles (CNPs), sized between 100-500nm, were suspended in filtered, deionized water flowing through an agar-based vessel phantom. A separate passive cavitation detector (Olympus Corp., fc=15MHz, focus 75mm) was used to verify the presence of inertial cavitation. Experimental results confirm the strong presence of inertial cavitation when US is combined with NCs and CNPs but no cavitation with just US alone. Cavitation is reliably and repeatedly instigated at pressures below 1.5MPa with both particles. CNPs display an extended presence of cavitation energy that does not diminish, while NCs bubble nuclei deplete on excitation. The US system was found to be capable of real-time adjustment of the therapy focus in depth and angle. Simultaneously, the system allowed for B-mode US image guidance as well as real-time overlaid PAM that displayed only cavitation in the vessel when NPs were present. Adjustment of focus and PAM feedback allowed for complete treatment coverage of the vessel volume. Use of an open-platform US system allowed for rapid development of complete US enhanced drug delivery system allowing image guidance, therapy delivery, and real-time monitoring of delivery. Formulated NPs significantly lower the cavitation threshold permitting use of diagnostic imaging system and providing a mechanism for treatment monitoring. Through real-time focusing and PAM an entire volume can be covered over the course of a treatment cycle, increasing chances of complete therapeutic agent delivery. Future work focuses on correlating release of therapeutic agents with cavitation maps in *in vivo* preclinical models.

Design and development of thoracic aortic aneurysm (TAA) stent-graft using nanocomposite material and shape memory alloy

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Background: Thoracic aortic aneurysm (TAA) is an enlargement of thoracic aorta to a size greater than 1.5 times of its normal diameter. TAA affects between 6 and 10 in 100,000 people annually. The overall mortality rate of ruptured TAAs is up to 97%. Genetics, certain connective tissue disorders, trauma, heavy smoking and hypertension are factors causing the disorder. Treatment options for TAA are open surgery and endovascular stent graft replacement. **Aim:** The aim of this project is to design a stent graft using polyhedral oligomeric silsesquioxanes-poly (carbonate-urea) urethane (POSS-PCU) nanocomposite and Nickel-Titanium (Nitinol) shape memory alloy. POSS-PCU is a novel material developed by our research team at UCL. It has superior properties such as viscoelasticity, anti-thrombogenecity, durability and MRI compatibility, which makes it an ideal graft material for endoprosthesis. POSS-PCU has been successfully used in many applications such as Trachea, bypass graft and heart valve and is currently being used and further developed in many other applications. On the other hand, Nitinol is a self-expandable, image-compatible and biocompatible alloy, which represents the metal scaffold of the stent-graft. **Material and method:** In order to fabricate the suture-less, tapered endoprosthesis, moulds of different material (glass, stainless steel, PTFE) were made based on the size of the pig's aorta. Dip-coating method was used to make a stent-graft with nitinol rings sandwiched between two layers of polymer. The mechanical properties, water permeability and the uniformity of the polymer over the device were tested. **Results:** Among different moulds, glass was the easiest one to coat and resulted in the most uniform graft. Regardless of polymer thickness, the young's modulus of the graft material was 4.75 MPa and the tear strength was 67.7 N/mm. The contact angle between water and polymer was 107°, which indicates the hydrophobicity of the polymer. **Conclusion:** The development of thoracic stent-graft is promising and further test are in progress include fatigue tests, haemodynamic tests and in vivo large animal studies.

Keynote: Professor Colin Caro in Conversation with Professor James E. Moore Jr

Business Pitches

Developing a novel wound dressing aiming to promote healing in patients with chronic wounds, namely, diabetic ulcers

Basil Richard Fansa
Imperial College London

There is still an unmet need for an effective wound dressing that will facilitate faster & higher quality healing in patients with diabetic ulcers, amongst other chronic wounds such as venous ulcers. Out of the 3 million (and increasing) diabetic patients in the UK, a quarter of these will develop an ulcer at least once in their lifetime. The NHS spends around £650 million annually on treating diabetic foot ulcers (DFUs), including the dire outcome of 5,000 amputations a year. The problem extends globally, as there are 11.3million patients with DFUs worldwide. Conventional dressings that are commercially available and in use, may have their individual merits however, in terms of effective wound healing, success is limited and most wounds will often take around a year after presentation to heal depending on the depth and area size of the wound, even with the best nursing care available. 13% diabetic foot ulcers still fail to heal even after a year from presenting. In this project, a novel dressing has been developed which is a composite, whose primary component is a bioactive glass. Early prototypes involving different manufacturing techniques have been produced, and have been shown to release ions when incubated in aqueous buffers. The ion release profiles from these have been measured using Inductively Coupled Plasma Optical Emission Spectrometry (ICP-OES). A combination of surface topography imaging (Scanning Electron Microscopy) & Fourier Transform Infrared (FTIR) spectroscopy techniques have been used to identify changes in glass & composite structure, crystallinity (evidenced by X-Ray Diffraction) and presence of hydroxyapatite (HA) on our samples, when exposed to Tris Buffer & Simulated Body Fluid, which has been used to mimic physiological ion concentrations in blood plasma. The results obtained have shown that there is potential for the materials developed to be used as a chronic wound dressing.

Preventing Breast Cancer Related Lymphedema

Karthik Ravichandran
Imperial College London

1 million women worldwide will develop breast cancer every year and 20% of these women will develop breast cancer related lymphedema (BCRL). The surgical technique used to remove lymph nodes cut the main drainage pathway for lymph flow which causes the arms to swell up. There is no cure once the disease progresses. There is nothing we can do for these women who survived breast cancer and been through tough emotional and physical times. Currently we can only try to manage the condition through bandages, massages and exercising. In UK there are 9000 new cases of oedema every year. Our proposed solution is to ensure at the time of surgery when surgeons remove lymph nodes they implant our device to replace the lymph node to provide new pathways for lymph flow. We want to start the prevention at the earliest point as possible thus reducing the risk of developing oedema. The potential market for our device is for all patients who undergo lymph node biopsy because we do not know which patients are going to develop lymphedema. The potential market will be 52,400 surgeries every year giving us potential UK annual market of £52 million. In the US the market size is five times the size of the UK. Later we envisage to target other types of cancers where lymphedema is a problem. We have the chance to prevent and make a real difference for women who survived breast cancer. The current lymphedema population have very little hope that their condition will be cured.

Stent Tek: Enabling Percutanous Creation of Vascular Access in Dialysis Patients

Sorin Popa, *Robert Dickinson*
Imperial College London

Stent Tek is an engineering company developing a novel catheter based system that provides a better way for patients to receive hemodialysis (HD) for kidney failure. These patients require chronic vascular access (VA) which can be achieved in one of three ways: native arteriovenous fistulas (AVFs), arteriovenous prosthetic grafts (AVGs), or central vein catheters. Although AVFs are considered the gold standard due to longer patency rates and a decreased risk of infection they have a higher incidence of early failure compared to AVGs and less than 15% remain patent for the entire length of a patient's HD treatment. In the US, the healthcare system spends $10 billion a year on the dialysis population to treat failed VA sites. Our novel catheter device percutaneously creates a reliable access site that is functionally similar to an AVG. Two catheters are aligned at the appropriate site in the arm using a proprietary electronic system and a stent graft is deployed to create the anastomosis. This is a

minimally invasive procedure that can be performed outside of the operating room by surgeons or radiologists and is significantly simplified compared to the traditional surgical approach. In the US, vascular access devices and accessories are $4.5 billion a year market. Ours is a high tech single use device that costs $500 to manufacture and will sell for $4000 with the overall procedure estimated to cost less than half of what is currently the standard. A detailed business plan and financial forecasts show that we forecast a conservative yearly revenue in five years of $50 million in the US alone; expanding into Europe is expected to double this figure. Currently, a first generation prototype of the catheter system is near completion and the next milestone is to conduct animal trials within 18 months. We are seeking $1.2 million to reach first in man trials in 30 months.

LOBSTER: LOw-cost Bimanual System for physical Therapy and Enhanced Rehabilitation

Flavia Tempesti, Etienne Burdet
Imperial College London

Each year approximately 15 million people worldwide have a stroke, over 70% of these require arms and hands rehabilitation and around 10 million people are paralysed on one side due to stroke. Rehabilitation of hand function is paramount to activities of daily living (ADL) and thus a priority for people affected by neurological disease such as stroke, spinal cord injury and cerebral palsy to regain an active life. Rehabilitation of the hand function has also been shown to improve the arm function (while the converse is not true). The few rehabilitation device developed so far are bulky, expensive and demand additional safety measures. Working alongside physiotherapist we developed the LOBSTER, acronym of: LOw-cost Bi-manual System for physical Therapy and Enhanced Rehabilitation, a bi-manual rehabilitation device that can help patients with this kind of paralysis. Thanks to a mechanical connection between the two handles, the healthy hand guides the movement of the impaired one providing the appropriate forces. This natural actuation decreases the overall cost and increases the security of the system, making the device more suitable for home-based use. LOBSTER is portable, easily reconfigurable and allows training of at least three upper limb movements. By combining LOBSTER with a tablet, the movements and the improvements of a patient can be tracked in real-time and this allows a more engaging rehabilitation experience.

Assessment device to quantify the severity of Parkinson's symptoms

Paolo Angeles, Mike Mace, Ravi Vaidyanathan, Etienne Burdet
Imperial College London

Parkinson's Disease is an incurable disease that affects 6.3 million people worldwide. More specifically, there are 1 in 500 sufferers in the UK with 80 % of those receiving some form of treatment. Current treatments are initially through medication and if refractory to this treatment, deep brain stimulation will then be offered. The amount of treatment is dependent on the severity of the symptoms. Delivering the correct amount of medication and stimulation is extremely difficult as symptomatic assessment is subjective between clinicians and often requires many unnecessary re---evaluation sessions. Tremor and slow movement can be measured to some extent however the final main symptom, muscle rigidity cannot. Time and cost can be saved for the clinician and patient, if the treatment given was optimised in the first instance. We propose a device to offer a more quantitative view on assessing the severity of each Parkinson's symptom and to offer objective feedback to the clinician. The clinician would then be able to make more effective judgments based on this quantitative result. This result will be based on the Unified Parkinson's Disease Rating Scale (UPDRS). The device will give a more refined resolution feedback based on the UPDRRS and clinicians will also not need to change or alter in anyway their methods of diagnosis by using this device. This means that standard practices to evaluate Parkinson's symptoms will remain unchanged. Moreover pharmaceutical and medical device companies can now have proper symptom feedback on new treatments that they are trialling. Initially the device will objectively measure one of the main symptoms, rigidity, and future work will look to measure tremor and slow movement as well.

Company Presentation
2D, 3D, 4D – Advancing implant and device design *(Materialise)*

Lars Neumann, Daniel Daryaie
Biomedical Engineering Department, Materialise NV, Biomedical Engineering Department, Materialise NV

Human beings are incredibly diverse in their physical makeup and personalisation is proving itself as an opportunity to advance health care and create novel, previously impossible intervention strategies. This growing trend towards personalisation and the advent of 3D medical imaging combined with 3D printing techniques have strongly driven biomedical research and engineering in academia and industry. Software has been a key in the creation of accurate digital patient representations from medical images, and in the design and evaluation of novel implants and devices based on patient data. In this presentation, I will show how software enables researchers and engineers to combine different image modalities pre- and post-operatively to assess device fitting and maximise the knowledge gain from medical trials.

Sensing and profiling of circulating cell-free nucleic acids with fluorogenic PNA probes: A high-throughput and minimally invasive approach for early-stage diagnosis and improved prognosis of cancer

Gavin AD Metcalf, *Hinesh Patel, Sylvain Ladame*
Imperial College London

Cancer, a heterogeneous disease with over two hundred classes that can develop in over sixty organs, is a global burden with escalating incidence and mortality. Current diagnosis relies upon the presentation of clinical signs and symptoms within the patient, which can often be in late stages of the disease with associated metastasis, resulting in a poor prognosis. Therefore, early detection of cancers in order to improve prognosis and survival remains a vital strategy for cancer management. A promising method of sensing cancer in early stages of growth relies on the detection of selected biomarkers. One such biomarker group is that of microRNAs (miRNAs), a class of circulating cell free nucleic acids (cfNAs) that are dysregulated in many tumours. Circulating miRNAs can be detected in biofluids (such as blood, urine, and saliva) that are sourced via minimally invasive means, thus avoiding conventional invasive biopsy acquisition procedures. The focus of this research is to develop a new technology based on peptide nucleic acid (PNA) fluorogenic probes, designed and engineered in-house, to detect specific miRNAs (and other cfNAs) biomarkers for cancer in a reliable and minimally-invasive manner. Work thus far has demonstrated that novel fluorogenic probes have the ability to sense miRNAs down to nanomolar (nM) concentrations and with high specificity (at the single nucleotide level) attesting the promise of these novel biosensors for early stage diagnosis and improved prognosis for cancer.

Predicting tumour responsiveness to chemotherapy treatment in volumetric Xenograft images

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The Nakagami distribution is a general model for ultrasonic backscattering envelope under various scattering conditions and densities where it can be employed for characterising image texture spatial interaction, but the subtle inter-heterogeneities are difficult to capture via this model. We propose a locally adaptive 3D multi-resolution Nakagami-based fractal feature descriptor that extends Nakagami-based texture analysis to accommodate subtle speckle spatial frequency tissue intensity variability in volumetric scans. Local textural fractal descriptors – which are invariant to affine intensity changes – are extracted from volumetric patches at different spatial resolutions from voxel lattice-based generated shape and scale Nakagami parametric voxels of interest (VOI). We found after applying an adaptive fractal decomposition label transfer approach on top of the generated Nakagami VOIs from ultrasound radio-frequency datasets produces results on complex speckle tissue textures superior to the state of art, and is, as well, effective when tested across different field-of-view ultrasonic scans. Experimental results on 3D ultrasonic pre-clinical xenograft images suggest that describing tumour intra-heterogeneity via this descriptor would remarkably facilitate better prediction of therapy response and improve disease characterisation.

Texture Analysis of 18F-FDG PET Imaging for Prediction of Neoadjuvant Chemotherapy Response in Oesophageal Cancer

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Oesophageal cancer is associated with high mortality and it is of vital importance to be detected and treated in early stage. In advanced disease, preoperative chemotherapy or radiochemotherapy can play an essential role in the improvement of survival for patients who respond to the treatment. There is a need for different treatment tactics for patients who do not respond to preoperative treatment in order to increase the probability of tumor control and reduce treatment-related toxicity. Therefore, the ability to noninvasively predict treatment response before therapy is of great interest and could allow oncologists to personalise future cancer treatments in the clinic. In this study, we measured heterogeneity of 18F-FDG uptake in pretherapy PET imaging of primary oesophageal cancers using texture analysis to determine the ability to predict response to neoadjuvant treatment. Texture analysis implements a variety of mathematical methods to extract texture features which can be used to measure the intralesional heterogeneity. Here, we use textural parameters which are extracted from statistical-based methods and are categorised into first order, second order and high order features. Using texture analysis, we extracted 103 statistical-based texture features from a cohort of 107 patients. We trained and tested a Gradient Boosting (GB) classifier using as predictor variables the 103 texture features. The GB algorithm computes a sequence of simple decision trees to provide a more accurate estimate of the response variable. The principle idea behind this algorithm is to construct the new decision trees to be maximally correlated with the negative gradient of the loss function, associated with the preceding tree. In order to assess the performance of our model we used a 11-fold cross validation technique in which our dataset was partitioned into 11 equally sized subsamples. Of the 11 subsamples, we retained a single subsample as the validation data for testing the model, and the remaining 10 subsamples were used as training data. Then we repeated the cross-validation process 11 times, each time training and testing our model on each of the 11 different combinations of training and validation datasets. Overall, we achieved 93.6% sensitivity and 95% specificity. In summary, we found that by using a GB algorithm incorporating 103 texture features from pretherapy 18F-FDG PET imaging of primary oesophageal cancer we can accurately predict histological Mandard treatment response to neoadjuvant chemotherapy. After further validation, this approach may offer the potential to stratify patients for preoperative therapy before surgery in the clinical and in clinical trials.

Calculating voxel-based radiotherapy dose in treatment of prostate cancer

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Radiotherapy is one of the most potent and cost-effective curative treatments for cancer. However its success depends on an accurate delivery of dose to the tumour, while avoiding damage (toxicity) to adjacent organs. This study is part of the inter-disciplinary VoxTox project aiming to estimate delivered dose and correlate that with clinical assessment of toxicity. The work described here focuses on rectal toxicity associated with treatment of prostate cancer. Over the course of a treatment of typically 37 days, changes in rectum shape will result in differences between the planned and delivered doses. In principle daily computed tomography images on the treatment bed can be used to find the location of the rectum. However the lower quality of these scans means the prostate and some parts of the rectum are not clear. A robust automated image analysis process is proposed, using standard algorithms combined with anatomical knowledge and information from the high-quality planning scan. To calculate the accumulated dose, material elements within the rectum need to be identified and tracked on the daily scans. A biomechanics approach is proposed to do this. The daily image is used to construct the outline of the rectum day-by-day and a finite element model predicts the movement of material elements within this defined shape. A tube of uniform circular cross section is expanded to the appropriate daily geometry. The resulting trajectory of material element movement is combined with dose map information to derive dose-volume histograms (DVH). Rectal deformation is found to have a significant effect on the delivered DVH. Given the project's aim of recruiting 1000 prostrate patients for the trials, workflow schemes have been implemented for robust and simple management of the data and analysis, drawing on experience within the High Energy Physics group. In conclusion, the work to date has established a methodology for calculating voxel-based dose delivered to prostate cancer patients. Further work is needed to validate the deformation model using phantoms and to apply the analyses to the cohort of patients being recruited. **Acknowledgements** Funding is gratefully acknowledged from Cancer Research UK for the VoxTox project.

Nanoparticle Induced Inertial Cavitation for Enhanced Drug Delivery to Tumours

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The potential of acoustic inertial cavitation, i.e., the radial collapse of a bubble due to ultrasound exposure, has been widely recognised for enhancing both transport and uptake of drugs in cancer treatment. For example, it has been proposed to provide a triggering mechanism for drug release from liposomes that extravasate into tumours due to the enhanced permeability and retention (EPR) effect and to increase the permeation of drugs throughout the tumour volume. In the past decade, much research has been devoted to initiating and controlling inertial cavitation using microbubbles. However for tumour therapy, microbubbles have a number of limitations: 1) they are too large take advantage of the EPR effect and 2) they are also rapidly destroyed following ultrasound exposure. Recently, there has been a surge in development of nanoscopic cavitation agents such as phase change nanodroplets and nanobubbles. Here, we present two novel solid nanoscopic particles that trap bubbles within nano-crevices that function as nucleation agents for inertial cavitation. We demonstrate that these particles reproducibly generate inertial cavitation for extended periods of time. Their inertial cavitation thresholds were predicted with a modified Raleigh-Plesset equation for crevice-stabilised bubbles. Additionally, these nanoparticles facilitate enhanced drug penetration in *in vitro* cancer mimicking models, opening up new avenues for enhanced drug delivery into tumours.

