Imperial College London

THE ROYAL BRITISH LEGION

THE ROYAL BRITISH LEGION
CENTRE FOR BLAST INJURY STUDIES
AT IMPERIAL COLLEGE LONDON

2013

CBIS Annual Report

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

August 2014

Imperial College London

Centre for Blast Injury Studies
Annual Report

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

http://www.imperial.ac.uk/blastinjurystudies

London, August 2014

Imperial College of Science, Technology and Medicine

Contents

Foreword

This second Annual Report represents a step change in the work of the Royal British Legion Centre for Blast Injury Studies at Imperial College London (CBIS). With the support of our Advisory Board, we have extended the remit of CBIS to include explicitly blast injury rehabilitation as a scientific theme. This has been made possible through the strong collaboration of the Defence Medical Rehabilitation Centre at Headley Court for which the Centre is grateful. We have also now started to address more of the clinical research priorities as defined in conjunction with the Surgeon General. For example, the appointment of Dr Tobias Reichenbach by Imperial College has brought a world-leading expert in hearing research to the Centre and he is now starting a major programme on blast-induced hearing loss in the military.

These two examples, the partnership with Headley Court and this new appointment with relevant expertise, reflect the approach of the Centre in which we lead in those areas where we have the expertise, support through collaborations where the leadership more appropriately lies elsewhere, and make new appointments where appropriate and required.

Not only has this year seen a growth in activity, but has also seen the Centre thrust into the media spotlight. In November HRH Prince Harry opened to great fanfare our newly refurbished laboratories that now allow us to conduct a whole new type of experiment that will primarily serve our blast biomechanics and blast biology and therapeutics themes.

I would also like to highlight that the Centre is dedicated to ensuring that our learning from the military experience is not confined to the armed forces, veterans and their families. We are committed to civilian transfer and this year our relationship with Find A Better Way, a humanitarian charity devoted to improving the lives of individuals and communities affected by landmines, has become established and with their support we are working on multiple civilian transfer projects. The new section in the report on Civilian Transfer is, therefore, very important to the Centre and should serve as a sharp focus to the researchers who, in the light of the withdrawal of British troops from Afghanistan and the significant reduction in casualties in recent years, should be devoted to capturing what can be learnt now before it is lost and engaging with what happens in the long run to those severely injured due to blast.

This last year has seen the Centre cement its place nationally and internationally as *the* leader in blast injury research. Our growth in numbers, outputs, and *effect* demonstrate not only the commitment to this work of the Ministry of Defence and our main funder, the Royal British Legion, but also that of Imperial College London itself. The strong personal support received by the Centre from Sir Keith O'Nions, the President and Rector of Imperial College is a key aspect of this commitment and we look forward to working with his successor, Professor Alice Gast, in subsequent years.

Professor Anthony M J Bull FREng

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

Introduction

The Royal British Legion Centre for Blast Injury Studies (CBIS) is a clinically-led research and translation centre based at Imperial College London. We seek to improve the mitigation of, and recovery from, blast injuries through clinically-led research. We then develop the science and engineering research and application across all relevant disciplines.

This report is not meant as a comprehensive survey of all the activities of the Centre, but is meant to give a flavour of the breadth and depth of the work with specific highlights.

The 2013 report summarises significant changes from previous year's work and, in particular, highlights the new research theme of Blast Injury Rehabilitation. Further information on the Centre's background, structure, and governance can be found in the 2012 Annual Report.

Following on from a description of the research themes, the report describes key clinical research outputs in 2013. The final main technical section of the report highlights three areas of engineering and science research that have seen significant development in 2013. These are: Noise-Induced Hearing Loss, Blast Lung Injury and Heterotopic Ossification.

In a new section this year, we have chosen to present how some of our alumni are now making a difference in other walks of life and we complete the report with a summary of our communication and outputs for the year.

Staffing, Governance and Finance

CBIS has maintained its high level governance structure with a strong advisory board, a research strategy group that acts as the main liaison between CBIS and the Royal British Legion as the main funder, and a management group that oversees day-to-day activities, resourcing, and prioritisation. 2013 has seen our Veteran's Representative, Captain Dave Henson, move to become a member of the Advisory Board in addition to his membership of the Research Strategy Group. Dave is a key part of the Centre and his involvement in 2013 extended from his representative role to becoming a research-active member of the centre as he started his Masters in Biomedical Engineering studies in the Department of Bioengineering at Imperial College with a project on novel implantable devices for through-knee amputees.

The Centre continues to grow through gaining significant extra resources from multiple sources. CBIS now comprises over 30 core and associated staff based at Imperial College. By maintaining strong links with The Royal Centre for Defence Medicine (RCDM), the Defence Science and Technology Laboratory (DSTL), and the University of Cambridge, CBIS is afforded unrivalled experience in the clinical management of combat injury, an interface with the MOD's defence and security requirements and world-class experimental facilities for the testing of hard materials and explosives. Through our partnership with charity Find A Better Way and others we can transfer the knowledge learned through our work with the military to the civilian arena.

Core funding from the Royal British Legion has been extended for a full year to run until November 2017. Given the extent of the areas comprising the subject of blast injury and resources currently available, not all of the subjects can be studied at once. In order for CBIS to address this shortfall, we will continue to source not only funding, but partner organisations conducting synergistic studies. Links with such institutions provide an opportunity to move into new areas, as well as extending the influence and adding to the expertise of the Centre. The Centre Management Committee and Research Strategy Group remain focused on identifying potential shortfalls and possible partners in order for CBIS to achieve its stated objective. As well as this, we are committed to exploiting the Centre's respective Intellectual Property.

The Centre activities are extensive in terms of research, dissemination, public engagement, outreach, education, and influencing policy. The academics and postdoctoral staff in the Centre are committed to extending the reach of the research and to resourcing additional activities through external sources. These activities are not only directly funded by the main stakeholders, as additional significant resource has been leveraged through the Centre's activities. These additional resources can be categorised in terms of manpower, research funding, and long-term committed resource. For example, we have been successful in securing research grants from Find A Better Way, Smith & Nephew, The Department of Bioengineering PhD Scholarship Scheme and Imperial Confidence in Concept Scheme.

Fourteen students that are enrolled in courses in the Faculties of Engineering, Natural Sciences and Medicine, conducted major projects associated with CBIS in 2013. These projects include third year group projects, final year BEng projects, final year MEng projects, MSc and MSci projects, and summer projects. All of these projects have been supervised by academic staff associated with the Centre and have utilised the unique experimental resources available in the Centre. These students were not funded by CBIS, but certainly contribute to the aims of CBIS.

As described briefly above, Imperial College London has funded the indirect costs of the research within the Centre. In addition, Imperial College has committed to the sustainability of the Centre by guaranteeing the permanent salary of an academic appointed to the Centre (Dr Spyros Masouros). A second, new member of academic staff is fully funded by Imperial College (Dr Tobias Reichenbach). He is leading the research on noise-induced hearing loss. Furthermore, Imperial College has a scheme to help the development of world-leading postdoctoral research staff through the Junior Research Fellow Scheme. The aim of this scheme is to help outstanding early career scientists and engineers establish their academic independence and make the leap from post-doc to permanent lecturer. CBIS has supported one of these fellow applicants who has successfully secured an additional three years of research. Focused on traumatic brain injury due to blast, Dr Mazdak Ghajari is expected to be in a position to obtain a permanent academic position at the end of the fellowship. These long-term, permanent positions have extended the clinical research of CBIS, as well as providing further sustainability of the Centre's activities.

