MeDe Innovation

EPSRC Centre for Innovative Manufacturing in Medical Devices

2014 Annual Review

CONTENTS

The EPSRC Centre for Innovative Manufacturing in Medical Devices – MeDe Innovation – is founded on a deceptively simple, but potentially ground-breaking, idea: to apply the concept of 'stratified medicine' to the medical device sector.

Stratified medicine subdivides patients into groups based on their risk of developing disease or their likelihood of responding to a particular drug – and then targets treatments where they will be most effective.

By segmenting the patient population based on how well particular designs of medical devices would work for each group, we believe this will enable a better match between device and patient and lead to a more successful long term outcome.

At MeDe Innovation, we aim to prove this concept in implanted orthopaedic devices, particularly 'Class III devices', which are those where the levels of uncertainty and risk are high.

We're taking a two-pronged approach. The first is to match each device to an individual patient, but to be cost-effective this will require new manufacturing techniques such as additive manufacturing, and so we're looking at how these might be employed nearer to the patient. Our second approach uses conventional design and manufacturing processes but improves the match by stratifying patients using the most relevant criteria and developing computer models that will show which product delivers the best 'fit and function'.

Our ideas immediately struck a chord: over 250 people from industry, academia and healthcare came to our launch event and our network continues to grow. With 15 companies and five universities investing as full partners within the Centre, we are already achieving our aim of building a collaborative community, involving the private sector, universities and clinicians working together on a portfolio of projects.

The research challenges we are addressing are those posed by the medical device industry itself. We already have over 40 projects underway in our first year, which is testament to the appetite within industry for solutions to these problems.

Manufacturing in the medical device sector should be seen as the 'whole value chain', from the product concept through to delivery to a patient, and the work of MeDe Innovation is an integral part of this broader manufacturing process. In a modern knowledge economy, value is rarely generated by the physical manufacturing itself, but rather through the innovation and creativity that goes into design and development. This is where we believe MeDe Innovation makes a difference – improving the UK's innovative manufacturing base and making things better for patients worldwide.

Professor John Fisher CBE
Centre Director

MeDe INNOVATION VISION & MISSION

The EPSRC Centre for Innovative Manufacturing in Medical Devices (MeDe Innovation) is developing advanced methods for functionally stratified design and near patient manufacturing, to enable cost effective matching of device function to the patient needs and surgical environment.

Our mission is to deliver “the **right product**, by the **right process** to the **right patient** at the **right time**” for enhanced reliability and performance.

GROWING AN INDUSTRY THAT MAKES A DIFFERENCE

UK MEDICAL TECHNOLOGY SECTOR

3,000

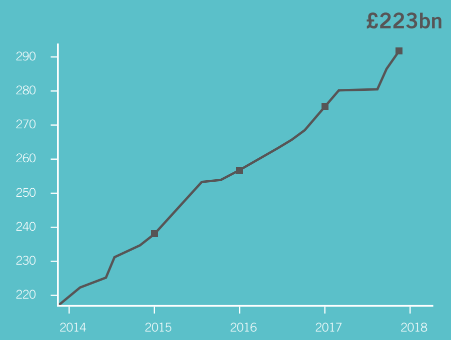
77,000

£17.6bn

The UK medical technology sector is comprised of more than **3,000 companies** (99% of which are SMEs), which employ close to **77,000 people** and have a combined **annual turnover of £17.6bn**

These companies are keen to innovate to access opportunities worldwide

Estimated global medical technology market growth



Estimated worth **£223bn worldwide with growth rates** forecast at **7% per annum** over the 4.5 years and a market size **approaching £291bn by 2018**

Supporting industry through regulatory changes

New developments in regulation and compliance has created a need for:

- enhanced pre-clinical simulation and testing
- robust designs
- fuller evaluation under the conditions the devices have to perform

Reducing the cost of care & failure rates

160,000

In England and Wales there are approximately **160,000 total hip and knee replacement** procedures performed **each year**

1 in 10

of them **are revisions** following failure

£2.3bn = £6m

The total **cost of hospital and social care** for patients with a **hip fracture** amounts to more than **£2.3bn per annum in the UK** - approximately **£6m a day**

Supporting Active Ageing

1 in 11 people are still in work at the age of 65 (from 2,500 in 1980 to 12,640 in 2010)

100 X 5

Over the last 30 years the number of centenarians (people aged 100 years or more) in the UK has increased five-fold from 2,500 in 1980 to 12, 640 in 2010

...CREATING A NEED FOR MORE ROBUST DESIGNS, PRODUCTS AND PROCEDURES IN A MORE EFFICIENT AND COST EFFECTIVE MANNER.

WORLD CLASS NATIONAL CENTRE

The EPSRC Centre for Innovative Manufacturing in Medical Devices (MeDe Innovation) is founded around five leading medical device manufacturing university research groups in the UK: Leeds, Newcastle, Nottingham, Bradford and Sheffield.

These partner universities currently have a medical devices manufacturing research portfolio of £87m in research grants (from a wide range of sources including EPSRC, BBSRC, TSB, NIHR, the Wellcome Trust and the ERC) that support the development of our technology, and £8.2m from industry. Collectively, research output and technology translation has generated £57m private sector investment in a small number of start-up companies based on IP generated by capabilities across the Centre and this is being used by these companies to support their growth and development.

Each individual university research group brings significant capabilities that are recognised nationally and internationally - creating a world leading centre that will address the innovative manufacturing needs of medical devices.

UNIVERSITY OF LEEDS

The Institute of Medical and Biological Engineering (iMBE) focuses on developing advanced methods of simulation which extend beyond current international standards, reflecting a wider range of clinical conditions; developing personalised functional computational models and models to predict functional biocompatibility.

iMBE also has significant capability in decellularisation processes for tissues. These biomimetic natural acellular scaffolds can be implanted directly and regenerated by the recipient's own stem cells. The scaffolds can be regenerated with differentiated stem cells or stem cells in-vitro in bespoke physically interactive bioreactors.

iMBE has the largest independent simulation facility in the world for total artificial joints. The facility houses more than 500m^2 of Class 2 cleanrooms and over 80 stations for full joint simulation.

NEWCASTLE UNIVERSITY

At Newcastle University, the Design, Manufacture and Materials Research Group focuses on the design, development, analysis and testing of novel materials, structures and processes.

Research addresses the design and manufacture techniques, processes and systems required to underpin the development and delivery of innovative materials and products, and much of the research is carried out with industrial partners.

UNIVERSITY OF NOTTINGHAM

The Advanced Materials Research Group (AMRG) is housed in the recently refurbished Wolfson Building, within the Material, Mechanics and Structures Research Division. The AMRG carries out research at the forefront of materials processing, materials science and materials engineering. Its research is underpinned by state-of-the-art processing and characterisation facilities.

The Group's strategic research themes include: nanotechnology (including hydrogen storage materials and novel forms of carbon); surface engineering and thermal spraying light metallic alloys and foams; novel photonic glasses; and laser processing.

UNIVERSITY OF BRADFORD

Advanced Materials Engineering research at Bradford is at the forefront of many of the new material development technologies such as electronic polymers, biomaterials, advanced ceramics, nanocomposites and 'smart' materials which are making an enormous impact on the lives of millions of people.

The Polymer Interdisciplinary Research Centre brings a unique capability in leading edge precision polymer processing, including micro moulding, small scale extrusion and solid phase orientation processing of polymers and biomaterials. The Bradford team offers novel manufacturing research in structuring polymers and biomaterials via high precision processing operations over the length scales, but particularly in small or micro scale processing, for which it leads an international network.