Inertial cavitation induced Doxorubicin release from nano-liposomes exposed to focused ultrasound using nano-scale cavitation nuclei

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Objective To develop and test inertial-cavitation sensitive Doxorubicin (DOX) liposomes for triggered drug release at acoustic intensities comparable to those achieved by diagnostic ultrasound (US) scanners in the presence of SonoVue® microbubbles (SV) and polymeric nanocups. **Methods:** Liposomes made of DOPE or DSPE, HSPC, cholesterol and DSPE-PEG 2000 were prepared using thin film hydration and size-reduced to 150-200 nm by membrane extrusion. DOX was actively loaded into the DSPE or DOPE liposomes by citrate or ammonium gradient method. DSPE liposomes were insonated using a 0.5 MHz spherically focused ultrasound transducer (FUS) driven with a pulse length of 100 ms at a 5% duty cycle for 30s, at peak rarefactional pressures (PRP) of 0.14, 0.5, 0.8, 1.2 and 1.5 MPa, in the presence or absence of SV. Acoustic emissions were measured using a 7.5 MHz passive cavitation detector coaxially and confocally aligned with the FUS transducer. DOX release was measured by fluorimetry whilst efficacy was assessed using an *in vitro* cancer cell line viability assay. *In vivo* studies were carried out by intravenously injecting luciferin loaded liposomes and SV in C57Bl6 mice bearing B16F10-luciferase tumors and exposing to US as described above at 1.2 MPa PRFP. Imaging of luciferin release was performed using an IVIS 100 system. **Results** Cavitation-triggered drug release was highly dependent on lipid composition with DSPE liposomes demonstrating a 30% increase in luciferin release compared to 0% with HSPC liposomes. Notably, in vitro studies showed no luciferin release from DSPE liposomes in absence of SV over the 0.14 -1.5 MPa PRFP range, demonstrating the requirement for co-administrating cavitation nuclei. Presence of SV triggered luciferin release from the liposomes only when 1.2 or 1.5 MPa US was applied and high levels of inertial cavitation, as evidenced by the detection of broadband emissions, were detected. When DOX was used as the payload instead of luciferin, similar results were observed. In presence of SV and nanocups, DOPE-DOX liposomes insonated with focused US showed triggered release of 34 and 18 % of DOX payload from liposomes. In vivo studies showed a 16-fold increase (p<0.001) in photons/sec/cm^2 in tumors of liposome+SV+US treated mice compared to non-US liposome+SV treated mice, suggesting significant enhancement of delivery of luciferin to the luciferase expressing cancer cells. **Conclusions** Drug release can be reproducibly triggered from DSPE and DOPE liposomes using modest acoustic intensities in the presence of commercially available SV and our proprietary polymeric nanocups, whilst passive cavitation detection provides a low-cost method for non-invasive monitoring of drug delivery in real time.

A novel framework for accurate and robust respiratory motion compensation in image-guided interventions using 3D echocardiography

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The clinical translation of respiratory motion modelling techniques in image acquisition and image-guided interventions is currently hindered by their lack of accuracy/robustness, and by the need for a subject-specific calibration scan that complicates the clinical workflow [1]. The subject-specific Bayesian motion estimation technique presented in [2] addresses the lack of accuracy/robustness by combining the robustness of a respiratory motion model with the real-time information provided by 3D echo images in a probabilistic framework. The Bayesian model as originally proposed uses the subject-specific calibration scan which often cannot be acquired due to patient considerations or complications to the clinical workflow. To address the requirement for the subject-specific calibration scan, a personalisation framework for population-based respiratory motion models was proposed in [3]. In this work, a subset from the population sample, rather than the entire sample, was used to model the respiratory motion of an out-of-sample subject based on similarities of the cardiac anatomy only, under the assumption that the anatomy of the heart is correlated to its respiratory motion. This work presents a proof of principle of the combination of the Bayesian motion estimation approach [2] and the personalisation framework [3], resulting in a personalised Bayesian respiratory motion model. Specifically, the personalisation framework presented in [3] is used to build the prior probability function, whilst live 3D echo images are subsequently used to form the likelihood and obtain the final Bayesian respiratory motion estimate. Therefore, the advantages of the two techniques are combined and exploited to overcome the limitations of current respiratory motion modelling techniques. The resulting technique is highly novel, being the first population-based indirect correspondence model ever proposed [1]. Results on 4 volunteer datasets show a median and 95th quantile value for the Target Registration Error in estimation accuracy lower than 1.5mm and 5mm respectively, enabling accurate and robust respiratory motion estimates that do not require interruptions or further complications to the clinical workflow. **References:** [1] McClelland, J. *et al.* "Respiratory motion models: A review." 2013,*Medical Image Analysis, 17, 19-42.* [2] Peressutti, D. *et al.* "A novel Bayesian respiratory motion model to estimate and resolve uncertainty in image-guided cardiac interventions." 2013, *Medical Image Analysis, 17, 488-502*. [3] Peressutti, D. *et al.* "Personalising population-based respiratory motion models of the heart using neighbourhood approximation based on learnt anatomical features." 2014, *Medical Image Analysis, In press.*

Wave Intensity Analysis in the Pulmonary Artery

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Introduction Wave intensity analysis (WIA) is a time-domain technique that uses simultaneous changes in the arterial pressure (dP) and flow velocity (dU) to determine the magnitude, origin, type and timing of travelling waves in a circulation. The objective of this study is to employ WIA in the pulmonary artery to assess the ventriculo-arterial coupling in man. **Methods** Simultaneous pressure and flow velocity measurements were obtained in the pulmonary artery (PA) during right heart catheterisation using a pressure and Doppler flow sensor tipped catheter. Recordings were made at rest and during a modified Valsalva manoeuvre and handgrip exercise. Wave intensity was calculated as $dI = dP{\times}dU$. Data were ensemble averaged using the R-wave of the ECG. To eliminate noisy velocity waveforms, an automatic procedure was used to exclude the beats that correlated poorly with the global velocity ensemble average. The relative time delay between velocity and pressure data was corrected by shifting the velocity data to achieve optimal linearity of the early part of the PU-loop. The slope of this line was used to calculate the local wave speed, which was used to perform wave separation. The variation in the PA pressure due to respiration was determined by low pass filtering at a frequency half-way between the peaks in the power spectrum identified as the heart rate and the respiratory rate. This was compared to the respiratory variations in the amplitude of the R-wave of the ECG. **Results** 7 patients (48 ± 14 years, 5 male) with normal pulmonary pressures were studied. In the main PA, WIA showed a forward (proximally originating) compression wave (peak $dI = 2.1 \pm 0.7 \cdot 10^5$ $Wm^{-2}s^{-2}$) in early systole caused by right ventricular ejection and a forward expansion wave (peak $dI = 0.7 \pm 0.3 \cdot 10^5$ $Wm^{-2}s^{-2}$) prior to closure of the pulmonary valve that decreased the pressure and flow in late systole. Backward (reflecting) waves were minimal. Wave speed was 2.64 ± 1.39 m/s. The wave pattern was unchanged by respiration and handgrip exercise, however, during Valsalva manoeuvre the magnitude of the waves reduced. **Conclusion** Minimal backward waves are present in the PA indicating well matched ventriculo-arterial coupling in individuals without pulmonary artery disease. Patients with pulmonary hypertension will be assessed in the continuation of this study.

Unilateral nephrectomy as a model of altered blood flow for the study of arterial permeability

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Introduction Development of atherosclerosis has been associated with elevated transport of circulating macromolecules into the arterial wall and with various hemodynamic forces acting on arteries. However, there have been few *in vivo* studies investigating the role of altered flow on wall permeability. Here we investigate the role of hemodynamic forces in determining arterial wall permeability in an *in vivo* model of altered blood flow using unilateral nephrectomy. Since patterns of atherosclerosis, haemodynamic forces and wall permeability change with age, two ages were investigated. **Methods** Nephrectomy of the left kidney and ligation of the left renal artery were performed in immature (13 weeks) and mature (1.5-2 years) male New Zealand White rabbits. Pulse wave velocity (PWV) was measured using photoplethysmography and blood velocity in the abdominal aorta was monitored using spectral Doppler ultrasound before the operation and for 4 subsequent weeks. Uptake of fluorescently labelled albumin by the aortic wall was mapped around renal branch ostia. Additional animals were used to obtain detailed geometries from computed tomography of resin corrosion casts of whole aortas. Flow simulations were run in star-CCM+ using the geometries and Doppler measurements as boundary conditions. **Results** A transient increase in PWV appeared 2 weeks after nephrectomy but was back to normal after 5 weeks, when tracer uptake was assessed. In control immature rabbits (n=5), tracer uptake was greater downstream than upstream of the left renal branch ostia, whereas in control mature rabbits (n=4) there was a relatively equal distribution upstream and downstream. Following nephrectomy, (n=5 at each age) mean tracer uptake was elevated by at least 70% and the pattern of uptake was reversed in the immature but not the mature animals. **Conclusions** Our preliminary data show an increase in macromolecular permeability around the origin of the renal artery following ligation in both age groups, and reversal of the pattern of permeability in immature rabbits only. These results causally link blood flow alteration to changes in wall permeability. (Funded by the BHF).

First in Man: Real-time magnetic resonance-guided ablation of typical right atrial flutter using active catheter tracking

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Introduction MR-guided electrophysiology (MR-EP) has the potential to improve catheter navigation, to visualize ablation injury and to avoid ionizing radiation. This study investigated the feasibility of an actively-tracked, fully MR-guided, electroanatomical mapping and ablation system. This represents first such system used in humans. **Methods** Two patients with typical right atrial flutter underwent cavotricuspid isthmus (CTI) ablation under MR guidance. The MR-EP suite integrated a Philips 1.5T Achieva scanner (Philips, Best, The Netherlands), an EP recording system (Horizon System, Imricor, Burnsville, MN, USA), an RF generator (St Jude Medical, St Paul, MN, USA), and a real-time image guidance platform (iSuite, Philips).Under anesthesia, a baseline MRI was performed. 3D right atrial shells were created by automated segmentation of a whole-heart MR scan (3D BTFE) and CTI anatomy delineated. Using the shell for guidance, deflectable MR-EP RF Vision catheters (Imricor) were placed in the CS and RA using MR-guided active tracking alone. Isochronal activation maps were created prior to ablation. RF ablation of the CTI was performed under active MR-guidance, with brief cine sequences for catheter position confirmation (35-40W for 40-60sec). Post ablation, activation maps were repeated and native-T1 weighted, T2 weighted and LGE imaging of the lesions was performed prior to removal from the scanner. **Results** Both patients underwent ablation of the CTI without use of fluoroscopy, with no complications. High fidelity electrograms were recorded with minimal MR interference. Active tracking of the catheter tip was accurate, with tracking position corroborated by conventional imaging sequences prior to each energy delivery. Total procedure times were 307min and 315min, and total ablation times (first to final RF energy delivery) were 88min and 56min. Septal to lateral transisthmus conduction interval was lengthened to 142ms and 134ms respectively, and atrial flutter was uninducible post-ablation. Imaging confirmed both T2 weighted and late gadolinium enhancement of the CTI with no gaps identified. The patients remain free of atrial flutter at 44 days and 23 days respectively. **Conclusions** This study confirms feasibility in man of active-tracked MR-guided ablation of typical atrial flutter in man.

Comparison of USPIO uptake and wall stress in abdominal aortic aneurysms

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Introduction: Selection of patients for repair of abdominal aortic aneurysm (AAA) is based on maximum diameter however some AAA rupture at lower diameter and some with higher diameter never rupture. Alternative markers of rupture are based on peak wall stress (PWS) estimated using finite element analysis (FEA) and an MRI marker of inflammation based on the uptake of ultrasmall superparamagnetic iron oxide particles (USPIOs). There may be benefit in using both wall stress and USPIO uptake in diagnosis, therefore their relationship needs further investigation. **Aim:** To investigate the spatial relationship between wall stress and USPIO uptake. **Methods:** Patients have MRI pre- and post-infusion of USPIOs and USPIO uptake is calculated. Wall stress is calculated using a processing chain with CT as the input data. 3D reconstruction is performed using commercial software (VASCOPS GmbH, Sweden). Meshing is performed using Mimics (Materialise, Belgium) and FE analysis using Abaqus (Dassault Systemes, USA). **Results:** To date 100 aneurysms have been analysed and FEA/USPIO comparison performed on 10 patients using a simple 2D analysis. Regions of high USPIO uptake were co-located with high stress in 8 of 10 patients in the peri-luminal region. However, 2 out of 10 patients showed no co-location in this region. USPIO uptake around the lumen may be an artefact associated with USPIO trapping in the thrombus. Focal USPIO uptake away from the lumen was associated with low wall stress in 6 of 10 patients. Interestingly, in 4 of 10 patients where the thrombus was thin or missing high USPIO uptake was associated with high wall stress. **Discussion:** In the literature PET-FDG studies have demonstrated co-location of high wall stress and high inflammation. The results of this study suggest a co-location of stress and USPIO uptake at the region where the wall is thin but no co-location in focal regions of inflammation behind thrombus. The most likely interpretation is that USPIO uptake around the lumen does have significant true inflammation and is not solely artefact associated with USPIO trapping. **Conclusion / further work:** Co-location of USPIO uptake and wall stress is most pronounced in regions of the wall which are devoid of thrombus suggesting that some luminal USPIO uptake does represent true inflammation. The further 90 cases are being analysed and data will be presented on all 100 cases.

Macrophages accumulate preferentially in local regions of low shear stress in a hypercholesterolemic porcine model of atherosclerosis

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Introduction: Perturbed shear stress has long been associated with the development of atherosclerosis, including thin cap fibroatheromas (TCFAs). However, direct correlations between perturbed shear and markers of advanced atherosclerotic lesions remain limited, particularly on a local tissue scale. Herein, we address this deficiency and test the hypothesis that macrophages accumulate in areas of perturbed shear stress. **Methods**: Three Yucatan minipigs with hypercholesterolemia were implanted with a shear modifying stent in the left anterior descending (n=1) or circumflex (n=2) artery. The un-instrumented vessel served as the control. At baseline and 36 weeks, vessels were imaged with bi-plane angiography and intravascular optical coherence tomography for 3D reconstruction and computational fluid dynamics (Fluent) simulations to compute shear stress. Following euthanasia, vessels were perfusion-fixed, excised, sectioned, and stained for macrophages. The reconstructed lumen was also co-registered with histology sections (90 total per vessel). Thus, macrophage concentration and shear stress magnitudes were defined at each point over select regions of the lumen upstream and downstream of the stent. Statistically significant overlaps ($p < 0.03$) were determined between each of 9 metrics of perturbed shear stress and the macrophage stain. A Spearman correlation coefficient was then computed between each shear-stain overlap "map" and the original stain distribution. **Results**: The instrumented vessel of all pigs developed advanced atherosclerotic lesions in the post stent region. In comparison, the control vessels formed little plaque. Lesions contained a maximum of 18 ± 8% macrophages (n = 3; mean over all pigs ± SD). A new shear metric – low shear index, which computes changes in shear from the current time point (post-stent) versus baseline (pre-stent), showed the highest correlation to macrophage accumulation with a mean coefficient value of 0.68 ± 0.18. The next best correlative shear metric was transverse wall shear stress, which showed a mean value of 0.39 ± 0.08. **Conclusion**: Low shear stress appears to be the strongest shear-based promoter of macrophage uptake, which is a well-known risk factor for TCFA-formation and rupture.

Multi-Modality Image-Based Analysis of Hemodynamics in Aortic Dissection

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Objectives The objective of this research is to develop a non-invasive, image-based modelling protocol to characterise pressure and flow in true & false lumens of aortic dissection patients. Our primary goal is to understand how aortic haemodynamics are altered by the presence of the dissection flap. We will thus compare solutions obtained in "healthy" and "dissected" aortas, and investigate the impact of multiple connecting tears between true and false lumen. **Methods** Automatic segmentation techniques have been used to create a number of 3D CAD models of dissected and normal aortic geometries from CT data. Patient-specific 2D PC-MRI flow data was also acquired, together with 4D PC-MRI velocity fields. The incompressible Navier Stokes equations of motion have been solved using a stabilised semi-discrete finite element method implemented in our in-house flow solver. Reduced-order Windkessel models and a heart model have been used to represent the distal and proximal portions of the vasculature, respectively. Field-based mesh adaptation techniques were used to produce meshes up to 13.2 million elements in size. **Results** Our simulations managed to match the measured flow waveforms and the overall distribution of velocities in the aorta. Localised regions of significantly altered pressure gradients, wall shear stress (WSS), velocity and flow distributions have been observed in the dissection models. Our simulations also showed that cardiac workload increased by 14% in the dissected aorta relative to the healthy aorta. When secondary tears were occluded, simulations showed significant haemodynamic changes, particularly in the true lumen where mean flow was observed to increase over 200% and peak pressure to drop 18%. **Conclusions** Image-based patient specific modelling can reproduce the complex haemodynamics present in dissection and could be a useful tool for treatment planning treatment of these patients. It is clear there are significant haemodynamic changes in aortic dissection. These results also highlight the need for better imaging techniques to measure the motion of the flap over the cardiac cycle and to characterise the number and location of the secondary tears.

Novel Methods for Computational Simulation of Complete TAVI Devices and Application

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Aortic stenosis (AS), in which the aortic root becomes calcified and inefficient, is a common medical condition in the ageing population. Conventional treatment for AS is surgical valve replacement (SVR); however, this involves extremely demanding surgery which is too invasive for many patients. As a result the transcatheter aortic valve implantation (TAVI) was developed. A TAVI device can be implanted by means of a catheter which requires only a minor incision. Paravalvular aortic regurgitation (PAR) is a condition that is present to a severe degree in approximately 10-20% of TAVI cases and has been linked to early mortality [1]. Computational simulation of TAVI device deployment is a popular focal point for TAVI research groups. However, as of yet, the leaflets of the devices have been neglected. This inhibits the ability to computationally analyse important phenomena including leaflet damage during deployment and computational fluid dynamic analysis post deployment. Using Abaqus CAE, this research has resolved this problem. A computational simulation of a full TAVI device (Edwards SAPIEN XT 26mm), featuring the frame, cuff and leaflets has been developed which can be deployed into an aortic root model by means of a balloon (based on the Edwards NovaFlex+ delivery system). Currently, it is believed that this is the first reported successful simulation of a complete TAVI model. This simulation technique has been used to demonstrate the application of computational simulation on patient specific procedural planning, and to predict the occurrence, severity, location and best treatment of PAR. 1. Patsalis, P.C., et al., Incidence, outcome and correlates of residual paravalvular aortic regurgitation after transcatheter aortic valve implantation and importance of haemodynamic assessment. EuroIntervention, 2013. 8(12): p. 1398-406.