Areas of Research

Themes, Priorities and Core Facilities

The Centre's research is focused on the physical and biological effects of primary and tertiary blast (Figure 1). Secondary blast, in which fragments are energised by the blast wave, has not been a focus of the Centre to date as this is addressed by other research centres that have a focus on ballistics protection, for example. Our clinical work has led us to focus on primary and tertiary blast as these insults produce high numbers of surviving casualties and fatalities, cause a significant burden of pain and disability, and are amenable to an interdisciplinary research endeavour.

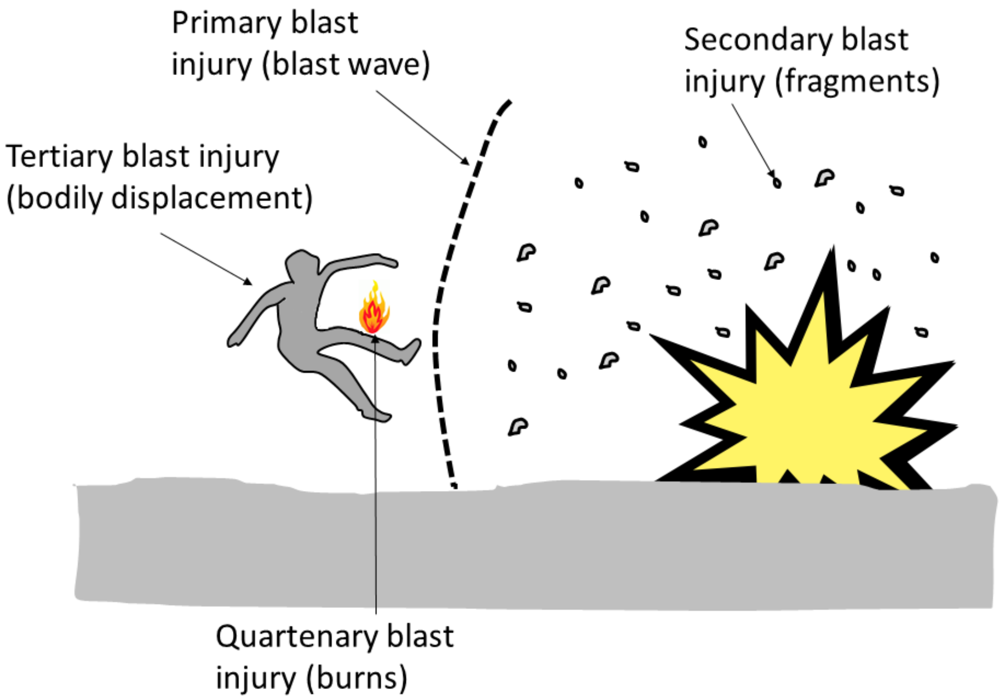


Figure 1: Modes of injury from explosions.

CBIS delivers its strategic research through resourcing specific research projects either in the form of PhD studentships or postdoctoral research staff, supporting associated projects through access to dedicated equipment or additional running costs, and through its core technical and administrative staff. The Centre has a series of clinical priorities and scientific themes (Figure 2). The addition of Blast Injury Rehabilitation this year brings the number of scientific themes to four. This new theme has priorities as described below. The other three themes articulated their research priorities in last year's annual report, and so brief updates only are provided here.

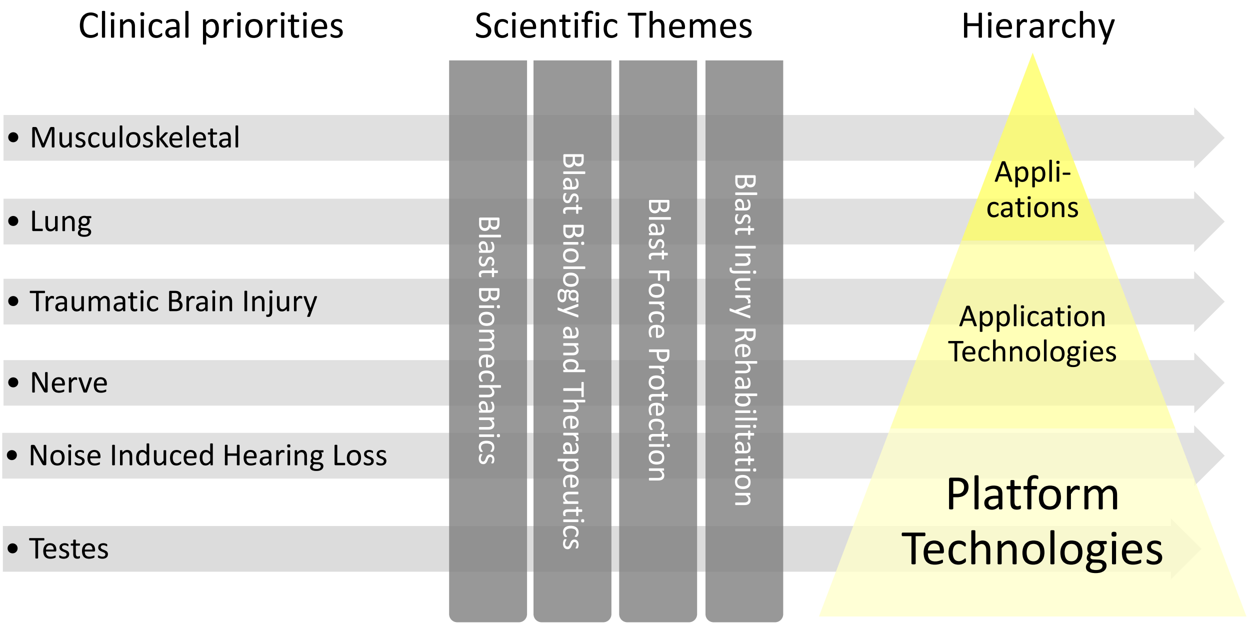


Figure 2: Centre research strategy

Core facilities for CBIS are provided within the various departments that house the researchers. Mainly these researchers are housed in the Department of Physics (Institute of Shock Physics), National Heart and Lung Institute, Department of Civil and Environmental Engineering and Department of Bioengineering. Within Bioengineering, 2013 has seen the development of major new laboratories for the use of the Centre's researchers (Figure 3). These comprise a dedicated facility for *in vivo* experiments with a *procedure room,* a *hotel* and a room for *physiological monitoring* and *behavioural analysis*, a new laboratory for underbelly blast simulation, and a room for cellular and molecular work using our state-of-the-art split Hopkinson Bar.

Figure 3: New Centre laboratory facilities opened in 2013

Blast Injury Rehabilitation

Background to Theme

Early in 2013 the CBIS Advisory Board encouraged the Centre Director to consider more seriously how rehabilitation could be incorporated into the Centre's activities. This followed on from a handover meeting in December 2012 with the new Surgeon General, Air Marshal Paul Evans who also encouraged CBIS to engage with Headley Court, the Defence National Rehabilitation Centre. The Royal British Legion were highly supportive of this development and, after, much positive interaction with Headley Court and their head of research, Wing Commander Alex Bennett, in September 2013 Blast Injury Rehabilitation was formally adopted as a Centre Theme.

Professor Alison McGregor from the Department of Surgery and Cancer at Imperial College leads this theme with close collaboration and leadership from Headley Court. These activities have only recently started and are also closely associated with the Centre's civilian-focused activities.

Theme Lead

Alison McGregor is a Professor of Musculoskeletal Biodynamics in the Department of Surgery and Cancer at Imperial College London, where she manages the Human Performance Group. She trained as a physiotherapist at King's College Hospital, qualifying in 1989, and then studied Biomedical Engineering at Surrey University which led to a PhD project in spinal mechanics and low back pain at the Royal Postgraduate Medical School. Her research focuses on the musculoskeletal system with respect to mechanisms of injury, effects of injury on function, and rehabilitation and injury management.

