



# **CBIS Annual Report**



The Royal British Legion Centre for Blast Injury Studies at Imperial College London May 2019

Imperial College London

# Centre for Blast Injury Studies Annual Report

The Royal British Legion Centre for Blast Injury Studies at Imperial College London www.imperial.ac.uk/blast-injury

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# **Invited Foreword**

It is with great pleasure that I write the foreword for this 2018 annual report. The Centre for Blast Injury Studies (CBIS) is a truly interdisciplinary endeavour that I am proud to support as an Imperial Centre of Excellence. CBIS puts clinical data at the heart of its research and brings together the expertise of clinicians, scientists and engineers from the civilian and military fields, all of whom are dedicated to deepening our understanding and tackling of the major challenges in blast injury research. This is a particularly exciting year, which marks a decade of triumphs for the Centre and Imperial Blast before it. Over the last ten years, the passion of the CBIS members alongside a truly multi-disciplinary focus on research has been fundamental to the Centre's continued success. I am delighted that this report takes this opportunity to reflect on all of these achievements.

The Centre is a unique synthesis of fundamental underpinning science and engineering, inspired by real-world problems and challenges. This report brings to life in a vivid and compelling manner the significant impact this research has had on the lives of many. The collaborative nature of the Centre and its many partnerships is central to its success, and Imperial College is proud to be working so closely with The Royal British Legion to deliver such impactful research to support the whole serving community. During my time as the Government's Chief Scientific Advisor for National Security I witnessed first-hand the value of people who were proud to serve their country, and I understand how important it is that we as a society support these people when they need it most. It is inspiring to see the commitment of the CBIS to supporting the serving community, from the point of injury all the way through to their rehabilitation and lifelong health. Without the close interworking of academia, governments, and charities, these many successes would simply not be possible.

There are a number of highlights for the Centre in 2018, ranging from the publication of seventeen journal articles, to a programme of events and extensive outreach activities. This year saw the Centre's first 'Blast Injury Conference,' which included an inspiring range of speeches and presentations exploring topics related to blast injury. It is wonderful to see the range of public engagement events that CBIS has delivered, and the increasing popularity of these. Imperial Festival was clearly a highlight, as it is for many at the College, and the Centre's stand was certainly busy during both the Schools' Day and the main weekend event. Members have been spreading the Centre's message through attending a range of high-profile national and global conferences. It is also very encouraging to see new initiatives for public engagement within the Centre, such as the 'Fragments' podcast, launched by two PhD students with the aim of promoting the work of the Centre to a wider audience. Blast injury is an important issue and we must effectively engage the public in order for our research to make the greatest impact. These activities are just a few of the exciting ways that we are celebrating and expanding the Centre's work. I am looking forward to seeing what other innovative approaches the CBIS members utilise in the coming years.

I hope that you enjoy reading about the Centre's achievements from 2018 as much as I have. This report encapsulates the commitment of the Centre's members to driving forward advances in blast injury research over this year, and the last decade. The work that the Centre's members do is at the cutting edge of medical science, and I look forward to seeing how they continue to be at the forefront of this life-changing research.

Professor Nick Jennings CB FREng Vice-Provost (Research and Enterprise), Imperial College London

# **Introduction from Centre Director**

This has been another great year for CBIS. Looking back at all the activities we have been a part of, including visits from lots of interested parties, to engaging the public and hosting a conference, it is clear that our impact is far reaching. I am also incredibly pleased with the research outputs from the Centre this year, with a number of very high quality research papers from a variety of groups.

Research and impact takes a long time to be achieved, but we are starting to see great moves forward in our knowledge of blast injuries and how we can mitigate, treat, and rehabilitate those affected. This year marks a decade of work for a number of us at the Centre, with Imperial Blast having been established in 2008, followed by the founding of the Royal British Legion Centre for Blast Injury Studies in 2011. There is still lots to be done, but since 2008 we have made great strides. The first section of this annual report summarises our achievements over the last 10 years, and putting all this together makes me incredibly proud. It is thanks to all the people who have committed research to this area, and because of the support of the Royal British Legion, Imperial College London, the Ministry of Defence and many other supporters, that we have been able to implement such changes.

To set the scene for this year's report, below is a brief overview of some of the highlights and key events from 2018, many of which will be discussed in more detail throughout the report.

JANUARY	We started 2018 by welcoming six new PhD students to the team (see page 22 for more information about them).
	This was followed by a visit from Air Commodore Richard Withnall and Dr Amarjit Samra, the military's Medical Director and the Director of Research respectively. We have a strong relationship with the military and visits such as these are important to keep the military up to date with the Centre's achievements and ongoing research.
	We also hosted a number of Royal British Legion fundraisers at the end of the month where they learnt more about what the Centre aims to achieve, and how the money they collect helps to enable our research.
FEBRUARY	Dr Emily Mayhew gave a seminar about the formation of the <b>Paediatric Blast Injury</b> <b>Partnership</b> . More information about the Partnership can be found on page 10.
MARCH	The Centre hosted members of the Royal British Legion's public relations, media and communications teams to learn more about the specifics of the Centre's work.
	Prof (Col) Jon Clasper also hosted a Defence Engagement Visit with important military guests.
APRIL	The <b>Annual Away Day</b> took place this month. This helped Centre members to get to know each other better and build relationships, as well as having some fun during the afternoon.
	CBIS was involved in <b>Imperial Festival</b> again this year, this time also taking part in the School's Day prior to the main weekend event. More information about this great public engagement event is on page 16.
ΜΑΥ	Dr Emily Mayhew and I spoke at the Imperial College London Institute of Global Health Innovation's (IGHI) Global Health Forum about the impact of conflict on health and post- conflict healthcare.
	The CBIS Advisory Board met for their first meeting of the year.

JUNE	Following on from the success of the CBIS stand at Imperial Festival, the Centre was invited to participate in the <b>Royal Institution of Great Britain's Family Fun Day</b> (page 18). We also hosted some more of the Legion's fundraisers and I spoke at the Legion's annual Poppy Appeal and Fundraising Conference.			
JULY	Dr Spyros Masouros went to the Royal British Legion's headquarters to speak about the Centre at one of their Poppy Appeal Organisers' seminars.			
AUGUST	Summer holidays were happening in various locations around the world.			
SEPTEMBER	<ul> <li>This was a very busy month of events for the Centre:</li> <li>Dr Spyros Masouros and Emily Ashworth were invited to speak at a team day for the Royal Centre for Defence Medicine in Birmingham.</li> <li>Dr Andrew Phillips gave a keynote speech at the Bath Biomechanics Symposium.</li> <li>The Legion's Legacy team held two days of events at Imperial for its supporters. This included presentations from Dr Spyros Masouros and Professor Alison McGregor about the Centre.</li> <li>The Centre also held its inaugural Military Amputee Research Advisory Group meeting (page 19) and launched its podcast series 'Fragments' (page 18).</li> </ul>			
OCTOBER	Two of our PhD students, who are leading on public engagement within the Centre participated in a Twitter Conference, sending a series of tweets about blast injury research and they also ran a stand at the <b>Science Museum</b> <i>Late</i> (page 18).			
NOVEMBER	The CBIS Advisory Board met for its second meeting of the year. The first annual <b>Blast Injury Conference</b> took place at the Royal Geographical Society and was attended by over 130 people (page 12).			
DECEMBER	The Centre's Management Group reflected on a successful year.			

We hope you enjoy reading this report and learning more about our work from 2018.

### Professor Anthony M J Bull FREng

Director, The Royal British Legion Centre for Blast Injury Studies at Imperial College London



Figure 1: 2018 – A Year in Numbers

This infographic provides an overview of the Centre's changes and its achievements across the year.

# A decade of success (and beyond)

The current Centre for Blast Injury Studies started in 2011, however, the precursor to the Centre was Imperial Blast. Imperial Blast was set up in 2008, to focus interdisciplinary research on the patterns of injury resulting from Improvised Explosive Devices (IEDs) and anti-vehicle mines. In this section of the annual report, we take the opportunity to reflect on 10 years of research into military blast injuries here at Imperial College London and the impact that we have had on service personnel and this research field. We want to thank all the people that have been involved to make this research so effective, from the Imperial Blast team through to former and current Centre members.

# **Vehicles and equipment**

We have influenced the awareness of the positioning of the **pelvic binder** in Role 1<sup>1</sup>. The positioning is taught in Battlefield Advanced Trauma Life Support (BATLS) courses, so will continue to have impact. This has now also been adopted by the US military.

CBIS' investigations into how **bone fractures** were affected by a subject's **environment** (e.g. in a vehicle or in cover, compared with free-field) have shown that lower limb injuries in survivors were significantly increased for those in cover<sup>2</sup>. The posture and position within a vehicle also had an impact on the injuries, both in terms of pattern and severity.

CBIS's work on the effect of **in-vehicle posture** on injury is widely published<sup>3,4</sup> and disseminated, and is being considered by vehicle manufactures and in retrofitting of the current UK armoured vehicle fleet.

All UK and US Service Personnel since 2012 will benefit from our contributions to work (in collaboration with others) on the introduction of **blast mats** in vehicles<sup>5</sup>. Work is ongoing.

Members of CBIS are consulted by, and have positions in, committees and workgroups, which define the protective levels of **personal protective equipment** and **vehicles**.

Dstl and companies such as Humanetics Innovative Solutions Inc., use models (physical and computational) that have been **developed at CBIS**.

<sup>&</sup>lt;sup>1</sup> Bonner TJ, Eardley WG, Newell N, Masouros S, Matthews JJ, Gibb I, Clasper JC (2011). Accurate placement of a pelvic binder improves reduction of unstable fractures of the pelvic ring. Journal of Bone And Joint Surgery-British Volume, 93(11): 1524-1528.

<sup>&</sup>lt;sup>2</sup> Ramasamy A, Hill AM, Masouros S, Gibb I, Bull AM, Clasper JC (2011). Blast-related fracture patterns: a forensic biomechanical approach. Journal of the Royal Society, Interface, 8: 689-698.

<sup>&</sup>lt;sup>3</sup> Grigoriadis G, Carpanen D, Webster CE, Ramasamy A, Newell N, Masouros SD (2019). Lower limb posture affects the mechanism of injury in under-body blast. Annals of Biomedical Engineering. 47(1): 306-16.

<sup>&</sup>lt;sup>4</sup> Masouros SD, Newell N, Bonner TJ, Ramasamy A, Hill AM, West ATH, Clasper JC, Bull AMJ (2012). A standing vehicle occupant is likely to sustain a more severe injury than one who has flexed knees in an under-vehicle explosion: a cadaveric study. Proceedings of IRCOBI Conference 2012, IRC-12-37.

<sup>&</sup>lt;sup>5</sup> Newell N, Masouros SD, Bull AMJ (2013). A comparison of MiL-Lx and Hybrid-III responses in seated and standing postures with blast mats in simulated under-vehicle explosions. Proceedings of IRCOBI Conference 2013, IRC-13-12.

# Surgical and clinical practice

Our biomechanical analysis has shown why unilateral below knee amputees get **accelerated arthritis** on their intact limb<sup>6</sup>. This will now be used to design better prostheses and surgical interventions. Through modelling loading patterns through sockets and prosthetics we are understanding why such high rates of osteoporosis are observed.

There are over 200 UK veterans with lower limb amputations from recent conflicts who could benefit from our work on **sockets**. Poor socket fit, socket misalignment and the build-up of temperature increase instability, discomfort, tissue breakdown and development of numerous conditions such as blisters, stump oedema and skin carcinoma. We have achieved the first step in developing a **smart amputee socket** that can help manage loading, skin health and function.

Military amputees with **osseointegrated implants** are being compared to those with standard prostheses as part of a prospective analysis of whether they do better. This work is generating the evidence which could benefit above knee amputees not tolerating standard prostheses in the future<sup>7</sup>.

Through-knee amputees have a significantly higher function than above-knee amputees. We have developed an **implant** to enable above knee amputees to bear load to re-create this function<sup>8</sup>.

Over 100 veterans were treated through the **Veterans Trauma Network** where many members of CBIS have been instrumental<sup>9</sup>.

CBIS plays a leading role in **ADVANCE** the 20 year follow up of the major war wounded from Iraq and Afghanistan<sup>10</sup>.

The above outputs would not have been possible without the investment the Centre has had from the Royal British Legion, Imperial College London and the Ministry of Defence. We believe the Centre will continue to make a significant impact in the field over the coming years as we further develop technologies and our understanding of blast injuries.

<sup>&</sup>lt;sup>6</sup> Ding Z, Jarvis HL, Bennett AN, Baker R, Bull AMJ. Development, validation and use of a musculoskeletal model for transtibial amputation: biomechanical evidence for increased rates of osteoarthritis of the uninjured limb. *In submission.* 

<sup>&</sup>lt;sup>7</sup> McMenemy L, Ramasamy A, Williamson B, Sherman K, Phillip R, Kendrew J (2018). Osseointegration in bilateral above knee amputees following blast: 2 year follow up results from the initial cohort of UK service personnel. Presented at the Combined Services Orthopaedic Society Conference, Birmingham, UK. May 2018.