Identification of atrial parameter by catheter measurements

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Atrial fibrillation (AF) is a common, progressive and complex disease, consisting of a supraventricular tachyarrhythmia characterized by uncoordinated atrial activation. AF is the most common arrhythmia and the consequent deterioration of mechanical function significantly increases the risk of other cardiovascular diseases, stroke and death. Crucial to the treatment of AF is the understanding of the pathophysiological mechanisms that underpin its initiation and sustenance. Personalized models represent a novel framework for understanding AF and offer a pathway for personalized treatment. Advances in medical imaging now provide high quality and robust descriptions of patient anatomy required for creating personalized models. However, the ability to characterize the electrophysiological material properties of the atria remains a challenge. The aim of this study is to develop an integrated approach that combines biophysical models, multi electrode catheters and tailored pacing protocols to efficiently and robustly characterize the local conduction velocity and action potential duration restitution properties in patient's atria during procedures. Local atrial electrophysiology was modeled by the Mitchell and Schaeffer 2003 action potential model. The pacing protocol was evaluated using simulated unipolar signals from a decapolar catheter in a model of atrial tissue. The protocol was developed to adhere to the constraints of the clinical stimulator and extract the maximum information about local electrophysiological properties solely from the time the activation wave reaches each electrode. A data base of simulation results for 3125 combinations of model parameters was created to provide a robust and rapid fitting method. This approach allows the best parameter set to be identified but also determines the uniqueness of the model fit to the clinical data. The proposed method enables automatic fitting of model parameters to patient data on clinical time scales and paves the way for personalizing atrial electrophysiology models to individual patient physiology and pathology.

Spatial Correlation between Atherosclerotic Lesion Frequency, Arterial Wall Permeability and three Wall Shear Stress Metrics in the Rabbit Aorta

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Atherosclerosis has a characteristic spatial distribution within the arterial system, particularly near branches. This distribution has been attributed to elevated uptake of plasma macromolecules by the wall, and to pro-atherogenic influences of low and/or oscillatory blood flow. However, the fundamental relationships between wall shear stress (WSS), permeability and lesion development have not been definitively established and may be age-dependent. This study investigated whether various hemodynamic metrics spatially correlate with permeability and lesion maps. Average maps for the area surrounding intercostal branch ostia in immature and mature rabbit aortas were produced for atherosclerotic lesion frequency (oil red O staining, n>112 ostia), arterial wall permeability (labelled serum albumin uptake, n>24) and three previously-defined WSS metrics: time-averaged (TAWSS), oscillatory (OSI) and transverse (transWSS), obtained from CFD analysis of vascular geometries (n>18). Hemodynamic maps were rank correlated with permeability and lesion maps, and a 95% confidence interval (CI) was obtained via a bootstrapping technique. Significance was assessed according to whether the CI included r=0. In young animals, lesions and regions of high permeability occurred distal to ostia. TransWSS strongly and significantly correlated with both permeability (r=0.616) and lesion prevalence (r=0.833). TAWSS weakly correlated with lesion prevalence (r=0.332) but non-significantly with permeability. OSI weakly correlated with both lesion prevalence and permeability (r=-0.271 and r=0.175 respectively). In mature animals lesions occurred lateral to the distal half of the ostia, whilst regions of high permeability occurred lateral to the proximal half of the ostia. TransWSS again strongly and significantly correlated with lesion prevalence (r=0.561), but non-significantly with permeability. TAWSS and OSI strongly correlated with permeability (r=-0.67 and r=0.598 respectively), but not with lesion prevalence. Thus only multidirectional disturbed flow (characterized by transWSS) correlated with the patterns of atherosclerotic lesion prevalence at both ages. The weak relationship between permeability and transWSS in mature animals needs further investigation. *Funded by the BHF and the BHF CRE*

Experimental and numerical study of approaches for treatment of aortic arch aneurysm

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In this presentation we will present a comprehensive numerical and experimental study of the hemodynamics in the aortic arch following three different endovascular treatment approaches for aortic arch aneurysm. In the study we examined the time-dependent flow field and hemodynamic parameters in models of (1) aortic arch with aneurysm, (2) aortic arch with total arch replacement, (3) hybrid stent graft and (4) chimney stent graft. The study included analyses of fluid dynamics in the aorta and branching arteries under time-dependent physiological conditions, using visualization in-vitro techniques and computational fluid dynamics simulations. The results show the effect of aneurysm on blood flow in the descending aorta and in aortic arch side branches. In the aneurysmatic case, the aneurysm provokes a highly disturbed flow and large recirculation regions, especially during diastole. Out of the two minimally invasive endovascular techniques, the hybrid procedure was found preferred from hemodynamics point of view, with less disturbed and recirculating regions. Although the chimney procedure requires less manufacturing times and cost, it is associated with higher risks rate, and therefore, it is recommended only for emergency cases. This study may shade light on the hemodynamic factors for these complications, and provide insights on ways to improve the procedure.

Heart sound segmentation using a logistic regression-based hidden semi-Markov model

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The identification of the exact positions of the primary heart sounds within a heart sound recording is an essential first step in the automatic diagnosis of pathological heart sounds. This process is called heart sound segmentation. The accurate segmentation of the primary heart sounds, or the first and second heart sound, allows the automatic analysis of the periods between these two sounds for the identification of systolic and diastolic murmurs. Early methods of segmentation used threshold-based techniques which work well on noise-free recordings. The recent use of more advanced methods, such as neural networks or hidden Markov models, has surpassed the capabilities of the threshold-based methods, especially in recordings contaminated with noise. In the case of hidden Markov models, segmentation accuracy is further improved by incorporating the expected duration of each "state", or type of heart sound, within a recording. This is then called a hidden semi-Markov model. This paper addresses the segmentation of the primary heart sounds within noisy, real-world heart sound recordings using a hidden semi-Markov model. The database used in this study comprised 405 recordings from 123 patients with over 20,000 ECG-labelled heart sounds. Eighty-three of these patients were found to have murmurs, confirmed using echocardiographic screening. The hidden semi-Markov model was extended in this study to use multinomial logistic regression to find the emission probability estimates, or the probability of seeing each observation in each state. The best reported alternatives in the literature were also implemented and tested on the same data. On a separate test data set, the extended hidden semi-Markov model method outperforms the best reported algorithm in the literature. Our new method achieves F1 scores of 95.5% and 91.2% for the first and second heart sound respectively, as compared to 94.2% and 88.7%. It was found that the extension of a hidden semi-Markov model with logistic regression-based emission probability estimation allows superior discrimination between the states of the heart sound recording, and therefore leads to more accurate localisation of the heart sounds within noisy recordings. This is further improved when using additional features as compared to the current state-of-the-art method.

Computational modelling of the placental amino acid transport system

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Placental amino acid transport is essential for fetal development and impaired transport has been associated with poor fetal growth, which may lead to chronic disease in later life. Placental amino acid transport is a complex process mediated by at least 18 specific membrane transport proteins, each of which can transport a subset of 20 amino acids. However, it is not fully understood how all these transporters function together to provide the fetus with the amino acids required for normal growth and development. The aim of this study was to therefore adopt a systems biology approach to develop an integrated computational model for placental amino acid transport. The first step was to develop and experimentally validate realistic individual transporter models that represent the different types of transporter mechanisms (i.e. secondary active (accumulative) transport, exchange and facilitated diffusion). Transporter models were developed based on carrier mediated transport. Specifically designed experimental studies using human placental membrane vesicles were carried out to test the transporter model over a range of experimental conditions, producing a detailed time course of substrate uptake data for model validation. In particular, the model was applied to investigate serine uptake via the LAT2 exchanger which is thought to display a 1:1 obligatory exchange mechanism (i.e. one amino acid molecule going into the cell, in exchange for one going out). However, previous experiments have consistently demonstrated amino acid uptake into such vesicles in the absence of any internal exchangeable amino acid (zero-trans uptake), which remained unexplained. Comparison of model predictions with experimental data clearly demonstrated a non-obligatory exchange component consistent with facilitated diffusion, thus contributing to an improved interpretation of previous vesicle studies and understanding of placental transporter function. Subsequently, this improved transporter model will be incorporated into an integrated modelling framework for multiple transporters and substrates, which will be validated against data obtained from ex vivo perfused placenta experiments. Ultimately it is hoped that this combined computational-experimental approach will lead to further insights for prevention of, and intervention in, poor fetal growth during pregnancy.

A novel high-throughput platform for siRNA transfection of primary mammalian cells

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Introduction: Cells respond to environmental cues with changes in gene signatures that may encompass gene networks of more than 1000 genes. Hence, validation of gene networks can only be achieved with high-throughput techniques. This abstract describes a highly modular siRNA platform, which uses ultrahigh parallelisation gene knockdown and monitoring techniques to validate the inferred networks. **Pilot work:** We have designed and validated a highly modular, high-throughput siRNA platform for (primary) mammalian cells. The platform consists of a variety of bespoke, components (highly efficient electroporator for mammalian cells, ultra-high precision robot dispenser, and a modular parallel plate chamber for experimental interventions) which are functionalised involving a series of procedures (dispensing, bespoke cell seeding, transfection and imaging). Each step of the assemblage has been carefully evaluated. The strengths of our siRNA platform resides in its high precision (<2%) and accuracy (<0.05%), its ultra-high parallelisation (500-2000 experiments), the presence of a bespoke electroporator which guarantees a high transfection efficiency in primary mammalian cells and its modularity which makes it possible to test for chemical, biological and mechanical intervention and adapt it to perform integrative experiments as proposed in this project. All components are compatible with standard microscopes enabling to perform automatic screening and high resolution imaging at a single cell level. The tests that were performed were i) dispensing accuracy and precision; ii) cell viability, transfection efficiency and cross contamination and iii) functional inhibition. **Conclusion:** We have developed a novel platform, which enables ultra-highly parallel siRNA transfection experiment for primary cells with high efficiency and high cell viability and with a control on the transfection time.

Generation of high affinity binders against clinically relevant cardiovascular biomarkers and their potential for the development of clinical diagnostics

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Due to medical advances, deaths from heart and circulatory diseases are falling faster than for other diseases; it still remains one of the UK's biggest killers, responsible for over a quarter of deaths in the UK in 2011. Cardiovascular disease is also one of the main causes of death in people under 75 in the UK. Both cardiovascular disease and coronary heart disease have significant economic costs for the United Kingdom. The prevalence of cardiovascular diseases is increasing at a rapid rate due to the increased life expectancy resulting from the technological and scientific advances. This is causing an unprecedented burden on the national health services warranting the development of novel therapeutic interventions. Assessing the risk for cardiovascular disease is an important aspect in clinical decision making and setting a therapeutic strategy, and the use of serological biomarkers may improve this. At the WELMEC Centre of Excellence in Medical Engineering based in the University of Leeds, we are involved in the development of novel protein biosensors for early disease diagnosis and improved patient targeting by integrating biomolecular systems with state-of-the art electronics. This involves the production of novel, robust antibody mimetics against panels of protein biomarkers involved in cardiovascular diseases. These artificial binding proteins are subjected to highly sensitive screening techniques and high affinity binding partners are selected to be immobilized on miniaturized electronic devices thus allowing highly sensitive label-free detection in clinical samples. The resulting multiplexed biosensor, which provides near real-time bedside monitoring, will have the potential to detect tens to hundreds of proteins in a single point-of-care test thus having a huge impact on the delivery of targeted and timely interventions.

Changes in bone cell stimulation during the temporal development of osteoporosis

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Introduction Osteocytes are mechanosensitive cells that orchestrate bone adaptation when their mechanical environment is unfavourable [1, 2]. Complex changes in bone mineralisation occur at the tissue level during the temporal development of osteoporosis [3, 4]. Such changes may alter the local mechanical environment, and thus mechanical stimulation, of osteocytes over time. However, the in vivo mechanical environment of osteocytes within osteoporotic bone has never been directly characterised. Therefore the objective of this research is to employ a custom-designed loading device, confocal microscopy and digital image correlation (DIC) techniques to characterise the strains experienced by osteocytes in situ in healthy and osteoporotic bone. Materials and **Methods** Femurs were extracted from sham-operated (SHAM) and ovariectomised (OVX) rats at 5 and 34 weeks post-operation. Cells were visualised using a plasma membrane stain, and were imaged during compressive loading of 3,000 microstrain ($\mu\epsilon$). DIC techniques were used to quantify cellular strains in ten cells per femur sample. **Discussion** We report for the first time that osteocytes in both healthy and osteoporotic bone experience strains ($31,028 \pm 4,213$ $\mu\epsilon$ and $40,548 \pm 6,041$ $\mu\epsilon$, respectively) that exceed 10,000 $\mu\epsilon$, which has been defined as the threshold for mechanobiological stimulation of bone cells through in vitro substrate stretching experiments [1]. Interestingly, osteocytes from osteoporotic bone experienced strain above this threshold in a greater proportion of their volume (15.74%), compared to those from healthy bone (5.37%), at the early stages of osteoporosis (5 weeks post-OVX). However, by 34 weeks post-OVX there was a significant decrease in the proportion of cell volume exceeding 10,000 $\mu\epsilon$, such that there was no longer a significant difference between healthy and osteoporotic cells. The temporal nature of these changes are particularly interesting as significant decreases in bone mass and quality are known to occur by 4 weeks post-ovariectomy in rats [5], and such changes might explain alterations in the mechanical environment reported here at 5 weeks. We propose that osteoporosis-related bone loss alters the mechanical environment of osteocytes initially, but that a mechanobiological response occurs to restore the mechanical environment of these cells during prolonged osteoporosis [6].References[1] You et al., *J Biomech Eng*, 122, (2000); [2] Birmingham et al., *Eur Cell Mater*, 23, (2012); [3] Brennan et al., *Eur Cell Mater*, 21, (2011); [4] Brennan et al., *Calcif Tissue Int*, 91, (2012);[5] Keiler et al., *Lab Anim*, 46, (2012); [6] Skerry, *Arch Biochem Biophys*, 473, (2008) Acknowledgements IRC EMBARK Scholarship, ERC Grant no. 258992 (BONEMECHBIO)

Stem cell differentiation increases membrane-actin adhesion regulating cell blebability, migration and mechanics

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Stem cell differentiation is known to influence cell mechanics leading to alterations in cell function. This study examined the influence of chondrogenic differentiation on the interaction between the cell membrane and the actin cortex and how this regulates bleb formation and mechanical properties. Micropipette aspiration was used to quantify cell membrane-cortex adhesion by measuring the critical pressure required for membrane-cortex detachment and bleb formation. The critical pressure increased from 0.15 kPa in human mesenchymal stem cells to 0.71 kPa following chondrogenic differentiation. In addition micropipette aspiration coupled with the theoretical standard linear solid (SLS) model was used to estimate the viscoelastic properties of cells. Differentiated cells were found to be stiffer with equilibrium and instantaneous moduli of 0.29 kPa and 1.33 kPa compared to stem cells with values of 0.15 kPa and 0.84 kPa respectively. This increase in membrane-cortex adhesion in differentiated cells was associated with reduced susceptibility to membrane blebbing and slower migration. Theoretical modelling of bleb dynamics successfully predicted the temporal distortion of the cells during aspiration and confirmed the importance of membrane-cortex adhesion in regulating the elastic modulus. Differentiated cells exhibited increased cortical F-actin organisation, a slower rate of actin turnover as well as reduced actin cortex remodelling following bleb formation. To investigate the mechanism of reduced blebability in differentiated cells we examined the expression of ezrin, radixin and moesin (ERM) proteins which are involved in linking the membrane and actin cortex. Differentiated cells exhibited increased expression of ERM at gene and protein levels. Stem cells expressing dominant active ezrin-T567D-GFP exhibited increased membrane-cortex bond strength confirming its biomechanical role. This study demonstrates that chondrogenic differentiation increases membrane-cortex adhesion associated with an up-regulation of ERM expression. This leads to reduced bleb formation and increased cell stiffness which in turn may regulate other fundamental aspects of cell function including migration and mechanotransduction.

Large heterogeneity of KLF2 and KLF4 in endothelial cells covering a plaque

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Introduction: High expression of Kruppel-like factor 2 (KLF2) and 4 (KLF4) in endothelial cells have been shown to be correlated to high shear stress areas in cultured endothelial cells. In patients with end stage atherosclerotic disease KLF2 is absent. As these two transcription factors regulate 60-70% of mechanosensitive genes in endothelial we monitored their expression over time in endothelium covering plaques. **Methods:** Female ApoE-/- mice were instrumented with a shear-modifying cast on the left carotid artery after 2 weeks on a high fat diet. Mice were culled 5, 7 and 9 weeks after surgery. Carotid arteries were collected and sectioned from aortic arch to carotid bifurcations. Sections of 64um intervals were stained for KLF2 or KLF4, with DAPI as a nuclear stain. We developed a new 3D histology technique which corrected for shrinkage, rotation in all directions and produced a digitized stack of endothelial distribution of KLF2 and KLF4. The cuff model is known to produce a vulnerable plaque upstream and a stable plaque downstream of the cuff after 9 weeks of the experimental protocol.
Results : The KLF2 expression in endothelial cells covering the vulnerable plaque deceased from 64% (5w) to 49% (9w) , while the KLF4 expression was low at 5w (3%) and remained low at 9 weeks (2%). In the stable plaque KLF2 expression was decreased (25%) and remained unchanged. KLF4 expression decreased from 85% to 25% over time. For both KLF2 and KLF4 the heterogeneity was very high and overlap between both transcription factors was minimal e.g. cell either expressed KLF2 or KLF4. **Discussion:** Expression of KLF2 and KLF4 in endothelial cells covering plaque depends on time and on their location. Remarkably, both stain showed large and unexpected heterogeneity. Endothelial dysfunction is a highly heterogeneous response of signaling modules.

A Mobile Android-based Platform for Intelligent Oxygen Therapy

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Chronic Obstructive Pulmonary Disease (COPD) is estimated to affect over 900,000 people. Long-Term Oxygen Therapy is the gold standard treatment in those who fulfill standard criteria, as it can increase exercise ability and improve long-term outcomes. Recent studies using portable oxygen monitoring (pulse oximetry) have discovered previously unseen periods of poor oxygen levels despite the use of oxygen therapy. These periods of insufficient oxygenation add to the progression of the condition and worsen heart function. Currently the fixed oxygen flow prescribed in oxygen therapy does not meet the changing patient needs during routine daily activities. We have developed a method of automatically regulating the oxygen flow via a feedback controller based upon pulse oximetry. A controller will work automatically to relieve periods of poor oxygenation, improving the efficacy of oxygen therapy. Previous work has used a fixed laptop as the controller, but this has now been replaced by a portable system. The system is based on an Android mobile phone. A wireless oximeter communicates via Bluetooth to give a continuous update of the patient oxygenation. The Android platform calculates the required Oxygen flow to maintain the SpO_2 at a target level, and controls a mass flow controller via a mini-USB connection to set the flow from a portable Oxygen cylinder. The whole system is stowed in a shoulder bag to permit patients to carry out normal daily activities whilst being treated. The system will also produce a time-log of the oxygenation that can be remotely downloaded to enable evaluation of the use of the new delivery system during initial clinical trials.