UNIVERSITY OF SHEFFIELD

At the University of Sheffield, the Bioengineering and Health Technologies Group undertakes pioneering research into advanced biomaterials and medical devices, making scientific and technical advances to restore the form and function of the head, neck and mouth. This is essential because the face defines human identity, and disease or trauma therefore undermines quality of life. Technological advances substantially improve clinical outcomes, and the group brings industry, clinicians, scientists and engineers together to make a difference to people worldwide.

RESEARCH LEADERSHIP

Professor John Fisher
Director of the Centre for Innovative Manufacturing in Medical Devices

Professor John Fisher is Director of the Institute of Medical and Biological Engineering at the University of Leeds, which houses the largest academic facility in the world for studying how artificial joints function and wear over time.

As a serial entrepreneur and founder of three spin out companies (one of which is AIM listed), Professor Fisher has extensive commercial experience; some of his designs for longer lasting joint replacements are now used worldwide and his international collaborations include the USA, Europe, China and Japan.

Professor Fisher's current research is developing simulation methods and models to improve the design of replacement joints, and the development of new tissue engineering techniques and regenerative devices for use in the musculoskeletal system.

Professor Fisher is a member of EPSRC Council, a Fellow of Royal Academy of Engineering and the Academy of Medical Sciences.

Dr Ceri Williams
Deputy Director of the Centre for Innovative Manufacturing in Medical Devices

Dr Ceri Williams has considerable experience of working in economic development and innovation delivery. Dr Williams provides operational leadership of MeDe Innovation to connect the Centre to UK and global academics, industry, clinicians and intermediaries including regulators and networks. She has considerable experience of leading research translation and has established innovation management systems and processes to give confidence to companies to invest in technologies delivered from university research.

Dr Williams is a member of the International Society for Professional Innovation Managers and has a PhD in Chemical and Process Engineering from the University of Leeds.

Professor Kenny Dalgarno
Deputy Director of the Centre for Innovative Manufacturing in Medical Devices

Professor Kenny Dalgarno is the Sir James Woodeson Professor of Manufacturing Engineering at Newcastle University, Deputy Director of the Arthritis Research UK Tissue Engineering Centre, and co-ordinator of the FP7 programme RESTORATION (Resorbable Ceramic Biocomposites for Orthopaedic and Maxillofacial Applications).

He leads a multi-disciplinary research team at Newcastle which is developing new biofabrication and 3D printing technologies for applications in biomedical engineering, tissue engineering and regenerative medicine. The research is supported by the EPSRC, the European Commission, Arthritis Research UK, the Carbon Trust and industry.

Professor David Grant
Co-Investigator, University of Nottingham

Professor David Grant is Head of the University of Nottingham's Advanced Materials Research Group where his own research focuses on biomaterials, coatings and energy storage. A particular interest here is in degradable coatings, nanostructures and composites for bone integration. Projects he is currently working on range from developing new materials right through to manufacturing devices and developing new structures for tissue-engineered projects.

Nottingham has a strong focus on 'delivering beyond blue skies' and Professor Grant's expertise in materials and manufacturing, along with his strong industrial links, have led to many partnership projects investigating biomaterial applications.

Professor Phil Coates
Co-Investigator, University of Bradford

Professor Phil Coates leads a team of over 50 researchers at the University of Bradford studying the processes and technology for manufacturing high-value polymer products for a range of sectors, including healthcare and medical devices. His research laboratory incorporates both the skills and the technology for leading edge in-process monitoring, analysis and control to develop scalable manufacturing processes with robust quality assurance and control.

His research has a substantial international dimension; he is Director of the internationally recognised Polymer Interdisciplinary Research Centre and of the RCUK Science Bridges China, a government-sponsored £8 million collaboration between UK and Chinese universities, focusing on advanced materials for healthcare technologies through a research and open innovation platform.

Professor Paul Hatton
Co-Investigator, University of Sheffield

Professor Paul Hatton's internationally leading research focuses on bioengineering and health technologies. A particular interest is in the use of biomaterials to promote tissue regeneration and restoration of function – an approach which he believes is preferable to drug-based therapies as the regulatory barriers are more manageable. More recently, Professor Hatton's research has included the evaluation of innovative manufacturing technologies for producing advanced biomaterials, medical devices and regenerative therapies.

Professor Hatton has more than 20 years' experience working with commercial partners, and has close links with the medical device industry as well as within the NHS.

WHAT IS 'STRATIFIED DESIGN AND MANUFACTURE'?

Stratified design and manufacture enables medical devices and implants to be more closely matched to a patient's needs, reducing the risks of adverse reactions and ensuring better long term performance. This is achieved either through customising a design to a specific individual, or by stratifying patients on the basis of relevant characteristics that enable the right design to be chosen to fit each group.

The research challenges

MeDe Innovation is applying the concept of stratified design and manufacture in Class III orthopaedic devices – such as replacement hips and knees – with the aim of substantially improving their longevity and reliability.

Class III devices are those where the outcome of the operation is most uncertain and the risk of failure the greatest. Lack of success is most commonly due to a mismatch between the design of the implant and the different variables within patients. Improving the match should therefore improve the outcome.

The first research challenge is to understand which variables most impact on the outcome of a procedure and to develop tools so these can be matched against different designs of orthopaedic devices. These variables might include genetic profile, ethnic background or the stage to which the disease has progressed. Once the most important variables are known, it should be possible to stratify patients into different groups based on which of these variables are present and match the most appropriate design to them.

The aim will be to take these variables into account at the design stage, enabling a range of devices to be created which can be manufactured in bulk using conventional methods – and so be very cost-effective – yet allow a more sophisticated match with each patient.

The second research challenge is to enable individualised designs to be manufactured in the clinic, while still remaining cost-effective. This cannot be done using conventional manufacturing methods as one-off devices need to use innovative manufacturing approaches, such as 3D printing. While specialist manufacturers can already produce devices to an individual design, if these could be made nearer to the patient – in the hospital or clinic, or even in the operating theatre itself – patients could be treated more quickly and be matched more closely to the medical device or implant. As this will require new methods of manufacture, a key aim of the research will be to understand how these manufacturing processes affect the materials from which the devices are made, to ensure the final products have the properties required.

INNOVATION CHALLENGES

1 STRATIFIED DESIGN AND MANUFACTURE OF MEDICAL DEVICES

Theme 1A: Functionally stratified design and manufacture of hip and knee joints

RESEARCH CHALLENGES

a) To develop models characterising variations in geometry, properties, surgical delivery and activities of the patient population.

b) To develop simulation models predicting biomechanical and biotribological function.

c) To apply these new approaches to hip and knee prostheses.

Theme 1B: Stratified bioprocesses for the manufacture and functional simulation of acellular scaffolds

RESEARCH CHALLENGES

a) To determine and control the variation in the manufacturing bioprocess for acellular bone and cartilage scaffolds, producing a product range which can be matched to surgical and patient needs.

b) Applying stratified design and simulation methods to match the properties of the acellular scaffold to the patient, based on functional performance.

Theme 1C: Stratified design and manufacture of nonwoven collagen scaffolds

RESEARCH CHALLENGES

a) To control the physical properties and reproducibility of collagen-based synthetic scaffolds, based upon a new, multi-route manufacturing platform.

b) To implement a functionally stratified approach to the design and manufacture of scaffolds so that the structure and properties meet specific patient needs.

Theme 1D: Manufacture of bioresorbable multiphase fixation devices and virtual modelling

RESEARCH CHALLENGE

a) The development and application of stratified design and manufacture processes for a new resorbable fracture fixation device. This is achieved by combining modelling for stratified patient groups with specific new manufacturing processing routes to enhance capability in delivering devices to order to customers.

