Imperial College London

THE ROYAL BRITISH LEGION

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CENTRE FOR BLAST INJURY STUDIES
AT IMPERIAL COLLEGE LONDON

2020 & 2021

CBIS Annual Report

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

January 2023

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

London, January 2023

Imperial College of Science, Technology and Medicine

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Introduction from Centre Director

"The COVID Years"

2020 and 2021 will forever be remembered as the COVID years. This is also the case for the Centre for Blast Injury Studies. We started 2020 full of hope: having been invited by Surgeon General to host a summit on traumatic brain injury we were able to bring together from across the globe a group of research leaders in London in early January 2020. This was the last international meeting that CBIS hosted. Our sister activity, the NIHR Research Group on Post Conflict Trauma (PrOTeCT) led by CBIS academics had an Advisory Board meeting in-person in early March under complex social distancing rubrics and little did we know that that would be the last time for a very long period we would be able to travel and bring people together in one room. The university closed its labs to everything that wasn't COVID-related a few days before the national lockdown started on the 23rd March and we immediately pivoted in a number of significant ways for which I thank all my colleagues and our amazing students.

One example is that we invited students and staff to work on the COVID response. We had medics who volunteered in the NHS, technicians making up alcohol-based hand sanitiser for our local NHS Trust, students manufacturing and assembling face masks for those on the COVID front-line and one of our CBIS PhD students worked on devising *a pandemic ventilator that could be deployed quickly*. The rest of us continued to work remotely on CBIS activity using technology (Zoom, phone and Teams.. some of us even used Skype), as well as making sure that we met in person when we could. For example, regular research meetings took place in my garden when permitted and colleagues went out for walks together as part of their daily exercise.

Many of us suffered personally through bereavement, anxiety and childcare and remote working pressures, yet the resilience and fortitude of all CBIS members has been truly astounding. This report is testimony to the excellence and productivity of the Centre members. We decided to cover the main COVID years in one report and have focused primarily on our research achievements over those two years.

We invite you the reader to contact the Centre if you have any comment on our activities or thoughts on how we can better serve our key beneficiaries: military personnel and veterans with blast injuries.

Professor Anthony M J Bull FREng
Director, The Royal British Legion Centre for Blast Injury Studies at Imperial College London

2020/21 – The COVID years in numbers

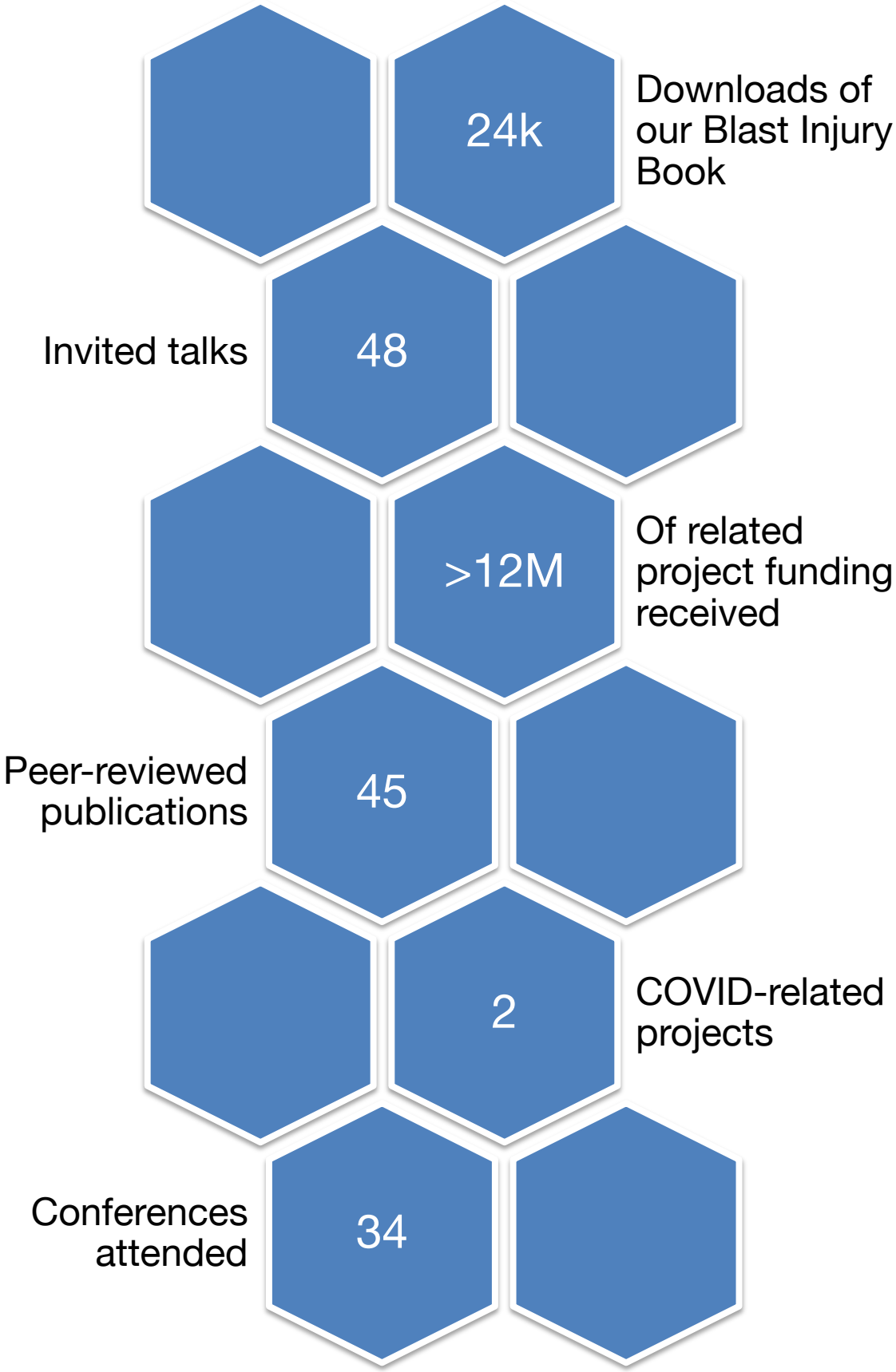


Figure 1: 2020/21 – The Covid Years in Numbers.
This infographic provides an overview of some of the Centre's achievements across the two years.

Impact

The Centre's unique collaboration between engineers, scientists, and clinicians, all with a focus on blast injuries, has produced important outputs over the last decade. This section briefly discusses some of the impact that the Centre has had in the field of blast injury.

Ballistic Protection

A project by Dr Spyros Masouros was funded by the 'Strategic Priorities Fund – Evidence-based policy making' from Research England through Imperial College, to generate the evidence to show that biofidelic backing is required when testing soft body armour. The results, obtained for two common ballistic fabrics across six different projectiles support the use of a biofidelic backing material in ballistic assessment of soft body armour.

The results have been published in the Human Factors and Mechanical Engineering for Defense and Safety journal, presented in LWAG and in GEMS, and sent to contacts in DE&S and DRDC, who sit in the NATO STANAG committee (2920) for ballistic protection.

Research Excellence Framework 2021

The Research Excellence Framework (REF) is the UK's system for assessing the quality of research in UK higher education institutions. First taking place in 2014 (replacing the previous Research Assessment Exercise), the exercise was repeated in 2021. REF is undertaken by the four UK higher education funding bodies from England, Scotland, Wales, and Northern Ireland. It is a process of expert review, carried out by expert panels for each of the 34 subject-based units of assessment, under the guidance of four main panels. For each submission, three distinct elements are assessed: the quality of outputs, their impact beyond academia, and the environment that supports research.

As part of this exercise, Imperial College London submitted a case study on *"Mitigation, Treatment and Influence within the Field of Blast Injuries"*, from the Centre for Blast Injury Studies. The case study outlined various contributions that CBIS has made to improve mitigation, advance treatment of blast injuries and influence policy and practice in the period 2014-2021. The following examples were taken from the case study, so were mostly conducted before the majority of this Covid Years Report.

Mitigation. The case study included Dr Spyros Masouros's contribution to a project related to a tender for new and improved UK Army gloves; this was supported by published work led by Dr Masouros and Dr Kedgley on quantifying the risk of injury to the small joints of the hand due to blunt impact and a report on assessing dexterity and protective ability of the existing gloves. The case study also included a significant amount of work of Dr Masouros's lab related to the mechanism of injury of military-vehicle occupants during an under-vehicle explosion.

With respect to **impact relating to treatment**, CBIS ensured the correct and accurate positioning of pelvic binders following blast injury. By emphasising the need for the training of military personnel in the correct use of the binder, those injured in this way have a much higher chance of survival. CBIS also co-led on the Paediatric Blast Injury Partnership and the development of the Paediatric Blast Injury Field Manual. The research investigates the injury patterns seen in children who are victims of blast injuries and has shown that some injury characteristics in children are distinct from those in adults. This will help to optimise care of children after a blast event with the Field Manual providing vital information to those treating child blast victims in the field.

The **rehabilitation** work included further investigation into the 'deck-slap' foot injury during the Afghanistan conflict. These were seen when mines detonated under a vehicle causing foot and ankle injury due to the rapid rise of the vehicle's floor. Results for the Direct Skeletal Fixation (DSF) for bilateral lower limb, above knee amputees showed improvements experienced by the initial cohorts.

Media Activity

Below are some images representing examples of our media activity in 2020/2021. To read a specific article, click on the relevant image.

Brain injury computer models brain blood vessels in highest resolution yet

Imperial College London News

July 2021

Precise mapping shows how brain injuries inflict long-term damage

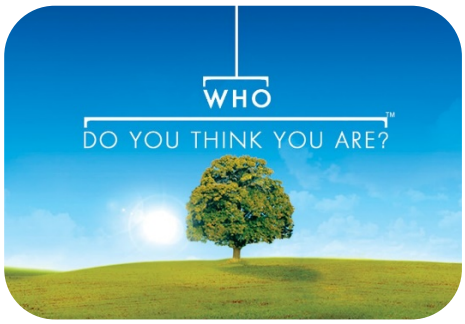
Imperial College London News

January 2021

Features about CBIS researchers

Blesma Magazine

October and November 2020, April 2021



Who do you think you are with actress Jody Whittaker

BBC One

October 2020

Trauma recovery: new science and technology for mental and physical health

The Royal Society

March 2020

Save the Children special with Emily Mayhew, James Denselow (Save the Children) and Dave Henson

Declassified Podcast

November 2020

COVID-19/Lockdown Activities

During the first national lockdown in March 2020, the Centre got involved in activities addressing the situation in various ways.

Emily's potato project

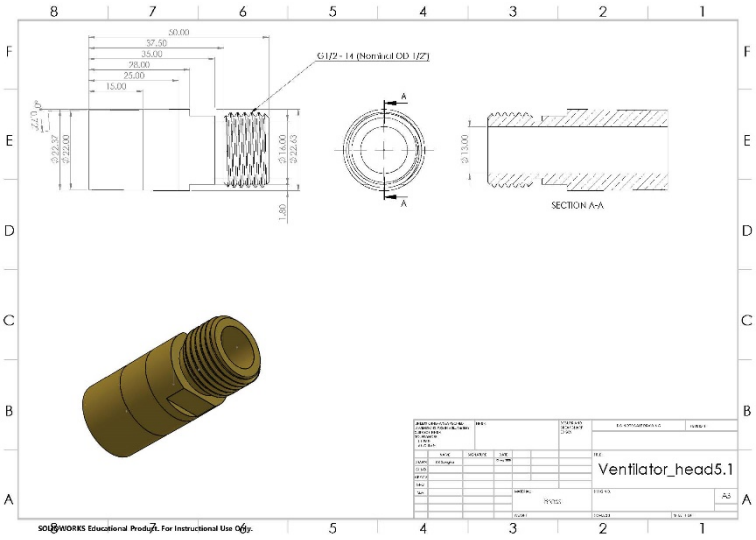
Dr Emily Mayhew, Historian in Residence at CBIS, created a "History of the Potato" series which she used to educate and entertain the children of the Bioengineering staff members during the first lockdown. Whilst working on a new book, Emily welcomed the distraction of developing an education series on a completely new subject. The subject matter was inspired by plans to introduce a natural history GCSE into school curriculum, and teaching something that could be useful to the students in the future.

The Potato Project comprised 12 learning sessions ranging from the evolution of the potato in the Andes and the development methods of the Incan farmers to make it a staple crop, through the potato famine in Ireland in 1845, to industrial production of potatoes for mash and crisps. Activities within the lessons included designing a new flavour of crisps, a recipe for mashed potato, and discovering the origins of Mr Potato Head. Both the students and Emily really enjoyed these lessons and came out of the series with a new appreciation for the humble potato.

Emily was also given a Thank You Award from the Department for her work with the children. An interview about the project can be found on the *Department of Bioengineering website*.

Jamvent ventilator design

During the lockdown, the Centre's Technical Supervisor, Satpal Sangha, was asked by the Jamvent team at Imperial College London (*https://www.jamvent.com/*), to help design a solution for connecting their system to the classic and universally used ventilation tubing. Satpal worked with a design brief from Jamvent to design a vent adaptor that took all aspects of the standard into consideration and was fitted with components that were readily available off the shelf. Whilst the first iteration worked satisfactorily, Satpal was keen to streamline the design and manufacturing process further to enable the vent adaptor to be fitted with greater ease and directly connect to the tubing. The final iteration managed to take everything into account and included a Computer Numerical Control (CNC) process which could complete the manufacture of the component in a matter of minutes. Speaking about the project Satpal said, "amongst many of the projects I was involved in during the height of the pandemic, this felt like a really rewarding piece of work as it helped unplug a blockage in the project and allowed for a vital piece of departmental work to progress."



Design of ventilators for COVID-19 patients

Dr Alastair Darwood, a PhD student within CBIS and an NHS clinical entrepreneur fellow teamed up with RedBull Racing and Project Pitlane, a consortium of Formula 1 teams, to produce a rapidly manufactured COVID ventilator following the request of the Government at the beginning of the first lockdown. The ventilator was based on Dr Darwood's design. In a matter of weeks, the teams finalized the design and testing for a production-based device and began the manufacture of 5000 units. Thankfully, the UK found no need for excess ventilators and the project was wound down, but Dr Darwood certainly found it an interesting way to spend lockdown. A YouTube video about the project is available on *https://www.youtube.com/watch?v=0wHhn1WapRY&feature=youtu.be*. Dr Darwood now continues his entrepreneurial design activities and we are sure to be highlighting him in a future annual report.

Governance and Staffing

Governance

The Royal British Legion

The Royal British Legion are the core funders for the Centre for the period 2011-2022 and provide oversight of the Centre's work. Members of The Royal British Legion attend events run by the Centre and Professor Bull meets with the Legion's Director of Operations for discussions about the Centre and formal reporting.

Imperial College London

Imperial recognises CBIS as one of its twenty Centres of Excellence. The Centre therefore provides an annual formal report to the Vice Provost of Research and Enterprise and smaller updates about activities every two months. The formal reports are considered and scored on the risk to sustainability, the Centre's original objectives, its outputs, and the leadership and governance. The institution's continued support of the centre is contingent upon good scores in these categories and gives CBIS a high-profile institutional backing.

Management Group

The Centre Director (Professor Anthony Bull), Clinical Lead (Professor Jon Clasper), three Associate Directors (Professor Alison McGregor, Dr Spyros Masouros and Professor David Sharp) and the Research Programme Manager (Dr Lucy Foss) meet monthly to discuss the Centre's strategic direction and operational workings.

Advisory Board

The CBIS Advisory Board continues to meet twice a year and provides advice to the Centre's 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 Advisory Group

The Military Amputee Research Advisory Group met in 2020 and 2021 for the fourth and fifth time since its establishment in 2018. The meetings were held online. The Group is chaired by Professor Alison McGregor and the meetings have included very useful discussions about rehabilitation and prosthetics. The Advisory Group provide input into projects that work with military amputees, giving advice about protocols and delivery. The Group's membership includes military amputees, military clinicians, and representatives from veterans' organisations.

Staffing

Throughout 2020 and 2021 the Centre was made up of just over 50 members from seven different departments within Imperial College: Bioengineering, Brain Sciences, Civil & Environmental Engineering, Dyson School of Design Engineering, National Heart & Lung Institute, Physics, and Surgery & Cancer. Our researchers continue to work at the interface of several different disciplines.

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) – *Centre Director*
- Professor Jon Clasper (Bioengineering) – *Clinical Lead*
- Dr Spyros Masouros (Bioengineering) – *Associate Centre Director*
- Professor Alison McGregor (Surgery & Cancer) – *Associate Centre Director*
- Professor David Sharp (Brain Sciences) – *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 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. Well done to all those listed below for their achievements in 2020/21.

- Professor Anthony Bull was appointed Inaugural Chair of Trustees of the Association of Biomedical Engineers, Medical Engineers, and Bioengineers
- Dr Spyros Masouros was a winner in 2021 of the Chief Scientific Advisor's to the MOD special commendation for his contribution to "optimising protection and treatment after blast injury".
- Dr Zepur Kazezian was chosen as member of Orthopaedic Research Society
- Dr Robert Dickinson was chosen as member of National Neurotrauma Association, Society for Neuroscience, British Neuroscience Association
- Professor Molly Stevens was appointed Fellow of the Royal Society
- Professor Molly Stevens also received the following awards:
    - Acta Biomaterialia Silver Medal (2020)
    - IET Achievement Medal (2020)
    - FEBS/EMBO Women in Science Award (2021)
    - Mabel Fitzgerald Prize, University of Oxford (2021)
- Dr Michael Bruyns-Haylett was appointed and served as a member of the local South Kensington Animal Welfare and Ethical Review Body (AWERB) committee.
- Dr Iain Rankin's paper on "Investigating Blast-Related Pelvic Injuries and Associations with Mortality" in the Journal of Trauma and Acute Care Surgery was selected by the US

Department of Defence Blast Injury Research Program Coordinating Office as the highlight publication of the month (August 2020) as 'significant research in the area of blast injury prevention, mitigation and treatment.'

- Professor Ravi Vaidyanathan won the Sony Start-up Acceleration Program (May 2021) Spinout company Serg Tech awarded (1 of 4 EU start-ups) a place in Sony corporation start-up boot camp (£45k prize plus Sony membership award) for work in human-robot interface.

New Postdoctoral Researcher

Dr Pouya Amiri joined CBIS in February 2020 in Professor Anthony Bull's group. Before joining CBIS, Pouya did his PhD on developing data driven models for the study of human postural control at McGill University Montreal, Canada. He is currently working to develop predictive forward simulations of amputee movements that maximize their performance and minimize the risk of developing long term pathologies. Subsequently, he will develop biofeedback training modules to train the amputees to adopt the new optimal movement patterns.

PhDs awarded

We would like to congratulate the following people who successfully defended their PhD theses in 2020 and 2021, in spite of the difficult situation with the pandemic!

Dr Dave Henson – May 2020: Understanding the musculoskeletal function of through- and above-knee amputees: Towards methods to improve the optimisation and individualisation of intervention techniques and therapeutic device design for lower-limb amputees.

Dr Suzanne Shanel – August 2020: Biomechanics of the hip and pelvis and predictors of injury during military load carriage

Dr Eduardo Rebelo – September 2020: Modelling of injury and protection of the foot and ankle in under-body blast

Dr Marina Saiz Alia – October 2020: Neural feedback mechanisms for speech-in-noise listening

Dr Xiancheng Yu – November 2020: Cavitation in blast induced traumatic brain injury: the mechanism, threshold, implication, and its mitigation

Dr Eduardo Rebelo – November 2020: Injury and protection of the foot and ankle in under body blast

Dr Iain Rankin – January 2021: Dismounted pelvic blast injury: mechanisms of injury, associated injuries, and mitigation strategies

Dr Louise McMenemy – February 2021: Improving outcomes following complex foot and ankle injuries

Dr Joshua Kaufmann – March 2021: Multiverse company bone changes in traumatic amputees

Dr Shruti Turner – July 2021: Visualising socket pressure in lower limb amputee.

Dr Biranavan Sivapuratharasu – September 2021: Understanding low back pain in amputees.

Dr Sarah Stewart – October 2021: Fracture non-union: using the blast wave to our advantage

Dr Adriana Azor – December 2021: Developing neuroimaging biomarkers of blast-induced traumatic brain injury

Leavers

We bid a very fond farewell to the following Centre members in 2020 and 2021. We wish them all the best in their new roles and look forward to continuing to collaborate with them in the future.

Dr Oluwalogbon Akinnola – working in industry as a Partnership Manager

Dr Mahmoud Keshavarzi – moved to Cambridge University as a Research Assistant

Dr Grigoris Grigoriadis – now working in Industry as a Project Engineer

Dr Eduardo Rebelo – now working in industry as a Management Consultant

Dr Zepur Kazezian – seeking pastures new

Dr Louise McMenemy – returned to work in clinical practice

Dr Sarah Stuart – returned to work in clinical practice

Academic promotions

Congratulations to the following Centre academics who have received promotions during the Covid years:

Dr Spyros Masouros – promoted to Reader in Injury Biomechanics

Dr Andrew Philips – promoted to Reader in Structural Biomechanics

Being a researcher in CBIS

Dr Xiancheng Yu – Postdoctoral Researcher

Before joining CBIS, I studied aeronautics and solid mechanics at the Northwestern Polytechnical University in China, where I obtained my bachelor's and master's degree. My work was mainly related to the impact mechanics of aeronautical structures, such as bird strike damage to aircraft wings. After finishing my master study, I decided to change my research direction to biomechanics as I was fascinated by the complex system of the human body. In 2016, I was awarded a PhD studentship by the Royal British Legion to start my PhD project at CBIS. I joined Dr Mazdak Ghajari's group to study blast induced traumatic brain injury (TBI). In 2020, I completed my PhD study and obtained my PhD degree. I chose to continue my research on TBI as a post-doctoral researcher at Imperial.