<sup>&</sup>lt;sup>8</sup> Barnes SC, Clasper JC, Bull AMJ, Jeffers JRT. Micromotion and push out evaluation of an additive manufactured implant for above-the-knee amputees. Journal of Orthopaedic Research, (in press)

<sup>&</sup>lt;sup>9</sup> https://www.nhs.uk/using-the-nhs/military-healthcare/veterans-physical-injuries/

<sup>&</sup>lt;sup>10</sup> https://www.advancestudydmrc.org.uk/

# Foot and ankle injuries – a case study

#### Background

Combat-related extremity injuries are common. In recent conflicts, over 80% of wounded Service Members sustained at least one extremity injury. The frequency and severity of these combat-related extremity injuries required the greatest utilisation of resources for treatment and have caused the greatest number of disabled soldiers. Specifically, severe foot and ankle (F&A) injuries were a common injury pattern identified for mounted troops (those in vehicles, rather than on foot), secondary to an explosive insult of the vehicle. Work conducted by Imperial Blast collected epidemiological<sup>11</sup> and follow-up data for the UK casualties<sup>12</sup> and identified that F&A injuries are associated with very poor outcomes, with few casualties returning to active service or pre-injury levels of activity. Blast injury to the F&A therefore became a clinical priority for the Centre.

#### Pathophysiology and protection

Key to protecting against a severe F&A injury is to understand the mechanism by which the injury occurs and the parameters which affect it. Being the first of its kind internationally, an anti-vehicle, underbody, blast-injury simulator was designed and built in the Centre to replicate in a highly controlled setting the loading environment seen by the occupant of a vehicle when attacked by a mine<sup>13</sup>. Combining this capability and standard high-rate loading equipment in the CBIS laboratories, experiments were carried out to look at the loading profiles required to produce a severe F&A injury, to measure the effect of occupant posture on probability of injury, to test the ability of anthropometric test devices (ATDs or dummies) used in NATO standards to predict the probability of F&A injury, and to measure the effect of protection such as postural changes or equipment (e.g. combat boot and blast mats) to reduce the severity of injury.

We conducted a series of cadaveric tests in which specimens were mounted in a range of different postures of knee and foot angle, including 2 standing postures<sup>14,15</sup>. For the same insult, standing postures (with the knee at full extension of hyperextension) presented the most severe of F&A injuries. The next most severely injured posture was that with knee and ankle both at 120° (Figure 2). Out of all postures tested, the one with the knee and ankle at right angles (90°) produced the least severe injuries. This is the posture specified in NATO testing protocols. Our results suggest that occupant posture affects the probability of injury and so it should be taken into account in vehicle design and vehicle qualification tests.

A series of tests on ATDs loaded under the same conditions as cadaveric specimens allowed us to assess their biofidelity; that is, their ability to predict the behaviour of the human leg<sup>16</sup>. We showed that the standard Hybrid-III leg used in most qualification tests around the world significantly exaggerates the deformations and loads seen in the human leg, and in doing so, also likely exaggerates the protection offered by mitigation systems and equipment such as the combat boot. We have tested a number of

<sup>&</sup>lt;sup>11</sup> Ramasamy A, Hill AM, Phillip R, Gibb I, Bull AMJ, Clasper JC. The modern "deck-slap" injury—calcaneal blast fractures from vehicle explosions. (2011). Journal of Trauma and Acute Care Surgery 71 (6): 1694-1698.

<sup>&</sup>lt;sup>12</sup> Ramasamy A, Hill AM, Masouros SD, Gibb I, Phillip R, Bull AMJ, Clasper JC (2013). Outcomes of IED foot and ankle blast injuries. The Journal of Bone and Joint Surgery – Am, 95: e251-e257.

<sup>&</sup>lt;sup>13</sup> Masouros SD, Newell N, Bonner TJ, Ramasamy A, West ATH, Hill AM, Clasper JC, Bull AMJ (2013). Design of a traumatic injury simulator for assessing lower limb response to high loading rates. Annals of Biomedical Engineering, 41: 1957-1967.

<sup>&</sup>lt;sup>14</sup> Grigoriadis G, Carpanen D, Webster CE, Ramasamy A, Newell N, Masouros SD (2019). Lower limb posture affects the mechanism of injury in under-body blast. Annals of Biomedical Engineering. 47(1): 306-16.

<sup>&</sup>lt;sup>15</sup> Masouros SD, Newell N, Ramasamy A, Bonner TJ, Hill AM, Clasper JC, Bull AMJ (2012). A standing vehicle occupant is likely to sustain a more severe injury than one who has flexed knees in an under-vehicle explosion: a cadaveric study. Proceedings of IRCOBI Conference 2012, IRC-12-37.

<sup>&</sup>lt;sup>16</sup> Newell N, Masouros SD, Bull AMJ (2013). A comparison of MiL-Lx and Hybrid-III responses in seated and standing postures with blast mats in simulated under-vehicle explosions. Proceedings of IRCOBI Conference 2013, IRC-13-12.

different types of combat boot procured for troops in the UK<sup>17</sup>, the USA, and the Netherlands on a number of testing platforms to quantify their overall protective ability and the shock absorbing capacity of each of their components.





We have used the above experimental results to develop and validate computational models of the lower extremity<sup>18</sup>, of the ATDs<sup>19</sup>, and of the combat boot<sup>20</sup>. Computational models are inexpensive alternatives to physical tests; they not only allow multiple virtual tests with varying parameters to be run, but they also enable quantification of parameters which we cannot measure physically. We use these to look closely into the mechanism of injury of the F&A and in order to design new mitigations systems (Figure 3).



Figure 3: (a) Computational models developed in CBIS and used to investigate the mechanism of injury of the F&A. (b) Results show that the heel bone is the site most prone to injury. (c) The computational model is now used to investigate mitigation designs within the combat boot.

<sup>&</sup>lt;sup>17</sup> Newell N, Masouros SD, Pullen AD, Bull AMJ (2012). The comparative behaviour of two combat boots under impact. Injury Prevention, 108: 109-122

<sup>&</sup>lt;sup>18</sup> Grigoriadis G, Carpanen D, Bull AMJ, Masouros SD (2016). A finite element model of the foot and ankle for prediction of injury in under-body blast. Proceedings of IRCOBI Conference 2016, IRC-16-63.

<sup>&</sup>lt;sup>19</sup> Newell N, Salzar R, Bull AMJ, Masouros SD (2016). A validated numerical model of a lower limb surrogate to investigate injuries caused by under-vehicle explosions. Journal of biomechanics 49 (5), 710-717.

<sup>&</sup>lt;sup>20</sup> Newell N, Salzar R, Bull AMJ, Masouros SD (2016). A validated numerical model of a lower limb surrogate to investigate injuries caused by under-vehicle explosions. Journal of biomechanics 49 (5), 710-717.

Blast mats are force-absorbing structures that may be placed on the vehicle floor in order to reduce the load transmitted to the occupants' feet when the vehicle is attacked by a mine, and therefore reduce the severity of injury to the lower limb. We have tested commercially available mats in our under-vehicle simulator and identified their protective capacity. We have used our understanding of the injury mechanism and of these tests to design mats that could outperform the ones currently available. We have used our computational models to trial various designs / geometries before manufacturing the one that we are predicting would perform best. We have now tested the design in our injury simulator and compared it to those that are commercially available (Figure 4).

### **Treatment and rehabilitation**

Work in both the US and the UK military rehabilitation centres indicates that a custom ankle foot orthosis (AFO) reduces pain and allows some patients to carry out activities that bring their quality of life close to pre-injury levels. These orthoses allow enhanced lower limb propulsion to enable activities such as running and jumping. Early results demonstrate that 80% of US service personnel considering amputation pursued limb salvage having been prescribed the AFO. The outcomes and injury profiles, however, of the UK cohort that benefit from the AFO are unknown, as is the capacity of the AFO to offload the injured F&A and reduce pain.



Figure 4: (a) Test setup to quantify the protective ability of blast mats in under body blast loading. (b) Comparison between commercially available blast mats and the one under development in CBIS.

Work in the Centre aims to produce a clinical decision tool to indicate which patients will most benefit from an AFO so that the, often painful, attempts at limb salvage rehabilitation in unsuitable patients are prevented. It also aims to understand the mechanism by which the AFO reduces the load seen by the F&A by combining gait data with computational tools (Figure 5). This may allow us to optimise and tailor the AFO to individual injuries, based on our evidence and technology.





# **Compensation scheme**

The research on foot and ankle injuries that CBIS has undertaken has been used to inform the compensation scheme for military personnel who had suffered from these injuries. The Armed Forces Compensation Scheme Medical Board upgraded the compensation for those who had suffered a calcaneal fracture, to bring it in line with compensation for below knee amputations.

# The Paediatric Blast Injury Partnership (PBIP)

Written by: Dr Emily Mayhew (Imperial Lead) and Dr Michael von Bertele (External Lead), Paediatric Blast Injury Partnership

What lies beyond CBIS? As we know from our television screens all too well, a global cohort of blast injured human beings who live in conflict zones exists, most of whom are children. There are brutal facts behind these images. One in every six children lives in a conflict zone, where on a daily basis they run the direct risk of being injured by explosive devices. Additionally, the indirect effects of life in conflict zones such as malnutrition, disease and the breakdown of healthcare systems and general infrastructure make treating blast injuries very difficult. Children continue to be in danger once conflicts have been resolved, and they are much more likely than adults to be injured by unexploded or legacy ordnance as they return to normal life. A recent photostory in *Time* magazine highlighted the dangers for children of running or walking to school or simply playing outside in countries where war never quite goes away.





In January 2018 a Partnership was formed between Imperial College London and Save the Children UK to focus on the global emergency of paediatric blast injury. As well as thinking strategically about the issue, the Partnership also wanted to make a practical contribution as quickly as possible to benefit both patients and their caregivers. With the help of medical organisations in places like Syria, Yemen and Iraq, we determined there was an immediate need to provide practical support for clinicians in conflict zones to adapt existing trauma and care systems to successfully treat children, even where resources are severely constrained.

So, in May 2019 we will publish a Field Manual that provides simple technical guidance and key action points for every stage of the care pathway of paediatric blast injury from point of wounding, through pre-hospital care, paediatric ICU, surgical care, ward care and rehabilitation. Integrated into each section will be material on psychiatric and psycho-social support for both patients and their caregivers. The first edition of the Field Manual will be simple to use, small and portable, readable in low light, and printed on durable, waterproof pages, and our partners in Save the Children will distribute it to organisations who can put it to use straight away.



The Field Manual is just a start. The Partnership recognises that at present there is no coordinated focus for research into treatment of paediatric injury and its outcomes. If we are to make significant progress in this area, then we will need an evidence base. Our External Partnership Lead, Michael von Bertele, has initiated a programme to develop both the methodology and coordination of data collection, primarily by designing and setting up an international Trauma Register that records all aspects of child conflict injury including blast. The programme will seek collaboration from as many organisations as possible; local health providers and responders, local and international NGOs, military medical services, and others, in as many places in the world as possible, and at all different stages of the care pathway. The Trauma Register will aim to gather data in a simple and shareable format that can be accessed by all collaborators to stimulate research and understanding across the entire continuum of injury, including mental health sequelae. This programme will seek to guide and support future work on research, models of care, treatment policy and planning, at a global level.



None of this work would have been possible without CBIS. Although funded and directed from outside the Centre, it is their expertise in the understanding of blast injury that has enabled the Partnership to move forward. From CBIS, the Partnership has learned how essential it is to analyse the mechanisms of injury to fully assess effects and make progress towards solutions, and that in order to achieve these goals, both comprehensive data collection and a broad range of interdisciplinary research will be required. Like CBIS, the Partnership is founded on recognition of the need to treat the entire blast casualty continuum, from point of wounding through rehabilitation and beyond, as part of a broader effort to recognise and treat all of the effects of conflict on children. Thus, the Partnership shares with CBIS the commitment to securing survival and life beyond survival, for the entire blast injury cohort in the UK and everywhere around the world, today and tomorrow.

# **Events**

There have been a number of important events for the Centre throughout 2018. Some of these are discussed in more detail over the following pages.

#### **Blast Injury Conference 2018**

Following the successes of the CBIS Networking and Research updates in previous years, the Centre made the decision to move toward running a conference from 2018 onwards. The first of these, the Blast Injury Conference 2018, took place at the Royal Geographical Society on 22 November, and was a predominantly national event, bringing together researchers from around the UK.