2 MANUFACTURE AT THE POINT OF NEED

Theme 2A: Minimally invasive implantation of bioactive materials

RESEARCH CHALLENGES

a) Development of micro-scale extrusion and droplet deposition equipment which can be operated through an arthroscope.

b) Creation of mechanically robust and biologically enhanced structures in-vivo.

Theme 2B: Processes for in-clinic manufacture

RESEARCH CHALLENGES

a) Co-processing of cells and structural biomaterials whilst maintaining mechanical and biological function.

b) Development of micro-factories for in-clinic use.

Research
Challenges

THEME 1A: FUNCTIONALLY STRATIFIED DESIGN AND MANUFACTURE OF HIP AND KNEE JOINTS

Around the world, populations differ - not just in the size and shapes of their bodies but also in the way they live their lives – and this has an impact in terms of wear and tear on their hips and knees. This area of MeDe Innovation research is helping medical device companies develop both a range of designs for replacement hip and knee joints that can respond to these variations and methods of choosing the design that best matches the needs of different patient groups.

What’s the challenge?

The way replacement hip and knee joints are currently designed doesn’t take into account the huge variation that exists around the world in terms of patient anatomy, the way joints are used, surgical techniques and national healthcare systems. For example, people in the East tend to squat, whereas in the West people spend more time sitting down, young people are typically more active than older people and this means their hip and knee joints – and diseases that affect them – are very different. But not all differences impact on how well a replacement joint will work – so a key challenge is to identify which parameters are the most important and should be taken into account in the design.

“There are thousands of possible parameters that might affect the outcome of a hip or knee replacement. We need to identify the most important, which will have the greatest impact on patients.”

Professor John Fisher, University of Leeds

Our approach

We’re gathering new data and using existing data – such as patient x-rays following surgery and implant retrievals – to help us define the most important variables which affect the outcome of a hip or knee replacement.

We’re working on a number of research projects in areas where we’ve identified key variables and differences that have the most impact. We're developing computer models and simulation systems that allow us to predict function and performance for different combinations of these variables. For each of these projects, we can then carry out experimental simulations on a limited range of designs, to understand and validate how they perform in different situations and the impact of each variable on the final outcome, so that we can determine which design would be most effective for each group of patients.

Working with industry, we aim to help companies adopt enhanced design, simulation and testing systems more quickly into their product development processes, to enable new stratified product ranges to be created.

In some cases this might help companies gain the necessary approvals for their devices in particular markets, such as China or India. For hips – where surgical positioning is one of the key factors – it might lead to a new design that can more effectively take into account variations in surgery or help develop new guidelines on the level of surgical precision required.

“By analysing the biological consequences of wear of hip and knee joint replacements, we can predict more accurately how joint replacements will work in patients, resulting in a better design.”

Professor Eileen Ingham, University of Leeds

PARTNERS

University of Leeds:
Professor John Fisher
Professor Eileen Ingham
Dr Louise Jennings

Xi'an Jiaotong University, China

NIHR Leeds Musculoskeletal Biomedical Research Unit

Simulation Solutions Ltd

DePuy Synthes

PARTNERS

University of Leeds:
Professor Eileen Ingham,
Professor John Fisher and
Professor Ruth Wilcox

NHS Blood and Transplant
Tissue Services

Tissue Regenix Group plc

THEME 1B: STRATIFIED BIOPROCESSES FOR THE MANUFACTURE AND FUNCTIONAL SIMULATION OF ACELLULAR SCAFFOLDS

Cartilage and the bone to which it is attached are often damaged by injury or general wear. Current repair methods do not provide a fully functional, long-lasting solution, increasing the risk of osteoarthritis. This area of MeDe Innovation research is developing grafts or scaffolds that can regenerate in the patient's body to create a better, longer-lasting repair while ensuring these implants can be efficiently manufactured and still work as required.

What's the challenge?

Existing approaches used to produce acellular biological scaffolds for the replacement of ligaments and heart valves have been shown to have limitations for use with cartilage due to its distinctive structure, in which the collagenous matrix is filled with a gel. This gives the cartilage its unique ability to dissipate loads and protect the joint. Established decellularisation methods lead to loss of this gel. The challenge is to develop a decellularisation process that maintains the structure and function of the cartilage matrix. These implants need to be matched to the patient, enabling the patient's own tissue to grow into them to create a more natural repair. They also need to be designed in such a way to enable efficient manufacture at scale.

"If we can analyse how the graft behaves when the match between the patient and the material is less than perfect, we can find out what level of mismatch can be tolerated. This will help improve the manufacture of these biological scaffolds and help control their variability."

Professor John Fisher, University of Leeds

Our approach

We're applying our existing expertise in implants and grafts – both in design and manufacture – to develop new cartilage-on-bone grafts. We're selecting the most applicable design and manufacture processes to create the most efficient process, which will be scalable for industrial production.

We're trying to gain a fundamental insight into how each part of the manufacturing process affects the final product, so we can improve the process. For example, graft products need to be sterile for safety, but chemicals used for sterilisation are incompatible with industry processes. We're working on how different methods of sterilisation will impact on our grafts, which in turn will inform how these are manufactured.

We're also ensuring that the range of products we develop matches the needs of the individual patient, using simulation and computational modelling to assess their performance in relation to different criteria. By trialling our grafts in knee joint simulators, we're able to see how different materials perform in different situations.

Using this data in our computational models will help us to develop tools to create a better match between the patient and the graft, so it can become integral to the patient's body, restoring and improving joint performance and reliability.

"We're defining the manufacturing processes for a range of products which match both the surgical procedure and the patient, ensuring enhanced performance and reliability."

Professor Eileen Ingham, University of Leeds

THEME 1C: STRATIFIED DESIGN AND MANUFACTURE OF NONWOVEN COLLAGEN SCAFFOLDS

Collagen is a protein in the human body, found particularly in skin, ligaments and tendon, which can be used to create material for use in surgery. Collagen is also a natural haemostat – it controls bleeding – which is an added benefit in surgical procedures. This area of MeDe Innovation research is using collagen to produce material for repairing bone and soft tissue in the mouth and jaw, which can be customised by the surgeon to fit the needs of each patient.

What's the challenge?

For material made of collagen to be used in surgery, it needs to create no adverse reaction in the patient, be strong and retain its physical properties when implanted. The human body is a damp environment and some collagenous materials can deteriorate in these conditions.

The material needs to be designed and manufactured so that it can be modified by the surgeon to fit each patient during the operation. However, to be affordable, it needs to be designed in such a way that it can be manufactured in bulk, but still be personalised for each patient.

"Customising the material to the needs of the individual patient increases the likelihood of its success, resulting in fewer complications and a permanent repair. We'll be putting together a demonstrator kit to show that it meets surgeons' needs, works well and is safe for patients."

Professor Stephen Russell,
University of Leeds

Our approach

We've developed a technique for making synthetic collagen following extraction from biological tissues, which will enable our material to be manufactured in bulk at an affordable price. We're developing a 3D fabric, using textile manufacturing methods, which will have the right properties and integral strength for use in bone and tissue repair. In particular, we're working on making the collagen stable in water, so it can absorb liquid but still retain its strength and other functional properties.

We're looking at two possible ways the surgeon can customise the material: cutting and shaping the material to the correct size and combining different components from a kit to create the right physical properties for each patient. We're designing the material so that it can be fixed in place and its mechanical properties can be customised using light that operates at specific wavelengths – a technique already used in dentistry.

The first applications for the material will be in dental and facial surgery, for example as a graft to repair bone defects, and we're working with dental clinicians to develop these. However, we also hope the material will be used in a wider range of bone repairs.