To date her work has largely focused on the lumbar spine by considering its function to be a composite of interacting systems including a:

- passive or skeletal system which permits segmental joint motion,
- muscular system which drives motion of the passive system, and
- control system (the central nervous system) which co-ordinates the muscles and body segments to produce function with a variety of projects in each of these areas.

She has also investigated aspects of management and surgical care including:

- surveys of practice,
- clinical cohort studies,
- development of evidenced-based information (*www.tso.co.uk/bookshop*), and
- a large randomised controlled multi-centre clinical trial investigating optimal post-operative management.

Professor McGregor leads a programme of research into rowing performance, with a focus on rowing kinematics and mechanisms of injury. This work has been in association with the GB Rowing team and contributed to the Team's success at the London 2012 Olympic Games. She also represented College as a Torch Runner for the London 2012 Games.

Alison is one of the investigators in the Medical Engineering Solutions in Osteoarthritis Centre of Excellence Funded by the Wellcome Trust and the EPSRC where she leads an initiative into the use of technology to further rehabilitation of this common disease process (*www3.imperial.ac.uk/osteoarthritis/research_objectives/rehabilitative_and_preventative_treatments*).

Aims and Approaches

The aim of the Blast Injury Rehabilitation theme is to develop evidence based novel approaches for supporting recovery and optimal return to function following blast injury. The focus is on musculoskeletal and neuromuscular recovery. This theme will utilise information derived from the other themes to understand the impact of the injury on the whole person in order to then determine how best to recover and compensate for such an injury. A strong focus of the theme is the use of novel technology to support rehabilitation particularly. Two key tools are those used for biofeedback (in which visual, tactile and audio feedback is provided during rehabilitation) and motivation. This theme will engage with the long term studies within CBIS in order to explore the long term implication of injury on health and well-being and so optimise long term outcome.

Theme areas include:

- Optimising recovery and return to function.
- Understanding the long term implications of injury.
- Developing of biofeedback tools to enhance delivery of, and compliance with, rehabilitation.

Initial Research

This theme has one full-time dedicated resource assigned from core funds. This three-year PhD studentship will allow a formal collaboration between Headley Court and CBIS to be established, will provide a coalescing point for other activities at Imperial College, for example, the Sports Innovation Challenge that focuses on devices and technologies for disabled athletes, and will act as the stimulus for new research directions. This theme will have very close interactions with the civilian transfer work mentioned later on in this report.

Whilst rehabilitation from lower limb amputation due to blast injury is successful, many long term issues remain unresolved, particularly in relation to pressure sores, heterotopic ossification and sustainability of prosthetic function. The first PhD project work will aim to develop ‘smart sockets’ as patient interfaces with the capacity to pervasively monitor activity, muscle movement, and force profiles. Recent advances in additive manufacture and wireless communication, coupled with the work of the supervisory team (Prof McGregor, Dr Vaidyanathan) in instrumentation and patient monitoring has the potential to produce a new generation of bespoke prosthetic interfaces with embedded physiological sensors. In addition to well-documented benefits of patient-specific support, these devices will provide quantifiable, real-world feedback that will empower patients and clinicians with objective markers of function, status, and improvement or deterioration. Clinicians are in strong need of patient physiological and performance data captured in non-clinical environments and patients will benefit from data to encourage compliance with rehabilitative activity. This work will provide a basis for targeted research that will demonstrate veracity of building as well as for testing cost-effective sensor-enhanced prosthetic sockets that will support clinical research and long-term patient care.

Blast Biomechanics Update

The Blast Biomechanics Theme has seven main project areas. The activity started with lower limb modelling and has progressed to more detailed work on fractures, head/neck, torso/lung and hearing. This reflects a significant increase in manpower resource as well as the ability to translate from one project area to another. The approach we are taking to deliver blast biomechanics research is a combination of experimental and computational techniques. Experimental and computational models of human injury and of mitigation technologies are necessary in order to understand the physical mechanisms involved and to allow for developing new and improved evaluation criteria, techniques, materials and designs in a cost-efficient manner.

Human Tissue Characterisation

In this project we develop test protocols and equipment able to quantify the physical response of human tissue specimens under high rate impulse loading in order to understand and explain their material behaviour. The information from these individual-component experiments allow us to build accurate computational models able to predict the behaviour of the 'structure' (organ level) based on the interaction of its components.

Fracture Models

Understanding the physical failure of tissues is a key part of the blast biomechanics theme. We are now developing multi-scale modelling and experiments to understand fracture at the nano level all the way up to the whole organ level. In addition, we are now producing a parallel set of 'engineering models' (these are fast running on standard computers) that allow the rapid investigation of whole-body fracture in order to investigate pelvic, spinal, and upper limb injuries to quantify muscle function in fracture mitigation. A computational approach for predicting the internal mechanical structure of the bone (structural model) based on loading conditions encountered regularly has been developed allowing rapid assessment of potential site of tissue failure.

Head/Neck/Brain Models

Dr Mazdak Ghajari was appointed in October 2013 as a Research Fellow in the Department of Aeronautics and is leading on the computational and experimental work on head and brain injury including the development of more appropriate surrogates for testing mitigation and projection.

A biofidelic headform featuring a glass-fibre skull and a gel brain has been developed using CT and MRI data of a human subject. It has been used in preliminary shock tube tests to investigate the effect of the helmet on the intracranial pressure. To represent better the kinematics of the head during blast, we are planning to connect the headform to the Hybrid III anthropometric test device (or dummy) neck and repeat the experiments.

A PhD student has been appointed to explore blast-related brain injury mechanisms (at the tissue level and the cell level) by developing, validating and using detailed multi-scale computational models of the human head. Advanced neuroimaging data will be implemented in the model. The student will provide a strong link between engineering and medicine disciplines.

Torso/Lung Model

This is a newer area for the Centre and work has accelerated with the appointment of Dr Hari Arora, a Research Fellow, at the end of 2013. The aim of this work is to look at the lung/torso structure as a whole and conduct experimental and numerical investigations to gain insight into the blast response of the thorax and the connotations towards lung injury. This involves characterising materials and lung function in blast and developing computer models that will allow us to perform simulations of blast injuries, such that we can then develop effective mitigation strategies.

Lower Limb Injury

2013 saw our first PhD student in this area, Dr Nic Newell, complete his work. We have now developed significant capacity in testing of the lower limb in high trate conditions that simulate blast. We have also looked at mitigation through vehicle design, posture, boot design, and vehicle floor mats. Furthermore, we are developing finite element models – a type of modelling that uses traditional concepts from stress analysis and continuum mechanics – for the lower limb that can predict the response to the high rate impulse loading we see in blast-related injury. We use the information from the experiments to inform and validate the models and so give us confidence that they are predicting accurately. We then use them to run multiple virtual experiments to develop, test, and evaluate mitigation strategies. 2013 has seen us focussing more on the foot as our clinical work has shown that it is associated with high disability rates.

Spinal Injury

This project has developed significantly since last year with the appointment of a PhD student, a military MD(Res) student, and a computational engineer to work with Dr Masouros and Professor Clasper to develop experimental models of spinal injury in blast and their finite-element model counterparts in an attempt to understand the mechanism of injury and so develop and test appropriate mitigation strategies.

Hearing Biomechanics

The aim of this project is to develop fidelic computational models of the biomechanics of hearing and hearing damage in order to develop new and evaluate existing mitigation strategies. This is a new area of the Centre and is reported on in full later on in this report.

Blast Biology and Therapeutics Update

In line with the specific objectives for this theme, as set out in the 2012 report, we report on our key activities below.