Blast induced TBI (BTBI) has been a prevalent injury over the last two decades, which is caused by blast waves, inertial loading, and foreign impacts. These loadings are usually generated by Improvised Explosive Devices (IEDs), which have been widely used in modern conflicts. Many soldiers have been affected by such attacks while in service. Nearly 20% of US and 10% of UK soldiers in combat roles deployed to Iraq and Afghanistan sustained a mild TBI. However, most military related BTBI victims are civilians rather than soldiers. According to the statistics of Action on Armed Violence (AOAV), in 2019 alone, 29,499 deaths and injuries were recorded from the use of explosive weapons worldwide, of which 19,407 (66%) were civilians.

Despite the prevalence of BTBI, its mechanisms are still not fully understood, particularly those linked to primary blast wave. Combat helmets are traditionally designed to prevent injuries caused by ballistic loadings, such as shrapnel and bullet strike. However, they cannot provide enough protection against blast waves propagating from the explosions. An interesting study compared the effectiveness of historical combat helmets (from World War I) and modern combat helmets in mitigating blast wave damage.[1] They found that the 100-year-old World War I helmet performed as well as the modern ones. This is primarily due to the lack of understanding of BTBI mechanisms, which highlights the importance and urgency of research in BTBI mechanisms.

My work at CBIS aims to improve our understanding of BTBI mechanisms. I focus on using advanced computational and experimental approaches (Figure 1) to investigate a potential BTBI mechanism: cerebrospinal fluid (CSF) cavitation. I developed a physical surrogate to represent the human head and exposed it to controlled blast wave. For the first time, my experiments showed the whole process of CSF cavitation onset and microjets formation, recorded by high-speed video camera. I further used a high-fidelity human head computational model to investigate how blast wave induced CSF cavitation. The key contribution of my work is that I proposed and proved a novel mechanism explaining CSF cavitation under blast exposure, which is based on difference of pressure wave transmissions in the skull and brain tissue.

[1] "Primary Blast Wave Protection in Combat Helmet Design: a Historical Comparison between Present Day and World War I" by Joost Op 't Eynde, Allen W. Yu, Christopher P. Eckersley and Cameron R. Bass, 13 February 2020, *PLOS ONE*.

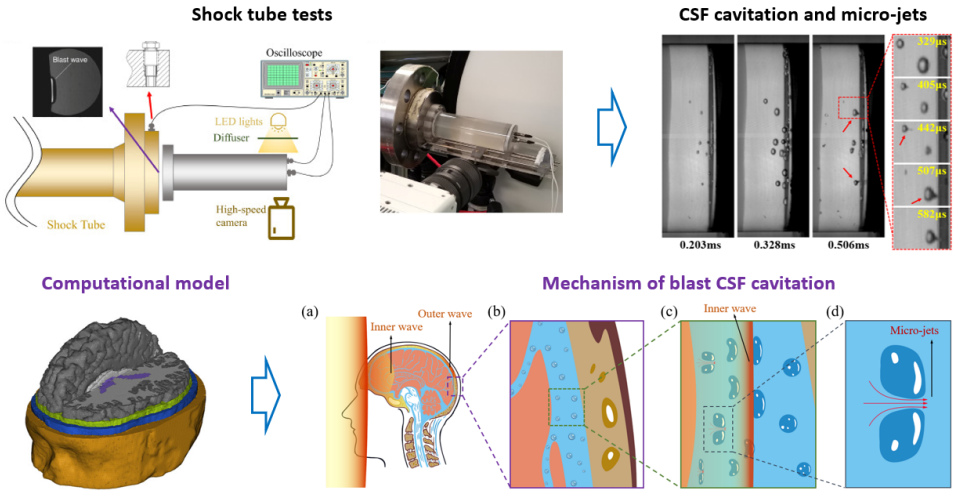


Figure 1: I first conducted shock tube tests on head surrogate and observed the whole process of CSF cavitation and micro-jets formation. Then, I used head computational model to study the wave transmission in the human head. Finally, I proposed a novel mechanism to explain how blast wave induced CSF cavitation.

I am very grateful that I had the chance to study and work at CBIS. Over the last six years, I produced research outcomes with both good quality and quantity. I have published five research papers in top journals and am working on two additional journal papers. More importantly, I have actively sought to build my research leadership, supervision, and management ability. I am currently the assistant supervisor of one PhD student at CBIS who is studying blast induced extremity injury. Ultimately, working on research projects that could lead to better protection for the human head and mitigation of brain injury is extremely rewarding.

Exemplar Research Findings

These two years were highly productive for the Centre in terms of peer review journal publications. Each key publication is summarised in lay language (as far as is possible). These papers represent a fraction of the work that our researchers are doing as many researchers are also working on projects outside of CBIS. Some of the associated projects are mentioned in the grants section on page 63.

Paper Collections

Because of the large number of publications presented in this report, and as they were published over two years, there is a narrative with many of these that shows the progression of the work. This serves to explain how such research can seem incremental, but when observed as a whole demonstrates a major contribution. We highlight some of these collections of papers here before the individual paper summaries.

Amputee Biomechanics

There is much Centre activity to investigate the unique issues associated with blast-induced military traumatic amputation for our cohort of young, fit, and healthy UK military service personnel and veterans. Musculoskeletal biomechanics has shown that amputee intact knees are at a greater risk of joint disease, and this is due to the increased *loading*. Reasons for this are due to how amputees move, but also their muscle volume *adaptations*, and so this information has been incorporated into the Centre musculoskeletal modelling *software* for use in analysing and implementing changes for other military amputees. This work has also required experimental *advances* to better enable the measurement of amputee motion in the lab.

Secondary Blast and Bone Fracture

One of the key areas of technical progress in recent years has been the development of secondary blast experimental capability. Secondary blast injury, that is, injury due to fragments energised by blast, is the most injurious of blast injury modalities in the dismounted and in civilians in the vicinity of the explosion. We have studied secondary blast injury to the *lower extremity* and the pelvis from *small secondary blast fragments* and are working on other parts of the body and *on soft armour*.

Short, Medium, and Long-term effects

CBIS continues to commit resource to investigating the outcomes of military conflict trauma; this work informs all our protecting, mitigation, treatment, and rehabilitation research. As an example, we followed-up the military amputee cohort who had received *direct skeletal fixation* to enable them to walk using prostheses. We co-lead with the Ministry of Defence and King's College London the prospective, longitudinal cohort study investigating the medical and psychosocial outcomes of United Kingdom combat casualties from the Afghanistan war: *the ADVANCE study*. The baseline measures, taken an average of eight years post injury, were completed in 2021 and results will be presented in future reports. We recognised early on that there was much to be learned from previous conflicts and so have invested some resource into investigating outcomes for amputees from the *First World War*. This work provides a comprehensive roadmap for future investigations into complex casualty and ageing, particularly with regard to pain.

Hearing

Another aspect relating to the effect of blast is hearing loss, or reduced hearing. CBIS has conducted research into the measurement of *otoacoustic emissions in the inner ear* to develop the *first computational model of the auditory brainstem response to naturalistic speech* which may help to diagnose hearing loss, especially in infants. They have used this methodology to identify methods for the improvement of *speech-in-noise recognition* and determined that this is similar *across subjects and is better than sham stimulation*. Other aspects of this include *brain stimulation in sync with speech rhythms*, a *deep recurrent neural network (RNN) for reducing transient sounds* and investigations into the method for processing *background speakers in the brain*.

Brain Injury

Blast-induced Traumatic Brain Injury (bTBI) is still not well understood, and so there is CBIS research dedicated to this aspect. It was determined that *rapid motion of the head produced by the blast wave* is the most likely cause of the initial injury. *Using rat models and computational finite-element analysis*, further analysis was conducted to investigate vascular injury and *damage in white matter two weeks post injury.* It has also been determined that the use of *xenon gas can protect the brain following severe TBI.*

Prosthetic Rehabilitation

A survey of clinicians and amputees was undertaken to determine the biggest frustration of those with lower limb amputation(s), which was *expanded with respect to work and social life*. It was determined that the main issue was socket fit, so an initial study into *a low-cost in-socket pressure sensor* was tested and then developed into a *visual biofeedback tool* that enables clinicians to better fit prosthetics.

Pelvic Injury, Amputation and Flail

CBIS research has also determined that *pelvic vascular injury* was the cause of death in casualties with severe blast injuries to the pelvis. The *mechanism of injury to the pelvis and lower limbs* was found to include the *secondary blast-injury mechanism* (energised environmental debris or fragmentation). A proof-of-concept *pelvic belt* was developed and proved that use of pelvic protection aimed at limiting limb flail can reduce the severity of pelvic blast injury.

Higher knee contact forces might underlie increased osteoarthritis rates in high functioning amputees: A pilot study.

Ding Z, Jarvis HL, Bennett AN, Baker R, Bull AMJ (2020)

Journal of Orthopaedic Research, 39(4), 850-860

Military transtibial amputees (TTAs) can achieve a very high level of function. This is as a result of the state-of-art prosthetics that they are given, the advanced rehabilitation and surgery provided by the military, as well as their high level of motivation. In fact, the way these military TTAs walk is indistinguishable from healthy individuals who have not had an amputation. What is known is that TTAs are more likely to develop knee osteoarthritis, a type of mechanical 'wearing out' of their intact limbs. (Their amputated limbs have a much lower rate of pain and osteoarthritis.) Osteoarthritis is known to be started by mechanical overload and can be treated in some cases by reducing the loading on the joint, so we decide to quantify the loading on the knees of TTAs using our advanced research tools developed at Imperial College. We had to measure the way our TTAs move in the lab and compare these to people who do not have amputations but are of a similar age to the amputees. We found very clearly that the mechanical load on the knee of the amputated leg was the same as the mechanical load for the people who do not have an amputation. However, the mechanical load on the non-amputated limb of the TTAs was much higher. This means that there is mechanical overload, and this explains why TTAs have a high likelihood of developing osteoarthritis on their intact limb.

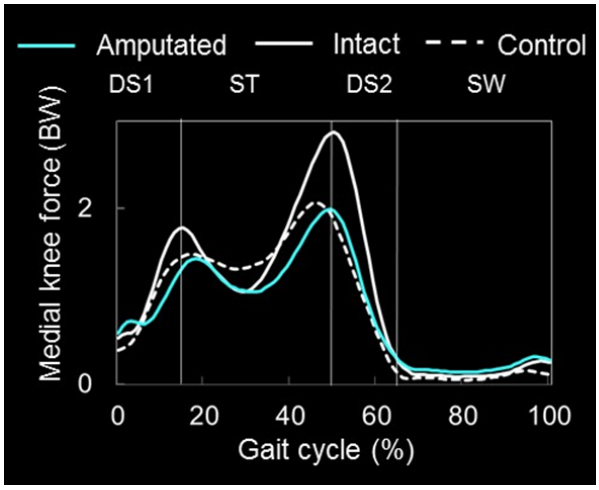


Figure 1: Knee loading for amputees and non-amputees, showing a higher load for the amputees' intact limbs

We also found that there were differences in the way the muscles worked as the amputees walked. This means that there are several possible ways that we could intervene to potentially stop, slow down, or even reverse this degenerative joint disease in our military amputees.

Military trans tibial amputees overload their intact legs

- This is the first study to have quantified mechanical loading of the knee for military unilateral trans tibial amputees
- Knee forces on the amputees' intact limb are greater than for non-amputees
- Amputee intact knees are at a greater risk of joint disease and this study explains that this is due to the increased loading
- We could potentially intervene by improving prosthetic foot control, socket design, and strengthening of the amputated muscles

Understanding lower limb muscle volume adaptations to amputation

Henson DP, Edgar C, Ding Z, Sivapuratharasu B, Le-Feuvre P, Finnegan M, Quest R, McGregor AH, Bull AMJ (2021)

Journal of Biomechanics, 125: 110599

Amputation due to blast produces a severe anatomical deficit. Muscles are reduced in size, lost, must be re-attached surgically, and end up being used in a very different way than in their pre-injury state. This means that some of these muscles get significantly bigger or smaller than for people who are uninjured. In order to understand the effect of these muscle changes on function (the ability to move), we measured the volume of all the main muscles of the legs of lower limb amputees as well as for a set of non-amputees who, in all other ways, are equivalent to the amputees.

We found very significant muscle volume loss in the amputated limb of highly active military unilateral amputees with little change in the intact limb. This means that there is a compensation strategy that is dominated by the intact limb. The findings for bilateral amputees were more subtle: they had expected significant muscle volume increases in very specific muscles and significant volume decreases in muscles that are expected to be heavily loaded during functional activities but have been surgically re-attached following the amputation. This second finding shows that future work should be looking at ways of potentially maintaining muscle volume through other surgical techniques, or even different rehabilitation strategies.

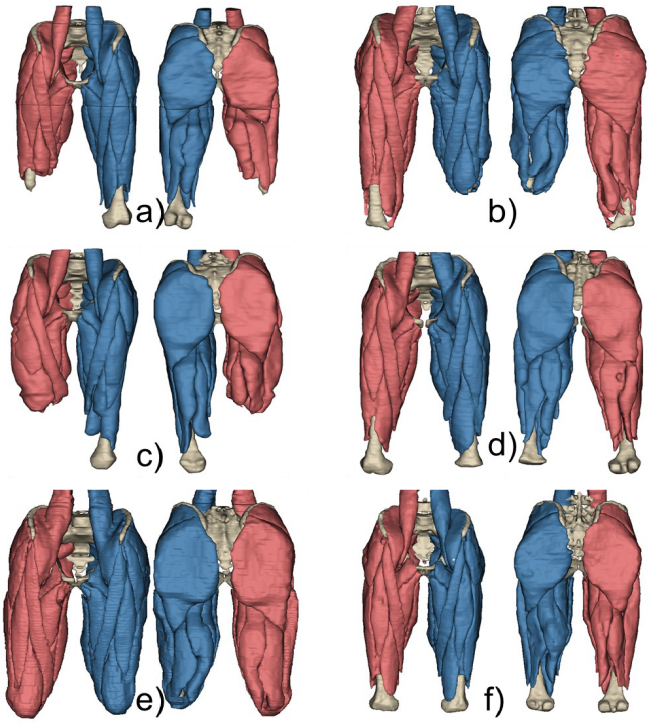


Figure 1: Muscle shapes and volumes for six amputees measured using medical imaging

This study presents a benchmark measure of how the volumes of all muscles of the lower limb change in lower limb amputees. We can now use this information in on-going studies to optimise rehabilitation, surgical techniques, and prosthetic devices.

How muscle volumes change in military amputees

- This information can be used in our current studies on optimising rehabilitation
- Muscles that require surgical re-attachment after amputation do not recover their normal volume, limiting the amputee's potential to achieve high levels of function

An anatomical atlas-based scaling study for quantifying muscle and hip joint contact forces in above and through-knee amputees using validated musculoskeletal modelling

Toderita D, Henson DP, Klemt C, Ding Z, Bull AMJ (2021)

IEEE Transaction on Biomedical Engineering, 86, 3447-3456

Musculoskeletal modelling is a powerful computational tool that can comprehensively assess muscle and joint contact forces. The commonly used linear scaled generic models are time- and cost-efficient, but do not account for anatomical variations between subjects. Amputees have a wide anatomical variability, and so, there are likely to be considerably great errors in linear scaling from one subject. However, the development of subject-specific models from magnetic resonance imaging (MRI) is time and computationally intensive. This paper developed a unique MRI-based anatomical atlas of 18 subject-specific above- and through-knee traumatic amputee models. Laboratory motion data were obtained, and musculoskeletal modelling used to quantify muscle and joint contact forces. The subject-specific models were then used to derive multiple linear regression models that showed that linear scaling to a model with the most similar pelvis width, body mass index and stump length to pelvis width ratio results in modelling outcomes with minimal errors. This study presents the first validated musculoskeletal model for bilateral above- and through-knee amputees. It provides robust tools to perform accurate analyses of musculoskeletal mechanics for lower limb amputees and enables such models to be used extensively for any other traumatic amputee without recourse to expensive imaging-derived anatomies.

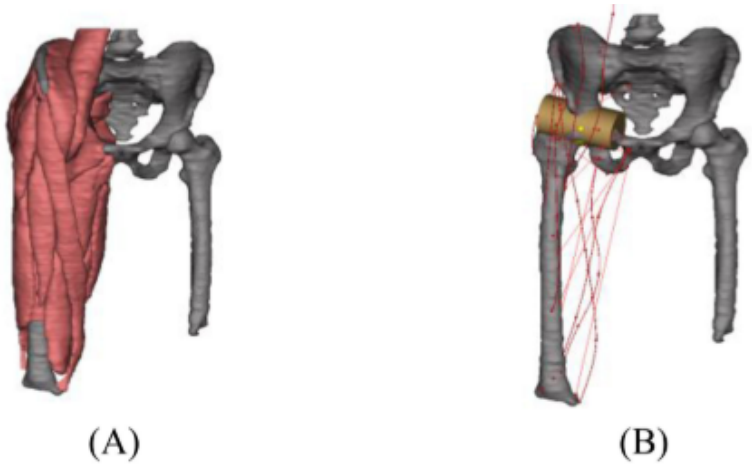


Figure 1: Lower limb anatomy of a representative subject (one limb of a bilateral above-knee amputee): (A) pelvis, femoral remnants and muscle 3D reconstruction. (B) muscle lines-of-action (red), hip joint centre (yellow point), wrapping object (yellow cylinder).

The aim of the study was to develop an MRI-based anatomical atlas for above and through-knee traumatic amputees and regression models that can be used for accurate musculoskeletal modelling.

Subsequent work uses this anatomical atlas and highlights differences in musculoskeletal function and loading for bilateral above- and through-knee amputees with fore-shortened non-articulated stubbies and full-length articulated prostheses. This is the first in a series of papers that demonstrate the clinical benefit of the musculoskeletal modelling described in the previous publication. Subsequent papers will show the developed musculoskeletal modelling tools applied to other datasets of unilateral above- and through-knee traumatic amputees, where biomechanics is used to explain the incidence of osteoarthritis in this amputee population.

Anatomical atlas-based scaling study for quantifying muscle and hip joint contact forces

- Linear scaling to a model with the most similar pelvis width, body mass index and stump length to pelvis width ratio results in modelling outcomes with minimal errors

A femoral clamp to reduce soft tissue artefact: Accuracy and reliability in measuring three-dimensional knee kinematics during gait

Ding Z, Güdel M, Smith SHL, Ademefun RA, Bull AMJ (2020)

Journal of Biomechanical Engineering, 142, 044501

A key focus of the Centre's work is to understand and influence the functional and joint health outcomes for military amputees. Musculoskeletal modelling is one of the tools that we use to do this, where accurate measurement of how the amputee moves is a critical component of the technology pipeline that we have developed. An important finding of our prior work is how the knee joint is loaded in unilateral amputees; in order to further understand how best to create interventions to protect the intact knee we must measure the full six degrees-of-freedom of motion of the knee (three rotations and three translations). However, this measurement is prohibited by soft tissue artifact (STA). The purpose of this study was to present and assess a new femoral clamp to reduce STA at the thigh. We hypothesized that our novel device could preserve the natural knee joint kinematics pattern and outperform conventional methods of measuring knee joint motion. In this study we measured the knee joint motion of participants while walking using multiple different methods, including the new clamp, and compared these to the gold standard knee joint kinematics measured using an X-ray based imaging technique.

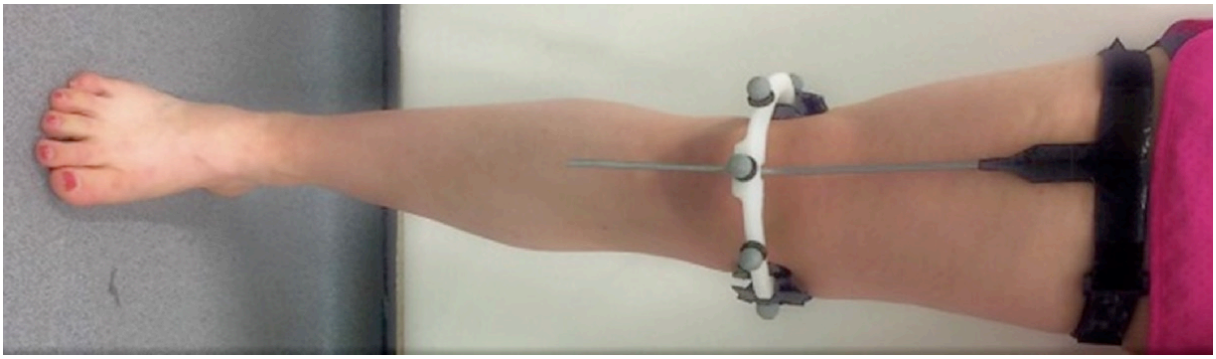


Figure 1: A femoral clamp to accurately measure knee joint motion

We found that the femoral clamp did not change how the participants walked in terms of speed and knee joint rotations. The clamp measurement reduced the rotation and translation errors measured using the standard techniques and also improved the interoperator reliability (i.e., greater consistency of the measurements when made by different observers) when compared to the standard technique.