We have the techniques and machinery to make collagen sheets continuously and are now in the process of meeting commercial collagen suppliers who can provide us with the quantities we need to industrially develop the material.

"We're adapting textile manufacturing methods to create a customisable biomimetic material and, by using natural polymers, we aim to reduce immunological reactions in patients. The challenge is to adapt large scale manufacturing techniques to a biomaterial like collagen without affecting its structure and biofunctionality."

Dr Giuseppe Tronci, University of Leeds

PARTNERS

University of Leeds:
Professor Stephen Russell
Professor David Wood
Dr Giuseppe Tronci
Professor Jennifer Kirkham
Professor Eileen Ingham
Dr Xuebin Yang

NIRI Ltd

Leeds Teaching Hospitals NHS Trust (LTHT)

Leeds Dental Institute

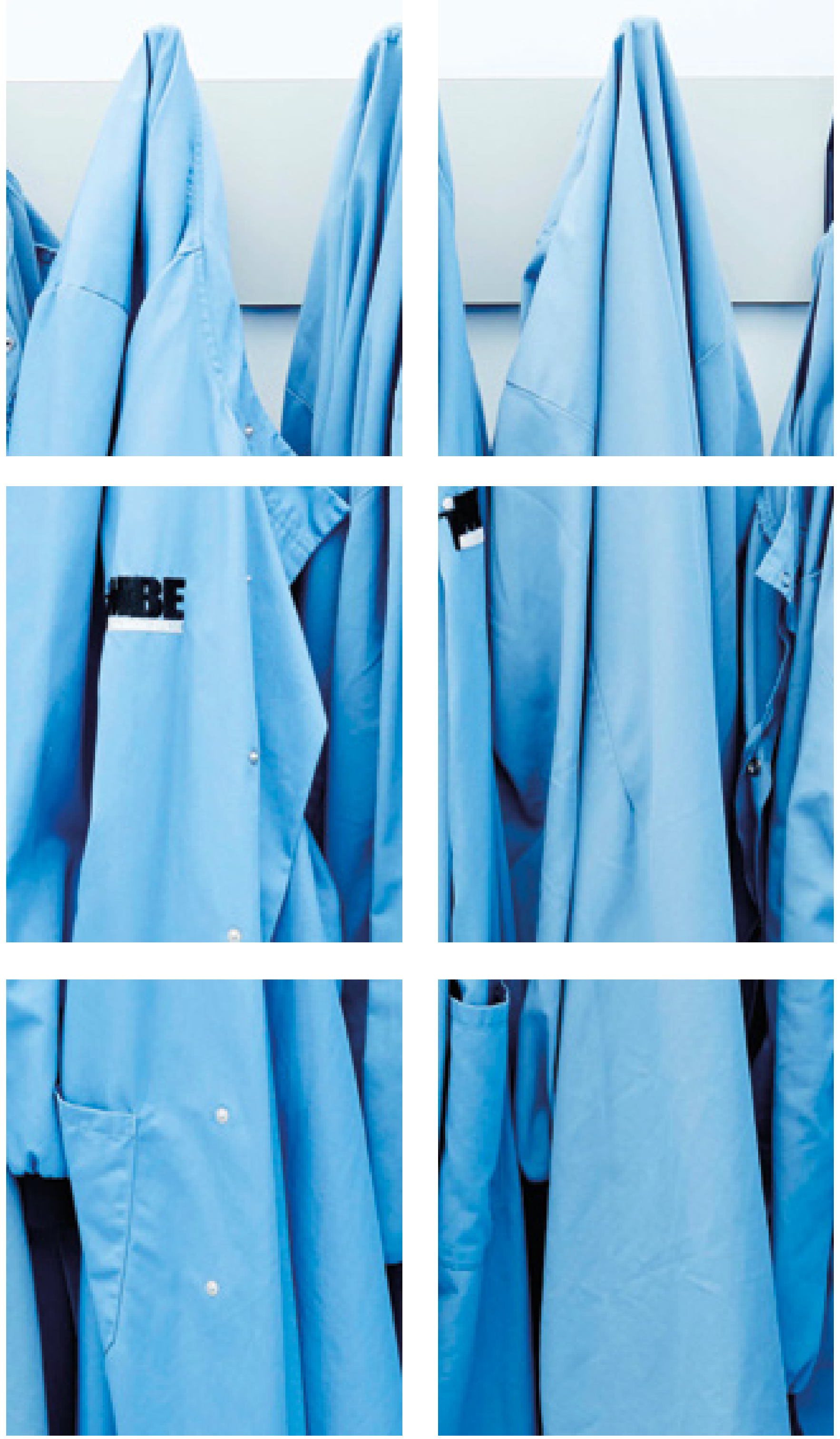
PARTNERS

University of Nottingham:
Professor David Grant
Dr Ifty Ahmed
Dr Donal McNally
Professor Nick Warrior
Professor Ed Lester
Dr Joel Segal

University of Bradford:
Professor Phil Coates
Dr Fin Caton-Rose

University of Leeds:
Professor Ruth Wilcox

Nottingham University Hospitals



THEME 1D: MANUFACTURE OF FULLY BIORESORBABLE MULTIPHASE FIXATION DEVICES TO ORDER

Current methods for healing multiple fractures often require the bone to be 'pinned'. Surgeons insert metal rods to hold the bone in place until it can mend. Removing the pins at the end of this process, however, requires another operation for the patient. MeDe Innovation is leading research into developing new fixation devices that can degrade naturally. The aim is to develop designs and manufacturing routes that will enable companies to produce devices tailored to specific patient groups.

What's the challenge?

Finding alternative materials for metal fixation devices is not straightforward: the material needs to be strong enough and stiff enough to support the bone while it heals, but then it needs to break down and be resorbed by the body. Once the devices have been designed, a further challenge is to identify cost-effective manufacturing processes, rapid turnaround for stratified patient groups, and clinical technologies that can support surgeons in implanting the devices accurately.

"We've already built a critical mass of projects around this theme which is helping us to move forward quickly and which have stimulated interest and collaborations from our clinical and industrial colleagues. It is exciting seeing these projects develop working together with our partners in Nottingham, Leeds and Bradford."

Professor David Grant, University of Nottingham

Our approach

We're using degradable phosphate-based glass fibres in a degradable polymer matrix as the basis for our implants. These can be tolerated by the body, but their degradation can also be closely controlled. We're also researching coatings to protect the surface of the implants, prevent bacteria from forming and promote bone growth. Studies into degradable glass-based coatings are still in their infancy and our aim is to produce a suite of materials that can be used in different medical settings and different medical devices.

Although new materials can improve the long term wellbeing of patients for whom implants are necessary, the challenge of inserting them accurately also needs to be addressed as this can be extremely difficult for surgeons to do.

To do this we are developing software that can convert traditional 2D images from MRI or CT scans and convert them into 3D representations. This will give surgeons much more accurate information about where to insert the device. Using computer technology to model the spine, we can provide a much clearer picture of the bone, or even use rapid prototyping to produce a model of the area that surgeons could use.

Device manufacturers will also find this extremely useful to be able to produce devices for specific patient groups. We're using device simulation and computer modelling techniques to evaluate some of the implants before they go forward into pre-clinical tests.

THEME 2A: MINIMALLY INVASIVE IMPLANTATION OF BIOACTIVE MATERIALS

Total joint replacement is an effective treatment for late-stage joint problems. However, when a patient consults a doctor about early-stage joint problems, there is currently no widely recommended treatment option available.