We have worked in collaboration with the blast force protection group, providing biological samples (cells and tissues) and appropriate analysis to develop experimental platforms to investigate the effects of high intensity compression waves (HICWs) on biological samples.

We have performed the first comprehensive analysis of the effects of high magnitude/dynamic pressure waves on living cells in suspension. Comparing the molecular and functional effects on neutrophils, schwann cells and mesenchymal stem cells. In summary, we have shown that HICWs cause destruction of a proportion of cells that is a function of the intensity of the blast, but independent of the density, size and type of cells, this work is currently being written up for publication. In addition, we have shown that when cells are subjected to HICWs they release microvesicles (MVs). This is significant because MVs are known to promote inflammation. It is possible that MV generation in response to blast injury may be one mechanism that contributes to blast-induced inflammatory responses, for example as seen in blast lung. Additional MoD funding has been secured for a military MD(Res) to further investigate this hypothesis.

Having successfully studied cells in suspension the challenge now is to study adherent cells and tissues. This will be addressed with a newly appointed Centre PhD student.

While blast injuries appear localised, for example, to the limbs, they are thought to initiate a more widespread inflammatory response that may contribute to the development of pathologies including blast lung and heterotopic ossification. The development and full calibration of the shock tube together with the establishment of new facilities for *in vivo* experiments has allowed us to initiate experiments to examine the inflammatory response to blast injury.

In terms of our policy on the use of animals in research as a centre CBIS operates according to the principals of the 3Rs:

Replacement - methods which avoid or replace the use of animals;

Reduction - methods which minimise the number of animals used per experiment; and

Refinement - methods which minimise animal suffering and improve animal welfare.

Replacement

We are developing systems to replace animal work by investigating blast injuries on living biological material at the cell and tissue level. In addition, we have a substantial activity on computational models that, once validated, can totally remove the need for animal testing.

Reduction

For studies investigating the biomechanical properties of freshly harvested tissues, we are obtaining tissues that would otherwise be incinerated from the control animals that are a part of other studies (from the Veterinary College in Cambridge). Where animal experiments are necessary, these are being co-ordinated in the Centre such that all tissues are used for multiple different studies. For example, in models of blast limb injury, designed to investigate the effects of blast on neuronal function we are also examining the systemic inflammatory response and effect on bone marrow mesenchymal cells.

Refinement

All our *in vivo* experiments have been designed in close consultation with vets to minimise suffering and optimise animal welfare.

Blast Force Protection Update

The year has seen significant progress for blast force protection engineering; this is described based on the equipment or technique used. Overall the systems developed mean that CBIS is now capable of producing loading to represent (a) the full blast process (b) the initial high pressure, high-rate loading (c) the momentum transfer associated with the main energy of the blast wave , and (d) the long low-pressure ‘tail’ of the loading. This means that the timescales and energy level required for different types of effect can be reproduced in the laboratory and the timescale and process for a specific type of injury can be defined; for example, is it the initial high intensity or the longer duration lower-level forces that produce a given injury or the combination of the two? Once this is known, the appropriate type of protection can be developed.

Challenges for the future include (a) developing a system for the tensile part of the blast loading, (b) having developed the loading system, we will focus on the diagnostic being used, including temperature rises seen in the samples (and seen in reality) and (c) ensure that all appropriate materials are studied under these well-defined and monitored conditions.

Split Hopkinson Pressure Bar

The spit Hopkinson pressure bar (SHPB) has been modified to allow for more variety in the nature and duration of the stress pulse as well as the type of sample that can be used.

The use of composite striker bars can subject samples to two-step loading pulses. This allows a low-level stress pulse to be applied to a material and then probe the damage done by applying a second, higher-level pulse immediately after. This means that incipient damage e.g. cracking to be studied.

The use of momentum capture has been studied by utilising two different approaches. This method allows a single pulse to be applied to the sample where the sample crushes under the load (stress and strain) or is subjected to the load without significant crushing. This is relevant to the subject of ‘pure’ blast compared to blunt, impact trauma.

Shock Tube

The shock tube has been fully calibrated in its ‘standard’ operating mode and is being developed to incorporate a variety of loading pulse shapes. The system can now reproduce known explosive outputs at given distance, produce pulse shapes associated with loading internal to vehicles and also for pulse transmission though granular, foam and sandwich materials.

The shock tube can produce pressure pulses which are associated with an explosive equivalent of 25 kg of TNT at 0.3 m, this can be reduced in a continuous fashion to mimic the effect of 25 kg of TNT at 12 m. This allows direct comparison between shock waves interacting on the samples and real-life explosion scenarios.

The system can now be used to reproduce effects within a protected vehicle or inside a bunker.

Sandwich panels and perforated metal plates have been studied in order to understand how effective mitigation measures are, and how the various structures of foams could be, used to protect hearing.

Drop Weight Loading

This is a technique used commonly in impact testing. We are utilising this technique to characterise the behaviour under impact of structures such as bone, ligament and the human heel fat pad, but also shock absorbing materials such as those used in combat boots. Furthermore, we utilise the drop tower to reconstruct in a fairly well-controlled environment injury mechanisms that we see in the battlefield, such as compression fractures of the spine.

Given the ‘soft’ nature of many biological tissues the stress load and the type of sample holders used in many conventional devices are less than ideal. A new system has been designed collaboratively between the Blast Impact Survivability Unit of the University of Cape Town, the University of Cambridge, Cavendish Laboratory and CBIS. This is designed to look at cell and tissue samples in a variety of matrices, paying attention to the loading that would be seen in blast injury whilst keeping the sample free of contamination.

Gas Gun

A gas gun has been developed and is in the process of calibration to produce shock waves in biological materials. The types of pressure and durations seen in this system reflected the first, high-intensity levels seen in the blast process. This capability was, therefore, a missing part of the armoury of testing facility and we can now produce microsecond (one-millionth of a second) duration loading and recover the sample for close biological analysis.

Clinical Priorities

Introduction

The clinical priorities for the Centre were set out in 2011 with the direct support of the Surgeon General and through the Centre's analysis of injuries, fatalities and clinical burden of pain and disability. We address these clinical priorities in two main ways: the first approach is to continue to gather clinical data and conduct clinically-based research on battlefield casualties. 2013 saw a series of papers published in this domain with highlights per paper provided below. Secondly, these clinical research outputs inform and direct our basic science and engineering research. In this report, we highlight our emerging research in the areas of noise induced hearing loss, blast lung injury, heterotopic ossification, and blast foot and bone failure.

Highlight Clinical Research Outputs

Identifying Future 'Unexpected' Survivors[1]

This research paper published in the British Medical Journal Open journal demonstrates the interdisciplinarity and collaborative nature of the Centre, and its potential clinical effect. Maj James Singleton conducted this work under the supervision of Col Jon Clasper and Prof Anthony Bull with collaboration from the Defence Centre for Imaging, Gosport; the Forensic Pathology Services, Abingdon; and the Academic Department for Military Surgery and Trauma, Royal Centre for Defence Medicine, Birmingham.

There is an imperative to analyse death data to minimise future potential loss of life. Therefore, we investigated the cause of death in modern battlefield fatalities following improvised explosive device (IED) blasts with cohorts of both dismounted (on foot) and mounted (in-vehicle) troops, in order to direct future research and treatment directions. This is the largest series of IED fatalities reported to date with comprehensive medical imaging and autopsy records. The results show very clearly for the first time that:

- For dismounted IED fatalities, extremity and junctional (groin/axilla/neck) haemorrhage are significant, potentially treatable, causes of death.
- In-vehicle IED casualties most frequently die of head injuries too severe to be treatable. Efforts to reduce the impact of such injuries should be made through mitigating/preventative strategies.