Accuracy measurement of knee joint motion in the lab

- We have devised and tested a device to measure knee joint motion in the lab
- The device outperforms all standard techniques in terms of accuracy and consistency
- This can now be used to better devise interventions to protect the intact knee of unilateral amputee

A review of through-knee amputation

Panhelleux B, Shalboub J, Silverman A, McGregor AH (2021)

Vascular Journal Vascular, 17085381211045183

Through-knee amputation is an umbrella term for several different surgical techniques, which may affect clinical and functional outcomes. This makes it hard to evaluate the benefits and need for a through-knee amputation approach. This article seeks to 1) determine the number of through-knee amputations performed compared with other major lower limb amputations in England over the past decade; 2) identify the theoretical concepts behind through-knee amputation surgical approaches and their potential effect on functional and clinical outcomes and 3) provide a platform for discussion and research on through-knee amputation and surgical outcomes. By reviewing NHS data from England and searching relevant literature, we found that in the past decade, 4.6% of major lower limb amputations in England were through-knee amputations. Three main through-knee amputation surgical techniques were identified. The classical approach keeps the femur intact and retains the patella. The Mazet technique shaves the end of the femur into a box shape. The Gritti-Stokes technique divides the femur at the end and attaches the patella to the cut end (see Figure 1). Studies reporting outcomes of through-knee amputation do not distinguish between the approaches, making direct comparisons difficult. Future studies that compare these approaches to one another and to other amputation levels are needed.

Figure 1: Schematic of the residual limb after through-knee amputation following different techniques. (a) Classical approach (b) Mazet technique, (c) Gritti-Stokes technique.

Procedure	Yearly average 2011-20 (± standard deviation)	% of total MLLA procedures
Amputation at or proximal to the hip (X09.1 and X09.2)	76 (±9)	1.5
Amputation of leg above knee (X09.3)	2457 (±97)	47.4
Amputation of leg through knee (X09.4)	242 (±24)	4.6
Amputation of leg below knee (X09.5)	2413 (±86)	46.5

Table 1: Yearly average numbers of major lower limb amputation (MLLA) procedures performed in England from April 2011 to March 2020, and as a percentage of total MLLA procedures between 2011 and 2020.

Through-knee amputation is thought to provide a better outcome (in combination with appropriate prostheses) to patients in the long-term. This could help many blast victims to enjoy a better quality of life after amputation of this sort. To determine this hypothesis, we are comparing the gait of people with a through-knee amputation to the gait of people with an above-knee amputation. We are comparing joint angles and moments as well as estimating muscle activations and joint contact forces in people with through-knee amputation.

Through-knee amputation

- Through-knee amputation is performed in 5% of major lower limb amputations in the UK
- There are three main surgical techniques for through-knee amputation: the classical, the Mazet, and the Gritti-Stokes techniques
- There is insufficient data on surgical outcomes of through-knee amputation to compare to other levels of amputation and more studies are needed

Mapping the risk of fracture of the tibia from penetrating fragments

Nguyen T-T N, Carpanen D, Stinner D, Rankin I, Ramasamy A, Breeze J, Proud WG, Clasper JC, Masouros SD (2020)

Frontiers in Bioengineering and Biotechnology, 8: 544214.

Penetrating injury caused by energised fragments from an explosion to the extremities, especially to the shin bone, is one of the most common blast injuries in both civilian and military settings. This injury is devastating and life altering; it has high risk of infection, slow recovery rates and can lead to amputation. The risk of such injury has not been quantified before. Knowing the risk associated with this injury can inform targeted protection, evacuation, and treatment.

This study mapped the quantified risk of fracture by a small metal fragment to the shin bone. The CBIS gas gun was used to launch the fragment at different aspects of the bone. The impact speed of the fragment was controlled to achieve different fracture severities, and the soft tissue. Intensive data collection and statistical analysis were carried out to obtain the fragment speeds associated with these fracture severities where the thickness of the muscle tissue was also considered. In order of severity (from no injury to maximum severity), these speeds were found to be 174, 190, 212, and 282 m/s for the lateral aspect – the most susceptible cortex to fracture, and 325, 426, 457, and 1045 m/s for the anteromedial aspect – the least susceptible cortex to fracture. These results can help improving the development of personal protective equipment and to assess and compare different mitigating strategies.

The experimental model will be repeated for a variety of FSPs so that other variables such as energy, momentum, and cross-sectional area, etc. can also be considered as the predictor variables, or as co-variates in the fracture-risk curves.

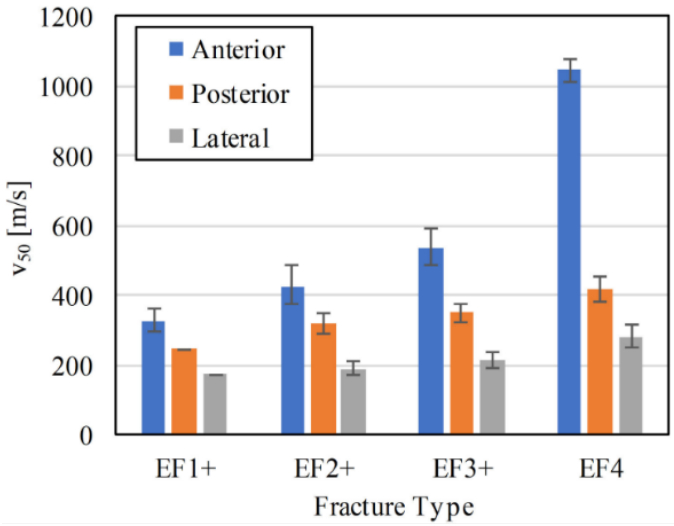


Figure 1: Thresholds of impact velocity at the soft tissue for the human tibia at three impact locations.

Fracture risk map of the tibia impacted by a blast fragment

- Blast penetrating injuries to the tibia is one of the most common wounding mechanisms in an explosion event, often with complicated clinical outcomes
- The lateral cortex was found to be the most vulnerable aspect to fracture by blast fragment penetration
- The anteromedial cortex was found to be the most resilient aspect to fracture by blast fragment penetration

The risk of fracture to the tibia from a fragment simulating projectile

Nguyen T-T N, Carpanen D, Stinner D, Rankin I, Ramasamy A, Breeze J, Proud WG, Clasper JC, Masouros SD (2020)

Journal of the Mechanical Behavior of Biomedical Materials, 102: 103525

Penetrating trauma caused by the fragments energised by the detonation of explosive devices, categorised as a secondary blast injury, is the most common injury among the blast injuries, especially to the extremities (45-75%). The penetrating threats can be anything from munition casings, soil ejecta, and small debris to bolts, nails, and bone fragments. The resultant injuries have high risk of infection, slow recovery rate and can lead to amputation of the limbs. The tibia is the long bone with the highest rate of penetrating injury (~45%); however, the risk of injury to it has not been thoroughly assessed.

In this study, the risk assessment of penetrating injury to the tibia was performed using a gas-gun facility with 0.78-g carbon steel cylindrical fragment simulating projectile. The tibia bone was either casted inside ballistic gelatine acting as soft-tissue simulant or on its own and compressed axially to simulate the standing gait prior to testing. The generated injuries were rated using the modified Winquist-Hansen classification. The experimental model was first applied to the ovine specimens and subsequently repeated on a small number of human cadaveric specimens for validation. After validating and scaling, the impact velocity at 50% risk (± 95% confidence interval) of EF1+ (front tibial fracture), EF2+ (punctured hole), EF3+ (larger posterior hole), and EF4+ (a comminuted fracture) fractures for a human tibia when impacted on the anterior surface were respectively 271 ± 30, 363 ± 46, 459 ± 102, and 936 ± 182 m/s. The scaling factor was found to be 2.5, which is the cortical thickness ratio of human to ovine tibia.

These results help identifying the thresholds for fragment penetrating injury to the tibia by small metal impactor. This information can improve the development of personal protective equipment, and thus the injury outcomes the tibia, as well as can be used to compare the efficacy of mitigating strategies.

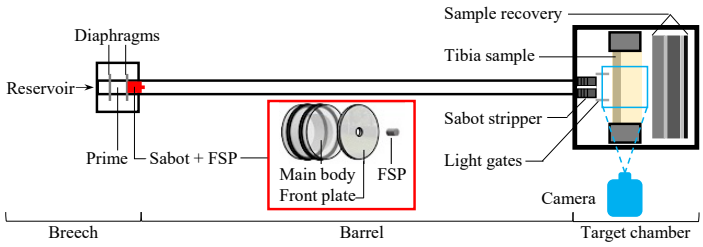


Figure 1: Schematic of the experimental set-up

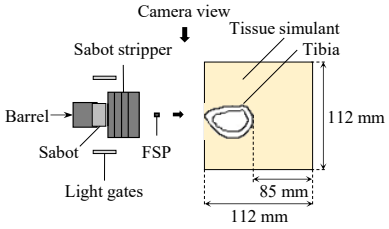


Figure 2: Zoomed view of the impact

The same experimental model has been used to address the injury thresholds for impacts by metal fragments to the tibia at different directions, taking into account the effect of the surrounding soft tissue. The result from this follow-up study can help advising on the protection priorities when designing protection clothing.

Fracture risk of tibia by a projectile

- The lower leg is the most common target for blast fragment penetrating injuries
- Thresholds have been defined for severe fractures to the tibia, thus enabling protective equipment to be designed to protect the lower limb

Gelatine backing affects the performance of single-layer ballistic-resistant materials against blast fragments

Nguyen T-T, Meek G, Breeze J, Masouros SD (2020)

Frontiers in Bioengineering and Biotechnology, 8: 744.

Energised fragments are an inevitable product and the most common cause of injuries from an explosive event. These fragments can be part of the detonating device like the casing shrapnel and some objects (such as ball bearings, nails, or bolts) purposely included to cause harm, or the by-products such as glass and debris from collapsing structures. These fragments have been found to damage mostly the extremities, head, and neck of individuals in the military population.

This study examined the protective performance of seven commercially available ballistic fabrics (figure below). A single layer from each fabric was impacted by a small metal fragment launched at various speeds by the CBIS gas gun, with ballistic gelatine mimicking the behaviour of muscle as the backing material. The fragment speed limits for perforation as well as the damage to the gelatine backing were used to assess the performance of the chosen materials. The results showed that a thin layer of some of these fabrics can offer meaningful protection against a small metal fragment. These findings can be utilised to inform future protective clothing. In addition, the backing material was shown to influence the perforation response and is thus deemed necessary for testing the protective ability of fabrics.

The experimental model is being applied to a range of fragment simulating projectiles with different shapes and sizes to confirm the essential role of the backing material in assessment of soft body armours.

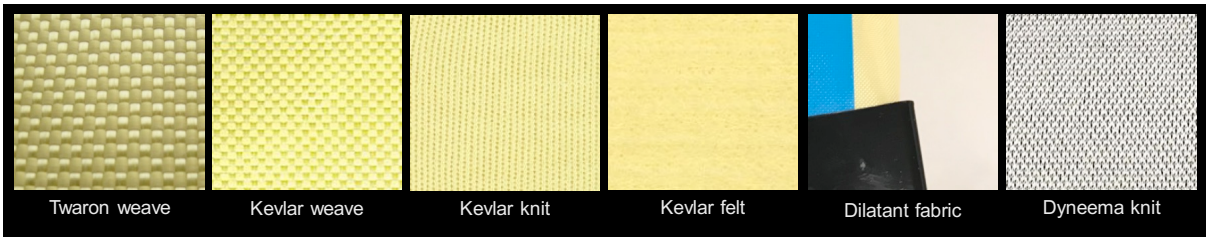


Figure 1: Commercially available ballistic fabrics used in the study

Assessing Soft Ballistic Fabrics Against Blast Fragment

- A gas gun system was used to assess the performance of seven commercial ballistic fabrics against the threat of impact by blast fragment
- A single layer of the tested soft ballistic fabrics can provide meaningful protection against penetration by a metal blast fragment
- A biofidelic backing material is essential in testing the performance if the soft body armour

A study protocol for a prospective, longitudinal cohort study investigating the medical and psychosocial outcomes of United Kingdom combat casualties from the Afghanistan war: The advance study.

Bennett AN, Dyball D, Boos CJ, Fear NT, Schofield S, Bull AMJ, Paul Cullinan P (2020).

BMJ Open, 10(10): e037850.

As mentioned in the CBIS 2019 Annual Report, the ADVANCE Study ADVANCE Study is a longitudinal study which is investigating the outcomes of battlefield casualties from the UK Armed Forces who were deployed to Afghanistan between 2002 and 2014. It looks at physical and psycho-social outcomes. The study is a collaboration between the Defence Medical Rehabilitation Centre (DMRC), Imperial College London and King's College London. Professor Anthony Bull is a member of the study's Project Board which ensures strong links between the Centre and the study. Members of CBIS and the CBIS Advisory Board are also members of the ADVANCE Charity Board of Trustees.

This first publication presented here highlights the methods employed in the study in which 1200 Afghanistan-deployed male UK military were to be recruited, half of whom will have sustained combat trauma and half of whom did not. This comparison group will be frequency matched based on deployment to Afghanistan, age, sex, service, rank and role and means that the comparison between groups is robust and able to investigate differences between groups in areas such as cardiovascular disease (CVD), CVD risk factors, musculoskeletal disease, mental health, functional and social outcomes, quality of life, employment and mortality.

The ArmeD SerVices TrAuma and RehabilitatioN OutComE (ADVANCE) Study

- The unprecedented survival of military personnel suffering severe conflict trauma in Afghanistan has produced a large cohort of inviduals for whom the long-term effects of their injuries are not known and require investigation
- ADVANCE has been established to address this gap and is a collaboration between academia and defence
- ADVANCE will provide high levels of evidence to influence future healthcare of these combat trauma patients

Direct Skeletal Fixation in bilateral above knee amputees following blast: 2 year follow up results from the initial cohort of UK service personnel

McMenemy L, Ramasamy A, Sherman K, Mistlin A, Phillip R, Evriviades D, Kendrew J (2020).

Injury, 51(3) :735-743

Direct skeletal fixation (DSF) represents a new way to attach a lower limb prosthesis for amputees. An implant is placed in the thigh bone with an attachment sticking through the skin to which the prosthetic leg is attached. This avoids complications experienced by amputees with skin breakdown and poor fit of the prosthetic leg. There are however associated risks of infection and the thigh bone breaking. The aim of the study is to evaluate the clinical outcome and complications from the initial cohort of blast injured bilateral lower limb, above knee amputees who underwent Direct Skeletal Fixation (DSF).

Seven bilateral above knee patients all injured by blast were followed up post DSF. Following surgery, all patients walked with improvement in the 6-minute walk test. Patients also performed better on physical and mental tests than the average able-bodied population. At follow up, no patient required removal of the implant. Each had been prescribed a minimum of 1 course of antibiotics with no evidence of deep infection.

DSF is an option for amputees who, due to the nature of their injuries, may not be able to tolerate traditional suspension socket prostheses and have exhausted all other treatment options. At minimum of 2 year follow up, the absence of significant infective complications suggests DSF may be used in the blast injured. Longer term surveillance of these patients is required.

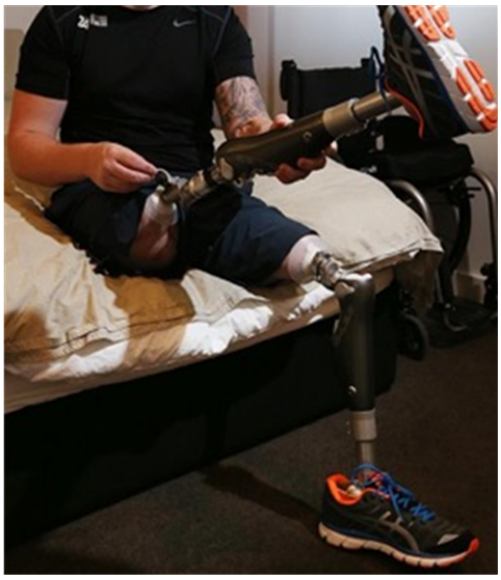


Figure 1: Donning a DSF prosthesis for a bilateral above knee amputee.

The aim of the study is to evaluate the outcome and complications from the cohort of blast injured bilateral lower limb, above knee amputees who underwent Direct Skeletal Fixation (DSF).

This work demonstrates that DSF is a safe and effective option for bilateral above knee amputees. It is not without risk and therefore should be offered only to those who have exhausted all traditional options.

Direct Skeletal Fixation in bilateral above knee amputees

- DSF is a safe and effective operation for patients who have exhausted all traditional options
- DSF is not suitable for all amputees and should be considered on a case-by-case basis
- Life-long follow up is required to establish long term outcomes

An analysis of the surviving pension records (PIN 26) of British Army First World War veterans 1914-1985

Dixon Smith S, Henson D, Hay G, Rice ASC (2021)

Journal of Military, Veteran and Family Health, 2: 64-73

The First World War created the largest amputee cohort in history. Current studies estimate > 80% of military amputees will experience residual or phantom limb pain, yet its long-term impact on health and quality of life has not been researched in detail. Medical pension files recently released by the UK's National Archives have enabled the first lifelong injury effects survey for an injured veteran cohort, allowing investigation into prevalence of chronic post-amputation pain in First World War veterans, prevalence of physical comorbidities, and the impact of aging. This is currently the only lifelong data set available to researchers and policymakers interested in long-term consequences of conflict wounding and likely medical and societal needs of large, disabled, and aging veteran cohorts in decades after injury.

The study focused on PIN 26, British government records for 22,829 First World War veterans and these were searched for amputees with chronic pain or other related conditions, revealing 100 relevant cases from 1914 to 1985. Incidences of pain, physical comorbidities and their treatment were recorded. Chronic post-amputation pain was reported by 76% of these amputees, supporting current estimates of prevalence. Twenty-one forms of treatment were identified; however, few appear to have been successful in significantly reducing pain. Fifty-two long-term health conditions directly resulting from amputation were recorded and 63% of patients reported more than one. In one third of cases, these conditions were considered severe enough to warrant an increase in disability pension. Lower limb amputees appear to have been particularly susceptible to pain and comorbid conditions.

The findings of this project have informed a systematic review investigating the professional medical conversation around the assessment and treatment of chronic postamputation pain in First World War veterans and which will also be submitted for publication.

Despite the century between the First World War and the recent Afghanistan conflict, injury patterns and post-acute treatments for amputation are remarkably similar. These historical files provide a comprehensive roadmap for future investigations into complex casualty and ageing, particularly with regard to pain. This project's findings are of particular relevance for veterans injured in Operation HERRICK as two thirds of extremity injuries in UK personnel were to the lower limbs. It is hoped by identifying likely conditions and periods of onset, the findings of this project will be of use to the strategic planning for today's cohort of military amputees and the long-term impact of their injuries becomes more evident.

Chronic post-amputation pain & blast injury, 1914-1985

- 76% of amputees reported chronic post-amputation pain, supporting current estimates of prevalence in military cohorts
- 63% of pensioners reported a long-erm health condition directly resulting from their amputation
- Historical records can be a valuable source for retrospective cohort studies

Otoacoustic emissions evoked by the time-varying harmonic structure of speech

Saiz-Alia M, Miller P, Reichenbach T (2021)

eNeuro, 8:0428

The human auditory system is exceptional at comprehending an individual speaker even in complex acoustic environments. Because the inner ear, or cochlea, possesses an active mechanism that can be controlled by subsequent neural processing centers through descending nerve fibers, it may already contribute to speech processing. The cochlear activity can be assessed by recording otoacoustic emissions (OAEs) but employing these emissions to assess speech processing in the cochlea is obstructed by the complexity of natural speech. Here, we develop a novel methodology to measure OAEs that are related to the time-varying harmonic structure of speech [speech-distortion-product OAEs (DPOAEs)]. We then employ the method to investigate the effect of selective attention on the speech-DPOAEs. We provide tentative evidence that the speech-DPOAEs are larger when the corresponding speech signal is attended than when it is ignored. Our development of speech-DPOAEs opens a path to further investigations of the contribution of the cochlea to the processing of complex real-world signals.

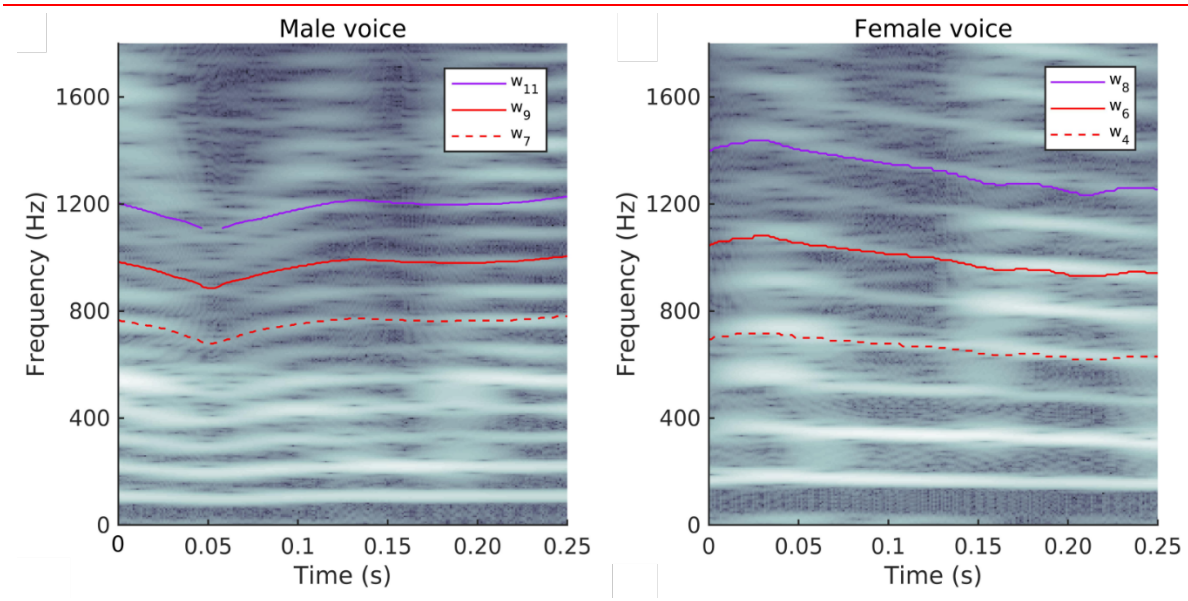


Figure 1: We developed a method to elicit emissions from the inner ear in a manner that ties them to the temporal fine structure of speech (pitch).