Problems involving damage to the cartilage and underlying bones in the hip, knee and other joints are known as osteochondral defects. If more of these defects can be treated earlier, and in a minimally invasive way, then the patient's rehabilitation – and the cost to the healthcare system – can be minimised.

What's the challenge?

The challenge in using minimally invasive approaches is that any synthetic plug used in the treatment of osteochondral defects must be small and strong enough to be inserted into the joint using the special surgical instruments used for these procedures. In addition, to enable faster repair, the plugs must also be bioactive – capable of interacting with the body. Ideally they would also be resorbable, meaning the plug will break down and be absorbed by the body once the repair is made, leaving natural tissue. Potential solutions to this challenge must show benefits for both the surgeon and the patient.

There are several resorbable materials currently used in surgery but these are not robust enough to be used with minimally invasive surgical instruments.

"We believe that the technologies we're developing are stronger from the collaborative relationships that we're building and we intend to create a pipeline of developments to maintain that momentum."

Professor Kenny Dalgarno, Newcastle University

Our approach

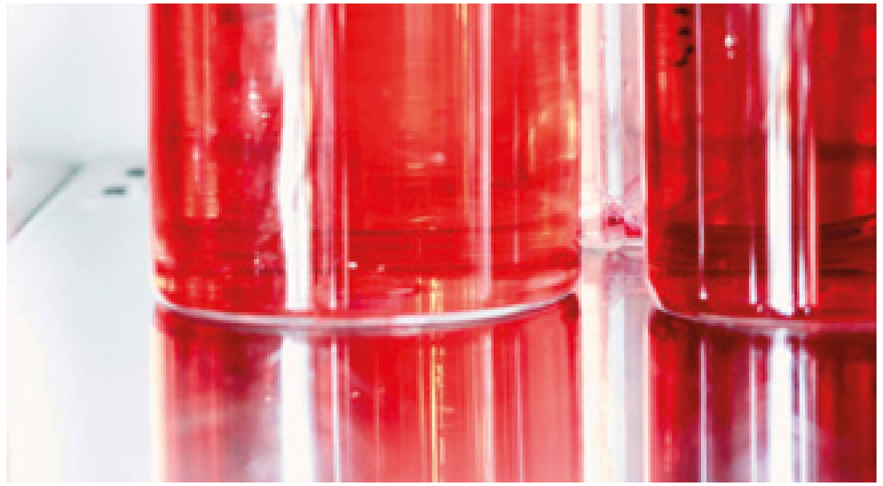
We're examining two approaches: (i) developing a resorbable bioactive material that can be implanted as a liquid and which then quickly hardens to form a plug; and (ii) developing a solid plug which is robust enough to be inserted in a minimally invasive procedure. These would restore function to the joint faster and enable a shorter recovery time.

As collaborative partners, we're combining our research strengths and industry specialisms to develop these approaches. Using novel polymer processing we're looking at coating the implant site with an effective temporary shield to protect other parts of the body when it's being implanted, whilst allowing the bioactive materials to repair the damaged area. We're also developing the best bioceramic structures for implantation. Our industry partners are working with us to develop the software we need for accurate imaging and to advise on surgical instrumentation and device design.

We're also working closely with clinicians on this project, to make sure that the identified solutions will be fit for purpose in a clinical setting.

"We're working on implantable devices that boost tissue regeneration and restore function, and this technology could be adopted and adapted for a whole range of other areas such as craniofacial surgery."

Professor Paul Hatton, University of Sheffield



PARTNERS

Newcastle University:
Professor Kenny Dalgarno
Dr Matthew German
Dr Oana Bretcanu
Dr David Fulton

University of Bradford:
Professor Phil Coates
Dr Pete Twigg
Dr Fin Caton-Rose

University of Nottingham:
Professor David Grant
Dr Ifty Ahmed

University of Sheffield:
Professor Paul Hatton

University of Cambridge:
Professor Andrew McCaskie

Materialise NV

JRI Orthopaedics Ltd

Surgical Innovations Ltd

Glass Technology Services Ltd

Ceramisys Ltd

PARTNERS

Newcastle University:
Professor Kenny Dalgarno
Dr Matthew German
Dr Oana Bretcanu
Dr David Fulton

University of Bradford:
Professor Phil Coates
Dr Pete Twigg
Dr Fin Caton-Rose

University of Nottingham:
Professor David Grant
Dr Ifty Ahmed

University of Cambridge:
Professor Andrew McCaskie

Materialise NV

JRI Orthopaedics Ltd

Surgical Innovations Ltd

Glass Technology Services Ltd

THEME 2B: PROCESSES FOR IN-CLINIC MANUFACTURE

Medical implants that are personalised to an individual patient are already a reality, but they are currently manufactured to order by specialised companies, adding time and cost to the process. If surgeons could make these implants themselves in the clinic – even during an operation itself – patients could be treated more quickly and efficiently. Because the manufacture and customisation would take place with the patient present, sometimes in response to what's found during an operation and incorporating the patient's own cells, the resulting implant could also be a closer fit, resulting in a longer lasting repair.

What's the challenge?

To ensure repairs to bone and cartilage are successful and long-lasting, the patient's tissue needs to grow around it, and this can be accelerated by incorporating a patient's own cells or other biological material into the implant. The high temperatures required in most manufacturing techniques for implants damage human cells, so a key challenge is to develop techniques which enable both cells and biomaterials to be processed together, while still retaining their mechanical and biological properties.

For use within a clinical environment the machines need to be straightforward to operate, and if an implant is to be made during an operation, the process also needs to be quick. The second challenge is to develop 'micro-factories' able to make personalised implants for use in bone and cartilage operations that are cost-effective, fast and automated.

"Novel materials won't necessarily make a good product. You need to understand how those materials behave during the manufacturing process and then adapt those processes in order to get the results you need."

Professor Phil Coates, University of Bradford

Our approach

We're working on combining different materials and processing times to develop initial designs for implants for use in bone and cartilage surgery, which can be adapted to fit an individual patient.

We've developed ways to make structures of biopolymers and bioceramics into implants and scaffolds, into which the patient's own tissue can grow. Feasibility studies are already underway to test these new techniques.