Towards a Modeling Pipeline for Atrial Electromechanics

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Atrial fibrillation (AF) is a supraventricular tachyarrhythmia characterized by uncoordinated atrial activation with consequent deterioration of mechanical function. Affecting almost one million people in the United Kingdom, predominantly the elderly population, AF is the most common type of arrhythmia increasing the long-term risk of other cardiovascular disease, stroke, and death. Although cases of lone AF exist, this medical condition is often secondary to hypertension and heart failure, pathologies impacting the mechanical loading conditions of the atria. The complex interaction between electrics and mechanics provides multiple potential pathways through which heart failure and hypertension adversely affect atrial physiology and function. The combination of a progressively aging population and an anemic success rate in catheter ablation therapy, an invasive procedure routinely used to treat AF in drug-refractory patients, creates an urgent economical and social need to optimize patient selection and procedure planning. In order to investigate the effect of individual deformation modes associated with hypertension and heart failure on the initiation and maintenance of AF, clinical measurements and novel imaging modalities are employed to create personalized electromechanical models of human atria. Computational simulation techniques provide detailed insight into cellular processes at the micro- and the electromechanical environment at the macroscale. The comparison between healthy controls and patients with hypertension and heart failure allows us to quantitatively investigate the link between deformation and atrial electrophysiology and identify the capacity of the atria to sustain AF. In addition, the effect of *in silico* treatment of mechanical boundary conditions (i.e., the reduction of global blood pressure in hypertensive patients) on the predicted arrhythmogenic risk for individual patient types is determined.

Managing the burden of Cardiovascular disease in resource-constrained regions using mHealth

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Introduction and Purpose Cardiovascular disease (CVD) is an established cause of mortality and morbidity in Lower and Middle Income Countries (LMIC). Inadequate preventive measures along with epidemiological and demographic transitions contribute to increasing chronic disease burden in low-resource healthcare systems that have not innovated on the traditional, physician-centric system equipped to treat acute care conditions. Despite the recent surge of interest in mobile health (mHealth) technologies, there is a lack of evidence on clinical impact or scale in resource-constrained settings, as well as a paucity of innovative applications for health providers. Our study focuses on the development and evaluation of a Clinical Decision Support (CDS) tool for CVD risk assessment and management in resource-constrained environments. **Design and Methods** The CDS-based CVD tool was built on the Android platform and supported by server-side infrastructure including an online medical record system. The CVD risk prediction and management algorithm underwent a stringent validation process including external physician validation. Design was user-centric and informed through alpha and beta tests with proper engagement of Non-Physician Health care Workers (NPHW), Primary Health Centre (PHC) physicians and local communities. The tool was pilot tested and a mixed-methods evaluation was performed to determine feasibility and acceptability within the context of a primary care setting in rural India. **Results** The CDS tool was field tested on 292 adults aged over 40 years. End-users were 3 PHC physicians and 11 NPHWs. In over 72% of the participants screened, the end-users agreed the CDS tool was easy to use. No user gave the tool a rating below 3 on a scale of 4, with 4 being most user-friendly and 1 being the least. Qualitative findings indicated that all users found the CDS tool useful and felt it enhanced their capacity. Both NPHWs and PHC physicians also found the tool adaptable into their workflow. Technical and system-level barriers specific to the use of CDS tools in resource-poor settings were identified. **Conclusion** To maximise adoption, enhance capacity building, and achieve full utility in resource-constrained environments, mHealth tools need to be iteratively designed with the end-users, including local communities and health care providers. Our mobile-based CDS tool when integrated with existing PHC system could contribute to improved CVD detection and management in the Indian primary health care system. Lessons from our pilot implementation shall inform further refinement of the CDS tool. The improved tool will subsequently be evaluated in a cluster randomised clinical trial involving 54 villages and over 16000 people in southern India.

Robust Estimation of Respiratory Rate from Pulse Oximeters

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Respiratory rate (RR) is one of the most important vital signs to estimate accurately, because derangements in RR can precede serious physiological deterioration in hospital patients. However, it is also one of the most difficult vital signs to measure accurately in a non-invasive manner. Respiration is known to modulate the electrocardiogram (ECG) and photoplethysmogram (PPG), which may be acquired non-invasively using patient-worn sensors; many RR-estimation methods have been proposed in the literature. We present a quantitative analysis of the efficacy of the leading existing methods from the literature, and demonstrate that, when applied to very large quantities of data acquired from hospital patients, they lack the required robustness to be used in clinical practice. Existing methods typically fail to distinguish between periods of good- and low-quality input data, or are optimised to perform well on a single training set and which subsequently fail to perform as well on independent validation datasets. We propose a suite of new algorithms to overcome the lack of robustness of existing methods. These methods are based on the use of autoregressive models to determine the dominant respiratory signal in waveforms derived from the ECG and PPG. Robustness is achieved by (i) using robust pre-processing to identify good- and low-quality input data, and (ii) performing "model fusion", in which the outputs of multiple models are combined to yield a robust estimator of RR. We demonstrate that the proposed methods are sufficiently robust to estimate RR from the large validation datasets considered in this work. We also demonstrate that this increase in robustness can be achieved by discarding far fewer data than existing methods, allowing RR to be estimated for significantly longer durations than can be achieved using existing methods. The resulting algorithms and data have been combined into an "Oxford Respiratory Rate" toolbox, along with our implementations of existing methods from the literature. This toolbox will be made available as an open-source repository to allow our results to be reproduced, and to stimulate further research in the non-invasive estimation of RR from sensor data.

Case-Based Reasoning for Antimicrobial Prescribing Decision Support: A Solution for Critical Care?

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Background: Prescribing antimicrobials is complex, often undertaken by non-specialist doctors, and frequently based upon incomplete and disparate information. Existing decision support systems (DSS) to aid prescribing decisions are not fit for purpose, and a solution is urgently needed. We report the development of a novel antimicrobial prescribing DSS by a multidisciplinary team of engineers and healthcare professionals in the context of a teaching hospital network in London. **Objective:** To develop a case-based reasoning (CBR) DSS to aid critical care antimicrobial prescribing through adaptive, heuristic algorithms drawn from archived patient cases. **Method:** Iterative development included: requirements gathering; decision making analysis (with categorisation of clinical, pathology and demographic variables); mapping of existing and required information systems (and subsequent linkage); workflow modelling; and finally, an adaptive software development process. 28 parameters were identified to categorise cases, antimicrobials and outcomes; principal component analysis (PCA) was used to reduce the dimensionality of the data. The final product was ported as an mHealth application (App) for use on mobile tablets. Information governance was assured through use of the App as a thin client, with all communication within secure hospital firewalls. **Results:** Pilot data on 50 clinical cases showed 100% accurate retrieval of patient demographic, clinical and pathology data from disparate NHS information systems. Clinically the App is in case-accrual phase, but concurrently Monte Carlo simulations are being used to optimise case retrieval (i.e. case comparison and database organisation). Workflow modelling suggests a 40% reduction (62 hours per month to 37) in critical care infection-specialist time following App roll-out. **Conclusion:** An unmet need exists around decision support for antimicrobial prescribing, particularly in critical care. Following deployment, the DSS will optimise decision making by facilitating: personalisation of antimicrobial prescribing (adaptation of evidence based medicine by cohort level and patient level clinical and pathology results), continuity (point of care support for inter-professional communication), and education (of non-specialist doctors).

Electronic Acquisition of Vital Signs on General Wards

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INTRODUCTION Vital signs are routinely measured every 6 hours in general hospital wards using a spot-check monitor and typically recorded on paper. Newer monitors can transmit vital signs wirelessly to computerised charting and alerting systems. Research into their effectiveness is usually carried out by capturing vital signs wirelessly in parallel with paper charting. We report our experiences of using paper and wireless acquisition in parallel as part of a research study. **METHODS** The study aimed to acquire a physiological database from patients recovering from cardiac surgery. Patients were asked to wear wireless telemetry monitors throughout their stay on a recovery ward. Ward staff were trained to use Wi-Fi enabled spot-check monitors at the outset. They were asked to record vital signs on paper for clinical use, and electronically for research use, requiring minor workflow additions. Research nurses visited daily to support study patients and assist staff. Vital signs were acquired from 198 patients over 14 months. Two experts transcribed vital signs from paper charts using double data entry. **RESULTS** 372 (6%) out of 6432 vital signs sets were acquired electronically. The proportion acquired electronically decreased over the four quarters of the study duration: 18% (out of 626), 8% (2118), 2% (1867) and 3% (1813). We identified a number of issues contributing to poor monitor usage:1. There was no immediate positive reinforcement for acquiring vital signs electronically since staff did not have access to the electronic charting system.2. Ward staff were mainly encouraged to maintain telemetry monitor usage. They were not encouraged as strongly to maintain high levels of spot-check monitor usage since it was thought this may engender a negative response.3. Staff turnover and use of temporary staff was high. Therefore during the study an increasing number of staff had not received full training on the monitor.4. We did not have a local champion from within the ward staff with adequate time to encourage usage. **CONCLUSION** Engaging clinical staff in research data collection can be difficult. Data collection tasks should be aligned as closely as possible to their existing workflow. Adequate engagement, incentivisation and training are also required. These tasks may require significant resources throughout a study.

Keynote: Professor Martin Knight, Queen Mary University of London

Employing synthetic biology and shear stress sensing to tackle atherosclerosis

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Introduction: The response of endothelial cells to mechanical forces is essential in the development and maintenance of the cardiovascular system and plays an important role in diseases like atherosclerosis. Endothelial cells are exquisitely sensitive to mechanical cues, as they are equipped with a variety of mechanosensors. Currently, the function of these mechanosensors has hardly been studied and consequently specific interventions are unknown. Herein, we fill this gap by using novel methods in synthetic biology to monitor the activity of a mechanosensitive G-PCR. **Methods:** We have developed an assay that allows the monitoring of shear stress sensor activity of the B2 Bradykinin G-Protein Coupled Receptors, built in to a synthetic network. The network consists of a G-PCR modified with a tTa transcription factor, an Arrestin coupled to a protease and a tTA responsive fluorescent read out. The network is activated by flow in an in-house developed flow device that delivers linearly increasing shear stress (in the 0-5 Pa range) along the length of the flow channel. The pump used provides pulsatile flow along the flow channel, more accurately modelling physiological conditions. Modified cells are exposed to shear for 24 hours, before fixation and staining. **Results:** The synthetic gene network, transfected in HeLa, EA.hy926 and HMEC-1 cells was proven functional by bradykinin activation. In HMEC-1 cells, the network was switched on by 24 hour shear stress exposure in the flow device. When imaged, eGFP expression is seen to be highest between 2–4.5 Pa. Control experiments, where the flow direction was reversed, where shear stress decreases along the flow axis, did not show a large effect, indicating that paracrine signalling is not involved in the activation of the shear stress sensor. **Conclusions and Future Work:** This assay allows for screening of compounds that affect the function of mechanosensors in the presence of shear stress, allowing further insight into the effect of disrupted flow on endothelial cells. This network, the first of its kind, holds promise for investigation in other states that are governed by changes in mechanical force, due to its modular design and inherent flexibility.

Back to life: fresh osteocytes spreading their processes for optimum mechanotransduction near microdamage in dead bone

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With increasing life expectancy, pathologies related to massive bone loss occur later in life and carry a high financial burden on the healthcare system. Adult human bone is composed of trabecular and Haversian tissues with a heterogeneous composite structure resulting from continuous remodeling. Microdamage are constantly resorbed by osteoclasts before tubular lamellar osteons are formed by osteoblast from Type I collagen fibrils mineralized by hydroxyapatite nano platelets glued together with non-collagen proteins. Trapped osteoblasts then differentiate into mechanosensitive osteocytes able to sense stimulation produced by microdamage. Because osteocytes regulate healthy bone turnover, it is essential to quantify the relationship between *in situ* mechanical stimulation and the cell biological response. Osteocytes have the particularity to bear 40 to 60 cytoplasmic processes extending into canaliculi and create a syncytial network via gap junctions with neighboring cells. In this work, we investigated the morphological and biological activities of live MLO-Y4 osteocytes repopulating fresh human cadaver bone under controlled micro tension. Osteocytes were monitored *in situ* near nascent damage using multi-modal SEM, UV light and fluorescence microscopies. Dual experimental and numerical hierarchical investigations quantified the cell cytoskeleton and membrane rearrangement and the ECM mechanical environment by finite element analysis in the explicit morphology subjected to the experimental displacements measured by digital image correlation. The biological response of the cells under stress was tracked by secreted and migrating osteocytic proteins and molecules marked by fluorochromes. Hybrid experimental and numerical investigations showed osteocyte lacunae and canaliculi morphology alterations in bone diffuse damage areas to be correlated to nascent sub-microcracks along the cell processes at local critical stresses close to HAP (hydroxyapatite) yield of 58-77 MPa up to strength of 108-216 MPa when mineralized collagen fibers still bridge cracks. Neighboring ECM and osteocyte chemical activity were shown by fluorochromes. With the support from NSF CMMI BMMB 1214816 and the Farman Institute

Mechanical forces play a crucial role during prenatal hip joint morphogenesis

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Introduction Despite considerable evidence to support the hypothesis that an abnormal mechanical environment leads to complications in skeletal development such as developmental dysplasia of the hip, the effects of mechanical forces during prenatal joint morphogenesis are not well understood. In this study, we propose a dynamic mechanobiological simulation of prenatal hip joint morphogenesis in which the effects of different range of movements during growth are explored. **Methods** A 2D biomechanical model of an idealised prenatal hip joint, consisting of two opposing rudiments, was constructed as a modified version of our previously published model [1]. All material properties were assumed to be linear elastic, isotropic and homogeneous (cartilage: E=1.1 MPa and v=0.49) [1]. Using the mechanobiological theory for cartilage, where growth and adaptation simulated based on growth due to biological (chondrocyte density) and mechanical (hydrostatic stress) factors [1], four different simulations of the growing joint were simulated with different ranges of movement: 1) no movements, 2) physiological movement; 3) reduced movement, 4) asymmetric movement. **Results** In the first three simulations, the acetabulum tended to open, becoming shallower, and the femoral head lost its sphericity. With larger range of motions these effects were reduced. The rates at which the acetabular depth and the femoral head sphericity decreased were inversely proportional to the ranges of movement. When the asymmetric movement pattern was simulated, the acetabulum opened only on the side on which movement occurred, showing asymmetry in its final shape. **Discussion** This research contributes to our understanding of the mechanical contribution needed for development of a functioning hip joint, where fetal movement helps to maintain the ball & socket configuration. With reduced movement, the congruity of the joint is reduced, making it less stable and increasing the risk of subluxation or dislocation of the hip. References 1. Giorgi, M., et al., Jbiomech, 2014. 47(5): p. 989-995.

Effect of PECAM-1 on patterns of permeability in the mouse aortic arch

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INTRODUCTION: The non-uniform distribution of atherosclerosis within the arterial system has been attributed to local variation in haemodynamic wall shear stress and in arterial wall uptake of circulating macromolecules. Platelet/endothelial cell adhesion molecule 1 (PECAM-1) may be involved; it is expressed by arterial endothelium and involved in sensing shear stress. Studies of hyperlipidaemic mice suggest that lipid deposition preferentially affects the inner curvature of the aortic arch. When such mice are crossed with PECAM-1 -/- mice, less atherosclerosis occurs at this location. Here we investigate the possibility that PECAM-1 acts through an influence on wall uptake of macromolecules. We also examine the influence of NO, since we have shown that variation in permeability of the rabbit aortic wall depends on NO synthesis. **METHODS:** Lesions in the excised aortas of apoE-/- mice fed a Western diet for 4, 8, 16 or 25 weeks from weaning were stained with oil red O, imaged by fluorescence microscopy and mapped with custom Matlab programmes. To assess macromolecule uptake, rhodamine-labelled albumin was administered to normal wild-type mice, to wild-type mice administered an inhibitor of NO synthesis (L-NAME), or to PECAM-1 knockout mice (a generous gift of Prof J Gibbins, University of Reading). 10 minutes later, aortic arches were fixed *in situ* and excised; uptake of the fluorescent tracer was imaged by confocal microscopy. **RESULTS:** In agreement with the previous studies, more atherosclerosis occurred in the inner than the outer curvature of the aortic arch. In wild-type mice, permeability was also significantly greater in the inner than the outer curvature of the arch. This difference was unaffected by administration of L-NAME, but was reduced to insignificant levels in PECAM-1 -/- mice. **DISCUSSION:** This study of the aortic arch demonstrated an anatomical correlation between patterns of uptake in wild-type mice and lesion prevalence in apoE-/- mice. Uptake was not affected by inhibiting NO synthesis but increased in the outer curvature of PECAM-1 -/- mice, suggesting that PECAM-1 normally reduces uptake in this region. PECAM-1 may affect lesion patterns through an influence on wall transport properties. *Funded by the BHF and BHF Centre of Research Excellence*

The effect of hemodynamics on inflammatory responses in endothelial cells

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We present the first, to our knowledge, integrative model that predicts inflammatory responses of endothelial cells (ECs) upon exposure to shear stress; responses that often constitute one of the first stages in a cascade leading to vascular remodeling and development of vascular diseases. We have developed a cell signaling model that describes the activation and nuclear translocation of NF-kappaB, the production of MMP-9 and the expression of cell adhesion molecules (CAM - e.g. VCAM-1 and ICAM-1) in ECs in response to shear stress. The model is inspired by, calibrated with and compared against existing experimental data. We apply the model to different flow environments with steady and pulsatile flow and study its behavior. The inflammatory cell signaling model includes three pathways: An inflammatory pathway that describes the activation and nuclear translocation of NF-kappaB via shear stress; A second pathway aims at the remodelling of the vasculature in which MMP-9 is produced by NF-kappaB and shear stress; The third describes the production of CAMs, which is initiated by NF-kappaB. Our model confirms experimental observations and we are pursuing in-vitro validation with cultured ECs in flow chambers by using different cell-imaging techniques. To study the effect of hemodynamics on gene expression, we have developed a numerical framework that combines computational fluid dynamics, cell signaling and mass transport in fluids (blood) and solids (tissue). We pattern the vascular wall surface with a "cell mesh" environment, representing a realistic ECs distribution that is coupled to a fluid and solid domain mesh. Each cell – divided into cytoplasm and nucleus - contains its own signaling system that reacts to shear stress, pressure and the local chemical environment. Additionally, cells secrete via luminal diffusion proteins into the blood and the surrounding tissue. We have implemented the inflammatory cell-signaling model into the fluid-cell-tissue framework. We study the inflammatory responses of ECs within a straight pipe, a backward facing step channel and two diseased vessels (aneurysm and stenosis). Our results confirm that low shear stress and irregular disturbed flows and low frequencies are favourable for NF-kappaB, MMPs and CAMs production, while regularity and normal frequencies are not. To our knowledge, this is the first model describing the production of NF-kappaB, MMPs and CAMs in ECs upon exposure to shear stress. Secondly, it is the first computational study of inflammatory reactions of ECs when exposed to different flow regimes. Furthermore, it is the first numerical framework that combines accurate hemodynamics, cell signalling and tissue diffusion. We believe that such a framework will allow progress towards understanding the enormous complexity of vasculature and the development of disease.

Neurotechnology

Keynote: Dr Simon J. Archibald, Integra: Pathways For Regenerative Medicine In Neurosurgery?