This work is now focusing both our medically-related research on treating haemorrhaging as well as our protection work on vehicle design and other in-vehicle preventative strategies.

[1] Singleton JA, Gibb IE, Hunt NC, Bull AMJ, Clasper JC. Identifying future 'unexpected' survivors: a retrospective cohort study of fatal injury patterns in victims of improvised explosive devices. BMJ Open 3, (2013), 8, e003130.

Primary Blast Lung in Fatalities[2]

Primary blast lung injury (PBLI) is an acknowledged cause of death in explosive blast casualties (Figure 4). What is not known is the injury profile, including PBLI incidence, for mounted personnel following an external explosion.

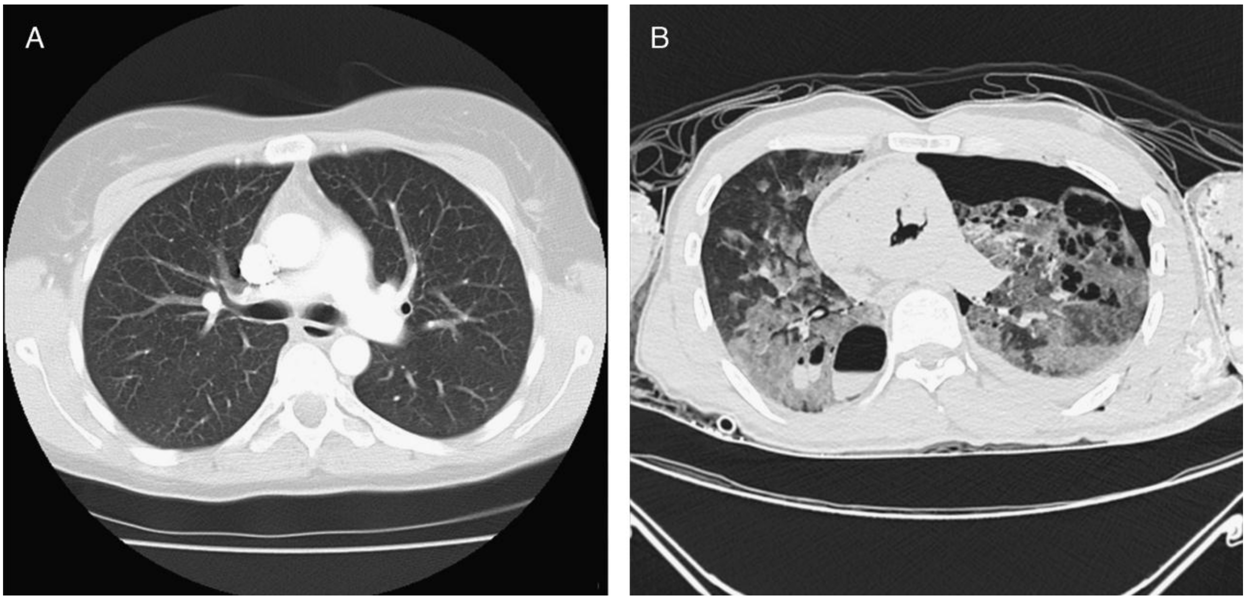


Figure 4: Medical images taken axially through the chest showing normal lung anatomy (A) and PBLI (B).

In this study we found that in-vehicle fatalities have a high incidence of PBLI, suggesting significant exposure to primary blast. This has not been reported previously and is a far higher incidence compared with dismounted (free field) blast casualties (Figure 5). A higher rate of associated thoracic trauma was also noted in in-vehicle compared with dismounted fatalities, another previously unreported phenomenon. When combining this work with that of the cause of death analysis, it is clear that further work is needed to understand better the mechanisms of blast injuries to the lungs, head, and extremities and to investigate the modulating effect of a blast victim's immediate environment on injury patterns and cause of death. Only by addressing all these areas can work to prevent, mitigate, and treat blast injuries be optimally focused.

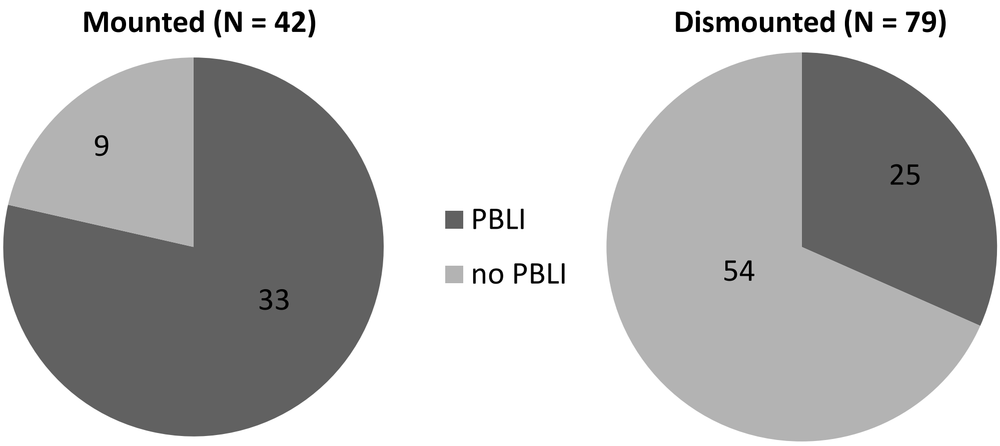


Figure 5: Incidence of PBLI and location of casualty at the time of wounding.

[2] Singleton JA, Gibb IE, Bull AMJ, Mahoney PF, Clasper JC. Primary blast lung injury prevalence and fatal injuries from explosions: Insights from post-mortem computed tomographic analysis of 121 improvised explosive device fatalities. J Trauma Acute Care Surg. 75(2 Suppl 2), (2013), S269-74.

Traumatic Amputation and Salvage of the Distal Femur[3]

Analysis of recent UK Armed Forces combat-casualty data has highlighted a significant number of through joint traumatic amputations (TAs), most commonly through knee amputations (TKAs). This is important, because TKAs fair far better in rehabilitation than amputations that cut across bone; this was shown by a consensus statement on lower limb amputation from the UK Defence Medical Services. We, therefore, sought to define the proportion of recent combat casualties sustaining severe lower extremity trauma with acute boney and soft tissue injury anatomy amenable to definitive TKA.

We identified all UK Armed Forces personnel (survivors and fatalities) sustaining a major extremity TA (through/proximal to wrist or ankle joint) between August 2008 and August 2010. All through-knee and below-knee TAs were grouped as ‘potential TKAs’ (pTKAs), that is, possible candidates for definitive TKA that would then have a functionally better outcome. Our results are shown in Figure 6 and Figure 7.

Detailed anatomical data on pre-debridement osseous and soft tissue injury levels were only consistently available for fatalities through medical imaging findings. Therefore further analysis of the soft tissue injury profile from the fatality data only showed that a definitive TKA in the pTKA group (all below knee amputations as well as TKAs) would have been proximal to the zone of injury (ZOI) in only 5% of cases.

Number of TAs per case	Survivors (N = 75)	Fatalities (N = 71)
1	30	15
2	35	45
>2	10	11
Total number of TAs	130	141

Figure 6: Number of traumatic amputations.

We confirmed in this study that traumatic TKAs following explosive blast are more common than previously reported and, importantly, the majority of lower limb TAs are skeletally amenable to a definitive TKA. Maximising residual stump length carries the risks of definitive level amputation within the original ZOI but this study demonstrates that the proximal extent of the soft tissue injury may frequently make this unavoidable. Further work is required to determine the relative merits of definitive below, through and above knee amputations in the short, medium and long term to ensure survivors are subject to minimal complications while maintaining capacity to achieve optimal functional outcomes.