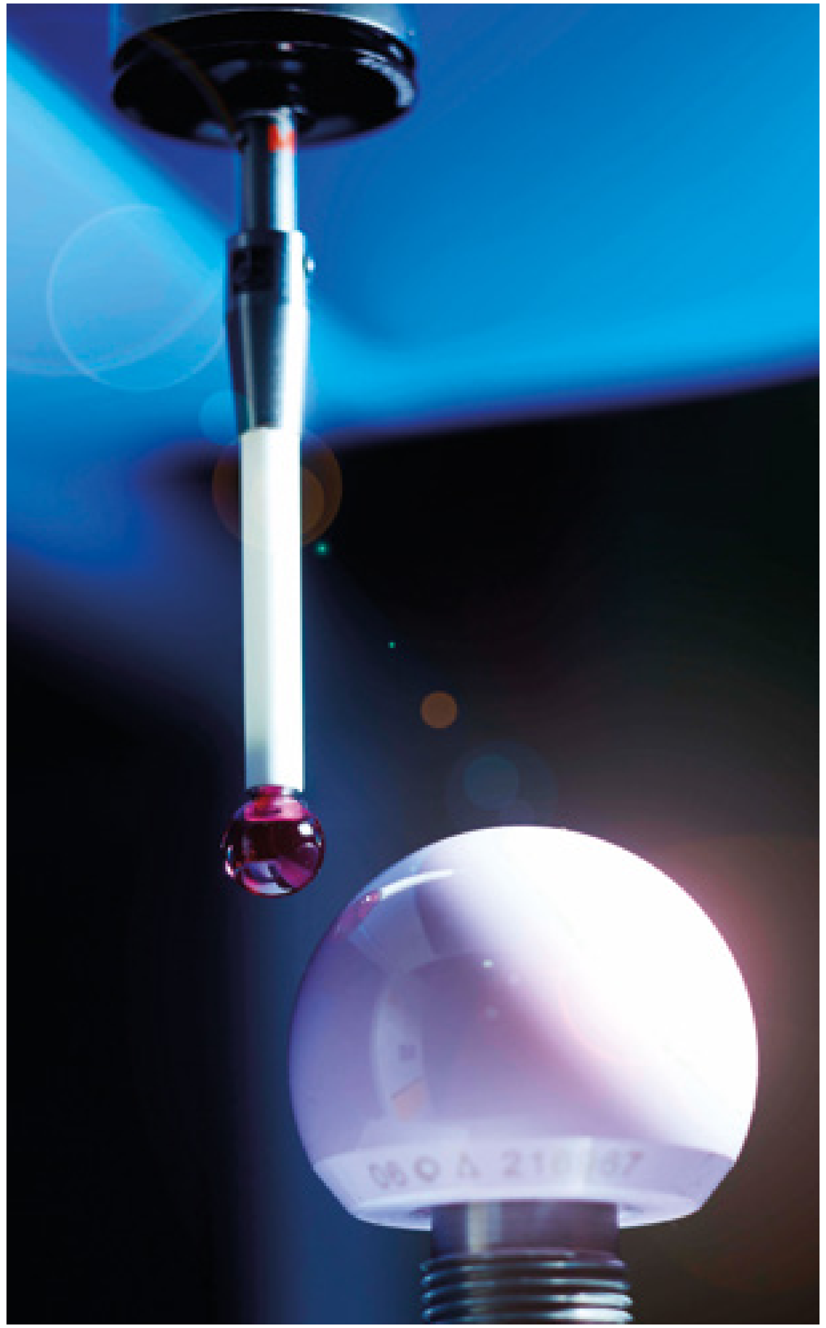
We're looking at how surgeons could combine cells and other biomolecules from the patient into the implant during the operation. To protect the properties of the cells while they're being processed, we've developed a process to coat the cells with polymers. The coating dissolves in the body, allowing the patient's cells to populate the implant and help the repair process.

Once the basic strategies for structural and biological material processing are in place, we will develop specific small size manufacturing units (known as micro-factories) for use within clinical environments.

"By combining fundamental research with manufacturing expertise we aim to create products that will enable patients to receive better treatment, faster."

Professor Kenny Dalgarno, Newcastle University

MEETING THE FUTURE NEEDS OF THE MEDICAL DEVICE COMMUNITY



Feasibility study funding winners: addressing key challenges in orthopaedic medical device design and manufacture

As part of MeDe Innovation's commitment to undertake and identify early-stage research ideas, the first tranche of feasibility study awards have been made to investigator teams from across the UK.

MeDe Innovation aims to widen its national reach whilst growing the research capabilities of the investigators supported by these awards. The successful projects have a defined clinical need, significant commercial potential and will identify the key challenges and questions that are not currently being addressed in orthopaedic medical device design and manufacture research.

The £50k awards will allow investigators to develop the evidence and refine the research questions that will underpin the development of full proposals for funding that can be submitted to existing national and global funding schemes.

A panel of experts from industry and academia selected the winners from proposals put forward by over 20 universities, clinicians and companies. The funded projects showed an exemplary fit with the research challenges that MeDe Innovation is addressing, offered significant potential and had support from industry. All three projects are due to start by autumn 2014.

Dr Ceri Williams, Deputy Director of MeDe Innovation, says: "We're looking for dynamic investigators with exciting, early-stage research ideas and the three projects selected have superb potential. We're planning a further call for Fresh Ideas proposals in the autumn and look forward to seeing more innovative research thinking."

The feasibility study projects are:

3D printing of lumbar fusion cage based POSS-nanocomposite biomaterial

Professor Alexander M Seifalian & Dr Deepak M Kalaskar, University College London

Lower back pain is a common problem and is considered to be a major health concern due to high treatment costs and rehabilitation time.

Using a combination of novel nanotechnology-based biomaterials and stem cells, the investigators propose to develop a new lumbar fusion cage, a device used in the repair and treatment of damaged discs and other lower back conditions.

"We're aiming to use a 3D printer to manufacture the lumbar cages and, during surgery, incorporate stem cells from the patient to the cage before implanting at the point of need," explains Professor Seifalian. "Our solution is minimally-invasive, personalised and regenerative, and will reduce both surgical time and patient recovery time. This award will crucially enable us to gather the data needed to prepare for pre-clinical testing and application for further funding."

Advanced manufacture of thermo-sensitive medical devices for targeted regeneration of endochondral bone at the bone-tissue interface

Dr Nicholas Dunne & Dr Helen McCarthy, Queen's University Belfast

Damage to the ligaments and cartilage in the knee following injury can often lead to osteoarthritis, one of the most common problems that requires surgical reconstruction.

The investigators will test the viability of the production and manufacture of a unique way to support the reattachment of soft tissues to the bone – a particular challenge when repairing the knee following injury. The new biomimetic method combines a number of technologies to create an interface between tissue and bone that would enable a minimally invasive treatment for patients.

"We are very excited to have received a feasibility grant award from MeDe Innovation," says Dr Dunne. "Globally, nearly one million cruciate ligament or meniscal rupture reconstructions are performed every year, and this award will give us the opportunity to develop our unique approach to tackling this societal and economic problem using minimally invasive surgical intervention."

Preliminary study of expandable osteochondral scaffolds in achieving mechanical stability and biological fixation for large osteochondral defect repairs

Dr Chaozong Liu, Prof Gordon Blunn & Mr Andrew Goldberg, University College London

Patients with severe damage to the cartilage within their joints suffer pain, experience mobility problems and often go on to require a total joint replacement.

This project will examine whether new expandable, biomimetic scaffolds produced by 3D printing are strong enough and fix in place effectively to repair the damaged joint cartilage and avoid joint replacement surgery.

Mr Andrew Goldberg, Consultant Orthopaedic Surgeon at the Royal National Orthopaedic Hospital, says: "If successful, this would allow the development of a one-step surgical treatment, which would offer the potential to improve patients' quality of life by easing their pain and recovering mobility much more quickly."

COMMUNITY BUILDING

Dissemination of research is central to MeDe Innovation's mission and we are already building a strong community to ensure we gain input from those working across the medical device sector in the UK:

MeDe Innovation launch conference

Our launch event was attended by over 230 delegates from across the medical devices sector – including many representatives from industry, clinical, design and manufacturing, regulatory and standards backgrounds.

Along with presentations on industry challenges from our collaborators, delegates were given the opportunity to question panels of experts in the sector; make contacts and learn more about our partners in the exhibition area; and to make suggestions and give feedback on how we can support the network of associate members.

230 ATTENDEES

85% MADE CONTACTS TO FOLLOW UP

During 2014, MeDe Innovation focused on raising awareness of its brand to academics, industrialists and clinicians interested in innovative manufacturing in medical devices through the sponsorship of existing events already successfully operating in the sector.

UK Medical Device Manufacturing Conference and Med Tech Innovation EXPO

"The event gave us the opportunity to show how our software solutions can be applied in the medical devices sector. Patients aren't the same - and we're looking forward to working with the other partners and MeDe Innovation to produce more robust design and manufacturing processes to accommodate variations in patients, populations and surgery," said exhibitor Dr Rebecca Bryan of Simpleware Ltd.