We were delighted that Stuart Hughes, BBC News Producer, was able to give our Keynote Speech at the conference. Stuart stepped on a landmine when he was reporting from Iraq in 2003 and he shared his experiences and reflections with the conference delegation. It was a truly inspiring and engaging talk, for which we were very grateful. The photo on the front of this report is from his speech at the conference.

The first session, chaired by Professor Anthony Bull, included presentations on topics ranging from the Paediatric Blast Injury Partnership to mental health and traumatic brain injury in UK Armed Forces. A panel discussion followed the presentations.

The following set of talks focussed on blast lung injury and heterotopic ossification. This session was chaired by Professor (Colonel) Jon Clasper, and featured delegates from the universities of Nottingham, Swansea, Oxford and Imperial.

The afternoon sessions showcased the work of the Centre's PhD students and postdoctoral researchers. Session three focused on musculoskeletal injury, discussing pelvic and lower limb injuries, as well as bone health and socket fit. The final session covered blast related traumatic brain injury, including the effects of this on hearing.

We would like to thank all of our speakers and poster presenters for taking part and we are already looking forward to welcoming delegates at the next conference in July 2019. The 2019 conference will be an international, two-day event.



# Visits from Royal British Legion fundraisers and staff

The Centre was incredibly pleased to have had a number of opportunities throughout the year to meet with the Legion's fundraisers and staff. Some events were held at Imperial College London, and members of the Centre presented to the visitors about the research that is funded by the Legion, and how important this research is for military personnel and veterans. The visits to the Centre were also an opportunity for the fundraisers and staff to see our facilities.

On a couple of occasions, members of the Centre also attended events organised by the Royal British Legion. Professor Anthony Bull spoke at the Poppy Appeal and Fundraising Conference in June, and Dr Spyros Masouros attended a Poppy Appeal Organisers seminar in July, both to raise awareness of the Centre. These talks are always very warmly received.

## **Global Health Forum**

Professor Anthony Bull and Dr Emily Mayhew took part in the Institute of Global Health Innovation's Global Health Forum run at Imperial. They were part of a panel of presenters that also included Mr Shehan Hettiaratchy and Dr Esmita Charani. The Forum was a chance to discuss the Centre's research with a different audience, and put its research within the context of the impact of conflict on healthcare, both in terms of military, but also civilian health. This was a well attended event that was live streamed.

# **Annual Away Day**

The Centre's Annual Away Day is an opportunity to bring together all members of the Centre, from across the different departments and faculties, to network with each other and to discuss research updates. Importantly, there is also the

opportunity for some fun and team building during the afternoon.

In the morning of the Away Day, all of the Centre's PhD students and postdoctoral researchers presented for 5 minutes about themselves and their research projects. This was a chance for new members to be introduced to the wider group, and for all members to refresh their knowledge of the variety of projects



being undertaken across the Centre's clinical priority areas.

The afternoon activity then saw the group (including students, postdoctoral researchers, academics and professional services staff) split into teams for a cryptic clue hunt around the Victoria & Albert Museum (South Kensington, London). The challenge was great fun, and there was certainly a competitive streak to many of the teams.

Activities and days together are a very important way to keep the identity of the Centre, and to ensure that all researchers continue to see their work as part of the broader context.

# **Media Activity**

Below are some images representing examples of our media activity in 2018. To read a specific article, click on the relevant image.



Fast-acting readily available gas may mitigate blast induced brain injury

Imperial College article February 2018



**Blast Proof** 



Discussing hearing loss in veterans

Imperial College article May 2018





**300,000 Veterans living with hearing loss in the UK** The Confederation of Service Charities May 2018



Imperial joint mechanics expert elected to World Council of Biomechanics Imperial College article July 2018



Blade runner Dave Henson: after the blast ABC Local October 2018



**Invisible Killers** 

Imperial College Magazine November 2018



Podcast: 1918 special to mark the First World War armistice centenary

Podcast: 1918 special to mark the First World War armistice centenary

> Imperial College article November 2018



**Prosthetic legs** 

Royal British Legion Festival of Remembrance Programme November 2018



Starburst galaxies and blast injuries: news from the College

Imperial College article

December 2018

# **Outreach and Engagement**

Outreach and engagement has been a very successful area for the Centre this year. We have used a range of activities, some that were aimed at school children, others for adults, and others that are accessible to a variety of audiences. Two of our PhD students, Sarah Dixon-Smith and Shruti Turner have taken a leading role in outreach for the Centre and we would like to thank them for their hard work this year.

### Imperial Festival – April 2018

Imperial Festival is always a highlight for the Centre, and for Imperial researchers generally. It is a wonderful opportunity for researchers and research groups to engage with the public and discuss their work. This year, the Centre's 'Blast Rehabilitation Gymnasium' was selected as one of just fifteen stands to participate in the Schools' Day, which takes place the day before the main weekend event.

Over the course of the Schools' Day, the stand welcomed 120 children and their teachers. Children at the stand split into two groups to look at the different areas. The first section of the stand had a selection of prosthetics that Mark Thoburn, a prosthetist from DMRC Headley Court, had kindly brought along. He discussed the different prosthetics with the children, highlighting their features and uses. The other half of the stand was set up as the rehabilitation gymnasium and CBIS volunteers took the children through a series of balancing exercises. The idea was for children to understand about balance and strength, and give them an insight into some of the exercises that amputees need to do whilst they are in rehabilitation. All the attendees seemed to have a great time on the stand and lots of questions were asked. Imperial College undertook an evaluation of the event using surveys from attendees and some comments about our stand were highlighted (see the next page).

Over the weekend of the main Imperial Festival event, more than 20,000 people were welcomed to the College's South Kensington campus. The CBIS stand was incredibly popular, with hundreds of visitors across the two days, and more than 150 entries to our competition to colour in, or design, a prosthetic limb.

Thank you to all the CBIS volunteers who helped to make this such a successful event.

Hundreds of visitors and over 150 entries to our colouring competition. "The best thing I did today was where you got to do lots of active things: race on crutches and balance on a ball. We learnt about fake arms and legs"<sup>1</sup> School's Day attendee "It's really hard to balance on one leg. I learned how people with disabilities get exercise and what exercise they can get from bioengineers"<sup>1</sup> School's Day attendee

> Old Oak Group K

> > "Volunteering at Imperial Festival is an ideal time to engage with the public and inspire people of all ages by not only sharing our research, but the reasons we do it" Shruti Turner CBIS PhD student

Imperial Festival School's Day participant being shown the difficulties of using crutches by CBIS PhD student Cheng Yu. Photo by Thomas Angus.

<sup>1</sup>Feedback about our stand from the Imperial Festival 2018 Evaluation Summary: https://www.imperial.ac.uk/media/imperial-college/be inspired/festival/public/Imperial-Festival-2018--Evaluation-Summary-v4.pdf

# 'Fragments' – a CBIS podcast series

Two of our PhD students, Sarah Dixon-Smith and Shruti Turner launched 'Fragments' in September, which is a podcast series from the Centre. The two students were keen to promote the work of the Centre and bring its research to different audiences in a new way. The topics discussed all relate to blast injury and recovery, and often the discussions connect developments made in the past conflicts to today. By the end of the year, five episodes had been released, all with a different theme:

- 1. Introductory podcast about blast injury and some of CBIS' research.
- 2. Casualty Evacuation Pathways links between WWI and what we are doing now.
- 3. 'Aftermath' at the Tate Britain a discussion of an exhibition about art in the wake of WWI.
- 4. Invictus Games parasports competition set up by Prince Harry.
- 5. Remembrance a discussion with Catherine Davis, Head of Remembrance for the Royal British Legion, talking about the Thank You 100 campaign.

The Centre is really proud of the work that Sarah and Shruti have put into these podcasts and looks forward to many more episodes in the future.

# Additional engagement events throughout the year

### **Royal Institution of Great Britain's Family Fun Day – June 2018**

Thanks to the success of the Centre's 'Blast Rehabilitation Gymnasium' at Imperial Festival, we were invited by the Royal Institution of Great Britain to take part in their Family Fun Day. We were delighted

to have been asked and the Centre volunteers had another wonderful day discussing blast injury and rehabilitation with members of the public. Both young people and adults were keen to have a go on the balancing activities.

#### **Twitter Conference – September 2018**

Sarah and Shruti took further initiative to try to engage more members of the public with our blast injury research. This time, the team were involved in a Twitter Conference run by the War Through Other Stuff Society. This was an exciting way to reach a different audience to our usual Twitter followers. The format consisted of 12 Tweets posted at a particular time about a particular topic – which for the theme was about 'Blast Injury and Rehabilitation'.

#### Science Museum Late – October 2018

In October, the *Late* was themed around engineering. The Blast Rehabilitation Gymnasium was present, along with a display of prosthetics. The activities were very popular with visitors and the stand attracted a large audience. The members involved from CBIS were Sarah Dixon-Smith, Shruti Turner, Peter Le Feuvre, Louise McMenemy and Martin Ramette.

#### STEM Day – October 2018

Michael Bruyns-Haylett gave workshops at Downe House School (Cold Ash, Berkshire), as part of their STEM Day for all year 11 girls. He used the workshop to inspire an interest in neuroscience by using illusions to explain how the brain uses heuristic shortcuts to perceive reality.

# **Governance and Staffing**

# Governance

### **The Royal British Legion**

As the core Funders of the Centre for Blast Injury Studies, The Royal British Legion have oversight of the work within the Centre. Professor Bull regularly meets with the Legion's Director of Operations to discuss the running of CBIS, and other members of The Royal British Legion attend events at the Centre.

### **Imperial College London**

CBIS is recognised as one of twenty Centres of Excellence within Imperial College. As such, the Centre is required to report on its progress to the Vice Provost of Research and Enterprise. This is achieved through annual reporting (which the Vice Provost's Advisory Group for Research considers), as well as providing updates about activities within the Centre every two months.

#### **Management Group**

The Centre Director (Professor Anthony Bull), Clinical Lead (Professor (Colonel) Jon Clasper), two Associate Directors (Professor Alison McGregor and Dr Spyros Masouros) and the Research Programmes Manager (Dr Lucy Foss) meet monthly to discuss operational management of the Centre and its strategic direction. Financial and scientific governance is also a key topic for the group. The Management Group works closely with The Royal British Legion and the Centre's Advisory Board.

#### **Processes**

The Centre's Management Group is constantly looking for any ways in which improvements can be made to the Centre's processes and governance. As such, the Group has implemented a more streamlined approach for when Centre members want to request additional funding e.g. for new PhD students or postdoctoral researchers. As such, a new process that includes external peer review has been put in place, and has been successfully run throughout the year. The addition of external peer review of PhD and postdoctoral research programmes is an important addition to our governance procedures as it provides independent external comment on the nature and direction of the Centre's research.

#### **Advisory Board**

CBIS is extremely lucky to have such an experienced Advisory Board. Chaired by Admiral of the Fleet the Lord Boyce KG GCB OBE DL, the Board meets twice a year to provide oversight to the Centre and advice to the Management Group. Members of the Board have academic, clinical, defence and industry expertise and provide strong support and guidance in these areas, with significant additional input provided outside the regular meetings.