Otoacoustic emissions

- Otoacoustic emissions could be stimulated in a way that related them to the temporal fine structure of a speech signal
- The emissions could be measured reliably in individual subjects
- The emissions indicated that attention to speech may already begin within the inner ear

Computational modelling of the auditory brainstem response to continuous speech

Saiz-Alia M, Reichenbach T (2020)

Journal of Neural Engineering, 17(3): 036035

Hearing function can be diagnosed by measuring the neural activity in the first stage of the auditory pathway, the auditory brainstem. This neural activity has traditionally been evoked through simple acoustic stimuli such as short clicks. However, a main function of our hearing system is to detect and process complex signals such as speech and music. We have therefore recently developed a technique to measure brainstem responses to naturalistic speech. In this paper we develop a computational model that provides a yet more refined understanding of how different parts of the auditory brainstem contribute to this response. We find that the speech-evoked brainstem response results predominantly from a midbrain structure, the inferior colliculus. We further find that frequencies up to about 8 kHz contribute relatively uniformly to the response, but that the response declines with increasing fundamental frequency. Our results can contribute to sharpen clinical diagnostics, for instance of hearing impairments in infants who cannot yet be assessed through behavioural testing.

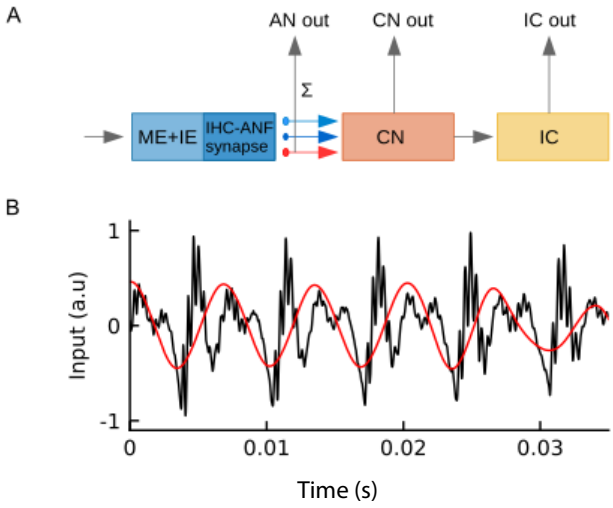


Figure 1: A, Our model of the auditory brainstem includes models of the middle ear (ME) and inner ear (IE), of the cochlear nuclei (CN) and of the inferior colliculus (IC). B, The input to the model is naturalistic speech (black). The brainstem response arises, for instance, at the fundamental frequency of such a speech signal (corresponding waveform shown in red).

The aim of the study was to develop a computational model for the neural activity in the auditory brainstem as elicited by speech. This model can now be used to gain a better understanding of how impairments to different parts of the brainstem alter this activity, and thus allow to better diagnose such impairments.

Model of the auditory brainstem response to continuous speech

- We have developed the first model of the auditory brainstem response to naturalistic speech
- The model reproduces previous experimental findings on this brainstem response
- The model reveals that the neural response originates primarily in the inferior colliculus

Transcranial alternating current stimulation in the theta band but not in the delta band modulates the comprehension of naturalistic speech in noise

Keshavarzi M, Kegler M, Kadir S, Reichenbach T (2020)

Neuroimage, 210: 116557

Two brain rhythms matter particularly for speech processing, the slower delta rhythm set by the rate of words, and the faster theta rhythm that corresponds to the rate of syllables. Here we employ non-invasive current stimulation to show that the theta rhythm but not the delta rhythm can be influenced in a way to affect human behaviour, that is, to modulate how well a person understands speech in noise.

Previous work has suggested that the brain's response to syllables might reflect lower-level acoustic processing of a speech signal, whereas the neural responses to words are linked to higher-level linguistic processing. Our results therefore suggest that transcranial alternating current stimulation can act on the lower-level acoustic aspects of speech processing, but not, or much less, on higher-level aspects.

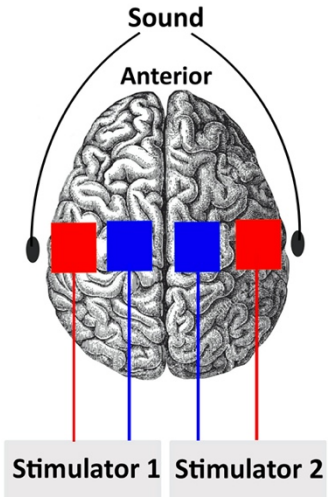


Figure 1: We applied non-invasive transcranial current stimulation in conjunction with speech in background noise and assessed how different types of neurostimulation waveforms influenced speech comprehension.

Our findings open the door to further refinement of current stimulation with respect to enhancing the comprehension of speech in noise, which would be of great benefit in particular to people with hearing impairment.

Neurostimulation in different frequency bands for speech-in-noise comprehension

- We employed non-invasive current stimulation paired to speech
- We found that stimulating with the theta rhythm, but not with the delta rhythm, altered the comprehension of speech in noise
- The optimal stimulation type could improve speech-in-noise comprehension beyond that obtained during a control stimulus

Modulation of speech-in-noise comprehension through transcranial current stimulation with the phase-shifted speech envelope

Kadir S, Kaza C, Weissbart H, Reichenbach T (2020)

IEEE Transactions on Neural Systems and Rehabilitation Engineering, 17(3): 036035

Auditory cortical activity entrains to speech rhythms and has been proposed as a mechanism for online speech processing. In particular, neural activity in the theta frequency band (4–8 Hz) tracks the onset of syllables which may aid the parsing of a speech stream. Similarly, cortical activity in the delta band (1–4 Hz) entrains to the onset of words in natural speech and has been found to encode both syntactic as well as semantic information. Such neural entrainment to speech rhythms is not merely an epiphenomenon of other neural processes, but plays a functional role in speech processing: modulating the neural entrainment through *transcranial alternating current stimulation* influences the speech-related neural activity and modulates the comprehension of degraded speech. However, the distinct functional contributions of the delta- and of the theta-band entrainment to the modulation of speech comprehension have not yet been investigated. Here we use transcranial alternating current stimulation with waveforms derived from the speech envelope and filtered in the delta and theta frequency bands to alter cortical entrainment in both bands separately. We find that transcranial alternating current stimulation in the theta band but not in the delta band impacts speech comprehension. Moreover, we find that transcranial alternating current stimulation with the theta-band portion of the speech envelope can improve speech-in-noise comprehension beyond sham stimulation. Our results show a distinct contribution of the theta- but not of the delta-band stimulation to the modulation of speech comprehension. In addition, our findings open up a potential avenue of enhancing the comprehension of speech in noise.

Modulation of speech-in-noise comprehension through current stimulation

- Neurostimulation with the theta-band but not with the delta-band part of the speech envelope modulates comprehension
- The modulation of speech comprehension with the theta-band current is consistent across subjects
- Theta-band current stimulation can enhance speech comprehension compared to sham stimulation

Transcranial alternating current stimulation with the theta-band portion of the temporally-aligned speech envelope improves speech-in-noise comprehension

Keshavarzi M, Reichenbach T (2020)

Frontiers in Human Neuroscience, 14: 187

Understanding speech in noise is a difficult task at which people without hearing impairment nonetheless excel. Here we employ non-invasive current stimulation to influence brain activity related to speech processing. We show that stimulating the brain in sync with certain speech rhythms can improve speech-in-noise comprehension. In particular, we stimulate with waveforms that are derived from the speech envelope, thus influencing cortical activity that is related to the rhythms of speech and that plays a role in speech processing. We then consider different temporal lags between the neurostimulation waveform and the speech signal. While long positive or negative delays do not have an impact on speech comprehension, we find that no delay or a relatively short delay of 90 ms can increase speech comprehension. This suggests that the neural mechanisms for speech processing on which the current stimulation acts occur relatively rapidly.

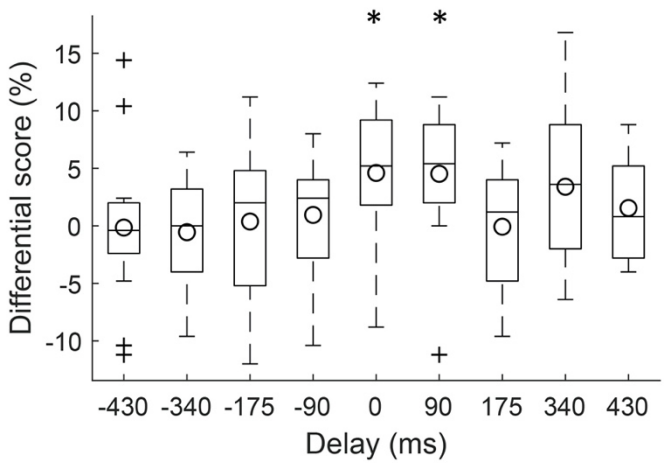


Figure 1: We determined the differential speech comprehension score, that is, difference between the speech comprehension score during transcranial current stimulation and the score during a sham stimulus. We found that no delay as well as a short delay of 90 ms between the stimulation waveform and the speech signal led to an improvement of speech comprehension.

Our findings can now be used to further investigate the neural mechanisms of speech processing and may pave a route to help people with hearing impairment to better understand speech in noise.

Brain stimulation in sync with speech rhythms

- We employed non-invasive current stimulation paired to speech
- We found that stimulating with speech rhythms, and in sync to speech, improved the comprehension of speech in noise

Transient noise reduction using a deep recurrent neural network: Effects on subjective speech intelligibility and listening comfort

Keshavarzi M, Reichenbach T, Moore BCJ (2021)

Trends in Hearing, 25:1

A deep recurrent neural network (RNN) for reducing transient sounds was developed and its effects on subjective speech intelligibility and listening comfort were investigated. The RNN was trained using sentences spoken with different accents and corrupted by transient sounds, using the clean speech as the target. It was tested using sentences spoken by unseen talkers and corrupted by unseen transient sounds. A paired-comparison procedure was used to compare all possible combinations of three conditions for subjective speech intelligibility and listening comfort for two relative levels of the transients. The conditions were: no processing (NP); processing using the RNN; and processing using a multi-channel transient reduction method (MCTR). Ten participants with normal hearing and ten with mild-to-moderate hearing loss participated. For the latter, frequency-dependent linear amplification was applied to all stimuli to compensate for individual audibility losses. For the normal-hearing participants, processing using the RNN was significantly preferred over that for NP for subjective intelligibility and comfort, processing using the RNN was significantly preferred over that for MCTR for subjective intelligibility, and processing using the MCTR was significantly preferred over that for NP for comfort for the higher transient level only. For the hearing-impaired participants, processing using the RNN was significantly preferred over that for NP for both subjective intelligibility and comfort, processing using the RNN was significantly preferred over that for MCTR for comfort, and processing using the MCTR was significantly preferred over that for NP for comfort.

A deep neural network for transient noise reduction

- A deep neural network was developed that can reduce transient distracting noise
- The noise-reduction provided by the network allows people to better understand a target speech signal

Cortical tracking of a background speaker modulates the comprehension of a foreground speech signal

Keshavarzi M, Varano E, Reichenbach T (2021)

Journal of Neuroscience, 41: 5093

Understanding speech in background noise is a difficult task. The tracking of speech rhythms such as the rate of syllables and words by cortical activity has emerged as a key neural mechanism for speech-in-noise comprehension. In particular, recent investigations have used transcranial alternating current stimulation (tACS) with the envelope of a speech signal to influence the cortical speech tracking, demonstrating that this type of stimulation modulates comprehension and therefore providing evidence of a functional role of the cortical tracking in speech processing. Cortical activity has been found to track the rhythms of a background speaker as well, but the functional significance of this neural response remains unclear. Here we use a speech-comprehension task with a target speaker in the presence of a distractor voice to show that tACS with the speech envelope of the target voice as well as tACS with the envelope of the distractor speaker both modulate the comprehension of the target speech. Because the envelope of the distractor speech does not carry information about the target speech stream, the modulation of speech comprehension through tACS with this envelope provides evidence that the cortical tracking of the background speaker affects the comprehension of the foreground speech signal. The phase dependency of the resulting modulation of speech comprehension is, however, opposite to that obtained from tACS with the envelope of the target speech signal. This suggests that the cortical tracking of the ignored speech stream and that of the attended speech stream may compete for neural resources.

Impact of the neural tracking of a background speaker

- The information contained in an unattended speech signal is still processed in the brain
- The neural tracking involved in the processing can be influenced through current stimulation
- Modulating the neural tracking of the background speaker impacts comprehension of an attended speech signal

Mechanisms of tensile failure of cerebrospinal fluid in blast traumatic brain injury

Yu X, Azor A, Sharp DJ, Ghajari M (2020)

Extreme Mechanics Letters, 38: 100739

Mechanisms of blast-induced Traumatic Brain Injury (BTBI), particularly those linked to the primary pressure wave, are still not fully understood. One possible BTBI mechanism is cavitation in the cerebrospinal fluid (CSF) caused by CSF tensile failure, which is likely to increase strain and strain rate in the brain tissue near the CSF. Blast loading of the head can generate rarefaction (expansion) waves and rapid head motion, which both can produce tensile forces in the CSF. However, it is not clear which of these mechanisms is more likely to cause CSF tensile failure.

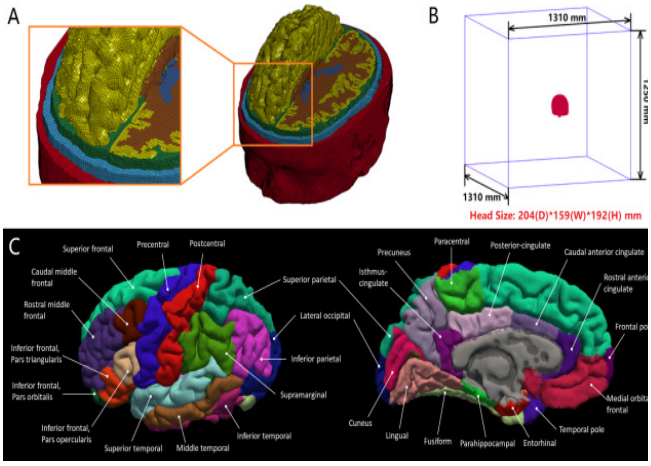


Figure 1: (A) Human head model. (B) The air domain. (C) Regions of interest (ROIs).

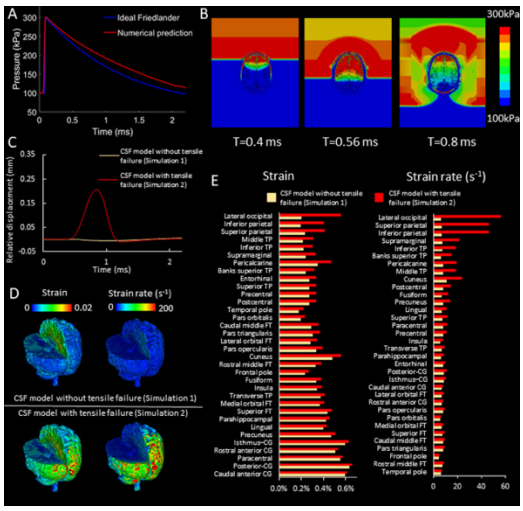


Figure 2: Simulation results of the frontal blast loading.

The aim of the study was to investigate the CSF tensile failure effect on brain deformation. In this study, we used a high-fidelity 3-dimensional computational model of the human head to firstly test whether the CSF tensile failure increases brain deformation near the brain/CSF boundary and to determine the key failure mechanisms. Then, we studied whether the rapid head motion or the rarefaction wave causes strain and strain rate concentration in cortex. Based on the findings of this study, we will design novel materials that can mitigate the CSF tensile failure effect on brain deformation.

CSF tensile failure effect on blast brain injury

- By exposing the head model to a frontal blast wave, we found that CSF tensile failure significantly increased strain and strain rate in the cortex
- We isolated the rapid head motion, and the rarefaction wave effects by conducting simulations with pure head motion loading and pure blast wave loading. Our results showed that the strain increase in the cortex was mainly caused by head motion. In contrast, strain rate increase was caused by both rapid head motion and rarefaction waves
- We showed that rapid motion of the head produced by blast wave is the key mechanism for CSF tensile failure and subsequent concentration of strain and strain rate in cortex. This finding suggests that mitigation of rapid head motion needs to be addressed in the design of protective equipment

Multiscale modelling of cerebrovascular injury reveals the role of vascular anatomy and parenchymal shear stresses

Faraizadeh Khosroshahi S, Yin X, Donat CK, McGarry A, Yanez Lopez M, Baxan N, Sharp D, Sastre M, Ghajari M (2021)

Scientific Reports, 11(1): 1-12

We used high resolution images of a rat brain vasculature to construct a finite element model of vascular injury biomechanics. We simulated controlled cortical impacts and predicted axial strain within the vessels. We compared our predictions of the location of maximal strains with the distribution of blood brain barrier (BBB) damage in a group of rats subjected to Controlled Cortical Impact (CCI). We show that in areas with BBB damage, vessels are subjected to larger axial strains. We found that an axial strain of 0.14 is likely to be enough to cause BBB damage. We also showed that vessels aligned with the direction of maximal strains in parenchyma are subjected to larger strain, showing the interaction between vascular anatomy, and loading distribution in producing larger axial strains in vessels and BBB damage.

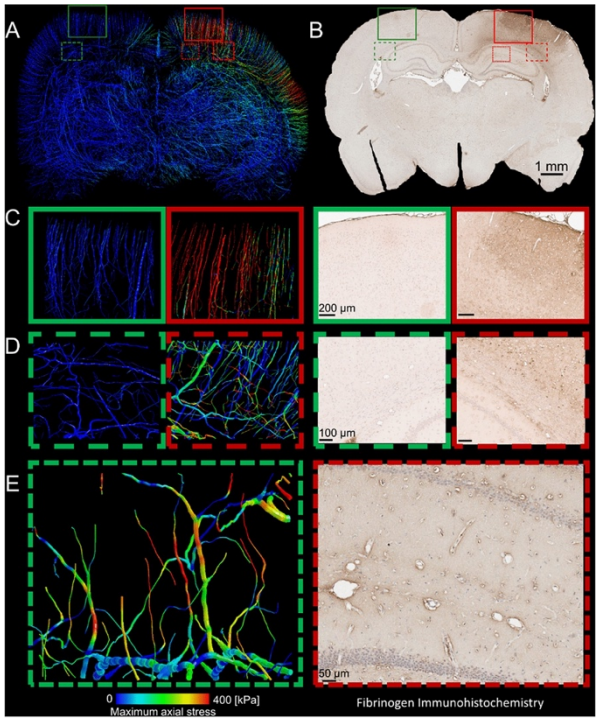


Figure 1: The distribution of axial strain in vessels (left) predicted from the finite element model and Fibrinogen extravasation (right) in a rat subjected to CCI.

The aim of this study was to understand whether vascular anatomy has an effect on producing large forces in vessels and causing vascular injuries during mechanical loading of the brain. The next step is to extend this study to human.

Multiscale modelling of cerebrovascular injury

- Vessels subjected to large axial strain are in locations where damage to the blood brain barrier is seen
- There is large difference in axial strain in vessels in proximity., such as those branching out from the same bifurcation point
- The anatomy of vessels and the distribution of brain deformation interact to produce vascular injury

From biomechanics to pathology: Predicting axonal injury from patterns of strain after traumatic brain injury

Donat CK, Yanez Lopez M, Sastre M, Baxan N, Goldfinger M, Seeamber R, Müller F, Davies P, Heellyer P, Siegkas P, Gentleman S, Sastre M, Sharp D, Ghajari M (2021)

Brain, 144 (1): 70-91

We hypothesised that the initial loading of the brain white matter can predict white matter damage post-injury. We used a controlled cortical impact (CCI) model in rats for this study. We developed a detailed finite element model of the CCI model and predicted the distribution of the strains and strain rate across the brain in the few milliseconds of the impacts. We subjected rats to the CCI with mild and moderate severities. We used high intensity MRI and quantitative histopathology to measure changes in the white matter 2 weeks post-injury. We found that the mechanical strain and strain rate can explain a substantial amount of the changes in white matter integrity and neuroinflammation, measured with diffusion MRI and histopathology. Our results prove that the initial mechanical loading is able to predict brain damage even two weeks post-injury, thus validating the use of computational biomechanics models for predicting brain injury.

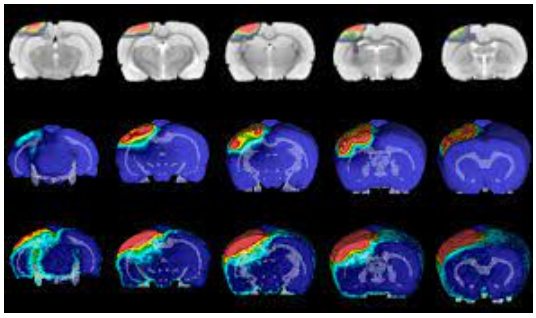


Figure 1: Rat brain after CCI. First row shows the lesion map, second row shows strain distribution in 1mm CCI and third row shows strain distribution in 2mm CCI.

From biomechanics to pathology

- Controlled cortical impact produces damage in white matter two weeks post injury
- The mechanical strain applied to the white matter during the loading can predict a large proportion of the changes in the brain tissue two weeks post-injury
- This validates the use of computational biomechanics models for predicting white matter injuries

Xenon treatment after severe traumatic brain injury improves locomotor outcome, reduces acute neuronal loss and enhances early beneficial neuroinflammation: A randomized, blinded, controlled animal study

Campos-Pires R, Onggradito H, Ujvari E, Karimi S, Valeo F, Aldhoun J, Edge CJ, Franks NP, Dickinson R, (2020).

Critical Care, 24(1): 667.