Next-generation medical diagnostics in natural environments based on low-cost wireless body sensor networks

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Our brain interacts with the environment through movement and we can efficiently control our body's 600+ degrees of freedom to perform complex motor control tasks. However, several neurological disorders such as Parkinson's disease or Multiple Sclerosis affect the way our brain controls motor behaviour. Therefore, understanding the neural control of behaviour is important for basic biomedical research and clinical applications such as rapid diagnostics and monitoring, brain-machine-interfaces and neuroprosthetics. We designed and implemented an ultra-portable and highly affordable body sensor network (BSN) that enables us to perform high-quality wireless recordings of real-life human motor behaviours and neurological signals in unconstrained, natural environments. This is of fundamental importance as everyday movements have the potential of telling us a lot more about the onset of a motor disorder than an experimentally predefined task or clinical assessment scales. Our system, ETHO2, deploys battery-powered embedded micro-controllers that collect high-resolution kinematic data using a commercial 9 DoF inertial motion sensor, in parallel to real-time muscle activations using our prototype mechanoacoustic (MMG) sensors. The data are wirelessly streamed to a remote base station for processing or storage. Our sensors have been experimentally proven to provide long-term stable recordings for more than 40 minutes and in combination with their millimetre scale size, they allow subjects to be absolutely free in their actions, meaning that the data obtained is not as stereotyped as the one obtained in rigid laboratory tasks. Our ETHO2 platform is currently being deployed in clinical trials for 1) testing a novel drug treatment for Friedreich's ataxia patients and 2) monitoring behaviour of subjects administered dopamine antagonist drug. Four sensor nodes are placed on the wrists and ankles of subjects and capture their kinematic activity while performing various daily-life tasks. Analysing the data will enable us to assess potential changes in behavioural patterns caused by the drugs. Furthermore, analysis of the data has the potential to reveal what methods evolution taught the brain to control a complex and high-dimensional system such as our body. This will drive us towards a new generation of BMI applications and the development of more advanced robotic controllers and natural prosthetics.

Mechanical Design of a New Cerebral Flow-Diverter Stent

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Purpose Using a stand-alone flow-diverter stent (FDS) to treat cerebral aneurysms has gained popularity recently as a safe and effective method. Currently available commercial FDS, such as SILK from Balt and PED from Coviden, adopt an interwoven mesh design that is braided from Nitinol wires. They are associated with high complication rates partially due to a low radial stiffness. A new FDS has been developed to provide adequate radial stiffness while retaining low porosity and excellent longitudinal flexibility. **Design** The new FDS is laser-cut out of a Nitinol tube. It comprises a low porosity region in the middle to be positioned across the neck of the aneurysm and high porosity regions (below 70%) at both ends to achieve a smooth transition between un-stented and stented parent artery sections. It is packaged to a small radius by first stretching it longitudinally and then crimping it radially, and self-expands when deployed in parent arteries. A stent of 2.05mm in radius has been successfully crimped into a 5F delivery system. The new FDS is deployed through an unsheathing process, and a stent placement device has also been developed to achieve quick and precise stent placement. **Mechanical properties** The radial force and longitudinal flexibility of a series of new FDS with varying geometrical parameters have been analysed numerically using Abaqus/Standard and compared with those of several currently available intracranial stents that are also laser-cut from Nitinol tubes, including Neuroform3, Enterprise, Wingspan and Solitaire (data from Krischek et al., Minim Invas Neurosurg, 2011). It has been found out that the new FDS has a relatively high radial force when the stent oversizing is 15%, comparable to that for Wingspan which has the highest radial force among those intracranial stents. In terms of longitudinal flexibility, numerical results show that the new FDS requires the smallest bending moment when bent into a 12.7mm arc, only around 10% of that for Neuroform3 which is the most flexible among those intracranial stents. **Conclusions** A new FDS that is manufactured through laser cutting technique has been developed for direct treatment of cerebral aneurysm. It has low porosity and excellent foldability and deliverability. Numerical results show that it has adequate radial stiffness and superior longitudinal flexibility in comparison with currently used intracranial stents, making it a promising candidate for intracranial applications.

A dynamic network model of essential tremor

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Essential tremor (ET) is a common movement disorder which affects as many as 4 out of 100 adults over 40 years of age. Though it's precise aetiology is unknown, it can be successfully treated by deep brain stimulation (DBS). This surgical treatment involves the chronic implantation of electrodes into disorder specific regions in the brain, which for ET is the ventralis intermedius (VIM) nucleus of the thalamus and zona incerta. While the treatment works well, achieving up to 90% improvement in symptoms (Deuschl et al, 2011; Baizabal-Carvallo et al, 2014; Mandat et al, 2011), the mechanisms by which the therapeutic effect is obtained are unknown. If we better understood these mechanisms, we could optimise the parameter setting process and minimise unwanted side effects. When undergoing DBS, intraoperative recordings from the implanted electrodes allow us to measure the neural activity patterns associated with ET in the form of local field potentials (LFP). We present LFP data which shows synchronised activity in the thalamus. We found peaks in the LFP power spectra within the tremor frequency band and at double tremor frequency. In order to understand the effects of DBS on such pathological neural activity, we adopt a computational modelling approach using a simple population representation of the network hypothesised to underlie ET. This network involves cortex, cerebellum and VIM and is based on previous descriptions of the essential tremor network (Raethjen & Deuschl,2012). The model is implemented using the Wilson-Cowan approach, which involves a set of coupled differential equations. The model was simulated by exploring the parameter space to uncover regions which produced oscillatory thalamic activity in the typical ET frequency range (4-12Hz). Consequently, the network exhibited oscillatory behaviour within the tremor range. By applying an input to the thalamus which simulates the effect of DBS (e.g. 150Hz square pulse), we found that these oscillations are suppressed. In conclusion, this study shows that the ET network has dynamic properties which support oscillations at the tremor frequency. Furthermore, the application of a DBS-like input to such a network disrupts synchronous activity, which could explain one mechanism by which DBS achieves therapeutic benefit.

Parcellation-Independent Multi-Scale Framework for Brain Network Analysis

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Structural brain connectivity can be characterised by studying diffusion MRI, tractography and the subsequent derivation of graph theoretical measures. The lack of a generally accepted paradigm for how the brain in subject populations such as neonates should be segmented, leads to the application of a variety of atlas- and random-based parcellation methods. However, this results in the yet unresolved challenge of comparing graphs generated from different numbers of brain regions and subsequently differing numbers of graph-nodes. In order to enable more meaningful intra- and inter-subject comparisons, this work proposes a parcellation-independent multi-scale analysis of commonly used network measures to describe changes in the brain. We apply our framework to a neonatal serial diffusion MRI data set to show its potential in characterising developmental changes.

Investigating mismatch negativity-like activity in the MAP2k7 schizophrenia model

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Mismatch negativity (MMN) is produced by subtracting event-related potential (ERP) components of the electroencephalogram elicited during an auditory oddball paradigm; i.e. when a series of infrequent 'deviant' stimuli are intermingled with identical 'standard' stimuli. Subtracting the averaged ERP waveforms in response to the standard stimuli from that to deviant stimuli produces the MMN response. This represents a disruption of sensory memory and is closely associated with the neuropsychiatric disease, schizophrenia. Auditory ERPs used to generate MMN are reproducible in humans and animals including rodents, providing means of studying this phenomenon in clinically relevant models. Further research is needed to characterise this potential biomarker and understand its generative mechanisms; specifically this study looks at genetic influence over neurophysiological processes measured by electrophysiological recordings. We combine three deviant oddball paradigms (duration, frequency, intensity) in an in-vivo electrophysiology study of wild-type (C57BL/6J) and genetic schizophrenia model (MAP2k7) mice. Recordings were taken from urethane anaesthetised animals in a sound attenuating, electrically shielded chamber, and sounds were played via a calibrated speaker. Electrodes were implanted bilaterally into the skull above primary auditory cortices to monitor auditory evoked potentials in response to the presented stimuli. Custom Matlab scripts, National Instruments USB-6211 data acquisition device, Intan Technologies RHD2000 Evaluation System and open source data acquisition software from open-ephys.org were used to implement this experiment. We highlight an analysis of wild-type vs. MAP2k7 electrophysiology data in context of its translational relevance for understanding schizophrenia risk genes.

The Influence of Reverse Shoulder Arthroplasty Implant Variables on Muscle Activation and Joint Load

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BACKGROUND: Reverse shoulder arthroplasty (RSA) has become widely accepted for the treatment of a number of shoulder pathologies. However, the effect of RSA design parameters on muscle and joint loading is poorly understood. Therefore, our objective was to evaluate the effects of various implant configurations on the deltoid forces required to produce active abduction and the resulting joint loads. **METHODS:** Seven cadaveric shoulders were tested using a validated *in-vitro* shoulder motion simulator which produces muscle driven glenohumeral abduction while simultaneously replicating *in-vivo* scapular rotation. The joint loads produced by these active motions were measured using a bespoke modularly adjustable, load-sensing RSA implant system. Three RSA geometric parameters were tested at three levels – humeral lateralization: 0,5,10mm; humeral polyethylene thickness: 3,6,9mm; glenosphere lateralization: 0,5,10mm – with all 27 permutations examined. The RSA system was initially implanted in its neutral configuration (0,3,0mm) using standard surgical procedures. **RESULTS:** Increasing humeral offset significantly decreased deltoid forces required for active abduction (0mm: 67.8±3.3 Percent Body Weight (%BW) vs 10mm: 64.9±2.9%BW, p=0.022), and had no adverse effect on joint loading. In contrast, increasing glenosphere lateral offset significantly increased the required deltoid muscle loads to achieve active abduction (0mm: 61.4±2.8%BW vs 10mm: 70.4±4.2%BW, p=0.007) and the joint loads (0mm: 53.4±3.0%BW vs 10mm: 69.7±3.7%BW, p<0.001). Additionally, increasing humeral cup thickness significantly increased deltoid load (3mm: 64.8±3.4%BW vs 9mm: 67.7±2.9%BW, p=0.03) and joint load (3mm: 60.0±2.8%BW vs 9mm: 64.0±3.3%BW, p=0.034). **CONCLUSIONS:** Humeral component lateral offset is the only variable tested that had a positive effect on joint and muscle loading and may be able to counter some of the negative effects resulting from glenosphere lateralization which is often implemented clinically. Increasing humeral cup thickness was found to have some unfavorable effects on deltoid and joint loading and should be used sparingly. These findings provide new insight into the effects RSA parameters and are not constrained by the configurations achievable using any one commercially available system.

Steep Cup Inclination can lead to Severe Edge Loading and Increased Wear under Surgical Translational Mal-position of Hip Replacement Prostheses

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Introduction Edge loading, which may occur due to rotational and/or translational mal-positioning [1], leads to increased wear rates [2] and acetabular rim fracture [3] of hip replacement bearings. The aim of this study was to determine the influence of cup inclination on the magnitude of dynamic microseparation, severity of edge loading, and the resulting wear rate of a ceramic-on-ceramic bearing, under translational mal-positioning conditions. **Materials and Methods** The Leeds II Hip Joint Simulator was used to test 12 ceramic-on-ceramic bearing couples (BIOLOX® delta, 36mm, DePuy Synthes, UK). Six acetabular cups were inclined at an angle equivalent, clinically, to 45° and six cups at 65°. A standard gait cycle was run. A fixed surgical translational mal-positioning of 4mm between the centres of rotations of the head and the cup in the medial/lateral axis was applied on all stations. The mean wear rates were determined and statistical analysis was performed (significance at 0.05). **Results** For the same level of translational mal-positioning of 4mm, the magnitude of dynamic microseparation was higher when the inclination angle of the acetabular cup was steeper (the mean± 95% CL were 1.4±0.3mm for the 65° inclination angle condition and 0.5±0.2mm for the 45° inclination angle condition). This resulted in significantly (p<0.01) higher wear rates of 1.01mm^3/million cycles for the steep cup inclination angle group of 65° compared to 0.32mm^3/million cycles for the 45° inclined cup group. **Discussion and Conclusion** An *in vitro* preclinical simulator model has been developed, not only to determine the wear of hip bearings under edge loading, but also to predict the occurrence and severity of edge loading due to rotational and translational mal-positioning taking into account many surgical variations, such as steep inclination and excessive version angles, medialised cups, head offset deficiencies, stem subsidence, and joint laxity. This study showed that cup inclination angle affects the magnitude of dynamic microseparation for a given surgical translational mal-position, thus leading to edge loading and significantly increased wear rates with increased inclination angles.**References**1. Fisher, J. JBJS-B, 20112. Nevelos, J.E., et al*.,* Biomaterials, 19993. Waewsawangwong, W. and S.B. Goodman, J Arthroplasty, 2012

Influence of lubricant and temperature on the wear of UHMWPE articulating against PEEK Optima

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Introduction UHMWPE articulating against PEEK-OPTIMA® has the potential for use as a novel bearing couple in joint arthroplasty due to its potentially low wear rates and the bioinertness of its wear debris. In this study, the wear of the bearing couple under different environmental and lubrication conditions was investigated in a series of pin on plate tests. **Methods** GUR1020 UHMWPE pins were tested against either PEEK (R_a~0.06μm) or cobalt chrome plates (R_a<0.01μm) in a 6-station multi-axial pin on plate reciprocating wear rig under kinematics to replicate those in total knee arthroplasty. Tests were carried out for 1 Million cycles at either room temperature (~20°C) or physiological temperature (~36°C) and in varying concentrations of bovine serum (0, 25 or 90%), wear was determined gravimetrically. Statistical analysis was carried out using ANOVA with significance taken at p<0.05. **Results** In tests lubricated with water, the wear rate of UHMWPE was very low against both PEEK and cobalt chrome under both physiological and room temperature. In 25% serum at room temperature, as per standard practice at Leeds, the wear of UHMWPE against PEEK was higher (p=0.07) than against cobalt chrome; at physiological temperature, the wear of UHMWPE against cobalt chrome was similar but against PEEK the wear was significantly lower (p=0.017). Testing under high protein concentration at room temperature significantly (p=0.003) increased the wear of UHMWPE against cobalt chrome compared to tests in 25% serum, this effect was not however observed against PEEK (p=0.38). Under elevated temperature, the wear of UHMWPE against cobalt chrome significantly (p=0.007) decreased compared to room temperature but against PEEK, the wear rate was similar. **Discussion** This study showed the wear behaviour of UHMWPE articulating against PEEK differs to that of UHMWPE against cobalt chrome. In tests lubricated with water, the results were considered not to be clinically relevant. When tested in serum, there are several factors which may contribute to the differing wear rates including; variations in surface topography of the plates, protein deposition, changing lubrication regimes, different frictional properties and protein precipitation. This study will enhance our understanding of UHMWPE-PEEK tribology prior to carrying out knee simulation.

3D Imaging Bone Quality: Bench to Bedside

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Measuring the health of bone is important for understanding the pathogenesis, progression, diagnosis and treatment outcomes for fragility. At present the most common method for measuring bone health in a clinical setting is to assess skeletal mass. The current gold standard is dual-energy X-ray absorptiometry (DXA) which models bones as 2D objects and measures areal bone mineral density (BMD). However, BMD only accounts for 50% of bone strength and the technique ignores other important factors such as cortical geometry and trabecular architecture, which are also significant contributors. Consequently a new concept of 'bone quality' has developed, the material and structural basis of bone strength and fragility. As yet though a suitable non-invasive method has not been developed or measuring quality in living patients. The aim of this paper is to discuss how bone quality might be visualised, quantified and applied in a clinical setting. The most useful imaging techniques are likely to be clinical-CT and MRI. Both modalities have been used successfully to characterise bone macro-structure in 3D e.g. volume fraction and orientation. More recently *in vivo* systems with high resolution (~0.100-0.200 mm) have been developed that can capture some aspects of bone micro-architecture. Alternatively 3D models created using clinical-CT and MRI can be used to virtually simulate loading on a computer and calculate bone mechanical properties. Analysed together these morphological and mechanical data sets might allow clinicians to provide screening programmes for osteoporosis and calculate individual fracture risk. Especially if applied as part of a holistic approach utilising patient meta-data on risk factors for metabolic bone disease (e.g. FRAX). As well as improve primary and secondary care by setting treat to target criteria for pharmacological therapies and planning surgical interventions or following up treatment outcomes. In the short to mid term the expense of 3D imaging and (in the case of CT) the risks associated with ionising radiation are going to restrict image resolution. Therefore, in order to achieve the goal of bringing bone quality from bench to bedside future research needs to be directed towards better analysis of 3D bone geometry at sub-optimal resolution.

Comparison of Stress on Knee Cartilage for Kneeling and Standing by Using Finite Element Models

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Kneeling is a common activity required for both occupational and cultural reasons and has been shown to be associated with an increased risk of knee disorders. While excessive contact pressure is considered to be a possible explanation, there are very few studies about the stress on cartilage in kneeling situation. So it is not clear whether and to what extent the stress during kneeling is different from that in standing. And it is also important to note that the reported stress on cartilage can vary dramatically among published studies. While this is understandable when we considering the individual differences and different measuring methods, it makes the comparison between kneeling and standing even more difficult. In this study, two finite element models for both postures are presented and the mechanical status of the cartilage are investigated. The models were established from Magnetic Resonance images of the same subject and assigned with identical material properties. The magnetic resonance images of knee joint were obtained from a healthy male volunteer under 90 degree flexed conditions. Using these images, the complete knee joint model was constructed including bony parts, cartilages, menisci and important ligaments. All of these parts are meshed by hexahedral elements, and the convergence of element size was tested. The material properties were determined from literatures. Compressive load up to 1000N was applied to represent the weight bearing. Muscle force (quadriceps 215N, biceps 31N, and semimembranosus 54N) was also involved according to the literature. The results show that with the same magnitude of compressive loads kneeling can result in greater stress on the cartilage and produce quite a different stress distribution when compared to normal standing. Parametric analysis was also carried out to determine the influence of cartilage elastic modulus and its Poisson's ratio. The higher stress and shifted loading area highlighted the risk of knee disorders for kneeling activity.

Engineering an In vitro 3D Bone Model for Implant Testing

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In-vitro and in-vivo testing of implants remain the gold standard for quality checks of orthopedic biomaterials. At present, in-vitro tests are limited in their lack of a dynamic environment while in-vivo experiments are limited by the difference in structure and cell behavior between animal and human bone. Our aim is to develop a tissue engineered bone construct that could be used for studying in-vitro bone formation around prototype implant materials. In this study, we investigated the use of polymer composite materials fabricated with electrospinning and particulate leaching (PL) techniques as a support for tissue engineered bone matrix. The scaffold therefore needs to have good mechanical strength and resilience with a high porosity and be osteoconductive. For electrospun scaffolds, polyurethane (PU) solutions made from 15%wt PU dissolved in 70/30 DMF/THF solvent were electrospun to attain scaffolds with either aligned or random fibres. To create Polyurethane-Hydroxyapatite (PU-HA) composites, PU solutions were doped with either micro or nano-sized HA particles in a ratio of 3 PU: 1 HA. For particulate leached scaffolds, solutions were combined with NaCl particles (~250 µm). SEM images analysed with ImageJ software, µ-CT imaging, FTIR spectroscopy, and mechanical testing were used to characterise fabricated scaffolds. For biocompatibility studies, MLO-A5 and hES-MP cells seeded on the scaffolds were assayed over a 28-day culture period. Calcium and collagen deposition were also undertaken as part of this study. FTIR characterization confirmed the presence of HA in all composite scaffolds, whilst µCT confirmed good pore interconnectivity. Although all scaffolds supported proliferation of both cell types and the deposition of calcified matrix, random electrospun polyurethane scaffolds with nano-HA enabled the highest cell viability amongst electrospun composite scaffolds. Interestingly, within the electrospun PU-only group, aligned fibres allowed better cell support than random fibres. For particulate leached scaffolds, PU scaffolds had the highest pore size but the lowest Young's Modulus and yield strength. However, with an average pore size of 190±75 µm, composites with nHA had the highest Young's Modulus and Yield strength of 0.671±0.080 MPa and 0.040±0.014 MPa, respectively. Fabricated scaffolds composed of highly interconnected macro and micro porous network (>60% porosity) with pore sizes previously described as optimum for bone regeneration (>180µm)[1], support bone matrix formation and have good mechanical properties in relation to their good porosity. We therefore propose the use of these scaffolds as a support for tissue engineered constructs, and for in-vitro studies of bone formation including testing of implant materials.