#### **Military Amputee Research Studies Group**

This year, Professor McGregor identified the need for an Advisory Group that could provide advice to the Centre and its researchers about ideas and protocols for working with military amputees. After various discussions, the Centre created the **Military Amputee Research Advisory Group**, which is a body made up of military amputees, military clinicians with expertise in this area, and representatives from veterans' organisations. The Group is chaired by Professor Alison McGregor (Centre Associate Director) and the external membership of the new Group is as follows:

Nick Beighton	Nick Beighton served as a Captain in the Royal Engineers but was injured in Afghanistan in 2009 when he stood on an IED and lost both his legs. In 2012, Nick competed in para-rowing at the Summer Paralympics in London and came fourth. He then subsequently became a member of the British Paracanoe squad and competed at the 2016 Summer Paralympics in Rio de Janeiro, winning the bronze medal in the Men's KL2 canoe sprint.
Josh Boggi	Josh Boggi joined the British Army in 2004 at the age of 17. In 2010, he stood on an Improvised Explosive Device (IED), resulting in the loss of both his legs and his right arm. Since then, Josh has competed in the Inaugural Invictus Games in London, where he won a bronze medal in the Cycling Time Trial and at the 2016 Games in Orden development of the provided by
Brian Chenier	Brian Chenier is a former military policeman who now works at Blesma, the Limbless Veterans charity, as a Support Officer for Prosthetics. Brian joined Blesma in 2013 to represent, lobby for and support limbless veterans for access to the best prosthetic provision available. Part of his role involves representing the charity on various committees, steering groups and networks.
Simon Harmer	Simon Harmer joined the British Army in 1997 as a Combat Medical Technician. In 2009, he sustained life-changing injuries from an IED explosion. Since being injured, Simon has taken part in numerous challenges, has become a volunteer ambassador for several service charities, and is a public speaker. He regularly delivers inspiring presentations at corporate meetings and educational talks in schools and colleges.
Shehan Hettiaratchy	Mr Shehan Hettiaratchy is a Consultant Plastic, Hand and Reconstructive Surgeon and the Lead Surgeon and Major Trauma Director at Imperial College Healthcare NHS Trust in London. He is currently a reservist with the British Army and has been involved in the care of military personnel in the UK. Shehan is the clinical lead for the NHS's Veterans Trauma Network and co-lead of the Trauma Bioengineering Network at Imperial College London
Jon Kendrew	Gp Capt Jonathan Kendrew is a Consultant Orthopaedic Surgeon at the Royal Centre for Defence Medicine working clinically at the Queen Elizabeth Hospital Birmingham. Jonathan is experienced in the acute and longer term surgical management of blast and GSW injuries including the management of complex amputation and the use of osseointegration.
Jon Kendrew Barry Le Grys	Gp Capt Jonathan Kendrew is a Consultant Orthopaedic Surgeon at the Royal Centre for Defence Medicine working clinically at the Queen Elizabeth Hospital Birmingham. Jonathan is experienced in the acute and longer term surgical management of blast and GSW injuries including the management of complex amputation and the use of osseointegration. Barry is currently the Chief Executive of Blesma, a Service charity that has specialised in assisting veterans overcome limb loss and loss of use since the end of World War One. He is also a Governor of Motability, Director of the Confederation of Service Charities (Cobseo), a Director of Veterans Scotland, and a Member of the Independent Medical Expert Group advising the Ministry of Defence on the relevance and validity of the Armed Forces Compensation Scheme.
Jon Kendrew Barry Le Grys Kate Sherman	Gp Capt Jonathan Kendrew is a Consultant Orthopaedic Surgeon at the Royal Centre for Defence Medicine working clinically at the Queen Elizabeth Hospital Birmingham. Jonathan is experienced in the acute and longer term surgical management of blast and GSW injuries including the management of complex amputation and the use of osseointegration. Barry is currently the Chief Executive of Blesma, a Service charity that has specialised in assisting veterans overcome limb loss and loss of use since the end of World War One. He is also a Governor of Motability, Director of the Confederation of Service Charities (Cobseo), a Director of Veterans Scotland, and a Member of the Independent Medical Expert Group advising the Ministry of Defence on the relevance and validity of the Armed Forces Compensation Scheme. Kate Sherman is the Clinical Lead Physiotherapist for Prosthetic and Orthotic Rehabilitation in the Complex Trauma Team at the Defence Medical Rehabilitation Centre at Stanford Hall. In 2011, Kate was one of six winners of the Barclays Women of the Year Award for her work in making a difference to the lives of British troops who had been wounded. In 2012, Kate completed her MSc in Rehabilitation Studies and is keen to further promote research and evidence based practice in the treatment and rehabilitation of complex injuries.

# Staffing

The Centre continues to be made up of about 50 members, spanning seven departments within the College; Bioengineering, Dyson School of Design Engineering, Civil & Environmental Engineering, Medicine, National Heart & Lung Institute, Physics and Surgery & Cancer. The ongoing collaborative nature of the Centre, where researchers work at the interface of different disciplines, continues to provide strong outputs from the research.

This year we have had two new postdoctoral researcher and nine new PhD students (more information about these new members is on the following pages). Our strong relationship with the military continues to thrive, with three of the new students being from the military.

#### **Centre academics**

We currently have 16 academics within the Centre who work across the different clinical priorities and who supervise PhD students and postdoctoral researchers.

Professor Anthony Bull (Bioengineering)	Professor (Col) Jon Clasper (Bioengineering)
Centre Director	Clinical Lead
Dr Spyros Masouros (Bioengineering)	Professor Alison McGregor (Surgery & Cancer)
Associate Centre Director	Associate Centre Director
Dr Robert Dickinson (Surgery & Cancer)	Dr Mazdak Ghajari (Dyson School of Design Engineering)
Dr Claire Higgins (Bioengineering)	Dr Angela Kedgley (Bioengineering)
Dr Andrei Kozlov (Bioengineering)	Dr Andrew Phillips (Civil and Environmental Engineering)
Dr Bill Proud (Physics)	Professor Sara Rankin (National Heart & Lung Institute)
Dr Tobias Reichenbach (Bioengineering)	Professor Andrew Rice (Surgery & Cancer)
Professor David Sharp (Medicine)	Professor Mark Wilson (Surgery & Cancer)

#### **Achievements**

Each year we like to celebrate the achievements of Centre members. These can range from awards for research to appointments on committees/councils.

- Professor Anthony Bull was elected to be a Member of the World Council of Biomechanics. There are only 40 members worldwide, and each member can only serve a maximum 12 year term.
- Dr Spyros Masouros was elected onto the Board for the International Research Council on the Biomechanics of Injury (IRCOBI).
- Dr Rita Campos-Pires was awarded the Mapleson Medal by the Anaesthetic Research Society for her presentation on Xenon Neuroprotection. Professor Helen Galley presented the medal to Dr Campos-Pires in Dundee (November 2018) (left and right respectively in the picture).
- Professor (Colonel) Jon Clasper was awarded the Alexander Memorial Prize. The prize is awarded annually for professional work of outstanding merit to promote the study and improvement of military medicine, military surgery, military preventive medicine or military



pathology. This is the Royal Army Medical Corps' (RAMC) premier prize and consists of a silver medal and a purse provided from a fund raised by public subscription in memory of Thomas Alexander CB FRCS(Ed), Director General Army Medical Department 1858-1860, who had taken an active and important part in the reorganisation of the Army Medical Department after the Crimean War.

- Professor Clasper also delivered the James IV Professorship lecture at the British Orthopaedic Centenary Conference in September 2018.
- The research paper "Characterization of lower extremity blast injury" by Webster CE, Clasper J, Stinner DJ, Eliahoo J, Masouros SD (Military Medicine, 2018, 183(9-10); e448-453) was selected by the US Department of Defense Blast Injury Research Program Coordinating Office as the highlight publication of the month (May 2018) as 'significant research in the area of blast injury prevention, mitigation, and treatment'.
- Louise McMenemy won the Philip Fulford Prize for best overall paper at the Combined Services Orthopaedic Society conference in May 2018 for her presentation entitled "Osseointegration in bilateral above knee amputees following blast: 2 year follow up results from the initial cohort of UK service personnel".

#### **New Post-Doctoral Researcher**



**Mahmoud Keshavarzi** graduated from the Shahid Chamra University, Iran, in 2010 with a BSc in Electrical Engineering, followed by an MSc in Electrical Engineering from the Sharif University of Technology, Iran, in 2012. Since then he has worked at the Sharif University of Technology and the University of Cambridge. Mahmoud joined CBIS in December 2018 to work with Dr Tobias Reichenbach on the neurostimulation of the cortex to find how the speech-in-noise comprehension is modulated by transcranial current stimulation with the speech envelope filtered at different frequency bands.

#### From PhD student to Research Associate



**Octave Etard** completed a BSc and then an MSc in Engineering at Ecole Centrale de Paris, France, before joining Imperial College London to study an MSc in Biomedical Engineering (Neurotechnology). Octave then joined Tobias Reichenbach's group to study for a PhD entitled 'Decoding human speech-in-noise processing from EEG recording' and has stayed on at CBIS as a postdoctoral researcher. He is building on the work from his PhD to investigate neural correlates of speech-in-noise listening and comparing control, blast exposed veterans and volunteers with Auditory Processing Disorders (APD).

#### **New CBIS PhD students**



Adriana Azor was awarded a BSc in Biology from the Lebanese American University, Byblos, Lebanon in 2016. She then moved to Imperial College London and completed an MSc in Translational Neuroscience in 2017. Adriana's MSc thesis title was 'Characterisation of brain abnormalities in Prader-Willi syndrome' and she was supervised by Dr Tony Goldstone and Dr James Cole. Adriana's PhD project is entitled 'Neuroimaging characterisation of blast-induced traumatic brain injury'. Professor David Sharp, Dr Mazdak Ghajari, Dr Peter Hellyer and Dr Stuart Harrison supervise the project.







**Sarah Dixon-Smith** has a BA in Archaeology & History from the University of Southampton and an MA in Public History from Royal Holloway,

Spyros Masouros and Lt Col Arul Ramasamy supervise the project.

Alastair Darwood joined the Centre in October 2018. He completed his medical degree at the University of Nottingham in 2016 and was based at West Middlesex University Hospital and then St Mary's Hospital for his two foundation training years. Alastair is the Technical Director and founder of two companies; Prometheus Surgical Ltd, and Lifeline Technologies Ltd. His work at the Centre aims to investigate cell lines involved with fracture healing and their response to simulated blast waves. Mr Peter Reilly, Dr



**Surg Lt Cdr Louise McMenemy** completed her medical degree at the University of London in 2010. She is a serving military officer and has been a Royal Navy Medical Officer since 2008, with various deployments between 2012 and 2015. Louise's PhD project at the Centre, supervised by Dr Spyros Masouros, is entitled 'Preventing amputation: Optimising treatment in complex foot and ankle injuries'. Here she is utilising the Bespoke Offloading Brace to improve outcomes in patients with complex foot and ankle injuries following limb salvage. She is also involved in ongoing work with the direct skeletal fixation group for military bilateral above knee amputees.



**Iain Rankin** completed his medical degree at the University of Glasgow in 2012 and graduated from University College London with an MSc in Evidence Based Healthcare in 2016. Between his undergraduate and PhD, he has completed multiple case reports, literature reviews and has designed a novel 3D-printed patient specific ACL femoral tunnel guide. Iain's PhD research is entitled 'Dismounted Pelvic Blast Injury' and investigates the mechanisms of pelvic injury in blast, as well as looking to develop mitigation strategies. His project is supervised by Dr Spyros Masouros and Professor (Col) Jon Clasper.



**Major Sarah Stewart** studied medicine at the University of Edinburgh and completed her foundation programme at the Queen Elizabeth Hospital, Birmingham. She subsequently attended the Royal Military Academy Sandhurst to complete her Army Officer training and undertook three years as a General Duties Medical Officer in the Army. Sarah is currently a registrar in Trauma and Orthopaedic Surgery on the Royal London Hospital rotation. She is undertaking a full time PhD at the Centre, studying the osteogenic effect of blast waves on stem cells and bone marrow. Sarah is supervised by Dr Spyros Masouros and Lt Col Arul Ramasamy.



**Shruti Turner** has a BEng in Aeronautics and Astronautics and an MSc in Biomedical Engineering from the University of Southampton. She joined CBIS in January 2018 and her PhD project is looking to understand the clinical utility of prosthetic socket sensors to improve prosthetic fit and rehabilitation. This is supervised by Professor Alison McGregor. Shruti has been working with Sarah Dixon-Smith to lead on the Centre's public engagement activities, building on her experience as an Outreach Coordinator at the University of Southampton.



**Enrico Varano** joined the Centre in September 2018 having graduated with a BEng in Engineering Design with Study in Industry from the University of Bristol. Enrico's PhD project is being supervised by Dr Tobias Reichenbach and is entitled 'Audiovisual hearing aids for APD treatment'. The project aims to employ non-invasive brain imaging techniques such as electroencephalography (EEG) to describe the effect of synthetic visual signals on speech in noise perception and auditory cortex response in healthy subjects, as well as sufferers of APD.

**Major Peter Le Feuvre** has a BA in Sports Science, a BSc in Physiotherapy, and an MSc in Physiotherapy. He has served within the Royal Army Medical Corp (RAMC), working at the Royal Centre for Defence Medicine (RCDM) and then at the Defence Medical Rehabilitation Centre (DMRC) Headley Court with battle casualties returning from operations (2006-2014). Peter joined CBIS in January 2018 and his PhD project entitled 'Defining a future rehabilitation pathway for lower limb military amputees: a consensus of clinicians, healthcare managers and patients' is supervised by Professor Alison McGregor.

### **PhDs awarded**

We would like to congratulate the following people who successfully defended their PhD theses in 2018!

David Sory – The effects of load and strain rate on biological systems – supervised by Dr William Proud.

Ben Butler – Adaptation of models to the study of blast injury – supervised by Dr Kate Brown.

Richard Pangonis – Blast biomechanics of the human head – supervised by Dr Mazdak Ghajari.

**Phill Pearce** – *Mechanisms of torso blast injury* – supervised by Professor Anthony Bull and Professor (Colonel) Jon Clasper.

Dan Zaharie – Mitigation of hard and soft tissue pelvic injuries – supervised by Dr Andrew Phillips.

#### Leavers

A number of Centre members have moved onto new positions and we would like to wish them all well in their new roles. We thank them for their valued input into the Centre over the years and we look forward to ongoing collaborations with them in the future.

Dr Erica Di Federico – moved to Queen Mary's University of London.

**Dr Grigorios Grigoriadis** – stayed at Imperial College London but has moved onto a project looking at low cost through-knee prostheses.