[3] Singleton JA, Walker NM, Gibb IE, Bull AMJ, Clasper JC. Case suitability for definitive through knee amputation following lower extremity blast trauma: analysis of 146 combat casualties, 2008-2010. J R Army Med Corps 160, (2014), 187-190.

Level of through joint traumatic amputation	Survivors	Fatalities
Shoulder	0	3
Elbow	2	4
Wrist	0	1
Hip	0	1
Knee	11	23
Ankle	0	2

Figure 7: Level of through joint traumatic amputations.

To summarise: TKAs are far more common than previously reported; the majority of lower limb blast-mediated traumatic amputations are skeletally amenable to a definitive TKA.; the proximal extent of the associated soft tissue injuries means that to retain a functional stump, the definitive amputation level may frequently remain in, rather than above the zone of injury. Long term outcomes need to be sought and linked to TA level and definitive amputation level to determine optimal management for patients with blast-mediated TAs.

The Mechanism of Traumatic Amputation: Opportunities for Mitigation[4]

The accepted mechanism of traumatic amputation (TA) due to blast is that the blast wave fractures the bone and then the limb is avulsed as it is energised by the blast wind. This generates an amputation that occurs transosseously (through-bone). As shown in our previous work we know that blast-mediated through-joint TAs are not as rare as originally considered, yet other prior work has suggested that TA is frequently associated with fatal primary blast lung injury (PBLI). Our new knowledge of the high prevalence of through joint TAs with high numbers of survivors suggests that the mechanism of TA and the link with fatal primary blast exposure merits review.

We identified all those with a blast-mediated TA in the 2 years from August 2008 and recorded all relevant details. Our results are summarised in Figure 8. As expected, the lower limb was most commonly affected (117/130 in survivors, 123/141 in deaths). The overall through-joint TA rate of 40/271 (15%) was high compared to previous work, with 85% of these being through knee.

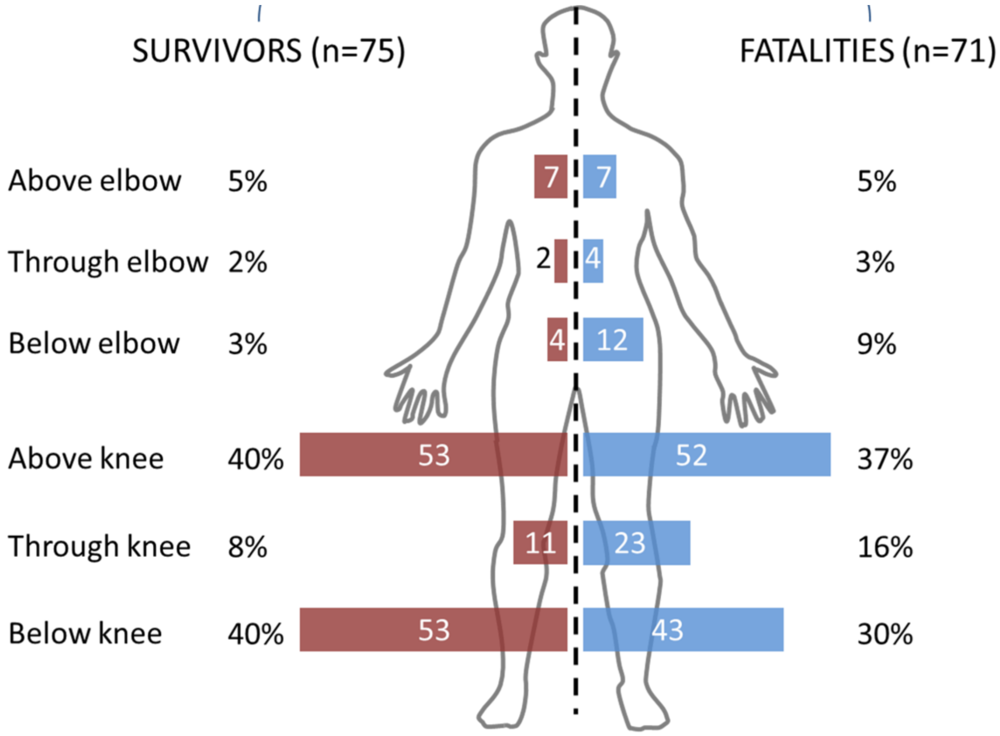


Figure 8: Level of blast-mediated traumatic amputations (TAs): survivors *vs*. fatalities (numbers in/by bars represent number of TAs).

Interestingly, only a quarter of the through-joint TAs had a fracture at the joint, meaning that the bones proximal to the joint were, by and large, intact. In this study there was no relationship found between PBLI and TA.

As the previously reported link between TA and PBLI was not present, this work calls into question the significance of primary blast injury in causation of blast mediated TAs. Furthermore, the accepted mechanism of injury can't account for the significant number of through joint TAs. The high rate of through joint TAs with either no associated fracture or a non-contiguous fracture is supportive of pure flail as a mechanism for blast mediated TA, where pure flail can be understood

[4] Singleton JA, Gibb IE, Bull AMJ, Clasper JC. Blast-mediated traumatic amputation: evidence for a revised, multiple injury mechanism theory. J R Army Med Corps 160, (2014), 175-179.

as the blast wind energising the lower limb that then causes disruption of all the soft tissues at the joint, but not the proximal load-bearing bone.

Severity of Foot and Ankle Injuries due to Blast[5]

Much of our previous clinical work (presented in previous annual reports and the Imperial Blast reports from our prior activity) has shown how prevalent and important foot and ankle injuries are. In addition, we know that improvements in protection and medical treatments have resulted in increasing numbers of modern warfare casualties surviving with complex foot and ankle injuries. Although much is known about the injuries, to our knowledge, there had been no prior analysis of foot and ankle blast injuries as a result of improvised explosive devices (IEDs) and the factors that are associated with a poor clinical outcome.

We identified UK service personnel who had sustained lower leg injuries (excluding traumatic amputations) following an under-vehicle explosion between 2006-08 and followed them up over a three year period. We obtained patient demographics, injury severity, the nature of the lower leg injury, and the type of clinical management. We then determined the ongoing clinical symptoms and recorded the need for amputation (Figure 9). At the time of final follow-up, 75% of the injured limbs had persisting symptoms related to the injury, and only 14% of the service members were fit to return to their pre-injury duties.

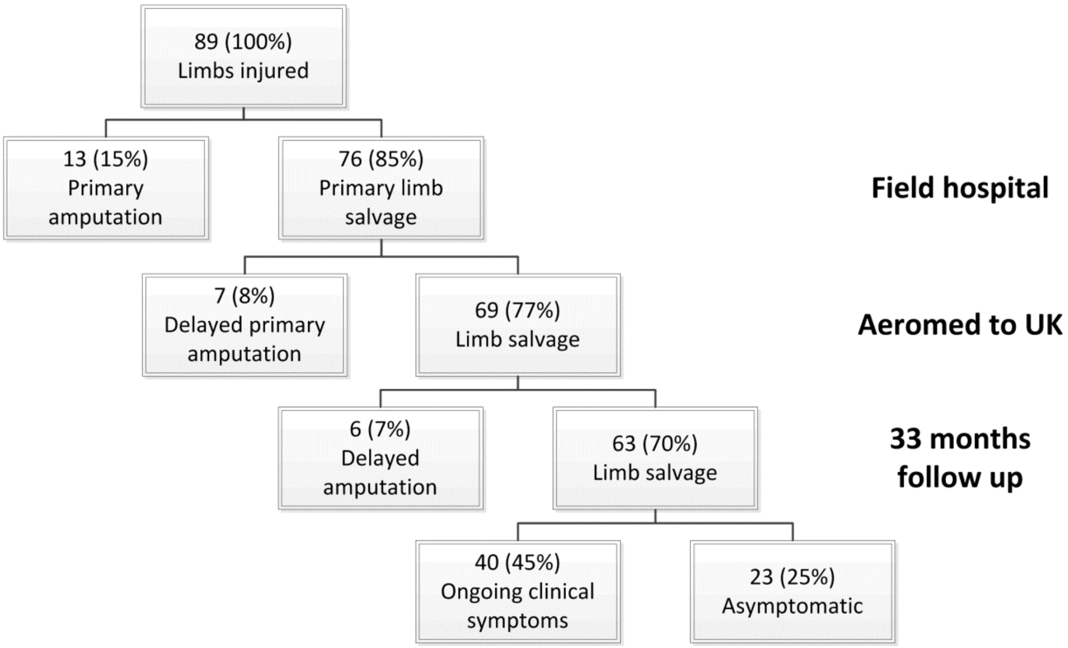


Figure 9: Flowchart depicting the outcomes of the foot and ankle blast injuries.