Traumatic brain injury (TBI) is a significant healthcare issue in both military personnel and civilians. Despite a greater understanding of the pathophysiology of TBI in recent years, current treatment is largely supportive, with no clinically proven treatments specifically targeting neuronal loss and secondary injury development. Our aim was to evaluate the potential of xenon as a neuroprotectant for treatment of TBI in a rat model of severe TBI. Xenon prevented or reduced neuronal loss in motor/association cortex and sensorimotor cortex, associated with locomotor and sensory deficits, and in the hippocampus and retrosplenial cortex, associated with cognitive impairments. Neuronal preservation was associated with an increase in number of microglia and astrocyte activation are consistent with microglia promoting repair and regeneration mediated by neuroprotective reactive astrocytes. This study supports the view that xenon could be an early neuroprotective treatment for TBI.

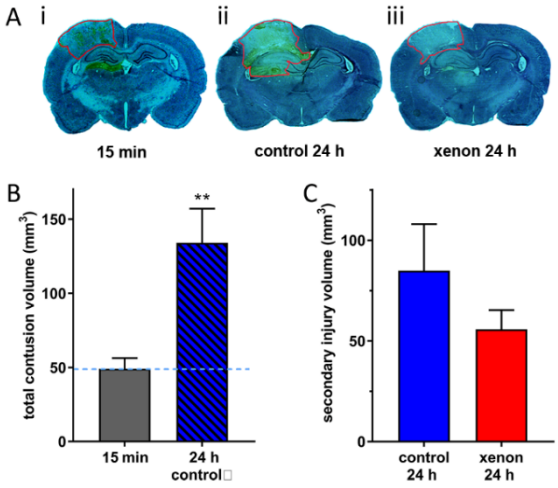


Figure 1. (A) Typical cresyl violet stained slices for (i) TBI primary injury at 15 min, (ii) TBI control at 24 h and (iii) TBI xenon at 24 h. (B) (i) In animals treated with control gas, the injury develops significantly between 15 min (grey bar) and 24 hours (dark blue hatched bar). The area above the dashed-line represents the secondary injury. (ii) Treatment with xenon (50%) (red bar) resulted in a 34% reduction in secondary injury compared to untreated control (dark blue bar). Secondary injury was calculated by subtracting the primary injury at 15 min from the total contusion volume at 24 hours

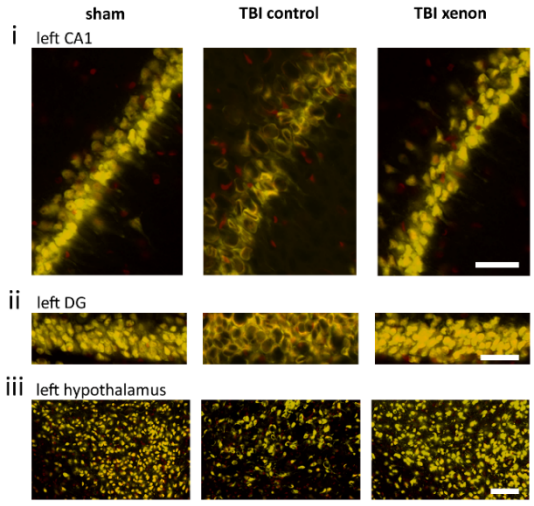


Figure 2. Xenon prevents neuronal loss in specific subcortical regions 24 h after TBI Typical immunostaining showing NeuN (yellow) and DAPI (red) staining from sham, TBI control and TBI xenon animals in (i) left CA1 hippocampal region, (ii) left dentate gyrus (iii) left hypothalamus. Live neurons show a strong NeuN staining combined with DAPI. The scale bars are 20 μm (i) and (ii); and 40 μm (iii).

Xenon is neuroprotective following severe TBI in rats

- Short duration (3h) treatment with xenon reduces lesion volume and improves locomotor function
- Xenon treatment attenuates neuronal loss in clinically relevant brain regions following TBI
- Neuronal preservation was associated with early beneficial neuroinflammation
- Our study suggest that xenon treatment may improve outcome after TBI in humans

Examination of the performance characteristics of velostat as an in-socket pressure sensor

Hopkins M, Vaidyanathan R, McGregor AH (2020)

IEEE Sensors Journal, 20(13): 6992-7000

The paper examines the development of a thin, flexible, and low-cost pressure sensor for measurements within lower-limb prosthetic sockets. Recent conflicts in Afghanistan and Iraq have produced amputees, often with numerous injuries and multiple amputations, as the result of blast injuries caused by improvised explosive devices (IEDs). Prosthetic sockets form the interface between the amputee's residual limb and their prosthesis and as such, have an enormous impact upon comfort and acceptance of the device. Socket fit is a complex problem with a real demand for quantitative information relating to factors such as pressure distribution. A low-cost device was produced using the material Velostat, the performance of which was examined under laboratory bench tests and within an above-knee socket with a single participant. The system was able to produce loading maps aligning with expected load distributions throughout the socket, however, had limitations with regards to accuracy and repeatability. The sensor has potential application in mapping contact regions within the socket to indicate whether expected load distribution is achieved across the soft tissue of the stump.

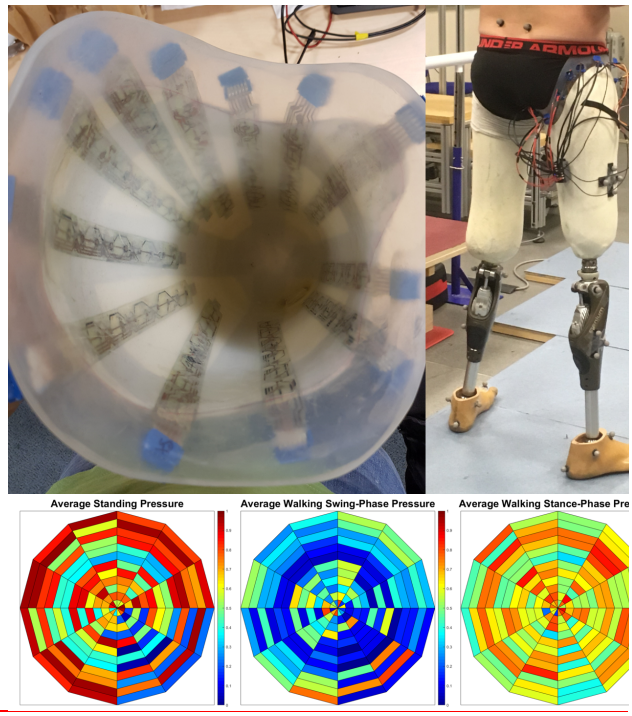


Figure 1: Top: The pressure sensing system as observed from inside and outside the socket. Bottom: Pressure profiles generated whilst standing, during walking swing-phase and stance-phase.

The aim of the study was to determine the suitability of a low-cost piezoresistive material for its application as a pressure sensor in lower-limb prosthetic sockets. The sensor is intended to inform prosthetists in their production of lower limb prosthetic sockets.

A low-cost socket pressure sensing device

- Socket fit is a complex problem that requires data to assist in driving effective production
- A low-cost pressure sensing device was produced and examined through mechanical bench tests and gait laboratory assessment involving participants with amputations
- The device was able to provide indications of in-socket loading patterns, however, it requires further work to improve accuracy and repeatability

Issues faced by people with amputation(s) during lower-limb prosthetic rehabilitation: A thematic analysis

Turner S, Belsi A, McGregor AH (2021)

Prosthetics and Orthotics International, 46(1): 61-67

The issues experienced by those undergoing prosthetic rehabilitation due to the loss of one or both legs have not been well documented, particularly compared to the medical and social consequences of poor rehabilitation outcomes. These personal experiences give an insight into the issues that should be prioritised from those going through prosthetic rehabilitation.

Lower-limb prosthetic rehabilitation

- The socket fit and associated medical complications were central issues, with far reaching consequences
- Along with other frustrations with the prosthesis and care, the overarching theme was the negative impact on the work and social life of individuals
- The results show a clear need for improving specific aspects of the rehabilitation journey to improve the quality of life of prosthesis users

Visual biofeedback tool for quantitative pressure monitoring in lower-limb prosthetic sockets

Turner S, Jain S, Patel A, Hopkins MO, McGregor AH (2021)

Prosthesis, 3: 394-405

The process of fitting prosthetics sockets is an iterative and subjective process, based on the feedback from users and the experience of clinicians. A good socket fit is vital for the successful rehabilitation and health of users. To aid the fitting process, as tool was created to provide objective pressure information from inside the socket.

Visual biofeedback tool

- Pressure sensors communicated with a device via bluetooth to collect this data, and a 3D visualisation was created so a colour map of the pressure in the socket can be seen
- The tool would allow users and clinicians to see the effect of changes to socket design on the pressure in the socket and help to prevent medical complications associated with too much pressure
- Adoption of this tool, and others providing objective information, could aid clinicians with the fitting process and prevent future medical complications and quality of life issues for users

Perceived effect of socket fit on major lower limb prosthetic rehabilitation: A clinician and amputee perspective

Turner S, McGregor A (2020)

Archives of Rehabilitation Research and Clinical Translation, 2(3)

A survey for individuals with lower limb amputation(s) and rehabilitation clinicians was deployed to find out their perspectives on their frustrations that have the biggest impact on lower limb prosthetic rehabilitation. There is lots of literature on the medical issues from having an ill-fitting prosthesis and on the impacts of amputation on quality of life. However, there was a gap in literature where the perspectives of those who experience are shown, particularly for military personnel. Previous research had not been found on whether the priorities for the military or different amputation causes were different.

The research showed that overall, issues during rehabilitation were similar for all groups, with socket fit being the top frustration. Those with amputations due to blast had similar perspectives on the impacting factors on rehabilitation to the rest of the cohort. It was noted that the private and military rehabilitation context was superior to the NHS one in terms of quality of prostheses and time to make and fix prostheses. While the different groups thought socket fit was the main issue, each described it differently – those with amputation(s) focussing more on quality of life, physiotherapists on gait re-education and prosthetists on socket design.

Table 1: Overview of the clinician survey participants, including the number of each who participated in the telephone interviews.

Table 2 Overview of the clinican survey participants, including the number of each who participated in the the telephone interviews

Job Role	Survey Participants	Interview Participants	Years of Experience in Role, Mean ± SD	Biggest Effect on Rehabilitation, %*	Biggest Frustration With Rehabilitation, %*	Biggest Frustration With Socket, %*
Total	44	8	12.97±8.14	65.7	40.9	56.8
Physiotherapists	16	5	12.65±8.18	62.5	37.5	62.5
Prosthetists	24	3	13.02±8.09	66.7	41.7	50.0
Other	4	0	14.00±7.11	50.0	50.0	66.7

NOTE. The percentage of socket fit related responses for each of 3 questions has been stated for the survey participants.
* Percentage of answers related to socket fit.

Table 2: Overview of the amputee survey participants with a summary of responses to key questions

Table 3 Overview of the amputee survey participants with a summary of responses to key questions

Characteristics	Participants, n	Biggest Effect on Rehabilitation, %*	Biggest Frustration With Rehabilitation, %*	Biggest Frustratio With Socket, %*
Total	50	52.0	42.0	52.0
Etiology				
Vascular	8	50.0	37.5	25.0
Cancer	5	40.0	40.0	80.0
Trauma (any)	29	51.7	48.3	51.7
Blast injury	7	42.9	57.1	71.4
Road traffic accident	15	40.0	33.3	46.7
Other trauma	7	85.7	71.4	71.4
Other	8	62.5	25.0	37.5
Level of amputation				
Transtibial	18	31.6	26.3	30.0
Knee disarticulation	1	-	0.0	100.0
Transfemoral	17	47.0	47	41.2
Hip disarticulation	1	100	100	0
Number of leg amputations				
Unilateral	30	30.0	33.3	30.0
Bilateral	8	37.5	37.5	50.0

NOTE. The percentage of socket fit related responses for each of 3 questions has been stated for the survey participants.
* Percentage of answers related to socket fit.

The aim of the study was to understand the main frustrations from key stakeholders in the rehabilitation journey to determine where future research should target to have the most benefit. The study provides the evidence that socket fit is a high priority amongst those most involved with amputee prosthetic rehabilitation. Therefore, has provided a clear mandate for future research to focus on this area to minimise the physical and quality of life impacts on amputees with poorly fitted sockets. Work is being carried out to translate pressure sensors that can be embedded inside the prosthetic socket into the clinical environment to assist prosthetic fitting and rehabilitation.

Effect of prosthetic socket fit

- The main frustration that impacts lower-limb prosthetic rehabilitation is an ill-fitting socket
- Socket fit is important for quality of life and higher function
- There is disparity in services between the military and private sectors and the NHS

A review of the biomarkers and in vivo models for the diagnosis and treatment of heterotopic ossification following blast and trauma-induced injuries

Kazezian Z, Bull AMJ (2021)

Bone, 143, 115765

Heterotopic ossification is the process of bone being formed in places where it doesn't normally – and shouldn't – form. It happens in approximately two thirds of military personnel with amputations due to blast injury. This rate is far higher than in cases of trauma and suggests that the blast effect itself is a major contributing factor. There is a huge amount of scientific literature on this area, yet there are many unknown. Therefore, we decided to review *all* the relevant scientific literature to understand both what is- and what isn't- known so that we could propose future research work for the Centre for Blast Injury Studies. We identified and reviewed all the relevant scientific articles of which there were 118.

We found that there are specific small proteins in the body called inflammatory cytokines that are crucial in the biological processes of how this condition occurs. This means that there are potentially ways of measuring these proteins in the blood at an early stage following blast injury and so giving us the opportunity to intervene with drug therapies.

This work links very closely with the Centre's other studies on the mechanical (loading) effects on heterotopic ossification, giving us the potential to intervene with drugs *and* with loading therapies.

The biological signals of heterotopic ossification following blast injuries

- This review found that there are clear biological signals that are associated with aberrant bone formation in blast injuries
- These signals can be harnessed to produce drug therapies
- On-going work in the Centre is continuing to develop the physical experiments to enable these drug therapies to be tested

Development of a rodent high energy blast injury model for investigating conditions associate with traumatic amputations

Kazezian Z, Yu X, Ramette M, Macdonald W, Bull AMJ (2021)

Bone & Joint Research, 10, 166-173

Heterotopic ossification (HO) is the aberrant formation of bone. It is highly prevalent in blast injured amputees. There are many ways to investigate HO, including computer models and doing experiments on bone. However, in order to fully understand the biological factors associated with HO in blast induced trauma, and so find ways of treating it, we must produce an experimental model that enables the effects of fracture, amputation and blast loading together to be investigated.

This study developed a preclinical model of blast-induced lower limb amputation. The blast, fracture, and amputation is induced by our shock tube which is a core CBIS facility.

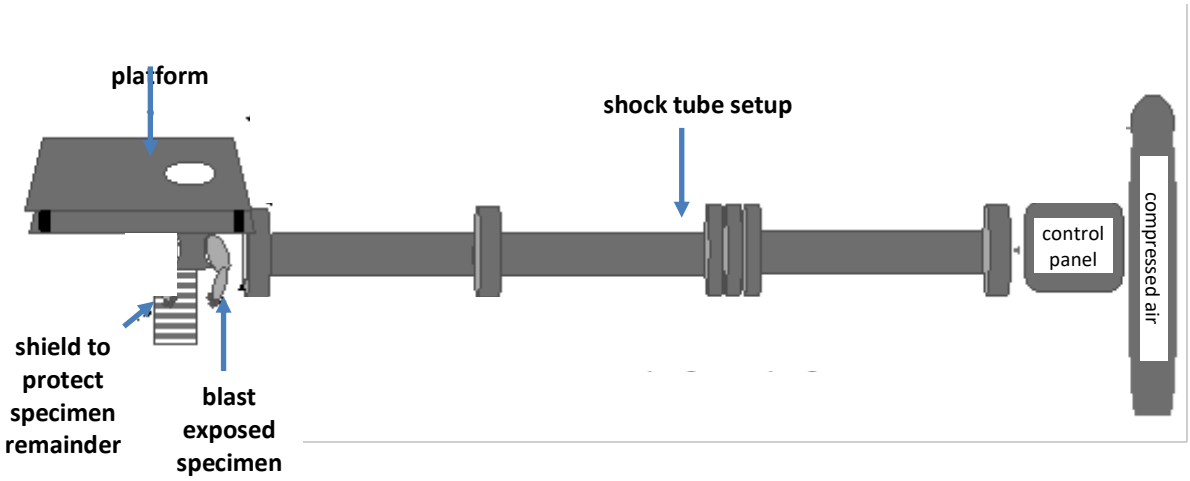


Figure 1: Schematic of the experimental set up for a preclinical model of blast-induced lower limb amputation

A preclinical model of blast-induced amputation

- Blast induced amputation is associated with biological effects such as heterotopic ossification, where bone is produced that causes pain and often requires surgical excision
- There is currently no experimental model that enables the biological effects of combined and simultaneous blast, fracture and amputation to be investigated
- This study has produced such a model that can now be widely applied

Formulation of a new gradient descent MARG orientation algorithm: Case study in robot teleoperation

Wilson S, Eberle H, Hayashi Y, Madgwick SOH, McGregor AM, Jing XJ, Vaidyanathan R, (2019)

Mechanical Systems and Signal Processing, 130 (1), 183-200

The paper culminates work that introduced and commercialised human-robot interface fusing bioacoustic and inertial signals. Specifically, the investigation introduced a new sensor fusion algorithm and hardware package for human-robot interface targeting control of upper limb prosthetics. Analytic and experimental results demonstrate faster convergence for multiple variations of the algorithm through changing magnetic inclination. Furthermore, decoupling of magnetic field variance from roll and pitch estimation is proven for enhanced robustness. The algorithm is validated for robotic hand and arm control, targeting use for amputees with artificial limbs. The validation study involves hardware implementation for wearable robot teleoperation in both Virtual Reality (VR) and in real-time on a 14 degree-of-freedom (DoF) humanoid robot. The experiment fuses inertial (movement) and mechanomyography (MMG) muscle sensing to control robot arm movement and grasp simultaneously, demonstrating algorithm efficacy and capacity to interface with other physiological sensors. To our knowledge, this is the first such formulation and the first fusion of inertial measurement and MMG in HMI. Higlights of the research include a keynote at the IEEE Swarm Human Blended Intelligence Conference, live demonstration at the Prime Minister's Technology Roundtable (10 Downing Street, 2018) and a keynote at the International Forum on Marine Robotics (2019). Robotics in the Dementia Research Institute Care-Research and Technology (DRI-CRT) program (£10mil; 2019-2023) extended from this investigation. The system is in the process of being translated by Serg Technologies (ICL spinout: *http://sergtechnologies.com/*) for support of patients with Parkinson's Disease, with subsequent translational work for use with artificial limbs underway.

Pelvic injury patterns in blast: Morbidity and mortality

Rankin IA, Webster CE, Gibb I, Clasper JC, Masouros SD (2020)

The Journal of Trauma and Acute Care Surgery, 88(6): 832-838

A retrospective study using the U.K. Joint Theatre Trauma Registry to examine the relationship between pelvic injury and mortality was performed. 159 male patients who had sustained pelvic injuries while deployed to either Iraq or Afghanistan between 2003 and 2014 were included. The mortality rate was 36 percent. A trend between pelvic vascular injuries and overall mortality rate was highlighted: amongst the injuries considered (traumatic amputation, perineal injury, unstable fractures, pelvic vascular injury, and combinations of them), pelvic vascular injury alone or combined with other injuries had the highest relative risk of mortality. Computed tomography (CT) imaging of 103 blast casualties demonstrated that lateral displacement of the pelvis was also significantly related to the development of pelvic vascular injuries.

Early intervention is essential to the treatment of blast-related pelvic injuries; within this cohort, 62 percent of the fatalities were unable to receive medical attention before succumbing to their injuries. Pelvic fractures, traumatic amputations, and perineal injuries were found to increase the risk of pelvic vascular injuries three-fold, with pelvic vascular injuries carrying the highest relative risk of death both in conjunction with and when compared to other injury categories.

The lateral displacement of the pelvis exhibited by these patients supports a previously published hypothesis of lower limb flail as a mechanism of primary blast injury to the pelvis, which has implications for injury modelling and the development of blast protection strategies.

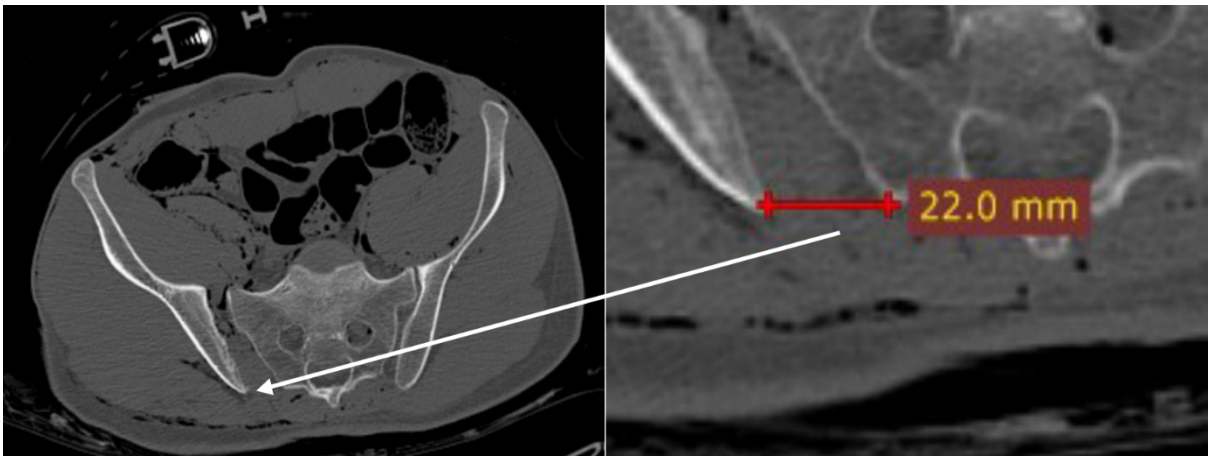


Figure 1: A CT showing lateral displacement of the sacroiliac joints, which was found to be significantly related to the development of pelvic vascular injuries

The aim of the study was to identify injury patterns associated with mortality followed by an explosive blast, in the casualty with severe injuries to the pelvis.