Dr Shabnam Kadir – became a Senior Lecturer at the University of Hertfordshire.

Dr Nic Newell – started a Fellowship in Mechanical Engineering on spinal biomechanics.

Sqn Ldr Phill Pearce – returned to full time surgery training.

Dr Darshan Shah – is undertaking a postdoctoral research position at KU Leuven.

LT COL Daniel Stinner – returned to the United States to continue his military and clinical duties.

Dr Fani Tsitouroudi – moved to working in industry.

# **Being a Researcher in CBIS**

### **Dr David Sory – Postdoctoral Researcher**

Since my earliest childhood, I have had a strong and inspiring interest in both life sciences and engineering. I followed a traditional education path in Latin and Science in Namur, Belgium and I gained my first degree with a 5-year program MSc course in Bioengineering, at the University of Liège. My inquisitiveness and passion for new technologies led me to the completion of a second MEng in Electromechanical engineering in Brussels. During the last academic year, I had the chance to do my Masters thesis within the context of a mobility program at the Israel Institute of Technology, Technion, in the Dynamic Fracture Laboratory, where I looked at stress wave propagation and dynamic tensile instabilities on split-Hopkinson pressure bar systems. Shortly after this international research experience, I moved to London where I undertook a cross-disciplinary PhD in cellular biomechanics of blast, funded by The Royal British Legion Centre for Blast Injury Studies (CBIS). My PhD took an interdisciplinary approach - combining technical expertise in shock physics and stem cell biology - to develop unique platform technologies that allow us to investigate the mechanical effects of improvised explosive device (IED) and landmine loadings on mesenchymal stem cells (MSC).

Due to the novelty of the research, this led me to pursue a post-doctoral research position in CBIS. My current research interests broadly encompass cell biomechanics under traumatic, non-physiological conditions, as recorded in near-field blast wave exposure. This project is particularly novel and quite challenging as this is the first research that incorporates the features of 3-D stem cell cultures under loading conditions replicating near-field blast wave exposure. My research as part of CBIS primarily focuses on understanding the effects of biomechanically-relevant loading to blast on cellular functions and integrity. This includes cell viability, cell proliferation and metabolic activity, and more importantly their ability to sense and respond to blast-like mechanical stimuli by producing bone- and cartilage-like tissue. My most recent work addresses the tailoring of transient mechanical stimuli to optimise the expression of osteogenic and chondrogenic markers in human MSCs.



Figure 6: A) Schematic of the split-Hopkinson pressure bar system we used to replicate loading conditions relevant to near-field blast loading. B) We developed a biocompatible pressurisation chamber to hold mesenchymal stromal cells in different 3D in vitro culture systems (e.g. single-cell suspension and 3D scaffold hydrogel). C) The loading conditions are tailored to match blast-relevant loading scenario.

Findings of my research would ultimately bring advanced knowledge on how adult MSCs respond to blast wave exposure events, specifically in the context of traumatic amputation due to IEDs and landmines, and the development of heterotopic ossification. My findings also raise the exciting possibility of using traumatic, non-physiological loading regimes as novel tissue engineering strategies for bone and cartilage regeneration.

Being a postdoctoral researcher involves a wide range of challenges and tasks on a day to day basis. Fundamental aspects of a researcher's job involve writing and reading. My typical day usually starts early in the morning, when it is the quieter, by writing, reading or analyzing data. This consists for instance of a quick search on the internet looking for new scientific publications which might be relevant in my research area, or the drafting of writing pieces that will be incorporated into a paper or an abstract for a conference. Thereafter, I complete some laboratory work, such as maintenance of cell cultures, preparing or finalising an assay, performing measurements and collecting data, or designing a new experiment.

There are a few key reasons why I really enjoy working as a part of CBIS. First, the Group is widely recognised at the national and international levels as the world-leading research group for blast injury studies. This is really rewarding. Secondly, it is a truly inspiring research environment where I get the chance to interact with lots of talented collaborators and partners across various fields. Finally, my job as part of CBIS allows me to pursue my career in cutting edge and novel areas of research that perfectly match my professional and personal interests. These help me to build my academic career plan on strong foundations.

## Biranavan Sivapuratharasu – Year Two PhD Student

As an undergraduate, I read Mechanical Engineering at Imperial College London. Throughout my degree, my interests were always with biomechanics. During my third year summer, I did a UROP with CBIS under the supervision of Dr Spyros Masouros. The project involved learning FEA software to model ligaments into a L4-L5 spinal structure to analyse the effect of the ligaments on the loading and posture of the spine. I then continued the work with CBIS and Dr Masouros for my master's project looking at gaining a better understanding of the motion of the intervertebral disc, its material properties and the parameters that affect it under quasi-static loading. I thoroughly enjoyed my experience with CBIS throughout my UROP and final year project. To me, research is much more enjoyable and therefore productive when you are able to collaborate with your colleagues. I enjoyed my research experience with CBIS so much, that I was convinced I wanted to further my research career by doing a PhD. As I could not find an appropriate PhD for me after graduating, I took up a job with Jaguar Land Rover as a graduate CAD/CAE engineer. I did not give up my intentions of doing a biomechanics PhD. I was ecstatic at the prospects I saw on the CBIS website for new PhD projects, I applied, and this is where I am now.

My PhD is on 'Understanding spinal loading in traumatic amputees'. Following the recent military conflicts, there is a huge number of amputees, and low back pain is a recurring problem amongst amputees. Although we know this pain exists, the cause in terms of the lower back mechanics is less clear. I use a motion capture system to monitor the movement of reflective markers on various anatomical locations of a subject in the laboratory during activities of daily living. I can observe posture, calculate the angles that different segments of the body make relative to another, and use a musculoskeletal model to calculate individual muscle forces. This tells which muscles are weak, and therefore causing any abnormal movements. This can help us feed back into the clinical world and instruct physiotherapists on how to improve amputee mobility.





Figure 7: Birana setting up motion capture system

Figure 8: Skeletal representation of the motion capture data

The two main challenges with my research involve recruiting amputees for participation and equipment limitations. Being part of CBIS has helped me jump over these hurdles easily. CBIS, as a research team is very collaborative; there will always be someone in the team that can and will help you. On a typical day, I start by going to the gym. Beyond this, there is no typical day – I could be experimenting, processing data, modelling, going to meetings or teaching. I love the fluidity of the work; never will I have two days that are the same.

It is amazing to be part of such a prestigious organisation, and my favourite part of it is that the focus of all the research that we do is the patient cohort. Research is only as good as its impact.

# Alumni

#### Dr Emma Burke – former Centre Manager

CBIS cemented the definition of 'multidisciplinary research' in my mind. I joined the Centre having worked in academia, industry and defence. I had years of experience engaging military and civilian personnel, engineers, medics and academics. I was well travelled and, consequently, had experienced a range of nationalities and cultures. Never before however, had I encountered all of this under one roof! CBIS prides itself on its collaborative nature, its focus on solving real world problems, and its practice of inclusivity in order to create benefit for all in society. I didn't need convincing to join the team.

I worked as Centre Manager at CBIS for three years from 2014. One of my first tasks in post was to coordinate the annual networking event, followed closely by the production of the annual report. To see the continuation and growth of both of these over the years highlights the commitment, drive and success of the team.

I left the Centre to pursue a role at UK Research and Innovation; a national body which works in partnership with universities and businesses to create the best possible environment in the UK for research and innovation to flourish. Working at CBIS taught me the importance of knowledge exchange, the value in translating lessons learnt, and the potential that resides in our universities. I now manage a programme of support for academic researchers to increase their capabilities in the commercial exploitation of their knowledge and expertise. This effort forms part of UKRI's aim to unlock greater economic benefit from our world-class research, and goes some way to keeping the UK in a competitive position on the world stage.

I witnessed several rewarding moments in my time at CBIS; the training of trauma surgeons from land-mine afflicted countries around the world (2016); the publication of the Blast Injury Science & Engineering textbook (2015) and a Lancet publication (2014). I look back fondly however at the time I convinced Prof Anthony Bull to do a bungee jump as part of Imperial College's RAG Week for Mines Advisory Group. I'm not sure he's forgiven me yet.

# **Exemplar Research Findings**

As you will have seen from the previous section, being a researcher in CBIS doesn't necessarily mean spending all your time in the laboratory. Research is a complex activity that involves significant amounts of planning, often technical development, reading and understanding the current level of knowledge in the field, securing funding for the work, spending time in the lab, on the computer, or conducting field work, and processing, analysing, and interpreting results. Almost none of this is done on your own; it is collaborative, and complex. Finally, and, most importantly, research has to be communicated. Sometimes research findings are negative in that a hypothesis is not proven, or the results are not what is expected and it is important that this is communicated so that others can learn from the work. Other times research produces important positive findings that can have significant impact. Impact can mean influencing other people's research, so that they can build on your findings, but it can also mean (and should mean) having societal benefit. The communication, therefore, is not just in learned publications, with rigorous peer review to maintain quality standards, improve communication, and provide credibility, but can also be in the popular press, through policy documents and by influencing people.

As such, the process of research can take a long time from start to finish and the publications that we highlight in this section may not represent the sole end point of research, but are an important marker of the quality and relevance of the work and represent years of work. The quality is highlighted by the work itself, but also the journals in which the work is published: excellent specialist journals (e.g. *Journal of Neurotrauma*) as well as general journals with broad readership (such as *Scientific Reports*). In the following pages we highlight some of the research outputs from the Centre in the past year. Many of the publications this year represent our historical and current strength in musculoskeletal research going all the way from clinical data on lower limb injuries through to computational modelling of bone, the formation of bone, and bone fracture. It is important to note that the computational work presented here represents major advances in technology that can now be applied to our priorities of protection, mitigation, treatment and rehabilitation.

It is also worth noting that as well as the research that CBIS produces each year and publishes in the open literature, many Centre members are involved in associated, non-CBIS, research projects. Whilst this associated research is not funded through the Centre, it is closely linked through the use of similar techniques, or working with the same patients or data. Centre members also have strong collaborations with researchers around the world to help drive their research forward. These close connections with other projects and other world-leading researchers ultimately helps to enhance knowledge and progress research in multiple fields. More information about associated grant funding and collaborations can be found on page 47.

#### Tibial osteotomy as a mechanical model of primary osteoarthritis in rats

#### Britzman D, Bull AMJ (2018) Scientific Reports, 8(1):5132

Military amputees have increased rates of knee osteoarthritis (wear and tear) in their nonamputated limbs. This means that, although they have the very best rehabilitation and prostheses, they are likely to end up with severe joint pain due to excessive loading on their good limbs. There are many approaches to experimentally understand and model this mechanically-induced osteoarthritis, yet noone uses a pure biomechanical approach: current models use surgery within the joint to induce osteoarthritis or use genetic approaches.

This study presented the first purely biomechanical surgical model of osteoarthritis in rats, which could be more representative of the human primary disease than intra-articular techniques published previously. A surgical tibial osteotomy was used to induce degenerative cartilage changes in the medial knee compartment of rats. Histology and serum analysis evaluated the arthritis changes. In-vivo biomechanical analyses were carried out using a musculoskeletal model of the rat hindlimb to evaluate the loading conditions in the knee pre- and post-surgically.

Qualitative and quantitative medial cartilage degeneration consistent with osteoarthritis was found in the knees of the operated animals alongside elevated serum II levels and increased tibial compressive loading.



Figure 9: Increased serum levels in the animals that subsequently produced osteoarthritis (left). Histology slides showing localised osteoarthritis on the medial side of the knee only (right).

This approach is a more physiologically fidelic way to model biomechanically-induced osteoarthritis such as that seen by military amputees.

## An in vivo model of biomechanically-induced knee osteoarthritis

- This is the first study to develop a biomechanical model of knee osteoarthritis that does not interfere within the joint, thus reduced the inflammatory component.
- This model can now be used to investigate the biology and mechanics of osteoarthritis post amputation.

# A novel in vitro model of blast traumatic brain injury

Campos-Pires R, Yonis A, Macdonald W, Harris K, Edge CJ, Mahoney PF, & Dickinson R, (2018) Journal of Visualised Experiments (142) e58400 doi 10.3791/58400 (2018)

Traumatic brain injury (TBI) is a leading cause of death and disability in military and civilian populations. The mechanisms that underlie brain trauma resulting from blast exposure are not fully understood, but are believed to be unique to this type of injury. Preclinical, *in vitro*, models are important in understanding blast-induced brain injury. We developed a novel *in vitro* blast TBI model using a shock tube to simulate open-field blast waves. This model can be used to understand the pathophysiology of blast trauma and to evaluate potential treatments for blast traumatic brain injury.