On presenting aspects of computational biomechanics to the non-specialists

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Computational investigations have acquired an important role in development of treatments and devices involving biomechanics. Accordingly, at the institute of Medical and Biological Engineering in Leeds (iMBE), attempts are made to enhance the way these are conveyed to the non-specialist. In keeping with the experience of public engagement within iMBE, a new tool was developed to communicate the computational modelling aspects of the institute's research. It combines the complex transition from clinical or pre-clinical image data to biomechanical models with a user friendly environment on a touch-screen application. This tool aims to increase the awareness on how 3D simulations can help to understand disease conditions and contribute to the development of novel treatment methodologies. It also aims to familiarise non-experts with the different steps involved in developing a patient-specific computational model and to introduce 3D image processing to the public. The available biomechanical models provide examples of the diverse aspects of how computer models can contribute to medical research and clinical practice. Technically, the tool consists of a code combining python libraries (www.python.org) and VTK (www.vtk.org) that outputs 3D image data and model results into interactive widgets. Using finger-tip control, the users are able to navigate through medical images and models, examine them from any direction, zoom in and out, and cut-through them to appreciate their full constituents. Over the past year, this tool has been used not only in local and national science fairs but also served to demonstrate the importance of computational models to patient events, student applicants and lab demonstrations. It has generated a real interest among visitors and led them to engage further within the iMBE stalls during fairs. In particular, it has interested younger generations who are used to touch-screen technology, and older people who are curious about the possibility to journey through 3D medical images. The tool was initially designed with a single application demonstrating most computational research aspects of iMBE. Since then it has been extended to particular aspects such as spine and bone microstructure. It is thus created as a flexible, portable, resource for the institute's public engagement strategy.

Wearable Technology in Osteoarthritis: A qualitative study of patients' perspectives.

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Recent technical advancements have brought an increased interest in wearable technology and its use in the management of movement disorders. Despite this, such technology is still a long way from being adopted in the clinical setting. User acceptance and clinical significance of measured parameters have been overlooked, thus preventing uptake in healthcare practice. The aim of the present study was to explore osteoarthritis patients' perspectives on wearable technology with specific regard to monitoring knee function. This information will maximise the acceptability of a novel sensor for use in clinical and home environments, to aid rehabilitation. Twenty-one adults suffering from osteoarthritis volunteered to participate to one of four focus groups. Each focus group lasted approximately 60 minutes was audio-recorded and a topic guide exploring patients' preferences on wearable technology was used. Focus groups were verbatim transcribed and a thematic analysis was conducted; key themes were identified from which sub-themes were specified. These were used to allow comparisons between focus groups and for data mapping and interpretation. Analysis of focus groups findings suggested five overarching themes patients associated with wearable technology: practical issues, utility/functionality, patient-doctor communication, social impact and empowerment. Overall a general positive response towards the use of wearable technology was identified and influenced by the discreetness, ease of use, and compatibility with every day routine. Patient also highlighted advantages in using a knee monitor device (for the management of knee osteoarthritis) with particular reference to an improved interaction with healthcare professionals and better provision of treatment. Participants also expressed the belief of enhanced patients' empowerment through the use of the device as well as an impact towards a better quality of life. Understanding patients' preferences is an essential step towards the adoption of new wearable devices in clinical domains. The outcomes from this study can have implications on the design of wearable technology. By combining the information obtained by the focus groups and the technology available we aim to design the optimal sensor to be used in a clinical context for the management of knee osteoarthritis.

BSN Analytics – A Tool for Pervasive Gait Analysis

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Gait analysis is an effective tool for clinical diagnosis and rehabilitation monitoring. However, detailed gait analysis is expensive and time consuming, and which has limited its used in rehabilitative care. With the recent advances in pervasive sensing technologies, a few wearable gait analysis devices have been introduced, such as the e-AR (ear-worn Activity Recognition) sensor, developed by Imperial College. Previous study has demonstrated the accuracy and feasibility of using the e-AR sensor for detailed gait analysis in laboratory and free-living environments. In deploying the technology for clinical use, a new gait analysis platform has been developed, called BSN Analytics. By integrating the e-AR sensor with a tablet computer and developing robust gait analysis algorithms into the tablet computer, the BSN analytics is a simple to use and low cost gait analysis system. The new platform provides readings on all temporal gait parameters, asymmetry derived parameters and also spatial gait parameters based on a user defined distance metric. In addition to capturing gait parameters using the e-AR sensor, synchronised videos are recorded in the BSN Analytics and which enables detailed data interrogation for the user. Furthermore, apart from quantitative analysis, qualitative questionnaires, such as the Oxford Knee Score, are also integrated in the platform for capturing qualitative metrics in monitoring patient recovery progress. The platform has been trialled clinically with 50 orthopaedic patients and promising results have been obtained (accuracy on temporal gait parameters in gait laboratory experiment: 17.9+-2.29ms, 36.9+-3.84, 35.5ms+-3.99ms for stride, stance and swing times, in free-living environment: 35.38+-3.22 and 73.05+-7.24 for heel contact and toe-off events).

Locating the Hip Joint Centre: Functional and Regression Methods vs. MRI

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Three-dimensional motion tracking techniques are commonly employed to quantify joint motions by non-invasive means. Standardized coordinate systems are created on each bone surrounding the joint of interest by digitising the locations of landmarks on the bones. On the femur, the hip joint centre (HJC) is used as one of the landmarks; however, due to its location in the pelvis, it clearly cannot be palpated. Since the hip approximates a ball-and-socket joint, dynamic motions have been used in conjunction with computational approaches, to estimate the position of the joint centre. The aim of this work was to compare the location of the HJC within the pelvis determined via functional and regression methods with that found with a direct anatomical measure, namely MRI. A nine-camera optical motion capture system was used to capture the motions of clusters of 14mm markers placed on the pelvis and thigh. The locations of the anterior and posterior superior iliac spines were digitised. 7 participants with no joint pathology performed a series of six different motion patterns: a cross, a cross and a circle, a quarter star and arc pattern (Quarter), random motion for 30 seconds, a half star pattern, and a half star and arc pattern. The HJC was calculated using two regression techniques based on static digitisations of the pelvic landmarks and three computational approaches that employed the motion trials. The calculated location of the HJC in the pelvic frame of reference was compared with that which was determined from pelvic MRI scans. The computational approach used to calculate the HJC using motion trials had a significant effect on the resultant location. However, the regression techniques proposed by Harrington et al. (2007) proved to be significantly more accurate than all other methods ($p < 0.003$). This approach resulted in a mean error in the position of the HJC of 11.4 ± 4.7mm and a maximum error of 19mm. These results illustrate that regression equations are the most accurate known method for determining the location of the HJC within the pelvic frame. Harrington ME, Zavatsky AB, Lawson SE, Yuan Z, Theologis TN. (2007) Prediction of the hip joint centre in adults, children, and patients with cerebral palsy based on magnetic resonance imaging. Journal of Biomechanics 40(3): 595-602.

Asymmetry of Step Characteristics in Acceleration Sprint Running

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Knowledge of asymmetry in sprint running has been described as being important from coaching, injury and data collection perspectives. The aim of the study was to examine asymmetries in step characteristics of field sport sprint performers during an acceleration sprint run. Twenty trained male field sport performers (mean±SD: age 21±1.9 years, body mass 78.7±7.7 kg and stature 1.78±0.06 m) participated in the study. Sagittal plane kinematic data was collected using a CODA motion analysis system sampling at 200 Hz during 20 m acceleration sprint running trials initiated from a standing start. Step velocity (SV), step frequency (SF) and step length (SL) were calculated for left foot touchdown to right foot touchdown (LR) and right foot touchdown to left foot touchdown (RL). The twenty performers were analysed using a multiple single-subject design. 18 out of the 20 performers displayed significant asymmetries ($p<0.05$) in step velocity, step frequency or step length between LR and RL steps. The findings suggest that there are significant asymmetries present in field sport performers step characteristics during an acceleration sprint run, and that these findings should be considered when designing strength and conditioning programmes or biomechanical data collections.

Early results of a method to measure short duration velocity fluctuations in human motion: A comparative study between average fitness individuals and marathon runners.

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Gait data was collected using an electro-goniometer at 100Hz sampling frequency from the knees of 10 participants of average fitness, and 2 elite marathon runners. Four motion types were examined: With the participant seated and feet clear of floor they were asked to swing their leg back and forth to a distance less than full extension (1), and to full extension (2). They were then asked to rise and reseat into a chair (3), and descend down and rise from a full squat position (4). Taking one event of flexion or extension as a motion, 1518 motions were collected in total. The data was subjected to a novel, though computationally simple means of analysis. The noise level of the data was manually assessed across all data at no more than 0.3 degrees, therefore a simple rounding to the nearest 0.5 degree was carried out. Ordinarily the data would have been passed through a more standard signal processing filter to remove noise, resulting in a perfectly smooth curve. Through simple calculation angular velocities were obtained in degrees per second and graphed, revealing the motions to be comprised of discrete patterns of 10-100 ms duration accelerations, periods of constant velocity, and decelerations in rhythmic sequences clearly not random in nature. A frequency analysis of the pulses of acceleration revealed them to range from 4-40hz, 21Hz average. This corresponds to known frequencies of motor neuron firing. Comparative analysis of the numbers of acceleration, constant motion and decelerations between the ten average fitness individuals and two marathon runners revealed they remained effectively identical. The durations of the events across all motions and motion types revealed the accelerations and decelerations were up to 16% shorter in duration, and the constant motions up to 15% longer in the marathon runners. With further work, this approach could provide a new simple and reliable means of measuring motor neuron activity and calculating forces within motions.

Decoding activity of leg muscles from motor cortex local field potentials in freely moving non-human primates

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Accurate decoding of upper limb muscle activity while performing various reaching and grasping behaviors has been achieved using action potentials (APs) and local field potentials (LFPs) from neural populations in the non-human primate motor cortex. Due to technical limitations, the ability to obtain similar decoding results of leg muscle activity during natural locomotion has not been deeply investigated. Here, we leveraged a recently designed multimodal neuromotor analysis platform to record population dynamics in the leg area of primary motor cortex (MI) in conjunction with electromyography (EMG) activity and whole-body kinematics in freely moving, unconstrained, and untethered non-human primates. Three rhesus macaques (Q19, Q21 and Q22, macaca mulatta) were implanted with (i) a 96-electrode cortical array (Blackrock, USA) in the leg area of left MI and (ii) an 8-channel EMG system (Konigsberg, USA) into four pairs of antagonist muscles spanning four joints of the lower limb (right leg). Both implants were equipped with modules for wireless data transfer which allowed us to simultaneously record wideband (30kHz) neuronal data and high fidelity EMG signals (2kHz) while monkeys walked freely on a horizontal treadmill at speeds ranging from 1.1km/h to 6.4km/h. EMG signals were high-pass filtered (50Hz cut-off), rectified and low-pass filtered (20Hz cut-off). Processed EMG activity was then decoded using a linear ridge regression from either (i) low frequency local field potentials (LF_LFPs) obtained by low-pass filtering neuronal recordings (5.5Hz cut-off) or (ii) spectral LFP amplitudes averaged over a wide high frequency band (WHFB_LFPs, Q19: 130-994Hz, Q21: 178-994Hz, Q22: 126-958Hz). Decoding accuracy, as measured by average ratio of explained variance (r^2), reached 0.38 and 0.53 when decoding EMG activity from LF_LFPs and WHFB_LFPs, respectively. For the first time, we demonstrated the ability to decode activity of lower limb muscles from motor cortex LFPs in freely behaving non-human primates. These results provide a first step for the development of brain machine interfaces to control exoskeleton movement, functional electrical stimulation of leg muscles, or spinal neuroprosthesis in order to re-establish locomotion in paralyzed individuals.

Taught Courses in Bioengineering

Augmented Reality for Assisting Learning of Biomedical Engineering Students

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The study of anatomy and physiology is crucial for understanding the clinical context behind biomedical engineering applications. At King's College London (KCL), this is supported by The Gordon Museum, which hosts the UK's largest anatomical specimen collection and provides medical and background information for each of its 8500 specimens. This project developed and investigated the effectiveness of an e-learning platform using a cutting-edge technology known as augmented reality (AR) in order to replace the traditional text-based information. The AR was used to automatically overlay interactive multimedia and annotations onto a live screen capture of the specimens on a mobile tablet computer, allowing biomedical engineering students to quickly orientate themselves with the specimen. AR was developed for six specimens using content hosted on a web-based online cataloguing system of photos, text and podcasts which was purpose-built for this study. Twenty-eight KCL students were block randomised to either an intervention or control group. The intervention group used AR-enhanced specimens, created with Layar (Layar B.V., the Netherlands) and delivered via a tablet device. The control group used specimens with text only descriptions as normally provided by the Museum. All participants completed an objective structured clinical examination (OCSE) to assess learning outcomes before and after two timed sessions. There were three specimens in each session with the first concerning myocardial infarction and the other cerebrovascular accidents. This was followed by a subjective assessment consisting of verbal and non-verbal (Likert scale) questionnaire.AR was shown to improve objective assessment results in both anatomy (+17.6%, $p<0.01$) and pathology (+11.1%, $p=0.09$) comprehension. Subjective assessment showed that students preferred AR (87% positive comments) to the control (52% positive comments).The results of this pilot study showed that AR was superior to traditional text descriptions when learning anatomy and physiology with specimens. Furthermore, students preferred the AR experience over traditional methods, and it enabled them to study the specimens in wider depth and breadth. In conclusion, AR is a powerful visual tool and may have an important role in enhancing learning for biomedical engineering students.

Effect of Decellularisation on the Biomechanical Properties of Porcine Meniscus: Experimental and Computational Study

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Introduction: Partial meniscus replacement can maintain the functional role of the meniscus and prevent early degenerative joint disease. A potential solution to the current lack of meniscal replacements is the use of an acellular biological scaffold produced from xenogeneic meniscus. This study investigated the effects of decellularisation on the biomechanical properties of the porcine medial meniscus through an experimental-computational indentation and unconfined compression creep study. **Materials and Methods:** Native and acellular porcine medial menisci were supplied by Tissue Regenix Group PLC, York, UK. On the day of testing, cylindrical specimens were cut from the central portion of the anterior, middle and posterior sections of the menisci. The specimens were then cut to the specified thickness. Mechanical indentation and unconfined compression creep tests were conducted to determine the equivalent (full creep curve) and equilibrium (final 30% creep deformation) biomechanical properties of each specimen. Each specimen was subjected to creep-deformation at ~20ºC. The instantaneous (within 40ms) load was maintained until creep deformation reached equilibrium. Meniscal pins were kept submerged in PBS throughout testing. The linear-biphasic indentation creep problem was solved using a combined experimental, analytical and computational approach. This solution scheme allowed simultaneous computation of the three independent intrinsic biphasic properties of the menisci, assuming 74% water content. The biphasic unconfined compression creep problem was solved using the linear-biphasic solution [1]. **Results:** The sensitivity analysis showed that specimens of 1.5 mm thickness were sufficient to describe the biomechanical properties of the tissue. Moreover, there were no significant differences between anterior, middle and posterior meniscal regions (ANOVA, $p > 0.05$). The effect of water content (60-80%) on the predicted properties was insignificant. The predicted Poisson's ratio of native and acellular meniscus from indentation tests was zero. The predicted aggregate modulus for native meniscus from indentation and unconfined creep tests was higher than that of acellular meniscus. On contrary, the native meniscus had lower permeability than that which was predicted for acellular meniscus. **Discussion and Conclusion:** Acellular meniscus had lower aggregate modulus and higher permeability compared to that of native meniscus. This change in biomechanical properties was likely due to the reduction of glycosaminoglycans (GAGs) during decellularisation. However, the predicted properties were within the reported range for the human meniscus. In conclusion, an acellular porcine meniscus has potential for clinical use in partial meniscal repair procedures. **References:** [1] Armstrong *et al*. Biomechanical Engineering 1984.

Application of acoustic perfusion bioreactor for augmentation of cartilage tissue engineering

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Articular cartilage enables smooth joint movement by acting as a low friction shock absorber. Since the tissue has limited self-repair ability, if left untreated, articular cartilage damage can progress to osteoarthritis, the most common form of arthritis in the western world. In the absence of effective pharmacological agents to treat osteoarthritis, application of tissue engineered cartilage grafts is a promising approach to address the problem of articular cartilage regeneration. However, cartilage grafts generated using conventional tissue engineering strategies are characterised by low cell viability, suboptimal hyaline cartilage formation and, critically, inferior mechanical competency, which limit their application for articular cartilage repair. To address the limitations of conventional tissue engineering and generate robust scaffold-free cartilage grafts of human articular chondrocytes (HACs), the present study utilised custom-built perfusion bioreactors with integrated ultrasound standing wave traps. HACs were isolated from deep-zone articular cartilage pieces dissected from osteoarthritic femoral heads, and the cells were culture expanded in 2-D monolayer cultures. Cells harvested from confluent monolayer cultures were introduced into the bioreactors, which employed sweeping acoustic drive frequencies over the range of 890 to 910 kHz to levitate the cells, promote rapid aggregation of the cells into 3-D clusters/ agglomerates and levitate the agglomerates in the lumen of the chamber away from the influence of the solid substrate. Furthermore, chondrogenic culture medium was perfused continuously at a low-shear rate throughout the 21-day culture period to enhance chondrogenesis in the agglomerates via improved mass transfer rates and mechanotransduction. 'Live-dead' cell staining demonstrated negligible cell death in the explants, indicating no adverse effects from prolonged exposure to ultrasonic force fields. Histologically, the explants were reminiscent of native hyaline cartilage and characterised by lacunae containing SOX-9-expressing chondrocytes, embedded

in dense extracellular matrix constituted by proteoglycans and collagen Type II. The elastic modulus of the explants determined by indentation-type atomic force microscopy was comparable to native human articular cartilage. Moreover, in the organ culture partial thickness cartilage defect model, implantation of the explants into defects for 16 weeks resulted in the formation of hyaline cartilage-like repair tissue that adhered to the host cartilage and contributed to significant improvements to the tissue architecture compared to the empty defects. The study has demonstrated the first successful application of the acoustic perfusion bioreactor technology to bioengineer scaffold-free cartilage grafts of HACs that have the potential for subsequent use in the clinic for the repair of partial thickness cartilage defects.