Pelvic injury patterns in blast: morbidity and mortality

- Pelvic vascular injury was identified as the cause of death in casualties with severe blast injuries to the pelvis
- Lateral displacement of the sacroiliac joints, unstable pelvic fracture patterns, traumatic amputation, and severe perineal injuries were associated with fatal pelvic vascular injury
- Protection which limits lateral displacement of the sacroiliac joints of the pelvis may reduce the risk of pelvic vascular injury and death

A new understanding of the mechanism of injury to the pelvis and lower limbs in blast

Rankin IA, Nguyen T-T, Carpanen D, Clasper JC, Masouros SD (2020)

Frontiers in Bioengineering and Biotechnology, 8: 960.

Following on from previous research that showed limiting rapid outward movement ('flail') of the lower limbs following a blast wave to a reduction in fatal vascular injury, this current study set to develop protective equipment which incorporated this principle into its design.

Having previously shown rapid outward movement ('flail') of the lower limbs following a blast wave results in pelvic fractures and fatal pelvic vascular injury, the current study set to identify other contributing factors which may cause injuries associated with blast injury to the pelvis. A novel experimental setup utilising a cadaveric mouse model within a gas gun system, delivering high velocity sandy gravel soil ejecta, was developed. The results suggested that sand gravel soil ejecta following an explosive event can cause both soft tissue injury and skeletal fractures alike at high velocities. Progressive worsening severity of injuries with increasing ejecta velocity were seen and linked this mechanism of injury to traumatic amputation, and soft tissue injury to the legs, perineum, pelvis and abdomen. The findings implicated high velocity sand blast, in addition to limb flail, as a critical mechanism of injury in the dismounted blast casualty. The mechanism of injury to cause these injuries following blast to the on-foot casualty is described.

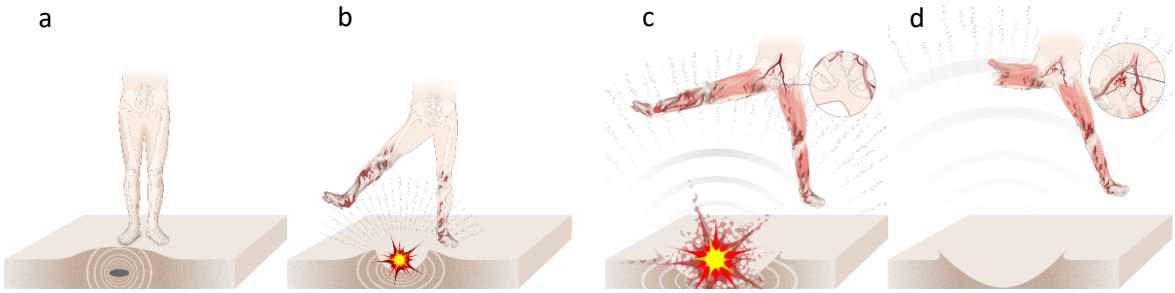


Figure 1: The mechanism of injury of blast injury to the pelvis. (a) Casualty stands on an IED which detonates, causing the initial blast wave to compress the surrounding soil. (b) Sand is ejected at high velocity towards the casualty, causing soft tissue injury and skeletal fracture. (c) The casualty is impacted by the blast wind, resulting in lower limb flail with separation of the front of the pelvis at the pubic symphysis. (d) The blast wind completes the amputation at the level of the initial disruption, whilst continued leg flail results in breaking of the pelvis at the back through the sacroiliac joint and pelvic vascular injury.

This work will guide future protective strategies to mitigate against this mechanism of injury.

A new understanding of the mechanism of injury to the pelvis and lower limbs in blast

- High velocity sand blast results in significant injury, including traumatic amputation, perineal wounding and pelvic fracture
- A novel mechanism of injury resulting in traumatic amputation has been described
- Future protective strategies should be developed towards protecting against high velocity sand blast to mitigate this mechanism of injury

The injury mechanism of traumatic amputation

Rankin IA, Nguyen T-T, McMenemy L, Clasper JC, Masouros SD (2021)

Frontiers in Bioengineering and Biotechnology, 9: 665248

One of the most common and defining injuries of an explosion is that of blast-mediated traumatic amputation. There has been no consensus on the mechanism of this injury; it's understanding is essential in order to improve future clinical outcome through mitigation strategies.

The aims of this study were to (a) replicate isolated traumatic amputation by high-velocity sand blast in a cadaveric small animal model for identifying the mechanism of sand blast mediated traumatic amputation, and (b) to investigate the effect of changes in sandy gravel soil size and moisture content on the risk for sustaining traumatic amputation.

Scaled sandy gravel soil in six test groups of different sizes and moisture conditions, based on NATO recommendations, was launched at cadaveric murine specimens. Statistical survival analysis was performed to examine the association between sandy gravel velocity and traumatic amputation for each test group. The results showed that sand blast caused significant injuries to soft and skeletal tissues, and that there was an increasing risk of traumatic amputation with increasing particle velocity across all groups.

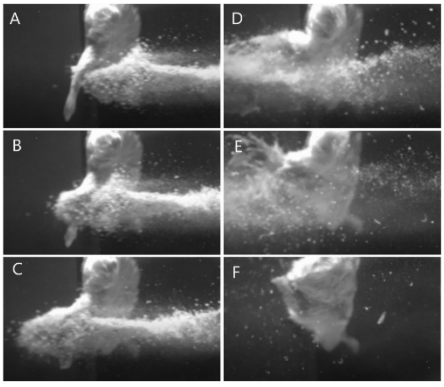


Figure 1: Stages of traumatic amputation by high velocity sand blast: (A) immediately pre-impact; (B) initial impact – sandy gravels move through and around lower limb; (C) foot pulled upward, skeletal and soft tissue above significantly fragmented and displaced; (D) lower limb entirely shattered and displaced, soft tissue stripping on the blast periphery; (E) remaining surrounding soft tissues tripped and displaced; and (F) completed traumatic amputation.

Figure 2: Radiograph of mouse injured with high velocity sand blast, sustaining a right sided lower limb traumatic amputation

The study findings are combined with previous work to describe fully the mechanism of injury. This produces a shift in the understanding of traumatic amputation due to blast from a mechanism predominately thought mediated by primary (initial shock wave) and tertiary (blast wind) elements, to now include secondary blast mechanisms (energised environmental debris or fragmentation) and inform change for mitigation strategies.

The injury mechanism of traumatic amputation

- Traumatic amputation due to blast is caused by a combination of the initial shock wave, subsequent energised debris and fragments, and finally the blast wind.
- The new understanding can initiate a shift in mitigation strategies

Pelvic protection limiting lower limb flail reduces mortality

Rankin IA, Nguyen T-T, Carpanen D, Darwood A, Clasper JC, Masouros SD (2021)

Journal of Biomechanical Engineering, 143(2)

Pelvic blast injury is one of the most severe injuries sustained by casualties of explosions. Pelvic fracture is a principal risk factor for mortality in the dismounted soldier. Our previous work showed the injury mechanism in a small-animal model to be secondary to blast-wave-mediated outward flail of the lower limbs: increasing lower limb flail led to increase in pelvic vascular injury. The pelvic personal protective equipment introduced to UK military personnel in 2011 has reduced genitourinary injury and fragmentation wound to the pelvis but does not protect against lower limb flail.

The aims of this study were to replicate dismounted pelvic blast injury in a small animal model and to provide proof of concept of the pre-application of a reinforced pelvic protective binder for reducing the incidence of pelvic vascular injury following blast.

Shock tube testing was conducted on fifty cadaveric mouse specimens. The specimens were either in standing or supine position with pelvic protection worn at the level of the lower pelvis and including the greater trochanters of the thigh (GT group), or at the level of the upper pelvis around the anterior super iliac spines (ASIS group), or with no pelvic protection (control group). Pelvic protection consisted of a 4.8mm wide by 1.2mm thick nylon belt with a tensile strength of 215.6 N.

The results showed that pelvic protection in the GT group limit flail and reduces pelvic fracture incidence from both front-on and under-body blast, with elimination of vascular injury in both scenarios. On the other hand, pelvic protection in the ASIS group did not limit flail, had no effect on fracture incidence, and was only associated with a minimal reduction in vascular injury.

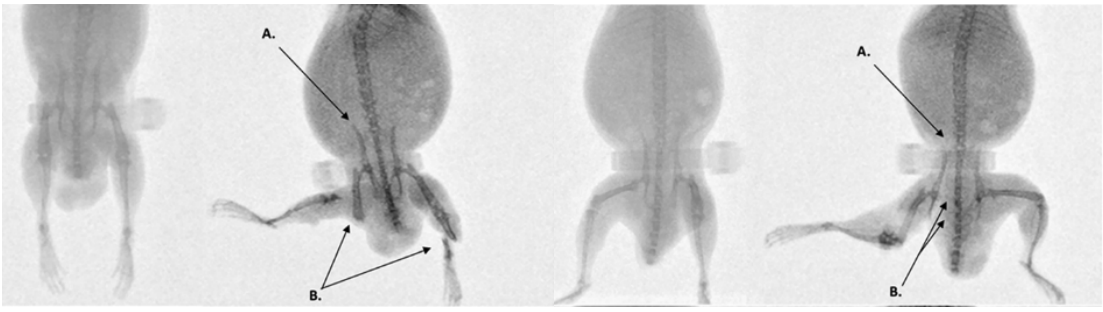


Figure 1: Left: pre-blast (left) and post-blast (right) radiograph of a mouse with pelvic protection worn at the level of the GT showing (A.) an uninjured pelvis with (B.) bilateral lower limb traumatic amputations. Right: pre-blast (left) and post-blast (right) radiograph of a mouse with pelvic protection worn at the level of the ASIS showing (A.) minimally displaced sacroiliac joint disruption with (B.) displaced pubic rami fractures.

This study proves the concept that use of pelvic protection aimed at limiting limb flail can reduce the severity of pelvic blast injury. Future development of protection for the soldier on routine foot patrol should consider allowing movement under low loading rates but prevent it at higher rates, such as those incurred with rapid movement of the limbs during a blast event.

Limiting flail reduces mortality

- A pelvic belt worn at the level of the greater trochanters prevents limb flail, pelvic fracture displacement, and vascular injury
- Wearing the belt above the greater trochanters is not effective in reducing the severity of injury

An experimentally validated finite element model of the lower limb to investigate the efficacy of blast mitigation systems

Rebelo EA, Grigoriadis G, Carpanen D, Bull AMJ, Masouros SD (2021)

Frontiers in Bioengineering and Biotechnology 9: 410

In this study a finite-element (FE) model of the leg was developed and validated in relevant vehicle-occupant blast-loading conditions (Figure 1), and then used to quantify the level of protection offered by a combat boot. A 35-year old male cadaveric leg was modelled. The leg was tested in the CBIS lab under blast-loading conditions and the results used to calibrate the FE model. The calibrated model predicted hindfoot forces that were in good (according to ISO18571) correlation with data from force sensors. The boundary conditions of the FE model were then changed to replicate pendulum tests conducted elsewhere. The simulation results of foot compression and peak force at the tibia were within the experimental corridors reported in the studies. A combat boot used by UK Forces was incorporated into the validated FE model. Simulations were run across a range of blast-related loading conditions. The predicted proximal tibia forces (Figure 2) and associated risk of injury indicated that the combat boot reduced the injury severity for low severity loading cases with higher times to peak velocity. The reduction in injury risk varied between 6 and 37 % for calcaneal minor injuries, and 1 and 54 % for calcaneal major injuries. No injury-risk reduction was found for high severity loading cases.

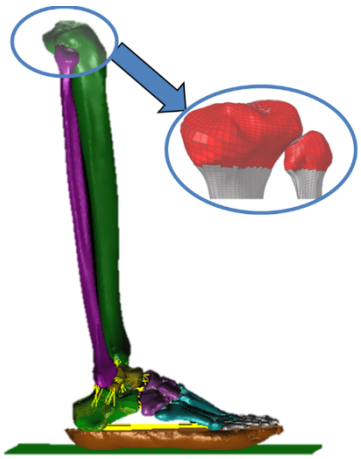


Figure 1: Finite-element model of the leg (the combat boot is not shown here)

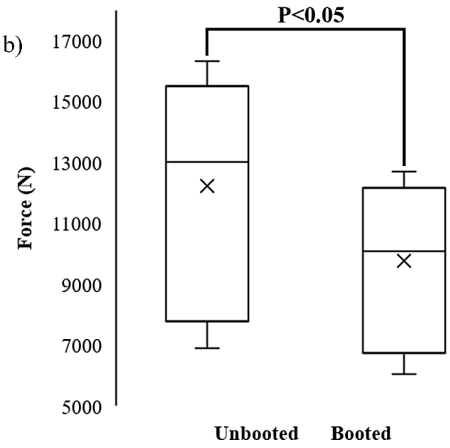


Figure 2: Comparison of the force at the tibia (which associates with risk of injury to the leg) for booted and unbooted configurations across the range of input underbody blast loads.

The validated FE model of the leg developed here was able to quantify the protection offered by a combat boot to vehicle occupants across a range of blast-related loading conditions. It can now be used as a design and as an assessment tool to quantify the level of blast protection offered by other mitigation technologies. Such use of the model is presented in a subsequent paper.

Blast mitigation systems

- A computer model of the leg under blast-loading conditions was developed
- Model results were in good correlation with multiple experimental studies across labs
- Model results showed that the combat boot offers some protection to hind-foot injury for low severity load cases, and that it does not offer any protection for high severity load cases

Biomechanical evaluation of a tool-less external fixator

Carpanen D, Masouros SD, Stinner DJ (2021)

BMJ Military Health, 2020-001766

Current external fixator systems used by the US and UK military for stabilising extremity fractures require specialised tools to build a construct. The goal of obtaining and maintaining limb length and alignment is not achieved if these tools are misplaced. An alternative, tool-less system is currently available, namely the Dolphix Temporary Fixation System.

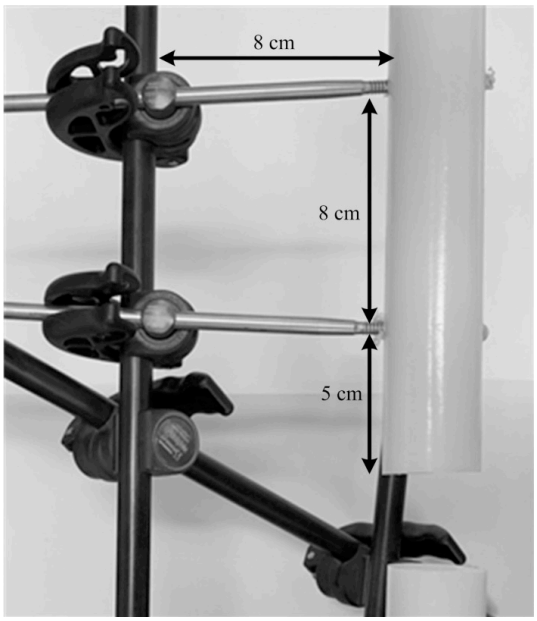


Figure 1: Picture of the tool-less construct tested. Two self-drilling pins were inserted into each bone segment at a set distance. A rod was then secured to both pins with pin-to-bar clamps 8 cm apart.

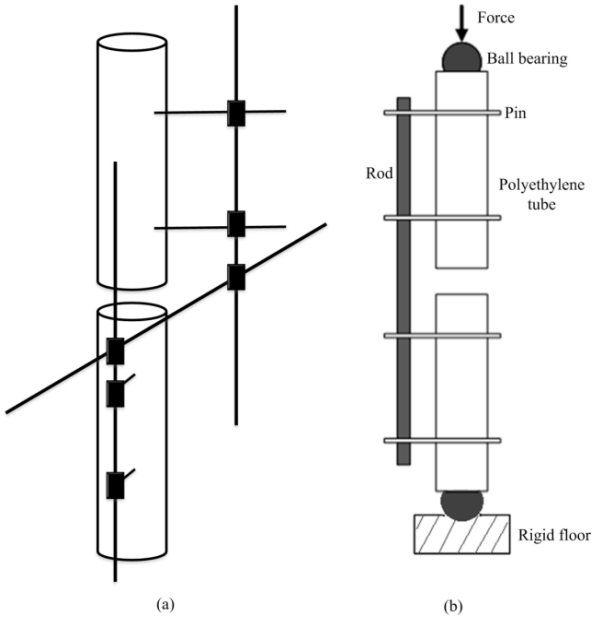


Figure 2: Schematics of (a) the Z-shaped construct assembled for mechanical testing, and (b) the axial compression test conducted

The aim of the study was to compare the stiffness of the Dolphix system with the existing Hoffmann III system. Three constructs of each system were assembled on a bone (tibia) surrogate. A 30 mm fracture gap was created to simulate a comminuted proximal tibia or distal femur fracture. The constructs were then tested in cyclic axial compression once daily for 3 consecutive days.

Length and alignment of the surrogate limb was restored following each testing cycle with both external fixation systems. The stiffness of the constructs was maintained throughout each sequential test, with the Dolphix exhibiting 54% the stiffness of the Hoffmann III construct. Given the Dolphix's performance in mechanical testing and the unique advantage of having a tool-less manual locking clamp mechanism, this system should be considered for use in the mobile austere environment.

Biomechanical evaluation of a tool-less external fixator

- A tool-less external fixator was shown to restore length and alignment, and to exhibit approximately half the stiffness of the standard Hoffmann III construct used to stabilise extremity fracture
- The tool-less aspect of the fixator tested makes it an attractive alternative to currently deployed external fixator kit, especially in the mobile austere environment

Replicating landmine blast loading in cellular *in vitro* models

Sory DR, Amin HD, Chapman D, Proud WG, Rankin SM (2020).

Physical Biology, 17(5): 056001.

Trauma arising from landmines and improvised explosive devices promotes heterotopic ossification, the formation of extra-skeletal bone in non-osseous tissue. To date, experimental platforms that can replicate the loading parameter space relevant to improvised explosive device and landmine blast wave exposure have not been available to study the effects of such non-physiological mechanical loading on cells. Here, we present the design and calibration of three distinct *in vitro* experimental loading platforms that allow us to replicate the spectrum of loading conditions recorded in near-field blast wave exposure. We subjected cells in suspension or in a three-dimensional hydrogel to strain rates up to 6000 s−1 and pressure levels up to 45 MPa. Our results highlight that cellular activation is regulated in a non-linear fashion—not by a single mechanical parameter, it is the combined action of the applied mechanical pressure, rate of loading and loading impulse, along with the extracellular environment used to convey the pressure waves. Finally, our research indicates that PO MSCs are finely tuned to respond to mechanical stimuli that fall within defined ranges of loading.

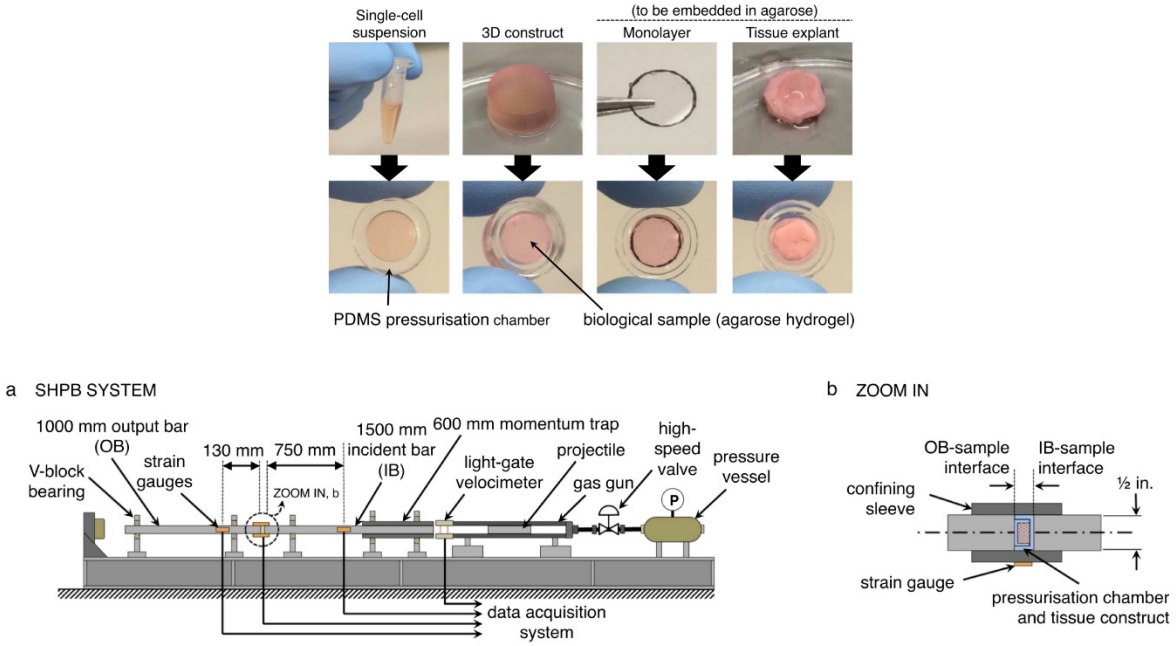


Figure 1: (top) Cellular *in vitro* models used in the pressurization chamber. (bottom) Schematic of the split-Hopkinson pressure bar (SHPB) and its diagnostics. (b) Setup of the pressurization chamber and the confining sleeve.

The aim of the study was to introduce and validate in vitro platforms capable of replicating loading conditions in 3D culture systems as recorded in IED/landmine blast avulsion of lower extremities.