Figure 10: Schematic of the shock tube device with the sterile bag holder frame. (A). The shock tube is a 3.8 m long stainless-steel tube, made of three 1.22 m long sections, connected by gaskets and flanges, with an internal diameter of 59 mm. (B) Inset shows the double breech assembly. One or two Mylar diaphragms can be clamped in the assembly with seal provided by rubber o-rings. (C) Sterile bag holder frame.

# A novel model of blast traumatic brain injury

- Our model uses a shock tube to simulate explosive blast in the laboratory.
- Brain tissue slices from mice are exposed to blast shockwaves.
- The injury is proportional to the blast intensity.
- Our model is very reproducible.
- Our model can be used to investigate mechanisms of blast trauma and to evaluate potential new treatments.

# Xenon protects against blast-induced traumatic brain injury in an in vitro model

Campos-Pires R, Koziakova M, Yonis A, Pau A, Macdonald W, Harris K, Edge CJ, Franks NP, Mahoney PF, & Dickinson R (2018)

#### Journal of Neurotrauma, 35: 1037-1044

The aim of the study was to evaluate the potential of the noble gas xenon as a treatment to prevent or mitigate the effects of blast injury on the brain. Blast-traumatic brain injury (blast-TBI) is a "signature injury" of recent military operations. Despite an increasing research focus on blast-TBI pathophysiology, there are no clinically proven treatments to prevent or limit ongoing brain injury following blast-TBI. We used a novel *in vitro* model of blast TBI developed in the Royal British Legion Centre for Blast Injury Studies to determine whether xenon reduced injury to brain tissue following blast exposure. We showed that xenon treatment starting 1 hour after blast prevented the injury from developing. Our study showed that the xenon-treated brain tissue exposed to blast was not different from uninjured sham tissue. These findings suggest that xenon may be effective in treating blast TBI and further studies to evaluate xenon's potential are merited.





Figure 11: (A) Experimental timeline (B) A typical shockwave (C) Images showing (i) sham, (ii) blast (iii) xenon-treated blast slices. Red propidium iodide fluorescence indicates dead cells (D) quantification of intensity histogram Figure 12: Xenon-treatment prevents injury development after blast. Xenon-treated slices (red bars) are not significantly different to uninjured sham slices (white bars). Control blast shown as blue bars.

#### Xenon protects against blast TBI in vitro

- Injury is proportional to intensity of blast.
- Blast injury activates apoptotic cell-death pathways.
- Xenon treatment starting 1 hour after blast prevents injury developing.
- Xenon may be of benefit in treating blast TBI.

# Nano-scale mechanisms explain the stiffening and strengthening of ligament tissue with increasing strain rate

#### Karunaratne A, Li S, Bull AMJ (2018) <u>Scientific Reports, 8(1): 3707</u>

Ligaments are the structures that tether our joints. When muscles contract to rotate our joints then they produce shearing forces across the joints; these shearing forces are resisted by ligaments. Ligaments do not normally self-repair as, once torn, the ends of the ligaments are far apart and do not come together again. Ligament failure is a major societal burden causing disability and pain. Failure is caused by trauma at high loading rates. Prior work in the Centre has shown that, at the macroscopic level increasing strain rates causes an increase in failure stress and modulus (higher strength and stiffness; *Bonner et al, J Mech Behav Biomedl Mtls, 2104*), but the mechanism for this strain rate dependency is not known. The aim of this study was to investigate the nano-scale mechanical property changes of human ligament using mechanical testing combined with highly advanced X-ray diffraction imaging at the UK's national synchrotron science facility.

The study found that, with increasing loading rate, there was a significant increase in stiffness of the ligament fibrils and a reduction of fibril to tissue strain ratio. This shows that tissue-level stiffening is mainly due to the stiffening of collagen fibrils. Further, we found that the reduction in fibril deformation at higher strain rates is due to reduced molecular strain and fibrillar gaps, and is associated with rapid disruption of matrix-fibril bonding. This reduction in number of interfibrillar cross-links explains the changes in fibril strain. We also developed a computational model to investigate these effects and the model verified our experimental findings.





This study was able to show, for the first time, why ligaments stiffen with increasing loading rate, and why this is limited at very high loading rates. A computational model was developed that replicated the experimental findings. This fundamental understanding of scale-dependent mechanics at physiologically-relevant strain rates will allow us now to understand, simulate, and predict ligament injuries at loading rates found in blast. Specific areas of interest are the mitigation of bone fracture proximal to the knee in order to salvage through knee amputations that have higher functional outcome than above knee amputations. This information will also help to identify the optimum properties that are required for biomaterials and scaffolds to promote organisation, growth and differentiation of cells in the process of forming engineered functional tissues.

## Why ligaments stiffen and strengthen as loading rate increases

- We showed, at the nano-scale, why ligaments stiffen and strengthen as loading rate increases.
- Our computer model replicated the findings.
- These findings can now be used in designing tissue engineered ligament replacements as well as modelling the effect of mitigation at the knee to salvage the distal femur in blast amputations.

# Injury risk of the human leg under high rate axial loading

Mildon PJ, White D, Sedman AJ, Dorn M, Masouros SD (2018) Human Factors and Mechanical Engineering for Defense and Safety, 2: 5

# Initial adaptation of the injury risk of the human leg under high rate axial loading for use with a Hybrid III

#### Mildon PJ, White D, Girdlestone C, Keirl J, McGeehin W, Dorn M, Sedman AJ, Masouros SD (2018) Human Factors and Mechanical Engineering for Defense and Safety, 2: 6

These papers propose a new injury-risk function for the leg in loading relevant to under-body blast, and determine the correlation in response between the human leg and the surrogate leg most commonly used for vehicle qualification, the Hybrid III, in such loading conditions. The purpose of these studies was to improve the prediction of lower limb injury in live-blast vehicle tests.

In the first paper, the risk function considered proximal tibia force as the primary indicator of fracture, with age, sex and body mass considered as covariates. Previous studies considered age as a linear covariate to allow the elderly cadaveric population results to be mapped onto a younger population. The literature review as part of this study found, however, that bone strength varies non-linearly with age. Extrapolating bone strength linearly may therefore overestimate the strength of younger populations' lower limbs. This study used a non-linear variation of bone strength with age and optimised parameters within this function to produce a Weibull risk curve with a minimum spread.

The second paper determined a transfer function that relates the measurement from the lower tibia load cell of a booted Hybrid III to the axial force in a cadaver. By incorporating this transfer function into an existing injury risk function, a prediction of the likelihood of fracture within the human leg can be obtained from the Hybrid III data. The transfer function is based on a combination of published experimental data, new experiments, and computational modelling. This imposes limitations on the applicability of this prediction process and its accuracy. This tentative prediction process indicates that the 10% probability of fracture for a 55 kg female under 40 years old and for an 85 kg male under 40 years old wearing a desert combat boot is related to forces measured by the lower tibial load cell of a Hybrid III wearing the same boot of 7.2 and 11.7 kN, respectively. The transfer function suggested here is the best tool to date for interpreting Hybrid III leg forces into risk of injury to the human leg.

#### Blast-injury risk prediction for the leg

- The most commonly used surrogate in vehicle-blast tests the Hybrid III was not developed for blast injury and therefore does not predict injury risk accurately.
- This study combined international efforts on the leg's injury risk in under-body blast into a single risk function and produced the best tool to date for interpreting Hybrid III leg forces into injury risk to the human leg.

# Biomechanics of the human intervertebral disc: A review of testing techniques and results

#### Newell N, Little JP, Christou A, Adams MA, Adam CJ, Masouros SD. (2018) Journal of the Mechanical Behaviour of Biomedical Materials. Vol. 69 pp 420-434

Many experimental testing techniques have been adopted to provide an understanding of the biomechanics of the human intervertebral disc (IVD). The aim of this review article is to amalgamate results from these studies to provide readers with an overview of the studies conducted and their contribution to our current understanding of the biomechanics and function of the IVD. The review found that intervertebral disc behaviour can be strongly influenced by the testing environment, preconditioning, loading rate, specimen age and degeneration, and spinal level. Component tissues of the disc (anulus fibrosus, nucleus pulposus, and cartilage endplates) have been studied to determine their material properties, but only the anulus has been thoroughly evaluated. Animal discs can be used as a model of human discs where uniform non-degenerate specimens are required, although differences in scale, age, and anatomy can lead to problems in interpretation.



# Figure 14: Graphical representation of a spinal motion segment. ALL and PLL refer to the anterior and posterior longitudinal ligaments, respectively. The capsular ligament encloses the zygapophysial joint. The intertransverse ligaments (ITLs) are not shown but they extend between upper and lower borders of the transverse processes.

The aim of the study was to review the literature to determine the research that is required to ensure that the material properties of the intervertebral discs in the spine are well understood for blast related research. The output has shown that high rate characterisation of the discs is necessary. This will be the direction of future research.

## **Review of intervertebral disc properties**

- A wide range of experiments have been performed to characterise the properties of intervertebral discs, predominantly at slow strain rates.
- This review summarises results from these experiments in a format useful for experimentalists and computational modellers.
- The behaviour of intervertebral discs is rate dependent; therefore, this behaviour must be fully characterised at high strain rates for blast related application.

# Analysis of isolated transverse process fractures sustained during blast-related events

Newell N, Pearce AP, Spurrier E, Gibb I, Webster CE, Clasper JC, Masouros SD. (2018) Journal of Trauma and Acute Care Surgery, 85(15): S129-S133.

Personnel have sustained a range of devastating blast injuries during recent conflicts. Previous studies have focused on severe injuries, including to the spine; however, no study has specifically focused on the most common spinal injury—transverse process (TP) fractures. Although their treatment usually requires limited intervention, analysis of TP fractures may help determine injury mechanisms. Data were collected from victims with spinal fractures who were injured in improvised explosive device attacks, from the UK's Joint Theatre Trauma Registry. The level and side of each TP fracture were recorded, as well as associated injuries, whether they were mounted or dismounted, and outcome (survivor or fatality). Most (80%) of the TP fractures were lumbar. More bilateral (both left and right fractures at the same level), and L5 TP fractures, were seen in fatalities than survivors. In the mounted group, lumbar TP fractures were statistically significantly associated with fatality, head injury, noncompressible torso haemorrhage, pelvic injury, and other spinal injuries. In the dismounted group, thoracic TP fractures were associated with head, chest wall, and other spinal injuries; and lumbar TP fractures were associated with pelvic and other spinal injuries.



Figure 15: Axial slice of a CT scan showing a typical lumbar spine transverse process fracture

The aim of this paper was to analyse TP fractures sustained by both mounted and dismounted soldiers due to IED explosions during recent conflicts to determine a) the levels at which TP fractures are common, b) how the distribution of fractures changes across the spine in mounted and dismounted casualties and fatalities, and finally, c) which other injuries are associated with TP fractures.

# **Transverse process fractures in blast incidents**

- Different injury mechanisms of the TP in the mounted and dismounted groups are likely. Inertial forces acting within the torso due to rapid loading being transferred through the seat, or high intraabdominal pressures causing the tensile forces acting through the lumbar fascia to avulse the TPs are likely mechanisms in the mounted group.
- Blunt trauma, violent lateral flexion-extension forces, or rapid flail of the lower extremities causing tension of the psoas muscle, avulsing the TP, are likely causes in the dismounted group.
- Isolated lumbar TP fractures can be used as markers for more severe injuries, and fatality, in mounted blast casualties.

# Simulating localised cellular inflammation and substrate properties in strain energy density based bone remodelling algorithm for use in modelling trauma

#### Rosenberg NM, Bull AMJ (2018)

Computer Methods in Biomechanics and Biomedical Engineering, 21(3): 208-218

There is a high incidence of heterotopic bone formation in the stumps of military amputees. As bone responds to mechanical stimuli, the analysis of its formation and development is amenable to engineering computational approaches, such as finite element analysis. This can be applied to heterotopic bone formation, yet to date, computational models that replicate bone formation do not include inflammation effects (i.e. they are 'biomechanics'-only), yet inflammation is a key component of bone repair in trauma and is known to be important in heterotopic ossification. Therefore, in this study a mechanobiological algorithm is proposed and tested that extends pre-existing computational modelling methods to include parameters that could be considered to represent the behaviour of bone remodelling when influenced by inflammation.

This novel algorithm regulates bone remodelling based on findings from recent studies into the nature of heterotopic ossification. These findings required the algorithm to take into account the distance from the zone of trauma, the density of mesenchymal stem cells that could potentially form bone, and the stiffness of the substrate as a trigger for cells becoming osteogenic, i.e. able to turn into bone.

The novel algorithm was tested on a simplified geometry that is standard in the scientific literature and shows that the algorithm can produce a range of structures depending on inputs that could be used in the future to replicate physiological scenarios such as blast-induced traumatic amputation and subsequent heterotopic ossification.



Figure 16: Different internal bone structures produced by varying key parameters of the new mechanobiological algorithm

The aim of the study was to create a new mechanobiological algorithm to be able to replicate bone formation in severe trauma. This will now be applied to cases of heterotopic ossification.