Med-Tech Innovation is a leading magazine, website and event platform for the UK medical device research, design and manufacturing community. It is the only information resource that provides dedicated technical, product, industry, academic and association content for and about the UK marketplace.

We hosted an exhibition space at the event, introducing MeDe Innovation and its focus to this key audience.

2014 saw the EXPO run in partnership with the UK Medical Device Manufacturing Conference, hosted by Medilink UK and ABHI (Association of British Healthcare Industries).

The event attracted around 1,200 visitors, at which MeDe Innovation Deputy Director, Dr Ceri Williams, delivered a keynote presentation on the latest drivers and trends in medical technology innovation and perspectives on the value of collaboration.

VISTORS PASS

1176 VISITORS TO THE EXPO, 63% MEDICAL DEVICE MANUFACTURERS

During 2014 MeDe Innovation also recruited associate members whilst exhibiting at:

2014 Materials Research Exchange: UK Advanced Materials Showcase, February, Coventry

Innovations in Healthcare, March, Sheffield

GREAT Technologies, July, Bradford

Bath Biomechanics Symposium 2014, September, Bath

Regener8 Annual Conference: The Pathway to Innovation for Regenerative Therapies, September, Leeds

Manufacturing the Future Conference, September, Glasgow Science Centre

Newsletters and website

MeDe Innovation provides a knowledge hub for the MeDe Innovation Network via our e-newsletters and social networks.

MeDe Innovation aims to not only inform, but also to connect, enabling businesses, policy makers, regulators, intermediaries, academics and clinicians to share information, knowledge and ideas and debate the challenges and issues facing the community.

This year we piloted the inclusion of news from our partners as part of these communications – adding value for members and further developing a sense of community for the network.

37 NEWS STORIES AND **23 EVENTS** SHARED TO OUR COMMUNITY

2,154 UNIQUE WEBSITE VISITORS

Membership

175 Academic members

144 Industry members

18 Clinical members

SHAPING THE FUTURE OF OUR RESEARCH

Disseminating research and crowdsourcing ideas

We are running three research workshops in 2014, focusing on each of our three of our key research areas.

These will provide an opportunity to:

- Hear updates on the latest scientific progress from MeDe Innovation's academic and industrial partners
- Gain regulatory, clinical and intellectual property perspectives from experts in the field
- Question expert panels for opinions and insights
- Identify new opportunities and collaborations to exploit the emerging research

THURSDAY 18TH SEPTEMBER 2014

HALIFAX HALL, UNIVERSITY OF SHEFFIELD

Biological and Biomimetic Materials for Medical Devices and Health Technologies

Biological and biomimetic materials offer unusual properties that underpin their use as orthopaedic medical devices.

Recent scientific advances have unlocked even greater potential for **improved clinical performance**, including regenerative properties, but at the same time this raises challenges for both manufacturers and regulators.

This workshop will explore both recent scientific progress and the regulatory environment, ultimately contributing to a strategy to further exploit the opportunities offered by these exciting materials.

Register at https://biological-biomimetic.eventbrite.co.uk

New Strategies for Treating MSK Disorders: in-clinic manufacture and minimally invasive implantation of materials

Surgical techniques must deliver the optimal patient experience at the lowest life-cycle cost.

MeDe Innovation is seeking to develop effective therapies which are customised to the patient and disease state, aiming for delivery with minimum disruption - ideally allowing the patient to go home the same day.

This combination of efficiency, personalised treatment and minimised hospital stays for musculoskeletal applications requires new thinking in terms of the **deployment of load bearing materials** - moving the fabrication of devices closer to the patient.

This research workshop will examine how new approaches to **materials processing and manufacture** can help us achieve the right product, by the right process, to the right patient at the right time.

Register at https://in-clinic-manufacture.eventbrite.co.uk

THURSDAY 30TH OCTOBER 2014

CENTRE FOR LIFE, NEWCASTLE

MONDAY 17TH NOVEMBER 2014

UNIVERSITY HOUSE, UNIVERSITY OF LEEDS

Functionally Stratified Design and Manufacture of Orthopaedic Devices

Patient and surgical variations have major effects on the failure rates, patient satisfaction, pain scores and other quality of life outcomes of many musculoskeletal interventions.

Matching the right patient to the right product at the right time remains a challenge in the way devices are designed and manufactured.

Through MeDe Innovation, a new approach is being undertaken **to improve testing methods** and implement **functional stratification** into the design and manufacture process.

This workshop will explore recent advances in **pre-clinical testing** which capture the effects of patient and surgical variability and the development of new products encompassing stratified design and manufacture.

Register at https://stratified-design.eventbrite.co.uk

MeDe Innovation Network: raising the profile of UK medical device manufacturing capability

We are creating a dedicated online database and easy access mechanism for UK medical device manufacturing capability.

The database will raise the profile and prominence of UK medical device manufacturing research, and highlight the very best of UK facilities and expertise to foster routes for academic and industrial engagement.

Join the MeDe Innovation Network to be the first to hear about the database launch.

http://mede-innovation.ac.uk/join-us/

MeDe Innovation Clinical Network: establishing a dedicated network of musculoskeletal surgeons

Led by Andrew McCaskie, Professor of Orthopaedic Surgery at the University of Cambridge, this network aims to support MeDe Innovation through bringing together clinicians and relevant scientists to refine and propose research.

OUR RESEARCHERS

The quality of our research is underpinned by the experiences, expertise and passion of our people. MeDe Innovation's early career researchers are essential to the delivery of our outputs, and ensuring they gain the essential experiences for their future career is at the heart of what we do.

In January 2014 we launched an Early Career Researcher (ECR) forum to further the professional development of rising stars in innovative manufacturing in medical devices. The initial meeting attracted over 40 researchers from academia and industry, keen to create a united voice and a support mechanism for the forum's membership.

Here are some examples of how MeDe Innovation is helping to broaden knowledge and experience of our rising stars.

Visiting a global manufacturer of orthopaedic implants

Dr Marlene Mengoni,
Research Fellow,
University of Leeds

"On 28 May 2014, the Early Career Researcher forum members visited JRI Orthopaedics Ltd's factory in Sheffield where its manufacturing, research, product development, customer service, marketing, warehousing and distribution is all centred.

Edward Draper, JRI's Innovation Manager, gave us an introduction to the company and an overview of its intentions for the existing product lines and new product developments. JRI faces some exciting times with the technologies underpinning joint replacement and regeneration changing rapidly – as are the manufacturing processes. The JRI team is working with MeDe Innovation to develop novel approaches to the design and manufacture of medical devices.

The factory tour started at the beginning of the manufacturing process. We were shown how the metals look on delivery and the control systems for logging the components' journey, through to close-up views and explanations of machining, metrology and polishing. We were then shown how one-off, unique implants are designed and made and, finally, the cleaning area, packing, sterilisation methods and warehousing.

I was most surprised by the large research grant portfolio this SME supports and leads, allowing it to explore new routes and technologies to further expand without compromising its core-business."

We would like to arrange more opportunities and visits for our ECR forum. If you would like to host a visit to your organisation email **info@mede-innovation.ac.uk**

Seeking new experiences to broaden horizons

Dr Mazen Al-Hajjar,
Senior Research Fellow,
University of Leeds

"I am a senior research fellow working on tribology of hip replacement – the science of wear, friction and lubrication. What we want to achieve is the prolonging of the lifetime of the hip replacement with designs that can last the lifetime of a young, active patient.

I'd been working as a postdoctoral researcher since being awarded my PhD in October 2012, but I felt like I had come to a crossroads and wasn't sure where I wanted my career to take me: industry or academia? Although I had previously completed a year-long student placement in industry - with global orthopaedics manufacturer, DePuy Synthes - I'd never worked in a lead product development role, so I asked for work experience at DePuy Synthes.