This proof of concept establishes a new window to address fundamental questions regarding IED/landmine blast biomechanics in screening a wide variety of cellular types and tissues.

Replicating landmine blast loading in cellular *in vitro* models

- Design, develop and calibrate *in vitro* experimental platforms that permit the exposure of cell cultures in 3D microenvironments to mechanical loading conditions mimicking blast trauma
- Showing that subjecting stem cells to a single-pulse mechanical loading shorter than 1 millisecond simulating blast traumatic loading is sufficient to prime stem cell differentiation towards the osteogenic lineage

Mechanotransduction in osteogenesis

Stewart S, Darwood A, Masouros S, Higgins C, Ramasamy A (2020)

Bone and Joint Research, 9(1): 1-14

This literature review aims to describe the fundamental physiology and biomechanisms that occur to induce osteogenic adaptation of a cell following application of a physical stimulus. Considerable developments have been made in recent years in our understanding of how cells orchestrate this complex interplay of processes and have become the focus of research in osteogenesis. This literature review discusses current areas of pre-clinical and clinical research exploring the harnessing of mechanotransductive properties of cells and applying them therapeutically, both in the context of fracture healing and de novo bone formation in situations such as non-union.

Factor	Vibrations and nanovibrations	Low-intensity pulsed ultrasound	Extracorporeal shockwave treatment	Electrical stimulation
Mechanism	Whole body vibration: 0.1% strain, 10 to 90 Hz Nanovibrations: nanoscale displacements of 1kHz	Ultrasound waves Intensity of 0.5 mW/cm² to 50 mW/cm² Application with probe over fracture or nonunion site	Pressure wave rapidly increasing to > 10 MPa over nanosecond timescale Applied externally or internally with a probe	Oscillatory electromagnetic fields generated around fracture site Multiple generation modalities in clinical use
Physiological action	Improvement in angiogenesis at the fracture site Some enhancement to bone stiffness and strength	Micromechanical stress at target site	Cascade of osteogenesis-inducing steps Generation of oxygen free radicals Hyperpolarization of cell membrane inducing osteogenic growth factor TGF-β1	Simulate an enhanced loading environment on bone via piezoelectric effect
Clinical relevance	Improving bone density No current use in fracture healing	Fracture-healing adjuvant therapy	Fracture-healing adjuvant therapy	Fracture-healing adjuvant therapy
Evidence base	Review of 19 studies of effect on fracture healing[72] No clear effect to make clinical recommendations	Review of 17 sham controlled trials failed to categorically confirm clinical utility[73]	Systematic review of level 4 studies reported overall union rate of 76%[74]	Recent Cochrane review inconclusive and unable to support widespread clinical use[75]

TGF-β1, transforming growth factor beta-1.

Table 1: summary of pre-clinical and clinical applications of mechanotransduction.

The aim of the study was to provide a comprehensive review on the fundamental concepts of mechanotransduction in osteogenesis, to enable researchers to develop novel ideas as to how cells can be mechanically stimulated to induce bone formation.

Mechnotransduction in osteogenesis

- Mechanotransduction underpins the biomechanisms in which bone cells adapt their function and behaviour based on their physical environment and forces exerted on the cell
- This represents an exciting area of research in orthopaedics, which has the potential to allow us to modulate the function of bone cells in vivo to create new bone

Fracture union rates across a century of war: a systematic review of the literature

Stewart SK, Tenenbaum O, Higgins C, Masouros SD, Ramasamy A (2020)

BMJ Military Health, 166(4): 271-276.

Fractures have been a common denominator of the injury patterns observed over the past century of warfare. The fractures typified by the blast and ballistic injuries of war lead to high rates of bone loss, soft tissue injury and infection, greatly increasing the likelihood of non-union. This systematic review highlights the ongoing difficulty of managing those fractures sustained by blast and ballistic injury in a conflict environment, with evidence to suggest that union rates have failed to improve across a century of warfare. It advocated the need for further research into therapeutic measures to treat or precent non-union.

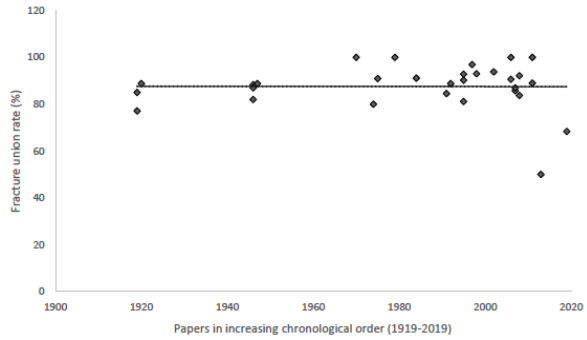


Figure 1: Rates of fracture union by date of publication of paper. Each data point represents the average union rate reported in an included paper

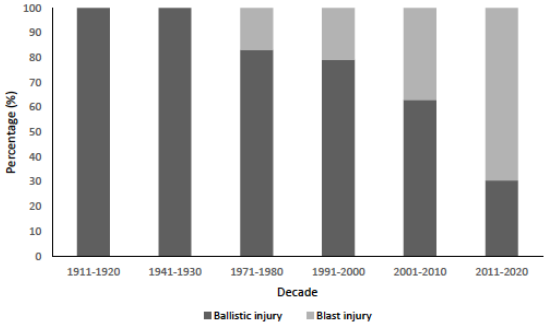


Figure 2: Proportion of blast versus ballistic injury for each decade of study. Omitted decades are a result of an absence of papers and/or absence of data

The aim of the study was to highlight the ongoing clinical difficulty in preventing and treating non-union in those fractures sustained from blast and ballistic mechanisms. It also serves as evidence that there is a research need to develop novel ways to improve fracture healing in those fractures caused by blast.

Fracture union rates across a century of war

- Fractures sustained in a combat environment are at high risk of progressing to non-union
- There does not appear to be a discernible improvement in the rates of fracture union over across a century of warfare
- Better survivability of individuals and increasing use of blast weaponry may be key factors contributing to this apparent failure in medical advancement of this condition

The pattern of paediatric blast injury in Afghanistan

Thompson DC, Crooks RJ, Clasper JC, Lupu A, Stapley SA, Cloke DJ (2020)

BMJ Military Health, 166(3): 151-155.

This paper reviewed 295 paediatric (aged 2-15 years) admissions with blast injuries to the Role 3 Field Hospital, Camp Bastion from June 2006 to March 2013. 76% were male, with an overall mortality rate of 18.5%. The most common blast mechanism was an IED (68%) causing 80% of fatalities. The lower extremities were the most commonly injured body region, accounting for 31% of total injuries and occurring in 62% of cases. 24.3% of children between 2 and 7 years suffered severe head or neck injuries compared with 19.8% of children aged between 8 and 15 years. 34% of head injuries were rated unsurvivable and accounted for 88% of fatalities. 77% of cases required an operation with a mean operating time of 125 min. The most common first operations were debridement of soft tissues (50%), laparotomy for abdominal injuries (16%) and lower limb amputation (11%).

The pattern of paediatric blast injury in Afghanistan

- Although paediatric blast casualties represented a small percentage of the overall workload at Camp Bastion Role 3 Medical Facility, the pattern of injuries seen suggests that children are more likely to sustain severe head, face and neck injuries than adults
- Despite UK military hospitals being staffed and equipped to deal with adults, provision for children still needs to be considered
- As well as specialist equipment and trauma management, staff need to be trained to deal with all aspects of paediatric care including their death

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.

Bennett AN, Dyball D, Boos CJ, Fear NT, Schofield S, Bull AMJ, Paul Cullinan P (2020). *A Study Protocol for a Prospective, Longitudinal Cohort Study Investigating the Medical and Psychosocial Outcomes of United Kingdom Combat Casualties from the Afghanistan War: the ADVANCE Study*. BMJ Open, 10(10): e037850.

Campos-Pires R, Onggradito H, Ujvari E, Karimi S, Valeo F, Aldhoun J, Edge CJ, Franks NP, Dickinson R (2020). *Xenon treatment after severe traumatic brain injury improves locomotor outcome, reduces acute neuronal loss and enhances early beneficial neuroinflammation: a randomized, blinded, controlled animal study*. Critical Care, 24(1): 667.

Ding Z, Jarvis HL, Bennett AN, Baker R, Bull AMJ (2021). *Higher knee contact forces might underlie increased osteoarthritis rates in high functioning amputees: A pilot study*. Journal of Orthopaedic Research, 39, 850-860

Ding Z, Güdel M, Smith SHL, Ademefun RA, Bull AMJ (2020)*A femoral clamp to reduce soft tissue artefact: Accuracy and reliability in measuring three-dimensional knee kinematics during Gait.* J. Biomech Eng 142, 044501

Kazezian Z, Bull AMJ (2021) *A review of the biomarkers and in vivo medels for the diagnosis and treatment of heterotopic ossification following blast and trauma-induced injuries.* Bone 143, 115765

Kazezian Z, Yu X, Ramette M, Macdonald W, Bull AMJ (2021) *Development of a rodent high energy blast injury model for investigating conditions associate with traumatic amputations.* Bone & Joint Research, 10, 166-173

Toderita D, Henson DP, Klemt C, Ding Z, Bull AMJ (2021) *An anatomical atlas-based scaling study for quantifying muscle and hip joint contact forces in above and through-knee amputees using validated musculoskeletal modelling.* IEEE Transaction on Biomedical Engineering, 86, 3447-3456

Hopkins M, Vaidyanathan R, McGregor AH (2020). *Examination of the performance characteristics of velostat as an in-socket pressure sensor*. IEEE Sensors Journal, 20(13), 6992-7000.

Wilson S, Eberle H, Hayashi Y, Madgwick SOH, McGregor AM, Jing XJ, Vaidyanathan R, (2019) *Formaulation of a new gradient descent MARG orientation algorithm: Case study in robot teleoperation*. Mechanical Systems and Signal Processing 130(1), pp 183-200 (not include in 2019 report)

Turner S, McGregor AH (2020) *Perceived impact of socket fit on major lower limb prosthetic rehabilitation: a clinician and amputee perspective.* Arch Rehabil Res Clin Transl. 2(3):100059

Henson DP, Edgar C, Ding Z, Sivapuratharasu B, Le-Feuvre P, Finnegan M, Quest R, McGregor AH, Bull AMJ (2021) *Understanding lower limb muscle volume adaptations to amputation.* Journal of Biomechanics 125:110599

Panhelleux B, Shalboub J, Silverman A, McGregor AH (2021) *A review of through-knee amputation.* Vascular Journal Vascular 17085381211045183

Turner S, Belsi A, McGregor AH (2021) *Issues faced by people with amputation(s) during lower-limb prosthetic rehabilitation: A thematic analysis.* Prosthet Orthot Int

Turner S, Jain S, Patel A, Hopkins MO, McGregor AH (2021) *Visual biofeedback tool for quantitative pressure monitoring in lower-limb prosthetic sockets.* Prosthesis 3, 394-405

Keshavarzi M, Kegler M, Kadir S, Reichenbach T (2020). *Transcranial alternating current stimulation in the theta band but not in the delta band modulates the comprehension of naturalistic speech in noise*. NeuroImage, 210: 116557.

Keshavarzi M, Reichenbach T (2020). *Transcranial alternating current stimulation with the theta-band portion of the temporally-aligned speech envelope improves speech-in-noise comprehension*. Frontiers in Human Neuroscience, 14: 187.

McMenemy L, Ramasamy A, Sherman K, Mistlin A, Phillip R, Evriviades D, Kendrew J (2020). *Direct Skeletal Fixation in bilateral above knee amputees following blast: 2 year follow up results from the initial cohort of UK service personnel*. Injury, 51(3) :735-743.

Nguyen T-T N, Carpanen D, Stinner D, Rankin I, Ramasamy A, Breeze J, Proud WG, Clasper JC, Masouros SD (2020). *Mapping the Risk of Fracture of the Tibia from Penetrating Fragments*. Frontiers in Bioengineering and Biotechnology, 8: 544214.

Nguyen T-T N, Carpanen D, Stinner D, Rankin I, Ramasamy A, Breeze J, Proud WG, Clasper JC, Masouros SD (2020). *The Risk of Fracture to the Tibia from a Fragment Simulating Projectile*. Journal of the Mechanical Behavior of Biomedical Materials, 102: 103525.

Nguyen T-TN, Meek G, Breeze J, Masouros SD (2020). *Gelatine backing affects the performance of single-layer ballistic-resistant materials against blast fragments*. Frontiers in Bioengineering and Biotechnology, 8: 744.

Rankin IA, Nguyen T-T, Carpanen D, Clasper JC, Masouros SD (2020). *A New Understanding of the Mechanism of Injury to the Pelvis and Lower Limbs in Blast*. Frontiers in Bioengineering and Biotechnology, 8: 960.

Rankin IA, Webster CE, Gibb I, Clasper JC, Masouros SD (2020). *Pelvic injury patterns in blast: Morbidity and mortality*. The Journal of Trauma and Acute Care Surgery, 88(6): 832-838.

Selected by US Department of Defense Blast Injury Research Program Coordinating Office as the highlight publication of the month (Aug 2020) as 'significant research in the area of blast injury prevention, mitigation, and treatment.'

Rankin IA, Nguyen T-T, McMenemy L, Clasper JC, Masouros, SD (2021). *The Injury Mechanism of Traumatic Amputation.* Frontiers in Bioengineering and Biotechnology, 9: 665248

Nguyen T-T, Breeze J, Masouros SD, (2021) *Penetration of Energised Metal Fragments to Thoracic Tissues.* Fournal of Biomechanical Engineering

Rebelo EA, Grigoriadis G, Carpanen D, Bull AMJ, Masouros, SD (2021) *An Experimentally Validated Finite Element Model of the Lower Limb to Investigate the Efficacy of Blast Mitigation Systems.* Frontiers in Bioengineering and Biotechnology 9: 410

Carpanen D, Masouros SD, Stinner DJ, *Biomechanical evaluation of a tool-less external fixator.* BMJ Military Health

Rankin IA, Nguren T-T, Carpanen D, Darwood A, Clasper JC, Masouros SD, (2021) *Pelvic Protection Limiting Lower Limb Flail Reduces Mortality.* Journal of Biomechanical Engineering 143 (2)

Saiz-Alia M, Reichenbach T (2020). *Computational modelling of the auditory brainstem response to continuous speech*. Journal of Neural Engineering, 17(3): 036035.

Kadir S, Kaza C, Weissbart H, Reichenbach T (2020) *Modulation of speech-in-niose comprehension through transcranial current stimulation with the phase-shifted speech envelop.* IEEE Trans. Neur. Syst. Rehab. Eng. 28:23

Keshavarzi M, Kegler M, Kadir S, Reichenbach T (2020) *Transcranial alternating current stimulation in the theta band but not in the delta band mmodulates the comprehension of naturalistic speech in noise.* Neuroimage 210:116557

Keshavarzi M, Reichenbach T (2020) *Transcranial alternating current stimulation with the theta-band portion of the termporally-aligned speech envelope inproves speech-in-noise comprehension.* Front. Hum. Neurosci 14:187

Keshavarzi M, Reichenbach T, Moore BCJ (2021) *Transient Noise Reduction using a deep recurrent neural network: Effects on subjective speech intelligibility and listening comfort.* Trends Hear 25:1

Keshavarzi M, Varano E, Reichenbach T, (2021) *Cortical tracking of a background speaker modulates the comprehension of a foreground speech signal.* J. Neurosci 41:5093

Saiz-Alia M, Miller P, Reichenbach (2021) *Otoacoustic emissions evoked by the time-varying harmonic structure of speech*. eNeuro 8:0428

Sory DR, Amin HD, Chapman D, Proud WG, Rankin SM (2020). *Replicating landmine blast loading in cellular in Vitro models*. Physical Biology, 17(5): 056001.

Stewart S, Darwood A, Masouros SD, Higgins C, Ramasamy A (2020). *Mechanotransduction in osteogenesis: current concepts and future research foci*. Bone and Joint Research, 9 (1): 1-14.

Stewart SK, Tenenbaum O, Higgins C, Masouros SD, Ramasamy A (2020). *Fracture union rates across a century of war: a systematic review of the literature*. BMJ Military Health, 166(4): 271-276.

Thompson DC, Crooks RJ, Clasper JC, Lupu A, Stapley SA, Cloke DJ (2020). *The pattern of paediatric blast injury in Afghanistan*. BMJ Military Health, 166(3): 151-155.

Turner S, McGregor A (2020). *Perceived Effect of Socket Fit on Major Lower Limb Prosthetic Rehabilitation: A Clinician and Amputee Perspective*. Archives of Rehabilitation Research and Clinical Translation, 2(3).

Yu X, Azor A, Sharp DJ, Ghajari M (2020). *Mechanisms of tensile failure of cerebrospinal fluid in blast traumatic brain injury*. Extreme Mechanics Letters, 38: 100739.

Faraizadeh Khosroshahi S, Yin X, Donat CK, McGarry A, Yanez Lopez M, Baxan N, Sharp D, Sastre M, Ghajari M (2021) *Multiscale modelling of cerebrovascular injury reveals the role of vascular anatomy and parenchymal shear stresses.* Scientific Reports 11(1), pp1-12

Donat CK, Yanez Lopez M, Sastre M, Baxan N, Goldfinger M, Seeamber R, Müller F, Davies P, Heellyer P, Siegkas P, Gentleman S, (2021) *From biomechanics to pathology: predicting axonal injury from patterns of strain after traumatic brain injury.* Brain 144(1), pp 70-91

Dixon Smith S, Henson D, Hay G, Rice ASC (2021) *Chronic post-amputation pain and blast injury: An analysis of the surviving pension records (PIN 26) of British Army First World War veterans 1914-1985.* Journal of Military, Veteran and Family Health, 2, 64-73

Books

Brust P, Deuther-Conrad W, Donat CK, Barthel H, Riss P, Paterson L, Hoepping A, Sabri O, Cumming P (2020). Preclinical and Clinical Aspects of Nicotinic Acetylcholine Receptor Imaging. Chapter in 'PET and SPECT of Neurobiological Systems', 2nd edition, Springer.

Mayhew, E (2021). The Four Horsemen and the Hope of a New Age, Riverrun Publishing (London)

Invited Talks

Ghajari M: *Predicting and preventing traumatic brain injury at the cutting-edge interface between engineering and medicine*. Distinguished lecture, University College Dublin, Ireland, January 2020

Mayhew E: *Blast Injury Long term effects*. University Womens Club, London, UK, January 2020

Masouros S: *How bones break: the mechanics of skeletal trauma*. Trauma Symposium. Royal Society of Medicine, London, UK, February 2020

Mayhew E: *Paediatric Blast Injury*. Society of Apothecaries, London, UK, February 2020

Reichenbach T: Seminar. Department of Computer Science, University of Hertfordshire, UK, February 2020

Reichenbach T: Seminar. Institute of Neurosciences, University of Barcelona, Spain, February 2020

Bull AMJ: *Amputee Biomechanics. It is not just about getting active* (plenary). Trauma recovery: new science and technology for mental and physical health conference. Royal Society, London, UK, March 2020

Henson D: *The Principles of (Recovering From) War*. Trauma recovery: new science and technology for mental and physical health conference. Royal Society, London, UK, March 2020

Mayhew E: *Unexpected Survivors: The Guinea Pig Club.* Kings College London veteran mental health conference, London, UK, March 2020

Dickinson R, *Xenon Neuroprotection in preclinical models of TBI*. Current Topics in TBI Online Webinar Series, April 2020, Online

Dixon Smith S: *Blast Injury & Chronic Pain*. The National Archives at Kew, UK, May 2020

Donat CK: *From TBI biomechanics to pathology - Validation of a finite element model of rat TBI using high field MRI, quantitative histology and blood biomarkers*. Frontiers in TBI conference 2020, London, UK, June 2020

Mayhew E: *Lockdown, the First Hundred Days with historical comparisons*. BBC Local Radio, multiple locations, UK, June 2020

Mayhew E: *A brief history of AMR*: IMSE invited webinar series, July 2020

Mayhew E: *Combat casualty – a history and future implications*. Army Medical Research and Development Infrastructure Planning, USA, July 2020

McGregor A: Talk on smart sockets to University of Moratuwa Engineering Research Conference July 2020

Mayhew E: *Forward Surgical Capability – a historical perspective*. 2 Med Brigade Study Day, Strensall, September 2020

Mayhew E: *V1 rocket attacks and their aftermath in World War Two*. Chelsea History Festival, London, UK, September 2020

Mayhew E: *Life beyond survival: from orthopaedic trauma to pathogen epidemics, what do endings really mean?* British Orthopaedic Association Annual Conference, Birmingham, UK, September 2020

Reichenbach T, Logitech Seminar, October 2020, Lausanne, Switzerland

Mayhew E: *Life Beyond Survival* (invited teaching sessions). Purdue University USA, October/November 2020

Mayhew E: *The Guinea Pig Club: surviving complex casualty*. CBS, USA, November 2020

Mayhew E: *Very Heavy Reckonings*. Colchester Medical Society, November 2020

Mayhew E: *Lessons from the Past, Today.* 204 (North Irish) Field Hospital Learning Day, November 2020

Stevens M, *Engineering the cell-material interface*, 11th World Biomaterials Congress, December 2020, Online

Bull AMJ: *Clinical biomechanics for amputee function – proposing new interventions.* Online keynote, Staffordshire Conference on Clinical Biomechanics (SCCB), April 2021

Stevens M, *Designing self-assembling and gradient materials for regenerative medicine*. MRS Spring, April 2021, Seattle, USA

Mayhew, E, *Military Medicine,* National Army Museum, April 2021, London, UK

Mayhew, E, *The Four Horsemen*, Stratford Literary Festival, April 2021, Stratford, UK

Mayhew, E, *Paediatric Blast Injury,* Naval Military Society, April 2021

Mayhew, E, *War Games podcast*, St Andrews University, May 2021, Online

Mayhew E, *The Four Horsemen for the modern age,* Imperial College podcast, June 2021, Online

Masouros SM, *Modelling blast injury: pathophysiology, protection and recovery*. International Research Council on Biomechanics of Injury (IRCOBI) 2021, June 2021, Online

Reichenbach T, Meeting of the Central Insitute of Medical Technology, Friedrich Alexander University, June 2021, Erlangen, Nürnberg, Germany

Reichenbach T, Sivatos Research Siminar, August 2021, Erlangen, Nürnberg, Germany

Pope D, Masouros SM, *Physics- and systems-based modelling techniques to nalyse human protection against blast and ballistic insult*. International Forum on Blast Injury Countermeasures (IFBIC) 2021, September 2021, Online.