## A mechanobiological algorithm for modelling bone formation in trauma

- Biomechanics alone cannot predict bone shape in an inflammatory-driven bone formation situation such as found in severe trauma.
- A mechanobiological algorithm was developed that takes into account important factors not previously modelled.
- The new algorithm is able to predict various bone structures and can now be applied to understand heterotopic bone formation in military amputees.

# Applications of a mechanobiological algorithm to investigate mechanical mediation of heterotopic bone in trans-femoral amputees

#### Rosenberg NM, Bull AMJ (2018) Scientific Reports, 8(1): 14196

Heterotopic ossification is the process of bone formation in tissues that do not normally contain bone. Approximately 2/3<sup>rds</sup> of those with blast-induced traumatic amputation develop heterotopic ossification and, as such, this is a major concern for the military. In particular, heterotopic bone forms in the soft tissues of the stumps of these amputees, causing pain, nerve impingement and affecting prosthesis fitting.

As with normal bone formation and remodelling, it is expected that heterotopic bone responds to mechanical stimuli. Understanding how mechanics influences heterotopic bone will give insight into the pathology.

Following on from prior work in the Centre for Blast Injury Studies (*Rosenberg and Bull, CMBBE, 2018*), the objective of this research was to investigate whether a novel mechanobiological algorithm could computationally simulate heterotopic bone formation in the residual limb of a trans-femoral traumatic amputee.

The study found that characteristic morphologies of HO were reproduced by changing the way that the residual limb is loaded, for example significant effects were produced by changing the loading direction on the femur; this is potentially associated with different initial surgical interventions such as muscle myodesis. Initial treatment such as negative pressure through a dressing was found to change the shape of the heterotopic bone produced.



Figure 17: Two dimensional computational models of heterotopic ossification demonstrating the effect of different geometries of stump as well as the effects of changing the loading on the stump. The models replicate the types of heterotopic bone seen in blast injured military amputees.

The aim of the study was to demonstrate the use of a novel mechanobiological algorithm developed in CBIS for the analysis of bone shape produced in blast injured military amputees.

The study demonstrated that, not only could the shapes of bone be replicated, but the bone mass and formation was significantly influenced by the loading changes on the stump; these loading changes could be modified by the initial treatment and rehabilitation and, as such, this work opens the way for future therapies.

#### Mechanobiology can explain the different bone formation in amputees

- The CBIS mechanobiological algorithm of heterotopic ossification was validated for an above knee blast injured amputee.
- Changing the loading on the stump significantly affected the shape and mass of heterotopic bone formed.
- This work can now be applied to develop mechanical therapies for heterotopic ossification.

# Rate and age-dependent damage elasticity formulation for efficient hip fracture simulation

#### Villette C, Phillips ATM. (2018) Medical Engineering and Physics, 61: 1-12

This study describes the development and application of an efficient bone fracture algorithm for use in structural finite element models, an example of which is given in the next paper summary. In computational modelling it is common to use a brittle material model in which once the material has reached yield it is considered to fail. This is a poor approximation of bone behaviour in which yield occurs at a lower strain than failure. A damage elasticity formulation in which Young's modulus is progressively lowered between yield and failure is an efficient way of representing the development of plastic strains without the need to define a complex yield surface and plastic flow criterion. The damage elasticity algorithm was developed based on datasets available in the literature, allowing for change in age and strain rate.



Figure 18: Fracture progression for a vertical load case acting on the femoral head using an Elastic Brittle (EB) and Elastic Plastic (EP) algorithm

The aim of the study was to apply the algorithm to a series of loading scenarios used in previous experimental studies to produce neck of femur fracture and then, in future apply this to bone failure due to blast loading scenarios. The damage elasticity algorithm was found to have superior performance compared to a brittle fracture algorithm, and was able to predict fracture initiation and progression as shown in Figure 18.

# Developing a bone fracture algorithm

- Damage elasticity algorithm superior to a brittle material model.
- Developed algorithm can predict fracture initiation and progression for use in blast loading scenarios.
- Can be used with structural and continuum finite element models.

# Characterization of lower extremity blast injury

Webster CE, Clasper J, Stinner DJ, Eliahoo J, Masouros SD (2018) <u>Military Medicine, Epub ahead of print</u>

The purpose of this study was to characterise lower extremity blast injury and to determine whether the amputation levels and associated injury characteristics correlate with a higher risk of mortality. The UK Joint Theatre Trauma Registry (JTTR) was interrogated to identify all lower extremity traumatic amputations sustained in Iraq and Afghanistan between January 2003 and the end of UK operations in August 2014. The mortality rates for each amputation level and associated injuries were determined. Of the 977 casualties, there were 679 (69.5%) survivors and 298 fatalities (30.5%). There was an increase in survivability from traumatic amputation throughout the conflict, however, traumatic amputations at the close of military activity in 2014 still had a substantial fatality rate of 23%. A more proximal level of amputation, an associated pelvic fracture, and an associated abdominal injury all correlated with an increased mortality rate.

Injury prevention and mitigation measures should be explored to minimize the risk of the associated injuries following blast that portend a higher risk of mortality. Current work is focusing on the protection of pelvic blast injury exactly due to its correlation with mortality.





## Lower extremity blast injury

- A more proximal level of amputation, an associated pelvic fracture, and an associated abdominal injury all correlate with an increased mortality rate.
- Due to the current battlefield limitations of haemorrhage control for junctional, intra-abdominal, and truncal injuries, mitigation efforts should focus on protecting lower extremity injury and mitigation of proximal extension of that injury to the pelvis and abdomen in order to increase survival rate following blast injury.

## Pelvic construct prediction of trabecular and cortical bone structural architecture

#### Zaharie DT, Phillips ATM. (2018) Journal of Biomechanical Engineering, 140(9): 091001

This study uses a combined musculoskeletal and finite element computational modelling approach to predict the structural architecture of the pelvis. A bilateral musculoskeletal model of the lower limbs is used to predict joint contact, muscle and inertial forces acting on the pelvic bones for the five most frequent activities of daily living (walking, ascending and descending stairs, sit-to-stand and stand-to-sit) with the resulting set of forces providing the loading envelop for the finite element model. The finite element model is a structural model, which used bar elements to represent trabecular bone and shell elements to represent cortical bone. Based on a mechanostat (similar to a thermostat but using a mechanical stimulus such as strain rather than temperature) the cross-sectional geometries of the elements in the finite element model were updated until the strains were within a target range when the loading envelop was applied. The resulting trabecular and cortical structures are shown in Figure 20.



Figure 20: Predicted trabecular (left) and cortical (right) structures across the pelvic construct

The aim of the study was to develop a structural model of the pelvis, which provides an efficient and low cost option for studying fracture initiation and progression that can be used in understanding pelvis failure in blast, in comparison to other finite element modelling approaches and experimental studies. An advantage of predicting a structural representation of the pelvic bone is that it provide information similar to micro-CT based on CT or MRI imaging to give the outer shape of the bone.

The developed structural model is now being used with the fracture algorithm detailed in the previous paper summary to assess potential fracture mechanisms of the pelvic construct under a range of loading scenarios, including blast. Future application of the model will assess the level of mitigation provided by protective devices. The model can also be developed to include vasculature. The model also allows for the additive manufacture of the predicted pelvic structure for use as a frangible surrogate.

# Predicting pelvic bone structure

- Process does not require detailed medical images.
- Predicted structure allows efficient and low cost fracture studies for use in blast.
- Predicted structure can be 3D printed using additive manufacture for use as surrogates in physical experiments.

# Appendix

## **Publications**

Below is a list of publications that have arisen from the work within the Centre. Journal publications are important platforms for disseminating research findings.

Britzman D, Bull AMJ (2018). *Tibial osteotomy as a mechanical model of primary osteoarthritis in rats.* Scientific Reports, 8(1): 5132.

Bull A, Mayhew E, Reavley P, Tai N, Taylor S (2018). *Paediatric blast injury: challenges and priorities*. The Lancet Child & Adolescent Health, 2(5): 310-311.

Campos-Pires R, Koziakova M, Yonis A, Pau A, Macdonald W, Harris K, Edge CJ, Franks NP, Mahoney PF, & Dickinson R (2018). *Xenon protects against blast-induced traumatic brain injury in an in vitro model*. Journal of Neurotrauma, 35: 1037-1044.

Campos-Pires R, Yonis A, Macdonald W, Harris K, Edge CJ, Mahoney PF, & <u>Dickinson R</u> (2018). *A novel in vitro model of blast traumatic brain injury*. Journal of Visualised Experiments, 142, e58400 doi 10.3791/58400

Logan NJ, Camman M, Williams G, Higgins CA (2018). *Demethylation of ITGA accelerates osteogenic differentiation in a blast-induced heterotopic ossification in vitro cell culture model*. Bone, 117; 149-160.

Karunaratne A, Li S, Bull AMJ (2018). *Nano-scale mechanisms explain the stiffening and strengthening of ligament tissue with increasing strain rate.* Scientific Reports 8(1): 3707.

Mildon PJ, White D, Girdlestone C, Keirl J, McGeehin W, Dorn M, Sedman AJ, Masouros SD (2018). *Initial Adaption of the Injury Risk of the Human Leg Under High Rate Axial Loading for Use with a Hybrid III.* Human Factors and Mechanical Engineering for Defense and Safety, 2: 6.

Mildon PJ, White D, Sedman AJ, Dorn M, Masouros SD (2018). *Injury Risk of the Human Leg Under High Rate Axial Loading*. Human Factors and Mechanical Engineering for Defense and Safety, 2: 5.

Newell N, Pearce AP, Spurrier E, Gibb I, Webster CE, Clasper JC, Masouros SD (2018), *Analysis of isolated transverse process fractures sustained during blast related events*. Journal of Trauma and Acute Care Surgery, 85 (1S): S129-S133.

Rosenberg NM, Bull AMJ (2018). *Application of a mechanobiological algorithm to investigate mechanical mediation of heterotopic bone in trans-femoral amputees*. Scientific Reports 8(1): 14196.

Rosenberg N, Bull AMJ (2018). Simulating localised cellular inflammation and substrate properties in a strain energy density based bone remodelling algorithm for use in modelling trauma. Computer Methods in Biomechanics and Biomedical Engineering, 21(3): 208-218.

Villette CC, Phillips ATM (2018). *Rate and age-dependent damage elasticity formulation for efficient hip fracture simulations*. Medical Engineering and Physics, 61; 1-12.

Webster CE, Clasper J, Stinner DJ, Eliahoo J, Masouros SD (2018). *Characterization of lower extremity blast injury*. Military Medicine, 183(9-10); e448-453

This paper was selected by the US Department of Defense Blast Injury Research Program Coordinating Office as the highlight publication of the month (May 2018) as 'significant research in the area of blast injury prevention, mitigation, and treatment'. Zaharie DT, Phillips ATM (2018). *Pelvic construct prediction of trabecular and cortical bone structural architecture*. Journal of Biomechanical Engineering, 140(9); 091001.

As well as the list of publications above, there are many other publications which are produced by Centre members. The above list has been kept to only those which are of direct relevance and funded by the Centre for Blast Injury Studies.

# **Book Chapters**

Pearce P and Clasper J (2018). *Conflict Surgery*. Chapter in Bailey and Love's Short Practice of Surgery. McCaskie A, O'Connell PR, Williams N (eds), 27<sup>th</sup> Edition, Taylor and Francis.

## **Invited Talks**

Bull AMJ: *Development of a new combined computational – experimental model of osteoarthritis.* Modelathon, Sheffield, UK. 2018.

Clasper J: *Military Trauma in the Military Setting – Managing Ballistic and Blast Injury.* Orthopaedic Trauma Society Meeting, Bristol, UK. January 2018

Clasper J: James IV Professorship Lecture. British Orthopaedic Association (BOA), Birmingham, UK. September 2018

Clasper J: Clinical Aspects of Blast. Military Medical Course, Cranfield, UK. October 2018.

Clasper J: Blast Injuries. TriService Radiology Conference, Camberley, UK. November 2018.

Clasper J: *The Centre for Blast Injury Studies*. University of Moratuwa, Sri Lanka. November 2018.

Le Feuvre P: Defining the components of Care. Defence Engagement visit, London, UK. March 2018.

Le Feuvre P: *Defining the components of Care.* Royal British Legion Supporters visit to CBIS, London, UK. June 2018.

Le Feuvre P: *A golden moment for Defence Rehab, or a glimpse of the future?* British Forces Germany Medical Rehab Update Day, RRU Sennelager, Germany. November 2018.

McGregor A: Invited talks for TRBL throughout the year.

Reichenbach T: *Decoding the brain's response to speech*. Speech in Noise Workshop. Medical Research Council Institute of Hearing Research, Glasgow, UK. January 2018.