Anisotropic scaffold to direct zonally distinct articular cartilage tissue regeneration

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Osteoarthritis (OA) is a debilitating condition that often arises when damaged articular cartilage is left untreated. In recent decades, cell-based therapies have seen potential as an approach in cartilage tissue engineering. However, a therapy that would direct the regeneration of articular cartilage with the native zonal organization of the tissue, thereby ensuring mechanical competence of the construct, remains elusive. Towards that goal, we have combined materials-based technologies (electrospinning, particulate leaching and directional freezing) to develop an anisotropic osteochondral scaffold that closely mimics the zonal organisation of native articular cartilage with distinct superficial, transitional, and deep zone morphologies to instruct proper tissue regeneration and positively impact tissue function. The tensile and compressive properties of the poly (ε-caprolactone) scaffold have been optimised to better match those of native articular cartilage and provide mechanical function during the tissue regeneration phase following implantation. Continued optimisation aims to implement the design with polymers that will render the scaffold more elastic such as poly (l-lactide-co-ε-caprolactone). Ongoing *in vitro* studies with bovine chondrocytes and human mesenchymal stem cells have demonstrated the production of sulphated glycosaminoglycan rich cartilage-like matrix that fills the porous structure of the scaffold. The gene expression profile and protein accumulation of key cartilage matrix markers including aggrecan and collagen type II were consistent with the histological results. Of importance, the scaffold directed zonally-distinct collagen fibre alignment within the tissue formed *in vitro*-tissue with fibres presenting an orientation parallel to the scaffold surface in the superficial zone and perpendicular in the deep zone with a more random arrangement in the transitional portion of the scaffold.

Bioactive membranes for bone regeneration

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Bone fracture is still a major problem. The periosteum plays a critical role during bone regeneration, and its incorporation as an active component of the surgical procedure has been demonstrated to significantly enhance bone regeneration[1]. Therefore, engineering periosteal grafts through membrane-based technologies is an attractive approach to improve bone healing. This work aimed to design, fabricate, and validate a bioactive protein-based membrane scaffold to be used as periosteal graft for applications in bone regeneration. Taking advantage of the biomimetic character of elastin-like recombinamers (ELRs) and the precision of micro/nanofabrication technologies, our strategy was to produce a highly tuneable and bioactive membrane exhibiting physical and biomolecular signalling to stimulate osteconduction and osteoinduction. ELRs molecules incorporated bioactive sequences designed to promote endothelial (REDV) and mesenchymal stem cell (RGDS) adhesion or mineralization (DDDEEKFLRRIGRFG, analog of the SN15 fragment of statherin) were used to fabricate ELR membranes by a recently reported drop-casting/evaporation technique[2]. We fabricated thin, robust, self-supported ELR membranes incorporating micro- nanotopographies, bi-lateral topographies, porous structures or multiple ERL layers. *In vitro* validation of our membranes showed that cells recognized both topographical patterns and bioactive epitopes incorporated in ELR molecules. Interestingly, an early expression of the osteoblastic transcription factor osterix at day 5 in non-osteogenic differentiation medium was strongly induced on smooth mineralization membranes[3]. In addition, these membranes exhibited the highest quantity of calcium phosphate (Ca/P in 1.78) deposition with and without cells. Finally, *in vivo* validation in a 5 mm-diameter critical-size rat calvarial defect model was analyzed for bone formation on day 36 after implantation. Animals treated with the mineralization membranes exhibited the highest bone volume within the defect as measured by micro-computed tomography and histology[4].These results demonstrate the capability to create thin molecularly designed membranes with both physical and biomolecular signals designed to orchestrate multiple biological processes. We found that ELR membranes displaying the bioactive sequence DDDEEKFLRRIGRFG, an analog of the SN15 fragment of statherin, exhibited the highest capacity *in vitro* to induce osteoblastic differentiation and mineralization and significantly improved bone regeneration *in vivo*. Membranes exhibiting selective bioactivity capable of eliciting specific biological responses may offer a more efficient periosteal graft alternative towards improving bone regeneration. [1]Zhang et al (2008). Clin Orthop Relat Res 466:1777-87. [2]Tejeda-Montes et al (2012). Acta Biomater 8, 998-1009. [3]Tejeda-Montes et al (2014). Acta Biomater 10, 134-41.[4]Tejeda-Montes et al (2014). Biomaterials, In press.

Evaluation of the Growth Environment of a Hydrostatic Force Bioreactor for Preconditioning Tissue-Engineered Constructs for clinical application

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Bioreactors are important tools to investigate the effect of physical forces on cells and cell-scaffold constructs and they further provide growth environments for engineered tissues. Since, cell fate and tissue development are affected by mechanical stimulation the evaluation of the bioreactor environment during culture is crucial to define outcomes. A novel hydrostatic force bioreactor imposing low levels of cyclical hydrostatic force at 0.005 Hz to 2 Hz frequency and 0-280 kPa on standard tissue culture multi well plates was developed in collaboration between Instron Tissue Growth Technologies, Ltd and Keele University. This study investigated the growth environment within this bioreactor to define outcome for regenerative medicine and clinical applications. Experimental measurements of changes in dissolved oxygen (O2), carbon dioxide (CO2), and pH after mechanical stimulation were performed. In addition, physical forces (pressure and shear stress) in the bioreactor were determined through mathematical modelling and numerical simulation. The effect of hydrostatic pressure on differentiation and maturation of different cell types was assessed using human bone marrow derived mesenchymal stem cells and chick femur fetal skeletal cells in monolayer and 3D hydrogel as well as organotypically cultured ex vivo chick foetal femurs and human embryonic stem cells. The concentration of dissolved O_2 and CO_2 in the medium increased after hydrostatic pressure was applied, whereas the pH of the medium decreased. These changes were dependent on the magnitude of the applied hydrostatic pressure and were reversible when samples were transferred to a cell culture incubator. The distribution and magnitude of physical forces were shown to be dependent on the shape and position of the cell-seeded hydrogels in the tissue culture well plates. Additionally, cyclic hydrostatic force worked synergistically with chemical cues resulting in increased mineralised densities of cell-seeded hydrogels and chick foetal femurs leading to enhanced osteogenesis. In addition, hydrostatic force enhances the bi-refringent properties of 3D collagen hydrogels which suggested increased alignment of collagen fibrils. The here described bioreactor allows the application of hydrostatic force for gas-liquid interface culture at physiological relevant pressures and provides a growth environment for engineered tissues. The application of hydrostatic pressure resulted in reversible changes of dissolved O_2, CO_2 and pH of the medium, which remained within the human physiological range. Furthermore, this bioreactor is alignable to culture in standard culture environments and might proof as suitable tool for pre-conditioning of cells and tissue for clinical tissue regeneration. **REFERENCES:** Y. Reinwald et al. (2014), "Evaluation of the growth environment of a novel hydrostatic force bioreactor" (in press, Tissue Engineering Methods C); J.R. Henstock, et al. (2013) "Cyclic hydrostatic pressure stimulates enhanced bone development in the foetal chick femur in vitro". Bone 53, 468-477. **ACKNOWLEDGMENTS:** The authors would like to thank the EPSRC Centre for Innovative Manufacturing in Regenerative Medicine (ECP007/1010) and Instron TGT, Ltd for funding.

Resorbable Calcium Phosphate Bone Cements Prepared by a Facile Synthetic Method

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Introduction Autologous bone is favoured as a natural graft, however, calcium phosphate cements (CPCs) are frequently used as synthetic bone substitutes due to their chemical similarity to the mineral component of bone. Their ability to conform to complex bone defects and excellent osteoconductivity also renders them excellent scaffolds for bone tissue engineering, although they do have their own limitations. In particular, the low resorbability of CPCs impairs new bone formation at the implant site. In this study we report a simple method of forming resorbable CPCs cement made of monetite ($CaHPO_4$). In addition, the early molecular responses of human mesenchymal stem cells (hMSCs) seeded on the monetite cements produced under mechanical stimulation are reported. **Matrerials and Method** Monetite cements ($CaHPO_4$) were produced as described by Cama et al. [1]. 60% by weight of a soluble porogen (sodium chloride, NaCl) with respect to the total calcium phosphate powder was used to produce a macroporous structure. The monetite cements were characterized in terms of porosity (Micro-CT analysis), chemical composition (X-ray analysis), setting properties (pH, temperature, enthalpy of reaction and variation of the chemical cement composition during the hardening process) and mechanical strength (compressive and diametral strength). Human mesenchymal stem cells (hMSCs) were seeded at a density of $1x10^6$ cell/ml on the macroporous structures and a dynamic compressive load between 1 and 10N at a frequency of 0.1 Hz was applied for 2h or 24 on the cell seeded cements. Gene expression was carried out to identify candidate transcriptional regulators and signaling mechanism induced by mechanical stimulation. **Results** The preparation method reported in this work considered the typical chemical reaction of brushite cement. However, the introduction of NaCl crystals in amounts higher than 6.2M was seen to drive the precipitation process towards monetite due to a decrease in the dissolution rate of precursor particles. The mechanical stimulation was seen to effect the cell biological responses with a significant increase in the expression of transcription factors in comparison to the cements maintained under static conditions. **Conclusion** The inclusion of common salt with the precursors provides a simple and effective method of forming resorbable monetite cements. hMSCs subjected to mechanical stimulation showed an up-regulation of genes involved in the differentiation process towards osteogenic lineage.

In vitro degradation of mechanical properties of porcine femoral head bone for development of an in vitro of avascular necrosis

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Various biological models of avascular necrosis (AVN) of the femoral head have been developed in vitro [1], however these do not demonstrate the mechanical failure observed clinically. A structural disease model would be advantageous when developing mechanically based treatments. This study assessed methods to degrade mechanical properties of bone plugs from porcine femoral heads; Brown et al. [2] demonstrated this to be 59% reduction in elastic modulus and 41% reduction in yield strength. Plugs were treated as follows (all at room temperature with agitation);Potassium hydroxide (KOH) 1M: 14, 7, 3 and 1 days Ethylenediaminetetraacetic acid (EDTA) 12.5%: 28, 14 and 7 days Hydrochloric acid (HCl) 1M: 48, 24, 18 and 6 hours. Computed tomography scans of the samples were obtained prior and after treatment to assess bone mineral density (BMD). Compression testing was carried out on control and treated bone plugs samples to provide offset yield stress and elastic modulus and compared. Significant reductions in BMD were seen in all groups treated with EDTA and HCl, though only samples treated in KOH for 7 days demonstrated a significant reduction. Conversely KOH samples soaked for shorter times demonstrated a slight increase in BMD, which may be due to absorption of potassium into the bone. Elastic modulus and yield stress values were significantly lower in all cases compared to control samples. A reduction of 47% elastic modulus and 46% yield stress was observed in samples treated in EDTA for 3 days, which is similar to the reduction in mechanical properties in AVN of human heads presented by Brown et al. [2]. HCl was more effective in reducing mechanical properties of bone in shorter time and may be more suitable in development of the in vitro model of AVN on whole femoral heads. Further work is required to establish optimum concentrations and treatment time for the final model. [1] Jones & Allen, Clin. Rev. Bone Miner. Metab. 9 (2011) 63.[2] Brown et al., Clin. Orthop. Relat. Res. (1981) 240.

Altered Mechanobiology of Schlemm's Canal Endothelial Cells in Glaucoma

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Glaucoma is a blinding eye disease associated with elevated intraocular pressure (IOP) that affects 60M people worldwide. Elevated IOP in glaucoma is caused by increased hydraulic resistance of aqueous humour outflow from the eye, with the source of outflow resistance located near to the endothelium of Schlemm's canal (SC) where aqueous passes through micron-sized transendothelial pores. SC pore density is reduced in glaucoma, which may contribute to elevated outflow resistance. In this project, we test the hypothesis that elevated biomechanical stiffness of SC cells contributes to impaired pore forming ability in glaucoma.SC cell lines were isolated from glaucomatous and non-glaucomatous human donor eyes. SC cells were seeded at confluence on track-etch filters, cultured for 2 days, and perfused in the basal-to-apical direction at 0, 2 or 6 mmHg for 30 minutes prior to fixation. Pore density (pores/mm^2) was measured by masked observers from scanning electron micrographs. Cell stiffness was measured by atomic force microscopy using spherical 10 μm tips on subconfluent SC cells, and Young's modulus (E) was calculated using a modified Hertz model. There was a statistically significant increase in pore density with perfusion pressure ($p < 10^{-4}$) in SC cell lines from non-glaucomatous donors. At 6 mmHg, pore density in glaucomatous SC cells was reduced 3-fold relative to non-glaucomatous SC cells ($p < 10^{-3}$). E was significantly larger in glaucomatous versus normal SC cells (1.24 ± 0.11 vs. 0.79 ± 0.10 kPa; $p < 0.02$). There was a significant correlation between increased SC cell stiffness and decreased pore density ($p < 0.002$).Pore formation in SC cells is a mechanosensitive process that becomes altered in glaucoma possibly due to elevated cell biomechanical stiffness. Drugs that selectively target SC cells to reduce their stiffness may thus be useful to promote pore formation and to lower outflow resistance as a potential glaucoma therapy.

Design and development of a synthetic biocompatible basement membrane for use as a treatment for Age-Related Macular Degeneration.

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Age-related macular degeneration (AMD) is a complex disorder causing irreversible loss of central vision in nearly 50 million individuals globally, with a direct cost estimated at approximately US$ 255 billion. The underlying pathology of this degenerative disorder is poorly understood, but impairment of the Retinal Pigment Epithelial (RPE) monolayer and its supportive Bruch's membrane (BrM) is a key feature of AMD progression. RPE cell replacement therapy has been recognised as a possible approach for the treatment of this degenerative disease, and injection of RPE cells under the retina has been suggested as a potential treatment to support photoreceptor cell function; however this leads to issues associated with lack of organisation and the likely movement of cells away from the injection site. To achieve this, we have developed a synthetic biocompatible scaffold which supports the growth of RPE cells that can be subsequently transplanted into the sub-retinal space. Major considerations in the design of this membrane, synthesised through the use of electrospinning techniques, were its ability to mimic the biochemical and biophysical properties of Bruch's membrane. Hence, we used a combination of methyl methacrylate (MMA) and poly(ethylene glycol) methacrylate (PEGM)), which we improved and optimised for long-term ocular applications. Modification of these parameters has allowed a greater flexibility in the thickness of the polymer membrane through the thinning of individual fibres, thus ensuring it accurately mimics human BrM in its thickness, porosity and mechanical properties. The fidelity and effectiveness of the PMMA:PEGM co-polymer as a suitable RPE scaffolding were tested using long-term cultures of primary murine RPE monolayers. We also studied the nature of RPE-extracellular matrix interactions with the fibres, and showed that our scaffold performed as an effective barrier, thus reproducing important features of Bruch's membrane. On-going studies are assessing the efficacy of this membrane in animal models of AMD.

Intervertebral disc composite mechanically stimulated in bioreactor for tissue engineering of annulus fibrosus artificial replacement

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Back pain is a disease, chronic in many cases, for which there is a lack of definitive cures (Hudson et al. 2013). Current surgical procedures alter normal spine biomechanics while intervertebral disc (IVD) mechanical prosthesis do not integrate with the surrounding tissues (Jin et al. 2013; Raj 2008). Therefore they are not deemed to be the optimal solution to address back pain in the long term (Park et al. 2012; van den Eerenbeemt et al. 2010). In order to overcome the drawbacks of the above mentioned therapies, we engineered an artificial cellularized tissue for replacement of the annulus fibrosus (AF), the outer part of the IVD, which was subject to mechanical stimulation in order to maintain cells in conditions close to those found *in-vivo*. For this purpose we used biocompatible PCL (Mn=70-90 kDa), electrospun into micro- and nano-fibres with different diameter and orientation degree, as support for human mesenchymal stem cells (hMSCs) growth. Cells morphology observation was carried out by means of both electron and fluorescence optical microscopy. For the latter actin filaments and nuclei were stained with phalloidin Alexa Fluor-555 and Hoechst 33342 whilst, for vinculin, rabbit primary polyclonal and goat secondary polyclonal Alexa Fluor-488 conjugated antibodies were used. Viability was periodically monitored through Alamar blue (Invitrogen) test. A model for multilamellar IVD-like constructs was built by wrapping electrospun bilayers with hMSCs around agarose discs. Mechanical properties of the agarose discs alone were compared with those of complete IVD-like structures. Hence, seeded IVD-like scaffolds were loaded into in a bioreactor (5900 BioDynamic, BOSE) able to exert cyclical mechanical stimulation that mimics spine compression by finely controlling the test parameters. HMSCs viability of cells seeded on electrospun PCL monolayers and bilayers constructs showed an increasing trend over 25 days demonstrating the good biocompatibility of PCL matrices used without any post-processing modification. Double layer scaffolds, superimposed by keeping the reciprocal 60° angle of AF collagen fibres, clearly showed to provide topographical cues on cells. HMSCs were found to migrate and assume an elongated shape, adopting the same orientation angle of the fibres of both the top and bottom layer. The presence of the electrospun bilayer surrounding the agarose cylinders noticeably enhanced both the ultimate tensile strength and the strain at break. Currently only preliminary tests have been carried out, showing the feasibility of medium-long term experiments with cellularized scaffold. In the future the bioreactor will be connected to a hypoxic chamber in order to keep the environment more close to that found in the natural IVD, characterized by low O_2 concentration. Bibliography: Van den Eerenbeemt, K.D. et al., 2010. Total disc replacement surgery for symptomatic degenerative lumbar disc disease: a systematic review of the literature. *European spine journal*, 19(8), pp.1262–80.Hudson, K.D. et al., 2013. Recent advances in biological therapies for disc degeneration: tissue engineering of the annulus fibrosus, nucleus pulposus and whole intervertebral discs. *Current opinion in biotechnology*, 24(5), pp.872–879.Jin, L., Shimmer, A.L. & Li, X., 2013. The challenge and advancement of annulus fibrosus tissue engineering. *European spine journal*, 22(5), pp.1090–1100.Park, C. et al., 2012. Clinical Outcome of Lumbar Total Disc Replacement Using ProDisc-L in Degenerative Disc Disease. *Spine*, 37(8), pp.672–677.Raj, P.P., 2008. Intervertebral Disc: Anatomy-Physiology-Pathophysiology-Treatment. *Pain Practice*, 8(1), pp.18–44.

The big impact of little things: vasculature bed can lead its footprint at the macroscopic scale of Magnetic Resonance Elastography data.