This study has shown that foot and ankle injuries from IEDs are associated with a high amputation rate and frequently (most often) with a poor clinical outcome. Although not life-threatening, they remain a source of long-term morbidity in an active population. Our work on predictors of amputation point to research requirements focused on protecting the hind foot in particular.

[5] Ramasamy A, Hill AM, Masouros SD, Gibb I, Phillip R, Bull AMJ, Clasper JC. Outcomes of IED Foot and Ankle Blast Injuries. J Bone Joint Surg Am 95(5), (2013), e25(1)-(6).

Clinically-Driven Research Examples

Blast-Induced Hearing Loss[6]

Hearing damage is one of the main service-connected disabilities, and causes accordingly high compensation (more than $1 billion in the USA; UK details are hard to come by). Auditory dysfunction is a particular problem in blast exposure; 60% of soldiers with blast-induced traumatic brain injury also have hearing loss. Hearing damage through blast accounted for 25% of all injuries during Operation Iraqi Freedom.

Blast exposure can cause hearing damage at different stages of the auditory system (Figure 10). First, regarding the outer ear and middle ear, the blast wave can rupture the tympanic membrane and/or disrupt the pinna, leading to conductive hearing loss and a loss of balance control. Second, hair cells inside the inner ear can be damaged. These cells normally convert the mechanical sound signal into electrical signals in nerve fibres. Their damage leads to sensorineural hearing loss that can have different severities at different frequencies. Third, the neurons and their connections in the auditory brainstem and the central nervous system can be damaged. This can lead to a difficulty in understanding speech in noise, in recognising a speaker, and in localising sound.

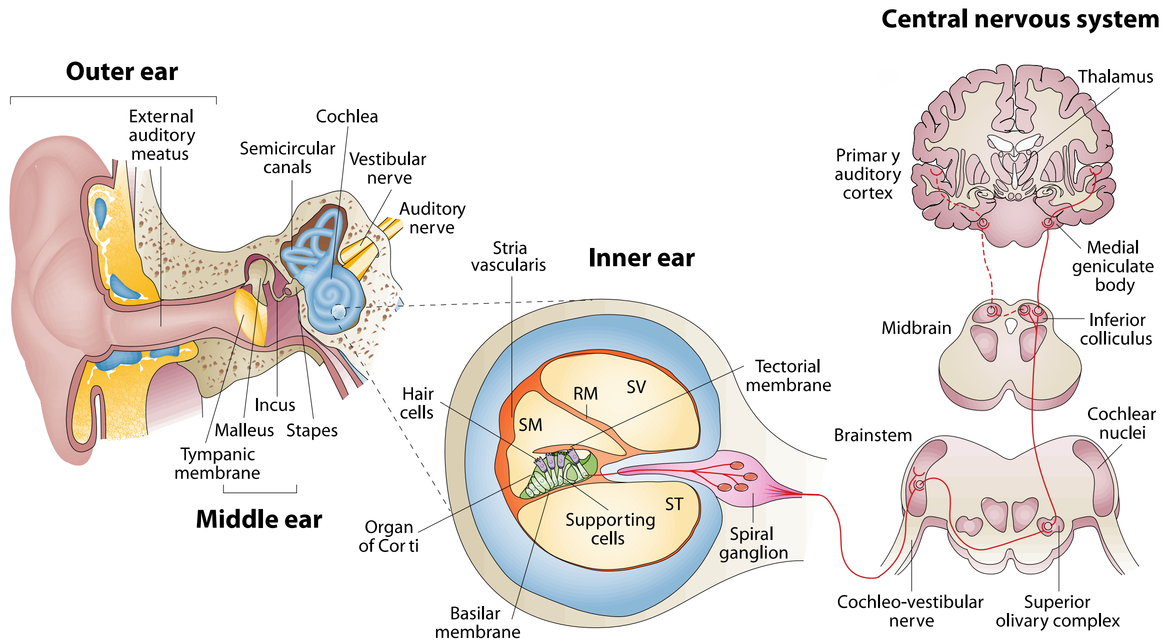


Figure 10: Hearing anatomy

An important advance in the welfare of service personnel who have been exposed to blast is to develop a method for detection and assessment of hearing damage early and objectively. Indeed, noise-induced hearing damage often accumulates and progresses over time. An early-detection method of hearing damage can help to identify members of the armed forces at the onset of hearing loss. Such members may then receive special care and assignments to prevent progressive hearing damage. Further, a quantitative assessment of functional hearing, such as understanding of speech and role-specific environmental sounds, will allow identifying which duties a member of the armed forces can perform reliably. Such an assessment will also allow making a quantitative

[6] This section summarises work primarily led by Dr Tobias Reichenbach and his research group.

prognosis regarding the effect of a member's hearing damage on future employment, and hence in assessing her or his compensation.

We have hence begun to work on improved detection and assessment of blast-induced hearing damage. Specifically, we want to develop an objective detection and assessment method of functional hearing impairment. Such a detection method should be able to identify hearing damage early and to quantify its effect on a person's functional performance such as understanding speech. It should also be objective, that is, not be based on a behavioural response.

The novel method for detecting and assessing blast-induced hearing damage will be based on recordings of a person's brain activity in response to complex sound signals such as speech. Brain activity will be measured from scalp electrodes (electroencephalography or EEG). This method is low-cost and already used clinically. Recent research has shown how hearing and auditory processing can be assessed from EEG recordings.

We have set up an EEG measurement system for the brain's response to auditory signals (Figure 11). We have demonstrated in previous work that in a person with healthy hearing, the brain activity tracks aspects of a speech signal, such as its fundamental frequency and its envelope (Figure 11). Because such tracking is absent or modified for an unattended signal, this is measure that can indicate the state of health of hearing. The next steps are now to optimise the recording paradigms in healthy people, to validate the method in people with hearing damage, and to assess veterans with blast-induced hearing damage. This will be performed by a PhD student who is sponsored by the Centre for Blast Injury Studies. Additional support will come from another PhD student who is funded through the EPSRC Doctoral Training Centre for Neurotechnology in Life and Health and who works on a related topic.