The role was intended to last for a few weeks, but was extended. It's really made me realise how complex the product development process is and how small, but significant, the science is within that process. The experience was invaluable in understanding the context of my research in the bigger picture. What I do at DePuy Synthes is one tiny part of product development that is probably several years away from the research getting to market.

I've also recently gained some significant experience from winning a place on the BORS International Fellowship. I spent four weeks on placements across the USA, Australia, Hong Kong, China and Germany with fellow winners (three from the UK) from surgical and biological backgrounds. It was a significant opportunity to understand how different countries carry out research and what else is going on globally in our focus area, such as how laboratories are set up, their priorities and what opportunities there might be.

I was also really keen to build up my connections for future collaborations. The highlight was meeting so many researchers from different countries – that was key for me – and understanding the differences in how we work."

Networking to develop opportunities

Dr Miquel Gimeno Fabra,
Post Doctoral Research
Fellow, University
of Nottingham

"Following my PhD which focused on metal organics frameworks and different nano materials, my PhD supervisor (Professor David Grant) mentioned the position at MeDe Innovation that he thought would be suitable for me. It links all my interests and expertise – glass fibre polymer composites for bone scaffolds and plasma glass coatings for implants – all fields that can mix easily with nano materials. The opportunity to get involved with lots of different projects at once is great as it gives me wings, it means I can work on a variety of topics and keep thinking out of the box.

Being part of MeDe Innovation has given me opportunities to meet other professionals who share similar challenges to me and who are interested in finding new ways of working together.

The MeDe Innovation launch event was a clear example of successful networking. I met a surgeon and an industry representative there and found we had some interests in common. Since then we have met, written and submitted a few proposals together. By just talking to people and finding out what they do you can quickly start working together. It's been particularly helpful getting to know a clinician as they can offer so much in terms of suggestions and solutions, and ultimately they're the end user of the work I'm doing."

ADVISORY BOARD

MeDe Innovation's External Advisory Board of global leaders in medical device innovation provides us with academic, industrial, clinical and regulatory perspectives. The Board members' valuable insights shape and steer the strategic direction of our programmes.

As we head into our second year, we will continue to seek the views of our External Advisory Board as a whole. We are also committed to gathering their individual perspectives on our key research areas and will incorporate these perspectives into our programme of research workshops and other outreach activities (see pages 28-29).

We would like to thank our External Advisory Board for their support and guidance throughout our first year:

Brian Jones
JRI Orthopaedics Ltd (Chair)

Dr Alan Ashby
DePuy Synthes

Janette Benaddi
NAMSA Inc

Dr Robert Bigsby
Biomet Europe

Professor Gordon Blunn
University College London

Mark Chapman
Medtronic Ltd

Professor Phil Coates
University of Bradford

Simon Collins
MatOrtho Ltd

Professor Kenny Dalgarno
Newcastle University

Sue Dunkerton
Health KTN

Peter Ellingworth
Association of British Healthcare Industries (ABHI)

Anne Farrow
Engineering and Physical Sciences Research Council (EPSRC)

Professor John Fisher
University of Leeds

Professor Peter Gore
ADL Smartcare Ltd

Professor David Grant
University of Nottingham

Suzanne Halliday
BSI Group

Professor Paul Hatton
University of Sheffield

Professor Jane Jiang
University of Huddersfield

Professor Steve Kurtz
Exponent Inc

Dr Ser Yong Lim
SIMTech, Singapore

Professor Andrew McCaskie
University of Cambridge

Professor Tony Miles
University of Bath

Neil Morgan
Innovate UK (Technology Strategy Board)

Dr Tim Morley
Smith & Nephew Healthcare

Professor Alan Silman
Arthritis Research UK

John Wilkinson
Medicines and Healthcare Products Regulatory Agency (MHRA)

Dr Ceri Williams
University of Leeds

Professor David Williams
Loughborough University

KEY CONTACTS

If you'd like to discuss any aspect of our work, or would like more information, our operational staff are ready to help:

Ms Lara McGann
Centre Co-ordinator

l.h.mcgann@leeds.ac.uk
+44 (0)113 343 8194

Lara is responsible for coordinating the day-to-day operation of the Centre and the delivery of the programme objectives. She also supports the work of the Director and Deputy Director, and works alongside the National Outreach Manager.

Dr Ceri Williams
Deputy Director

c.j.r.williams@leeds.ac.uk
+44 (0)113 343 0922

Dr Ceri Williams has considerable experience of working in economic development and innovation delivery. Dr Williams provides operational leadership of MeDe Innovation to connect the Centre to UK and global academics, industry, clinicians and intermediaries including regulators and networks.

Ms Rowan Grant
National Outreach Manager

r.h.grant@leeds.ac.uk
+44 (0)113 343 0923

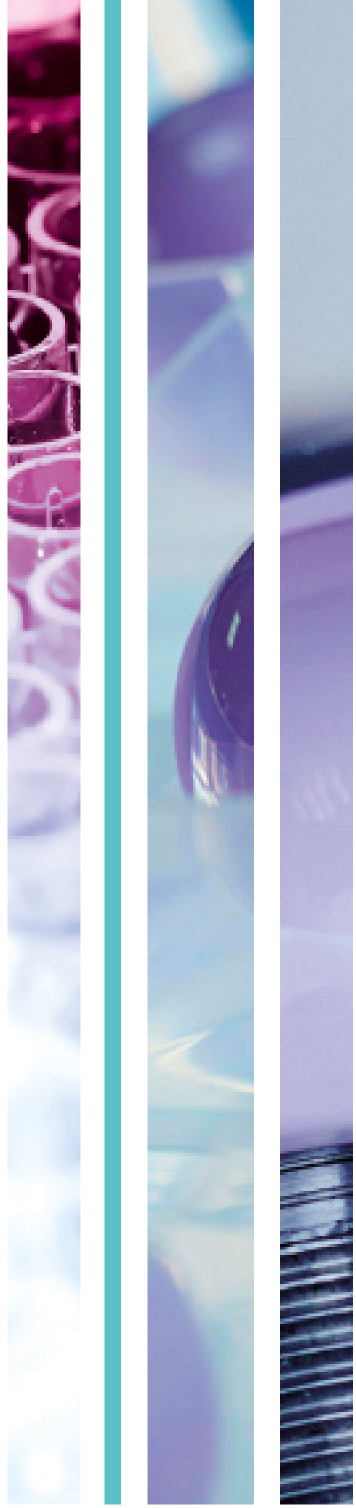
Rowan is responsible for the Centre's outreach activities. Along with management of all external communications activities for the Centre, she is responsible for the recruitment and coordination of the Centre's wider network.

The EPSRC Centre for Innovative Manufacturing in Medical Devices
c/o the Institute of Medical and Biological Engineering

University of Leeds, Leeds LS2 9JY
mede-innovation.ac.uk
Twitter: @MeDe_Innovation
LinkedIn: MeDe Innovation

MeDe Innovation

EPSRC Centre for
Innovative Manufacturing
in Medical Devices



MeDe Innovation
The EPSRC Centre for Innovative
Manufacturing in Medical Devices
c/o Institute for Medical & Biological Engineering
University of Leeds, LS2 9JT

+44 113 343 0923
mede-innovation.ac.uk
info@mede-innovation.ac.uk
@MeDe_Innovation

UNIVERSITY OF LEEDS | Newcastle University | The University of Nottingham | UNIVERSITY OF BRADFORD | The University Of Sheffield.

EPSRC
Pioneering research and skills