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Recently *in vivo* experiments using Multi-frequency MRE (MMRE) have shown that the exponent of the power law derived from MMRE data fitting with a power law could be more sensitive to specific pathologies such as fibrosis, steatosis or even inflammation. However these works lack fundamental understanding of the relation existing between the tissue microstructure with its macroscopic nature. We therefore concentrate our analysis on scattering induced dispersion using highly controlled micro-scatterers in size and density, and develop a theory from first principles which relates the spatial organization of micro scatterers to the exponent of the power law measured at the macroscopic scale. We present a straightforward link between geometrical organisation of the medium, description of multiple reflections of waves in that structure using a theory borrowed from geophysics, and the resulting impact on the macroscopic dispersion relations, i.e. the observation of frequency power law. Our theory explains how the waves' response translates from the micro-level through scales, and it is shown that this translation is possible if the microstructure is fractal-like. These theoretical findings are supported by magnetic resonance experiments and simulations using mechanical shear waves in the kHz regime. Dispersion properties of the shear waves are dramatically influenced by the presence of obstacles and are rather well predicted by the theoretical model developed here. Moreover, our discovery is in agreement with previously published results concerning the propagation of light or acoustic waves. We demonstrated that already a random distribution of mono-sized micro-scatterers exhibits fractal-like properties and that the spatial extent of this effective fractal-like region is actually of macroscopic size! Thus, waves which normally cannot resolve the presence of the microstructure due to an enormous discrepancy between wavelength and size of the scatterer are now able to reveal its presence in the dispersion relation. This allows stretching the limits of the resolution because the limiting factor is not anymore the size of the individual elements, but rather the spatial extent of the fractality. The generality of the proposed model allows immediate extension to more complex fractal structures. One potential application of the reported discovery is the characterization of vascular alterations that are inherently endowed with fractal character. As a perspective, we built a vasculature tree by 3D printing and we will measure dispersion of mechanical properties on a gel phantom with the embedded tree.

The use of XFEM to assess the influence of vascular canals in bone crack propagation

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Skeletal diseases lead to an increase in bone fracture risk. In particular, micro-porosity might have a profound influence on crack propagation. In osteogenesis imperfecta murine (*oim*) bones, which represent the condition of osteogenesis imperfecta in humans, a genetic mutation results in high bone fragility. *Oim* bones have more numerous and branched vascular canals compared to their wild type (WT) controls [1]. The aim of the current study is to use Extended Finite Element Method (XFEM) tools provided by Abaqus to characterize the role of vascular canals in mouse cortical bone during crack propagation. The topology of transverse cross sections of *oim* and WT tibial mid-diaphysis were captured with synchrotron radiation-based computed tomography and used to create 2D models. Although XFEM allows modelling crack propagation along an arbitrary, solution-dependent path, there are limitations when using this technique to model bone at the micro-scale, as the crack is not able to propagate through holes. In this study, two approaches were explored in order to overcome this limitation. The first approach consisted of assigning void material properties to the vascular pores. In the second method, we employed multiple partitions and assigned enrichment regions with independent crack growth possibilities. In both cases, the cohesive segment method was used with maximum principal stress failure criterion for damage initiation and an energy based damage evolution law for crack propagation. Bone was considered linear elastic and homogeneous and bone material properties were maintained constant for *oim* and WT, to explore the influence of porosity only. Results suggest that crack propagation is strongly affected by the micro-architecture, as the main crack follows the vascular canals both in *oim* and WT samples. However, the first approach does not capture the multiple sequential crack nucleation, revealed by the second method. In Abaqus XFEM, additional cracks cannot nucleate until all pre-existing cracks in an enriched feature have propagated. Thus, assigning material properties to the voids allows us to focus on one main crack, while sequential crack nucleation can be explored by specifying multiple enriched features in the model. We will combine these two methods to further analyse the influence of vascular canals in osteogenesis imperfecta.[1] Carriero *et al*, Bone, 61:116-24, 2014.

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Shuangyi Wang, James Housden, Davinder Singh, Kaspar Althoefer, Kawal Rhode
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71   An Investigation of Cochlear Dynamics in Response to Novel Hearing Implant Actuation
Yu Zhang, Masoud Zoka Assadi, Xinli Du, Peter Brett, Chris Coulson, Andy Reid, David Proops
Brunel Institute for Bioengineering, Queen Elizabeth Hospital

206   A Novel Endoscopic Scanning-Probe Device for Rapid Screening of Gastrointestinal Dysplasia
Fernando Avila-Rencoret, George Mylonas, Daniel S. Elson
Department of Surgery and Cancer, The Hamlyn Centre for Robotic Surgery, Imperial College London, Department of Computing , Imperial College London

285   Characterisation of Human Knee mechanics using a Robotic Testing System
Hadi El Daou, Kiron athwal, Christoph Kittl, Yasuyuki Kawaguchi, Breck Lord, Ryo Takeda, Ferdinando Rodriguez y Baena, Andrew Amis
Imperial College London, University of Hokkaido

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King's College London, Guy's and St Thomas' NHS Foundation Trust

109   Particle Tracking as a Tool in VAD Design: Focusing on Blood Damage and Residence Time
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King's College London, Division of Imaging Sciences and Biomedical Engineering, The Rayne Institute, St Thomas' Hospital, School of Physics and Astronomy, University of Birmingham, King's College London, Division of Chemistry

229   Continuous non-contact vital sign monitoring in the neonatal intensive care unit
Mauricio Villarroel
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270   An investigation of body worn sensors for lower limb monitoring and rehabilitation management
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Imperial College London, Queen Mary University London, Brain Sciences Foundation and Massachusetts Institute of Technology

Biomedical Imaging and Image Analysis

7   Serial changes in Apparent Diffusion Coefficient in Acute Ischemic Stroke

George Harston, Jacob Levman, Thomas Okell, Ian Reckless, Fintan Sheerin, Martino Cellerini, Stephen Payne, Michael Chappell, Peter Jezzard, James Kennedy
University of Oxford, Oxford University Hospitals NHS Trust

8   Identifying the ischaemic penumbra using pH-weighted magnetic resonance imaging

George Harston, Yee Kai Tee, Nicholas Blockley, Thomas Okell, Sivarajan Thandeswaran, Gabriel Shaya, Fintan Sheerin, Martino Cellerini, Stephen Payne, Peter Jezzard, Michael Chappell, James Kennedy
University of Oxford, University of Oxford, University of Oxford, University of Oxford, University of Oxford, University of Oxford, Oxford University Hospitals NHS Trust, Oxford University Hospitals NHS Trust, University of Oxford, University of Oxford, University of Oxford

23   Uniform B-spline Modelling of Tears, Discontinuities and Sliding Motion on a Manifold-projected Domain

Alberto Gomez, Graeme Penney
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24   Image-based view-angle independent cardiorespiratory motion gating and coronary sinus catheter tracking for X-ray-guided cardiac electrophysiology procedures

Maria Panayiotou, Andrew P. King, R. James Housden, YingLiang Ma, Michael Truong, Michael Cooklin, C. Aldo Rinaldi, Mark O'Neill, Jaswinder Gill, Kawal S. Rhode
Division of Imaging Sciences & Biomedical Engineering, King's College London

32   The cross-sectional relationship between osteoarthritis (OA) attributable bone area and traditional radiographic measures of OA: data from the Osteoarthritis Initiative

*Andrew J Barr[1], **Bright Dube**[1], Elizabeth MA Hensor[1], Sarah R Kingsbury[1], George Peat[2], Mike A Bowes[3], Philip G Conaghan[1]*
Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds and NIHR Leeds Musculoskeletal Biomedical Research Unit, [2]Arthritis Research UK Primary Care Centre, Research Institute for Primary Care & Health Sciences, Keele University,[3]Imorphics Ltd

33   Within-patient association between radiographic measures of pathology and MRI bone shape, using both knees in a large cohort from the Osteoarthritis Initiative

***Bright Dube**[1], Andrew J Barr[1], Elizabeth MA Hensor[1], Sarah R Kingsbury[1], Mike A Bowes[2], Philip G Conaghan[1]*
Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds and NIHR Leeds Musculoskeletal Biomedical Research Unit, Leeds, UK, [2]Imorphics Ltd, Kilburn House, Manchester, UK

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85   SPECT imaging of inflammation with antibody fragments directed against mouse Vascular Cell Adhesion Molecule 1

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97   Standardised unfold map of left atrial scar from 3D late gadolinium enhancement MRI datasets

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Paediatrics, University of Oxford, Institute of Biomedical Engineering, University of Oxford

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[1]Imperial College London, [2]Head and Neck Unit, The Royal Marsden Hospital, [3]Department of Echocardiography, Royal Brompton Hospital, [4]Imaging Department, Imperial College London, [5]Division of Imaging Sciences, King's College London

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Departments of Bioengineering, Aeronautics and Civil Engineering, Imperial College London

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Imperial College London, Wallace H. Coulter Department of Biomedical Engineering at Georgia Institute of Technology & Emory University School of Medicine

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Biomechanics group, Imperial College London, Tribology Group, Imperial College London

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*G. Daniel G. Langohr, **Josh W. Giles**, George S. Athwal, James A. Johnson*
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Diogo M. Geraldes, Ulrich Hansen, Andrew A. Amis
Biomechanics Group, Imperial College London

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Alexandra Smyth, Miriam Day, Nick Harris, Susan Partridge, Sophie Williams, John Fisher, Claire Brockett
University of Leeds, Leeds Teaching Hospitals NHS Trust

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University of Leeds, DePuy Synthes Joint Reconstruction

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Institute of Medical and Biological Engineering, School of Mechanical Engineering, University of Leeds

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Institute of Medical and Biological Engineering, University of Leeds, Biomaterials and Tissue Engineering, University College London

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Institute of Medical and Biological Engineering, University of Leeds

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Imperial College London, Georgia Institute of Technology & Emory University School of Medicine

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University of Leeds

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School of Engineering & Materials Science, Queen Mary University of London, Nanotechnology Platform

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204   Experimental and Computational Study of the Behaviour of Trabecular Bone-Cement Interfaces
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47   The effect of immobilisation on spine development of chick embryo
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106   Tribology of Osteochondral Graft Implantation
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107   Computational Modelling of Intraluminal Lymphatic Valve Mechanics
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157   Practical Identifiability of Cardiac Constitutive Laws Using 3D Tagged MRI
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167   The Impact of Lymphatic Network Structure on Lymph Propulsion
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169   A novel cost function for myocardial stiffness characterisation
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176   Cardiac Mr-Elastography: Towards Truly Intrinsic Biomechanical Properties
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237   Modeling Stability of the Shoulder
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256   Musculoskeletal modelling for ergonomics: shoulder loading in bricklaying
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Cardiff University

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Imperial College London, King's College London

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Daniel YF Chung, Omar S Al-Kadi, Fergus V Gleeson, J Alison Noble, Constantin C Coussios
Institute of Biomedical Engineering, Department of Engineering Science, University of Oxford, and Radiology Department, Churchill Hospital

277   Early screening of breast cancer recurrence by monitoring DNA methylation based biomarkers using semiconductor technology
Melpomeni Kalofonou, Christofer Toumazou
Imperial College London

282   Ultrasound Mediated Drug Delivery for Pancreatic Cancer
Hasnaa Shaddad
University College London

283   Enhancing bone repair by fine-tuning intracellular protein degradation by a putative anti-cancer target
Sandra Loaiza, Tamara Chinn, Katarzyna Parzych, Francesco Dazzi, Eileen Gentleman, Holger Auner
Imperial College London

284   Application of Gold Nanorods for Photothermal Effect in Upper Gastrointestinal Cancer Tissue.
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The Hamlyn Centre, Institute of Global Health Innovation, Imperial College London

286   Harnessing laser-plasma accelerated ion beams using Gabor lenses for medical applications
Christopher Hughes
Imperial College London

287   Directed assembly of a capillary bed on a microfluidic chip
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Department of Engineering, University of Cambridge

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Imperial College London

289   Ovarian cancer DNA methylation biomarkers in cell free DNA from blood

Kayleigh Davis, Kirsty Flower, Jane Borley, Charlotte Wilhelm-Benartzi, Robert Brown
Imperial College London

291   An in vitro blood vessel model for studying trans-endothelial migration dynamics of breast cancer

Cristina Bertulli
University of Cambridge

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Marta Varela, Ross Morgan, Oleg Aslanidi
King's College London

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Christian F. Baumgartner, Christoph Kolbitsch, Jamie R. McClelland, Daniel Rueckert, Andrew P. King
Division of Imaging Sciences and Biomedical Engineering, King's College London

30   Numerical Assessment of the Stiffness Index

Sally Epstein, Anne-Claire Vergnaud, Paul Elliott, Phil Chowienczyk, Jordi Alastruey
Department of Biomedical Engineering, St Thomas' Hospital, King's College, Department of Epidemiology and Biostatistics, St Mary's Hospital

44   A possible mechanism for arrhythmogenesis in the infarct border zone

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45   Transcriptome analysis of local shear dependent gene expression in endothelial cells during thin-cap fibroatheroma (TCFA) development

Takayuki Homma, Petronille Caurette, Hélder J. Silva, Ikuho Yamada, Elli Makrydaki, Sandra Bovens, Ryan Pedrigi, Enrico G. Petretto, Rob Krams
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54   Flow Patterns in Externally Stented Saphenous Vein Grafts Computational Fluid Dynamics Analysis Based On the Venous External Support Trial (VEST)

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Department of Bio-Medical Engineering, Afeka Academic College of Engineering, Department of Mechanical Engineering and Mechatronics, Ariel University

90   Effect of doxorubicin on left ventricular myocytes: a simulation study

Margarita Fernandez-Chas, Steven A. Niederer
King's College London

115   Developing a Model of Global Arterial Stiffening to Assess the Effect of Vascular Aging on Local Risk Factors for Atherosclerosis

Emma L Bailey, Peter Sowinski, Eleni Bazigou, Peter D Weinberg
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David Western, Ben Hanson, Peter Taggart
Department of Mechanical Engineering, University of Bristol,

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C. D'Onofrio, S. A. Rolland, K.W.Q. Low, R. Johnston, L.E. North, S. Brown, R. Phillips, J. Sienz, R. van Loon
Swansea University, Haemair Ltd.

134   Longitudinal predictive analysis of vulnerable plaques in a mouse model of atherosclerosis

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Imperial College London

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Jack Lee, David Nordsletten, Andrew Cookson, Simone Rivolo, Nicolas Smith
Department of Biomedical Engineering, Division of Imaging Sciences and Biomedical Engineering, King's College London,

177   Lumped parameter devices for experimental cardiovascular simulation: Effect on pulse waves
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183   Arterial Input Function Correction for Myocardial Perfusion Quantification
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189   Experimental and continuum modelling of arteriolar-scale microhaemodynamics
Joseph M. Sherwood, Stavroula Balabani
Imperial College London, University College London

198   Manifold learning for biophysical modeling and estimation of cardiac function
Radomir Chabiniok, Kanwal Bhatia, Eva Sammut, James Wong, Myrianthi Hadjicharalambous, Liya Asner, David Nordsletten, Reza Razavi, Andrew King, Daniel Rueckert, Nic Smith
King's College London, Imperial College London

200   Correction of wave speed measurement techniques in close proximity to a reflection site in elastic tubes
Nicola Pomella, Christina Kolyva, Ashraf Khir
Brunel University

203   Microscale 3D surface reconstruction of in vivo arterial endothelium: method for determining vessel wall strain
Ethan M Rowland, Emma L Bailey, Peter D Weinberg
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218   Novel Baseline Correction Method For Quantitative Analysis Of Myocardial Perfusion From Dce-Cmr Data Using Steady State T1 Relaxation Enhancement
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King's College London, Philips Healthcare

224   Modelling the mechanobiology of intracranial aneurysm evolution
Paul Watton, Haoyu Chen, Pedro Aparicio, Katia Mandaltsi, Thomas Eriksson, Justin Penrose, James Byrne
University of Sheffield, University of Oxford, University of Oxford, University of Oxford, University of Oxford, University of Oxford, ANSYS UK Ltd

252   A Virtual Contrast CFD Model Verified in Swine Sidewall Aneurysms
Thomas Peach, James Byrne, Jiayao Ma, Rafik Rizkallah, Yiannis Ventikos, Zhong You
Institute of Biomedical Engineering, Department of Engineering Science, University of Oxford, Nuffield Department of Surgical Sciences, Institute of Biomedical Engineering, University of Oxford

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Monica Rozeik, Terence Gourlay
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Rafik Rizkallah
University of Oxford

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Alexander Humphries, Srdjan Cirovic, Anthony M.J. Bull, Anthony Hearnden, Aliah F. Shaheen
Centre for Biomedical engineering, Department of Mechanical Engineering, University of Surrey, Imperial College London

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Phil Price, Conor Gissane, Dan Cleather
St Mary's University

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Daniel Bollag, Po Chan, Alistair Walker
Imperial College London

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David Britzman, Theofano Eftaxiopoulou, Anthony Bull
Imperial College London

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Maryam Imani Masouleh, Daniele Dini, Massimo Marezana
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Patricia Das Neves Borges, Antionio E Forte, Tonia L Vincent, Daniele Dini, Massimo Marenzana
Dept. Bioengineering, Imperial College London, Dept. Mechanical Engineering, Imperial College London, The Kennedy Institute of Rheumatology

223   Validating a simple indentation method for determining time-dependent mechanics of soft tissue
Robin M. Delaine-Smith, Saba Burney, Fran R. Balkwill, Martin M. Knight,
Queen Mary University of London

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S. Perazzolo, B. Hirschmugl, C. Wadsack, G.Desoye, R. Lewis, B. Sengers
University of Southampton, Medical University of Graz

77   Symbolic representation and inference of regulatory networks: Uncovering mechanosensitive gene networks
Nataly Maimari, Krysia Broda, Antonis Kakas, Alessandra Russo, Rob Krams
Imperial College London, University of Cyprus

78   A novel integrated platform for gene network inference and validation: Beyond the DREAM consortium
Nataly Maimari, Leila Towhidi, DongKyu Oh, Aliah Abuammah, Krysia Broda, Alessandra Russo, Rob Krams
Imperial College London

174   Investigation of biological pathways involved in brain development in preterm neonates using a multivariate phenotype and sparse regression
Michelle L Krishnan, James Boardman, Matt Silver, Gareth Ball, Serena Counsell, Andrew J Walley, A David Edwards, Giovanni Montana
King's College London, Royal Infirmary of Edinburgh, London School of Hygiene and Tropical Medicine, Imperial College London

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Hugo Sant'Ana Pereira, Jaisa Ahmed, Rob Krams
Imperial College London

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20 Are you more likely to develop osteoporosis because of who you are? A study on the effect of ethnicity on loss of bone mineral density – Case Study Lewisham & Greenwich NHS Trust
*Mansour Youseffi, **Q. Tammer**, Arfan Rashid*
University of Bradford, Lewisham and Greenwich NHS Trust

21 Development of Novel Hydrogels Based on Chitosan/Gelatin/B-Glycerophosphate for Replacement and Repair of Diseased Articular Cartilage: A Biological and Dynamic Characterization
*Mansour Youseffi, SA Khaghani, Tim Gough, **E Michailidou***
University of Bradford

168 Utilising High Resolution Imaging to Interrogate Blood Vessel and Bone Cell Interaction
***Juan A. Núñez**, Philipp J. Thurner, Ian Sinclair, Philipp Schneider, Claire E. Clarkin*
Centre for Biological Sciences, Institute of Lightweight Design and Structural Biomechanics, Vienna University of Technology, Faculty of Engineering and the Environment, University of Southampton

179 Rapid online decoding of receptive fields from multi-site tetrodes
***Kenny Ju Min Yeoh**, Paul Chadderton, Joseph Sollini*
Imperial College London

247 Implementation of multispectral polarization imaging in endoscopy
***Anne Pigula**, Neil T. Clancy, Daniel S. Elson*
Hamlyn Centre for Robotic Surgery, Institute of Global Health Innovation, Imperial College London

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