Mayhew, E, *Reckonings from Afghanistan,* National Army Museum, September 2021, London, UK

Mayhew, E, *The Guinea Pig Club,* BBC RAF History Podcast, September 2021, London, UK

Mayhew, E, *The Four Horsemen,* Chelsea History Festival, September 2021, London, UK

Mayhew, E, *The Paediatric Blast Injury Field Manual,* American Association of Paediatrics, September 2021.

Mayhew, E, *The Four Horsemen,* Gateshead History Festival, September 2021

Bull AMJ: *Enhancing computational musculoskeletal modelling with recent advances in computational methods and machine learning: clinical applications in ageing and trauma*. Plenary Keynote, European Society for Movement Analysis in Adults and Children 2020 (postponed to 2021 due to COVID), October 2021, Odense, Denmark

Mayhew, E, *The Four Horsemen,* Welles Literary Festival, October 2021

Bull AMJ: *Blast injury, extremity reconstruction and rehabilitation (a biomechanics perspective).* Plenary Keynote, Combined Services Plastic Surgery Society meeting, November 2021, Yeovil, UK

Masouros SM, *Modelling the lower extremity in under body blast*. IRCOBI Human Mdelling Applications Workshop, November 2021, Online

Masouros SM, *Modelling blast injury: from clinical data to pathophysiology and protection*. Unisa International Symposium in Biomedical Engineering Innovation (UNISA – ISBEI) 2021, November 2021, Online

Mayhew, E, *Stretcher Bearers of the Western Front,* Western Front Association, November 2021

Mayhew, E, *Stretcher Bearers of the Western Front,* 204 Field Hospital, November 2021

Conference Presentations and Involvement in Subject Specific Meetings

Government Experts on Mitigation Strategies, Minley, UK, January 2020
Nguyen T-N, Masouros S, *Secondary blast injury modelling*

Veteran Mental Health Conference, Kings College London, March 2020
Le Feuvre P, *Unity through diversity: Managing complexity in healthcare (poster)*

CBIS advisory board meeting, Imperial College London, London, UK, May 2020
Kaufmann J, *A combined computational and clinical approach to investigating bone health in lower-limb amputees*

Combined Services Orthopaedic Society Annual Meeting. May 2020 (virtual)
Stewart S, Darwood A, Masouros S, Ramasamy A, *Cell survivability following blast trauma influences the likelihood of non-union*

Brain Stimulation Workshop, Helsinki, May 2020 (online)
Reichenbach T

Frontiers in TBI, June 2020 (virtual)
Ghajari M, *Predicting traumatic brain injury pathologies using computational biomechanics* Organised and chaired the *Biomechanics* session

Virtual Conference on Computational Audiology (VCCA) June 2020
Saiz Alia M, Reichenbach T – *Computational modelling of the human auditory brainstem response to natural speech*

Federation of European Neuroscience Societies online meeting, July 2020
Valeo F, Campos-Pires R, Soumalias P, Martinez-Gili L, Chilloux J, Dickinson R, Dumas M et al., *Serum metabolic profiling following traumatic brain injury in rats using ^{1}H nuclear magnetic resonance spectroscopy*

ADVANCE Trustees meeting, London, UK, July 2020 (virtual)
Kaufmann J, *A combined computational and clinical approach to investigating bone health in lower-limb amputees*

International Association for the Study of Pain Virtual Series on Pain & Expo, July 2020 (virtual)
Dixon Smith S, Hay G, Mayhew E, Rice A, *Blast Injury & Chronic Pain: Mining First World War Pension and Medical Archives*
Dixon Smith S, Hay G, Mayhew E, Rice A, *A Systematic Review of the Professional Medical Conversation Regarding Conflict Related Chronic Post Amputation & Neuropathic Pain, 1914-1985*

The British Orthopaedic Research Society (BORS) Annual meeting, September 2020
Phillips A, Kaufmann J, *Taking a combined musculoskeletal and finite element modelling approach to investigating bone loss in transfemoral amputees*

Bernstein Conference on Computational Neuroscience, Germany (VCCA), September 2020 (virtual)
Reichenbach T – *Modelling the effects of transcranial alternating current stimulation (tACS) on the neural processing of speech*

European Society of Anaesthesiology meeting online, November 2020
Campos-Pires R, Mohamed-Ali N, Franks N, Aldhoun J, Dickinson R, *Hypothermia combined with xenon reduces secondary injury development and enhances neuroprotection by preventing neuronal cell loss in a rat model of traumatic brain injury*

World Innovation Summit for Health 2020, November 2020.
Henson D, *Session: The Children of the Frontline with Save the Children* (*https://www.youtube.com/watch?v=ML8VlW1a8E8)*

Virtual Physiotherapy Conference, November 2020
Le Feuvre P, *Unity through diversity: managing complexity following major trauma*

Society of Military Orthopaedic Surgeons (SOMOS), 2020 virtual annual meeting, November 2020
Rankin IA, *High-Velocity Sand Blast is a Significant Injury Mechanism Implicated in Blast Trauma*
Rankin IA, *Pelvic Protection Limiting Lower Limb Flail Reduces Mortality*
Rankin IA, *Tier 1 Pelvic Protective Equipment Reduces Injury from High Velocity Sand Blast*
Stewart SK, *Blast Waves Induce Osteogenesis in Mesenchymal Stem Cells*
McMenemy L, *Progress Since the Lower Extremity Assessment Project: A Systematic Review*
McMenemy L, *Predicting Outcomes following Rehabilitation with the Bespoke Offloading Brace*

Society for Neuroscience, January 2021
Campos-Pires R, Onggradito H, Ujvari E, Karimi S, Aldhoun J, Edge C, Franks N, Dickinson R. X*enon is neuroprotective and promotes beneficial early neuroinflammation in a rat model of sever traumatic brain injury.*

Group of Experts on Mitigating Systems (GEMS), Jaunary 2021
Nguyen T-T, Tsukada H, Breeze J, Masouros SD. *Soft ballistic protection against injuries due to energised fragments*
Rankin I, Webster C, Nguyen T-T, Clasper JC, Masouros SD. *Dismounted pelvic blast trauma: cause of death, mechanism of injury and mitigation strategies*

Injury Studies Networking Event, February 2021
Tsikonofilos, K. *Understanding blast-induced damage to the auditory cortex using multi-scale electrophysiology*

CBIS progress meeting, February 2021
May H, Cornelius D, Bruyns-Haylett M, Tsikonofilos K, Ghajari M, Sastre M, Sharp D. *Understanding the effect of biomechanics on the brain using rodent blunt and blast injury models*

GARDP Annual Conference, February 2021
Mayhew, E. *The Three Ages of AMR*

Wellcome Connecting Science's Longitudinal Studies, March 2021
Dixon Smith S, Rice A. *"A legacy of pain": A retrospective cohort study of veterans' healthcare*

Festival of Neuroscience run by British Neuroscience Association (BNA), London, UK, April 2021
Goodwin J, Bruyns-Haylett M, Kozlov A. *Electrophysiological signatures of blast injury in neural populations in the auditory cortex*

Virtual Conference on Computational Audiology, June 2021
Keshavari M, Varano E, Reichenbach T. *Cortical tracking of a distractor speaker modulates the comprehension of a target speaker*

Institute of Historical Research's History Lab, May 2021
Dixon Smith S. *From Raincoats to Royalty: The Blighty Tweed Company, 1916-1927*

International Association for the Study of Pain World Congress, June 2021
Dixon Smith S, Rice A, *A systematic review of the professional conversation regarding conflict related chronic post amputation & neuropathic pain, 1914-1985 [Project update]*

Weapons, Wounds & Warfare, University of Aukland (Hybrid), June 2021
Dixon Smith S, Rice A, *Blast Injury & the Continuum of Care: A Long-Term Cohort Study of Conflict Wounds in Veterans*.

Blast Injury Conference, London, UK, July 2021
Ghajari M, Conference Chair
Dixon Smith S, *An Interval of Comfort: A Very Long-Term Study of Blast Injury*
Bruyns-Haylett M, Tsikonofilos K ,May HG, Sharp DJ, Kozlov A, *A longitudinal study comparing same day resting state and auditory stimulus evoked EEG signatures before and immediately post blast in a rat model of blast induced mild traumatic brain injury*

May H, Tsidonofilos K, Bruyns-Haylett M, Donat C, Sastre M, Sharp DJ, *Axonal Injury as Consequence of. Last Traumatic Brain Injury: Evaluation of a Novel and Translationally Relevant Biomarker of Axonal Injury in a Rodent Model.*
Campos-Pires R, Yonis A, Pau A, Macdonald W, Harris K, Edge C, Franks N, Dickinson R, *Delayed xenon treatment prevents injury development following blast-neurotrauma in vitro*
Campos-Pires R, Hirnet T, Valeo F, Ong BE, Radyushkin K, Aldhoun J, Saville J, Edge CJ, Franks NP, Thal SC, Dickinson R, *Xenon improves long-term cognitive function, reduces neuronal loss and chronic neuroinflammation, and improves survival after traumatic brain injury in mice.*
Nguyen T-T, Clasper JC, Masouros SD, *Experimental Models of Secondary Blast Injury.*

38th National Neurotrauma Symposium, July 2021
Campos-Pires R, Onggradito H, Ujvari E, Karimi S, Leong I, Valeo F, Aldhoun J, Edge C, Franks N, Dickinson R. *The noble gas xenon is neuroprotective and promotes beneficial neuroinflammation following severe neurotrauma in rats*

RGS Conference, August 2021
Mayhew, E, *Forensic Humanitarianism*

International Conference on Phantom Limb Pain, Gothenbury, Sweden (Hybrid), September 2021
Dixon Smith S, Rice A, "*I did not expect the doctor to treat a ghost": chronic phantom limb pain in military amputees, 1914-1985.*

International Research Council on Biomechanics of Injury (IRCOBI), September 2021
Low L, Salzar R, Newell N, Masouros SD, *The role on non-linear stiffness in modelling high-rate axial loading of the spine.*

Personal Armour System Symposium, October 2021
Nguyen T-T, Carpanen D, Meek G, Rankin I, Ramasamy A, Clasper JC, Masouros SD, *Fragment Injury and Light-weight protection*

National Army Museum Conference, November 2021
Mayhew, E, *Military Medicine.*

Grants

Centre members received a number of grants in 2020/21 which relate to research funded by the Centre. The table below provides an overview.

Funder	Amount	Title	Lead applicant
The ADVANCE Study is funded through the ADVANCE Charity with support from: • The Headley Court Charity (the principal funder) • A direct LIBOR grant from the Chancellor of the Exchequer • Help for Heroes • Nuffield Trust for the Forces of the Crown • Forces in Mind Trust (FiMT) and The National Lottery Community Fund • Blesma – The Limbless Veterans • The UK Ministry of Defence	£12.5M	ADVANCE Study Charity	Professor Anthony Bull is the Imperial College lead Co-Investigator
Association of Paediatric Anaesthetists of Great Britain & Ireland	£39,925	The effect of xenon-treatment on the developing brain following paediatric neurotrauma	Dr Robert Dickinson (PI) and Dr Rita Campos-Pires (Co-I)
InnovateUK	£360,000	Smart Grants, Ultrasafe 3D printed helmets	Dr Mazdak Ghajari
Academies of Sciences (USA)	$105,064	NRC fellowship	Dr Andrei Kozlov
Scarfree Foundation	£47,677	Digital app to support long term health in amputees	Professor Alison McGregor
Innovate UK	£200,286	An AI-powered tool for reducing OA knee pain	Professor Anthony Bull

NIHR – costed extension	£483,813	NIHR Global Health Research Group on POsT Conflict Trauma (PrOTeCT)	Professor Anthony Bull
Road Safety Trust	£91,000	Rating bicycle helmets used on UK roads and disseminating results	Dr Mazdak Ghajari
RCI Rapid Spend Initiative: Defence Medical Services	£10,000	Determining the effectiveness of reinforcing the sleeves of clothing in reducing injury from explosive devices	Dr Spyros Masouros,Lt Col Arul Ramasamy and Lt Col John Breeze
Strategic Priorities Fund	£10,000	Generate the evidence to show that biofidelic backing is required when testing soft body armour	Dr Spyros Masouros
Innovate UK	£520,000	NURO.sense – An intelligent wearable to identify, assess and monitor the motor symptoms of neurodegeneration	Dr Ravi Vaidyanathan
NIHR	£1.1M	Closed-Loop Electronic Stimulation (ES) – Mechanomyogram Sensor (MMG) System for Passive Tremor Suppression Treatment	Dr Ravi Vaidyanathan
Funding through internal sources held at Imperial College London			
MedTech SuperConnector	£73,650	Bone Protector Cap for Amputee Stump Pain	Professor Anthony Bull and Dr Giovanni Milandri
EPSRC Impact Acceleration	£65,325		Professor Anthony Bull and Dr Dave Henson
EPSRC Impact Acceleration	£85,103	Delivery of Appropriate Low-Cost Prosthetic Devices	Professor Anthony Bull and Dr Dave Henson
EPSRC Impact Acceleration	£82,774	I-Fix: Local Manufacturing and Clinical Trial of Imperial External Fixator in Gaza	Professor Anthony Bull and Dr Mehdi Saeidi
EPSRC Impact Acceleration	£44,643	Orthopaedic Trauma Healthcare in Conflict, Post-Conflict, and Low-Resourced Settings – An Imperial College White Paper	Professor Anthony Bull, Dr Dave Henson and Dr Vassia Vardakastani
UKRI IAA Healthy Society	£96,642	Appropriate and affordable prosthetic locking liner and suspension system for low- to	Professor Anthony Bull and Dr Clement Favier

		middle-income countries and conflict zones	
Research proposal to assist evidence-based policy making (Imperial funding)	£22,000	Generate the evidence to show that biofidelic backing is required when testing soft body armour	Dr Spyros Masouros and Lt Col John Breeze

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 undertaken research with Centre members as part of the Undergraduate Research Opportunities Programme (UROP) this year. Below is an overview of some of the projects:

- **Dong Ruonan** – 'Lower limb amputee biomechanics' – supervised by Professor Anthony Bull and Diana Toderita. The project aimed to investigate the muscle and hip joint loading in bilateral transfemoral traumatic amputees and the effect of muscle atrophy on the generated contact forces at the hip joint.

- **John Goodwin** – 'An investigation of how environmental noise affects neural encoding of auditory stimuli in traumatic brain injury' – supervised by Dr Michael Bruyns-Haylett and Dr Andriy Kozlov. The project analysed neural population data (local field potentials) from the auditory cortex of rats in response to rat vocalisations. They collected these data from rats that have been exposed to a mild blast intensity at different time points post-blast, and the student is comparing these data with those from with healthy rats. John is attempting to identify markers of traumatic brain injury in these neural population data in order to provide evidence for, and insight into, a translational model of TBI induced auditory processing disorder.

- **Lois Galletly** – 'Determination of a proper objective function to resolve muscle-force sharing problem in amputee gait' – supervised by Dr Pouya Amiri and Professor Anthony Bull. The project's objective is to determine novel objective functions that can be used to determine muscle forces for amputee during walking.

- **Araminta Hampden Martin** – 'The impact of increased gait symmetry, facilitated via visual biofeedback, on reducing joint contact forces in transtibial unilateral amputees' - supervised by Dr Pouya Amiri and Professor Anthony Bull. The objective of the project is to develop a real time biofeedback training for unilateral transtibial amputee to help them generate similar forces on each foot and reduce the knee joint loading on the intact side.

- **Kay Raftery** – 'Segmentation of amputee spinal musculature from MRI scans' – supervised by Professor Alison McGregor, Biraravan Sivapuratharasu and Clement Favier.

- **Aime Keane** – 'Instrumentation development, testing and data capture for musculoskeletal and other clinical settings' – supervised by Professor McGregor and Dr Matthew Hopkins. The project examines the performance of low-cost pressure sensors produced in the laboratory, in comparison with commercial sensors produced by companies such as Tekscan and Novel. The aim is to perform comparative analysis to determine relative strengths and weaknesses of the laboratory device, relative to readily available alternatives.

- **Paul Courty** – 'Towards Audiovisual Hearing Aids' – supervised by Dr Tobias Reichenbach and Enrico Varano. The project aimed to develop audiovisual signals to improve speech in noise comprehension and test these both behaviourally and by employing brain imaging techniques.

- **Daria Morajska** – 'Towards Audiovisual Hearing Aids' – supervised by Dr Tobias Reichenbach and Enrico Varano. The project aimed to test audiovisual signals designed to improve speech in noise comprehension by employing ML methods to simulate human volunteer subjects in a behavioural experiment. The end goal being to develop a framework to hasten the pace of research in this field by providing a method to pre-select interesting experimental conditions. Another outcome of this project is that of providing explanation and insight into some of the behavioural results observed in humans.

Masters Projects

Centre members have been involved in the supervision of multiple Masters projects throughout 2020. Below are some examples of these projects:

- **Meghan Walker** – 'The effects of quadriceps loading on laxity evaluations in the knee' – supervised by Dr Spyros Masouros and Professor Anthony Bull. The project is a finite element study investigating the significance of the quadriceps muscle's contribution to the restraint of the tibiofemoral joint laxity. The ultimate goal is to inform the design of a novel robotic knee testing system.

- **Eszter Ujvari** – 'The Effect of Xenon on Microglial Activity in a Rat CCI Model of Traumatic Brain Injury' – supervised by Dr Robert Dickinson.

- **Shughoofa Karimi** – 'The role of xenon on astrogliosis in a rat model of severe traumatic brain injury' – supervised by Dr Robert Dickinson.

- **Isobel Fuller** – 'Characterizing a Model of Mild Blast Traumatic' – supervised by Dr Robert Dickinson.

- **Charlotte Boyles** – 'Categorising novel In Vivo Blast-Induced Traumatic Brain Injury Models through Neuronal Cell Quantification' – supervised by Dr Robert Dickinson.

- **Sanarya Aljaf** – 'The Effect of Blast-TBI and Xenon Treatment on Neuronal Loss in-vivo' – supervised by Dr Robert Dickinson.

- **Lorenzo Sani** – 'Auditory Blast Biomarkers' – supervised by Dr Michael Bruyns-Haylett, Konstantinos Tsikonofilos, Dr Tobias Reichenbach and Andriy Kozlov. The project focuses on uncovering electrophysiological signatures of damage to the auditory cortex, in a preclinical model of blast. The ultimate goal is to develop markers of auditory processing disorder, a debilitating condition for blast-exposed individuals.

- **Fatin Ahmed** – 'Neuroprotective effects of argon and xenon in traumatic and ischaemic brain injury: A pre-clinical systematic review and meta-analysis' – supervised by Dr Robert Dickinson

- **Andy Ko** – 'Characterisation of neuronal density and neuroinflammation in the rat thalamus after blast TBI' – supervised by Dr Robert Dickinson
- **Emilie Lai** – 'The effect of blast traumatic brain injury and xenon treatment on neurons and astrocytes in the rat thalamus – supervised by Dr Robert Dickinson
- **Isabelle Leong** – 'Investigating the effects of xenon on astrogliosis and neuroprotection following traumatic brain injury' – supervised by Dr Robert Dickinson
- **Min Liang** – 'A systematic review and meta-analysis of xenon and argon as novel teratments for acquired brain injury in animal models' – supervised by Dr Robert Dickinson
- **Valerie Sun** – 'Histopathological characterisation of a novel in vivo mild blast-induced traumatic brain injury model in rats' – supervised by Dr Robert Dickinson
- **Rulin Wu** – 'Acute signatures of blast-induced traumatic brain injury in EEG' – supervised by Dr Michael Bruyns-Haylett, Dr Konstantinos Tsikonofilos and Prof Andriy Kozlov. Traumatic brain injury (TBI) can significantly impair brain function and lead to long-term cognitive and sensory processing sequalae. TBI-induced chemical changes to the brain are known to be highly dynamic in the acute post-injury period, and it is expected that this will be reflected in the electrophysiological signal. In this project, resting state macroscopic (EEG) electrophysiological data from the early acute period in a rodent model of blast TBI were analysed for changes in the power of brain waves at different frequencies, as well as the dynamical regime of the resting brain. Compared to the uninjured brain, blast is associated with decreased power in the theta band (4-8 Hz) approximately two hours after blast, and with increased number of states that are present post-blast in the drain dynamics. These point towards promising early biomarkers of injury and a two-hour intervention window for candidate treatments.
- **Rory Horder** – 'Production and bonding of stretch dominated subchondrial bone mimics' – Supervised by Professor Molly Stevens and Dr Axel Moore. Mr Horder used computational solid mechanics modelling to predict the optimal structures for load bearing bone substitutes based on the material properties of different polymers. Cadidate structures were then produced using fused deposition modelling and analysed using micro-CT and unconfined compression. Mechanical competence, print accuracy and agreement with the theoretical modelling were used to define the optimal structure.

Imperial College London

THE ROYAL BRITISH LEGION

CENTRE FOR BLAST INJURY STUDIES

AT IMPERIAL COLLEGE LONDON