Reichenbach T: *Towards a smart hearing aid*. EPSRC Workshop: Changing perceptions: Hearing, Psychoacoustics and ICT, Bristol, UK. February 2018.

Reichenbach T: *Selective attention to speech: neuronal modulation in the auditory brainstem*. Newcastle Auditory Group, University of Newcastle, UK. February 2018.

Reichenbach T: *Selective attention to speech: neuronal modulation in the auditory brainstem*. Wellcome Centre for Neuroimaging, University College London, UK. June 2018.

Reichenbach T: *Towards real-time decoding of speech processing*. Neuromorphic Cognition Engineering Workshop, Telluride, USA. July 2018.

Reichenbach T: *Towards a smart hearing aid*. Imperial Audio Group, Imperial College London, UK. December 2018.

Rice A: *Doomed to go in company with miserable pain – the history of post amputation pain in First World War veterans.* Topical workshop on Chronic neuropathic pain as a consequence of warfare; using the medical legacy of the first world war to inform 21<sup>st</sup> Century medical research and practice. 17<sup>th</sup> World Congress on Pain, Boston, USA. September 2018.

Rice A: *Footsteps in the fire: burning feet syndrome in Far East prisoners of war.* Satellite Symposium Pain in Military veterans – after the conflict in the battle continues. 17<sup>th</sup> World Congress on Pain, Boston, UK. September 2018.

Turner S and Dixon-Smith S: Royal Society of Medicine, as part of a day organised by the military section of the Royal Society of Medicine. November 2018.

# **Conference Presentations and Involvement in Subject Specific Meetings**

Government Experts on Mitigation Strategies (GEMS), Cranfield, UK. January 2018

Pearce P, Masouros SD, Clasper J, Bull AMJ, Injury patterns within the underbody blast environment.

Perturbing and Enhancing Perception and Action using Oscillatory Neural Stimulation, Cambridge University, UK, January 2018.

Kadir S, Kaza C, Allaway G, Weissbart H, Reichenbach T, *Towards electrical stimulation for the treatment of auditory processing disorder* 

Midwinter meeting of the Association for Research in Otolaryngology, San Diego, USA, February 2018.

Etard O, Reichenbach T, *EEG-measured correlates of comprehension in speech-in-noise listening*.

Kadir S, Kaza C, Reichenbach T, Neuromodulation for enhancing the comprehension of speech in babble noise.

14<sup>th</sup> Annual Injury Biomechanics Symposium, Ohio, USA. May 2018.

Yu X, Sharp DJ, Ghajari M, The effects of CSF cut-off pressure and skull flexure on blast induced traumatic brain injury.

Auditory EEG signal processing symposium, University of Leuven, Belgium, May 2018.

Kegler M, Etard O, Forte AE, Reichenbach T, *Real-time decoding of selective attention from the human auditory brainstem response to continuous speech.* 

British Journal of Anaesthesia Research Forum, London, UK. May 2018

Campos-Pires R, Yonis A, Pau A, Macdonald W, Harris K, Edge CJ, Franks NP, Mahoney PF, Dickinson R, *Xenon is neuroprotective against blast traumatic brain injury in vitro*.

British Journal of Anaesthesia Research Forum, London, UK. May 2018

Campos-Pires R, Armstrong S, Sebastiani A, Luh C, Gruss M, Radyushkin K, Hirnet T, Werner C, Engelhard K, Franks NP, Thal SC, Dickinson R, *Xenon treatment improves short-term and long-term outcomes in a rodent model of traumatic brain injury*.

Combined Services Orthopaedic Society conference, Birmingham, UK. May 2018.

McMenemy L, Ramasamy A, Williamson B, Sherman K, Phillip R, Kendrew J, Osseointegration in bilateral above knee amputees following blast: 2 year follow up results from the initial cohort of UK service personnel.

Newell N, Pearce P, Spurrier E, Webster C, Gibb I, Clasper J, Masouros DF, Transverse process fractures in blast

Pearce P, Masouros SD, Clasper J, Bull AMJ, Injury patterns within the underbody blast environment

Webster C, Carpanen D, Clasper J, Masouros SD, The dismounted blast pelvis.

NAFEMS (National Agency for Finite Element Methods and Standards) UK Conference, Milton Keynes, UK. July 2018.

Grigoriadis G, Newell N, Carpanen D, Masouros SD, An inverse finite element method to quantify complex material behaviour.

World Congress of Biomechanics, Dublin, July 2018.

Grigoriadis G, Carpanen D, Webster C, Newell N, Masouros SD, *Lower limb posture determines the mechanism of injury in under-body blast.* Oral presentation.

Hopkins M, Vaidyanathan R, McGregor AH, Development of a smart socket sensor for pressure measurement in lower limb prosthetic applications.

Pearce AP, Clasper J, Masouros SD, Nguyen TT, Bull AMJ, *The biomechanics of blast related torso injury: Development of a small animal model of under body blast.* Oral presentation.

Basic Auditory Science Meeting, Newcastle University, UK, September 2018.

Saiz-Alia M, Forte AE, Reichenbach T, Hidden hearing loss and selective attention in the brainstem.

BioMedEng18, London, September 2018.

Pangonis R, Ghajari M, A novel mechanical testing apparatus for brain tissue.

Turner S, McGregor AH, Visualising complex 3D data in a clinical environment.

International Association for the Study of Pain World Congress, Boston, USA, September 2018.

Dixon-Smith S, *Blast injury and chronic pain: mining First World War pension and medical archives.* Poster presentation.

International Research Council for the Biomechanics of Injury (IRCOBI), Athens, Greece, September 2018.

Draper D, Newell N, Wernicke P, Fuchs T, Masouros SD, Peldschus S, A Comparison of the Compressive Behaviour of Lumbar Intervertebral Discs in Five Human Body Finite Element Models

Grigoriadis G, Carpanen D, Webster C, Newell N, Masouros SD, *The posture of the lower limb alters the mechanism of injury in under-body blast*.

Rebelo E, Grigoriadis G, Carpanen D, Masouros S, Protection of the Foot and Ankle in Under-Body Blast

Yu X, Sharp DJ, Ghajari M, Investigation of CSF volumetric response and skull flexure effect on blast induced traumatic brain injury.

War Through Other Stuff, Twitter Conference, September 2018

Dixon-Smith S, Turner S, *Blast injury and rehab*. Online presentation.

Defence Medical Services: Medical Innovation Conference, Birmingham, October 2018

Le Feuvre P, McGregor AH, Rehabilitation from Blast Injury.

Blast Injury Conference 2018, London, November 2018.

Azor AM, Ghajari M, Baxter D, Midwinter M, Hellyer PJ, Sharp DJ, *Effect of blast-induced traumatic brain injury on white matter integrity.* Poster presentation.

Bruyns-Haylett M, An investigation of simulated open field blast-induced damage of the auditory cortex at the level of cells and neural circuits using in vivo rat model. Oral presentation.

Dixon-Smith S, *Blast injury and chronic pain: mining First World War pension and medical archives.* Poster presentation.

Donat CK, Ghajari M, Yanez Lopez M, Goldfinger M, Baxan N, Gentleman S, Sastre M, Sharp DJ, Understanding the impact effects of Blast-related Traumatic Brain Injury through combination of high-field MRI, computational modelling and histology. Oral presentation.

Le Feuvre P, Sherman K, Neal P, Understanding the process of recovery for a military lower limb amputee. Oral presentation.

Sivapuratharasu B, Bull AMJ, McGregor AH, Understanding spinal loading in traumatic amputees: a systematic review & low back pain protocol. Oral presentation.

Turner S, McGregor AH, The impact of socket fit of lower limb prostheses on rehabilitation. Oral presentation.

<u>'Development of Medicine from the Crimea to the Present Day' at the Royal Society of Medicine, London,</u> UK, November 2018.

Dixon-Smith S, Turner, S, Long term effects of traumatic amputation'. Oral presentation.

## Grants

Within 2018, Centre members have received a number of grants that relate to our research. These include:

Funder	Amount	Title	Brief description
DSTL	£60k	Predicting penetration through skeletal tissue	Quantification of the risk of secondary blast injury to the chest wall and scapula
EPSRC and NIHR	£888K	Low cost through knee prostheses; TakeUP	Novel frugal technologies for through knee amputees in low and middle income countries
EPSRC	£1.7M	The Smart Implant Prototype & Manufacture Unit	Strategic equipment grant. In- house ability to make novel prosthetics and implants
MRC	£471K	Organ-on-a-Chip Technology Touching Lives Network	A network to expand Organ-on-a- Chip research in the UK

# **Collaborations**

Centre members have many collaborations across the world and collaborative working is an important aspect of furthering research. Within the UK we collaborate with Bristol University, University of Cambridge, University of Manchester, Manchester Metropolitan University, Oxford University, University College London, Blatchford Ltd, Royal College of Physicians, and Defence Medical Services. We also work with colleagues in Europe (Karolinska Institute (Sweden), the Université de Lorraine (France) and Saarland University (Germany)), the United States (Boston University, University of Iowa, Loyola Marymount University, University of Virginia and the Walter Reed National Military Medical Center) and Asia (Northwestern Polytechnical University and the National University of Singapore).

Below are some specific examples of the above-mentioned collaborations:

Dr Mazdak Ghajari invited Prof Li Yulong (Northwestern Polytechnical University), as well as members of his group, to visit CBIS. Together, they submitted an application for the Royal Society UK-China joint research travel grant.

Centre researchers working on blast traumatic brain injury have an ongoing collaboration with the National University of Singapore on non-human primate models of blast induced brain injury.

Dr Cornelius Donat spent one week at Boston University, within Professor Lee Goldstein's lab and he will be undertaking a longer placement to work on an animal model of blast traumatic brain injury in 2019.

Professor Anthony Bull has an ongoing collaboration with colleagues at the Walter Reed National Military Medical Centre about musculoskeletal modelling and gait analysis.

# **Education**

Centre members are involved in education through a range of activities at Imperial College London. This varies from teaching on courses for undergraduates and postgraduates to supervising students during projects of varying durations. Below are some examples of the activities that members have been involved in this year.

## **Undergraduate Projects**

A number of undergraduates have worked with Centre members this year. Below is an overview of some of the projects:

- Project 1: Peter Le Feuvre supervised an undergraduate medical student, Sereena Singh, on a project entitled 'Analysis of military prosthetic evaluation questionnaires'. The student spent two weeks at DMRC Headley Court where they organised and started to catalogue and record results from questionnaires completed by military amputees whilst they underwent their rehabilitation within the military. These questionnaires provide an indication of their satisfaction with their prosthetics, as well as additional issues they may have, such as lower back pain, and phantom limb pain.
- Project 2: Shruti Turner supervised two third year undergraduates (Shivali Jain and Akhil Patel) who looked at data analyses to identify sensory redundancy in the smart socket sensors and improvements to data visualisation.
- Project 3: George Meek was supervised by Dr Thuy-Tien Nguyen and Dr Spyros Masouros for a project entitled 'Protection from secondary blast injury'.
- Project 4: a large undergraduate group of engineers and medics was supervised by Professor Anthony Bull for a project to create a novel surrogate (crash test dummy) that is able to physically replicate the injuries due to very high accelerations of the shoulder and thorax.

## **Masters Projects**

This year, Centre members were also involved in the supervision of multiple Masters projects. Below are some examples of these projects:

- Project 5: Yann Tardy 'Decoding of auditory processing disorder' co-supervised by Dr Tobias Reichenbach and Octave Etard. The project began the decoding of auditory processing disorder from EEG recordings. To this end different machine learning classifiers were trained and evaluated on EEG recordings in response to speech acquired from patients with auditory processing disorder as well as from healthy control subjects.
- Project 6: Jessica Chadwick 'Vascular Damage in CCI Model of Traumatic Brain Injury' cosupervised by Dr Cornelius Donat, Dr Magdalena Sastre and Marc Goldfinger. The project aimed at quantifying damage to the neurovascular unit in an impact model of Traumatic Brain Injury. Injury caused widespread severity-dependent astrogliosis, aquaporin IV upregulation and collagenous thickening, in areas predicted by computational modelling.
- Project 7: Franziska Müller 'Relationship between neuroinflammatory responses and white matter changes in a controlled cortical impact model of traumatic brain injury in rats' – supervised by Dr Cornelius Donat, Dr Magdalena Sastre and Marc Goldfinger. The project aimed at identifying the relationship between chronic glial-mediated neuroinflammation and white

matter damage in an impact model of Traumatic Brain Injury. Upregulation of glial-markers, quantified using state-of-the-art machine learning, was observed ipsilateral to injury in white matter structures, along with corpus callosum thinning and neurofilament loss. This indicates a secondary neuro-inflammatory response in white matter structures, triggered by the initial biomechanical strain as predicted by computational modelling.

- Project 8: Tim Closs – 'A Novel Thoracotomy Device' which was supervised by Professor Anthony Bull.