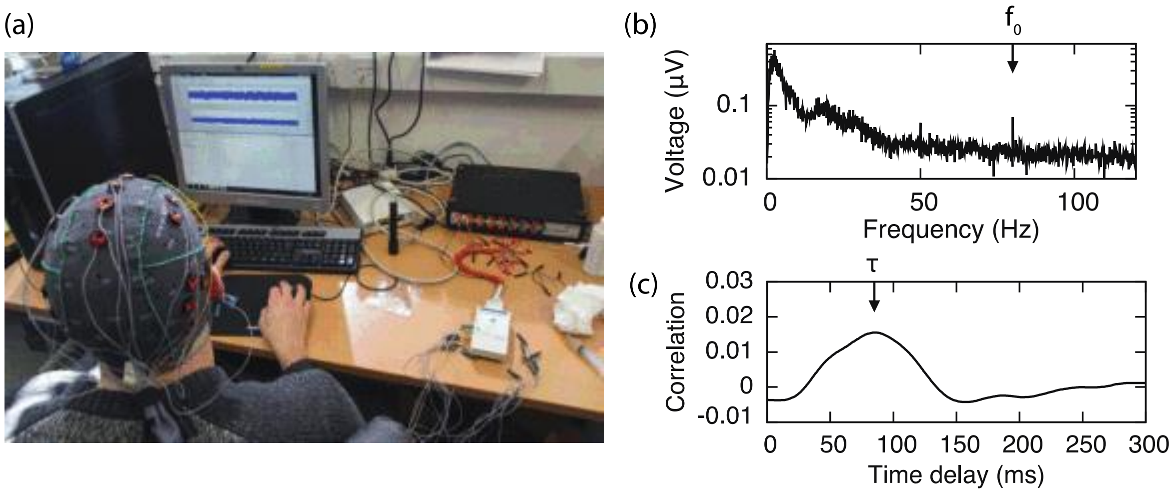


Figure 11: Towards an electroencephalographic (EEG) assessment of hearing. (a) An EEG measurement involves surface electrodes on the scalp. (b) The brain activity showcases the fundamental frequency f_0 of a speech signal. (c) The brain activity also correlates to the envelope of a comprehended speech signal, at a delay of τ=85 ms.

Blast Lung Injury[7]

Introduction

People caught in blast conditions whether combat (bomb blast) or civilian (bursting pressure vessels) are susceptible to sustaining primary blast injuries, with the soft organs such as the lung most vulnerable. The physical insult to the human can cause significant immediate and long term damage to the lungs. Clinical reports from others and from the Centre have identified the types of injury observed from the immediate insult such as: alveolar haemorrhage, emphysema, pneumothorax and parenchymal lacerations. The exact mechanisms of injury development have not been determined and this forms the basis of our research. The research is based across three main project areas: material characterisation and lung function under blast and post-blast conditions; system and thoracic structural response to blast; and inflammation of the lungs due to distal and direct thoracic blast loading.

Material characterisation and lung function in blast

This area of research aims to understand how different regions of the conducting airways and lung tissue behave under mechanical loading, as well as establishing the impact on function caused by a blast wave.

One aim of this work is to develop computer models that will allow us to perform simulations of blast injuries, such that we can then develop effective mitigation strategies. A fundamental requirement for this type of computer modelling is the knowledge of the biomechanical properties of living tissues. Much of the available literature analyses the biomechanical properties of tissue samples that have been fixed and/or stored and thus are not truly biofidelic. Through collaboration with the Veterinary laboratories in Cambridge and our research fellow working in the Cavendish Physics laboratories in Cambridge, we have been able to obtain tissue samples from piglets immediately post mortem (making use of tissue that would otherwise be incinerated) as part of a separate research project in the Veterinary College. This has allowed us a unique opportunity to assess the biomechanical properties of living tissues.

For example, we have conducted mechanical testing on skin at multiple strain rates. Sample data is shown in Figure 12 for strain rates in the low to medium range. Compared to literature data on skin, there is already noticeably greater strain rate sensitivity in the material tested here. In addition, we have conducted similar tests on the upper airways (larynx, trachea, bronchus and secondary bronchus or bronchioles).

---

[7] This section summarises work from many individuals, including Prof Sara Rankin, Dr Hari Arora, Mr Ashton Barnett-Vanes, Dr Theofano Eftaxiopoulou, Mr David Britzman, Dr Katherine A. Brown (Cambridge), Mr Benjamin J. Butler (Cambridge), Dr William G. Proud, Miss Thuy-Tien Nguyen, Dr Alun Williams (Cambridge), Dr Andrew P. Jardine (Cambridge), Dr Chiara Bo, and Miss Rachel L. Boddy (Cambridge).

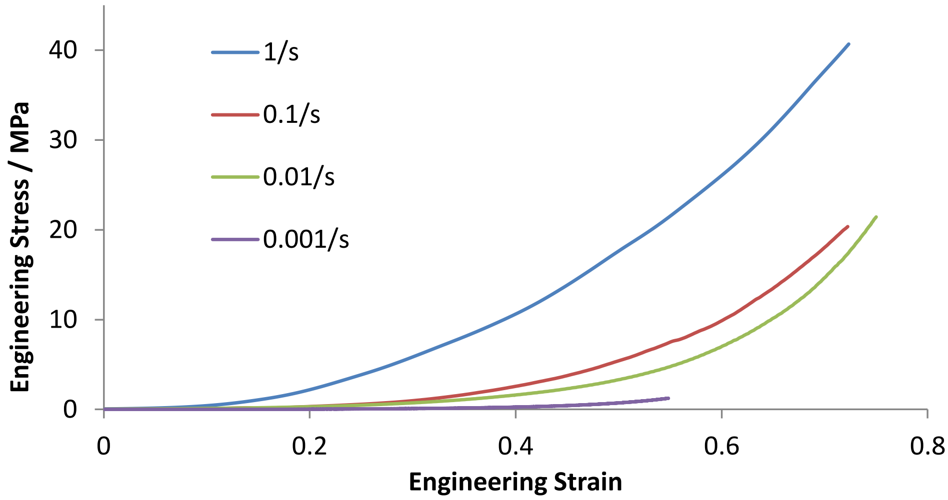


Figure 12: Material response of porcine rump skin samples at varying strain rates. A trend indicative of strain-rate hardening can be discerned.

Historically, mathematical models have been applied to these materials to try to capture their behaviour, however, there is no model that accounts for the inhomogeneity of the tissue. Our histology work has shown that skin has a layered structure and this allows us to develop more appropriate models of the constituent materials within these biological tissues using viscoelastic-plastic formulations. We are now working on these models.

The function of biological materials is also under investigation. Assays have been developed to allow mechanical loading as well as function to be evaluated. Early results highlight localised damage causing reduced function across areas of plates loaded by a shock, with some residual function. This method has been established to allow application on human trachea (to be obtained from University College Hospital).

Other experiments are planned to enable this material behaviour to be captured mathematically. Experiments are to be extended beyond the conducting airways to lung tissue.

System and thoracic structural response to blast

This area of research aims to look at the structure as a whole and conduct experimental and numerical investigations to gain insight into the blast response of the thorax and the connotations towards lung injury.

The work is looking into the physical variables at play and evaluating their influence on the biomechanical system. For example: locating the region of greatest stress concentration when subject to a shock as a function of pulse shape and orientation; or the dispersive or dissipative characteristics of the rib cage in blast. Imaging techniques are critical to these investigations, both during and after the event. High-speed imaging, used in conjunction with a number of image processing techniques such as image correlation and Schlieren, allow the deformation and shock wave interaction with a target to be evaluated. Post-test histological techniques are a primary tool for sample evaluation. A tool for whole organ histology imaging and 3D reconstruction has been used, called the histocutter. This tool can take automated image slices of a sample with a micron resolution in each axis. Figure 13 shows an example image of a mouse lung. This set of lungs was normal but allowed the sample preparation and technique to be evaluated for the quality of information that can be gained from this method. Other methods such as microCT are being pursued with the aim of having some direct comparison to data available from the military databases.

Several platforms are being established and licenses obtained for projects to look at direct thorax loading. The area of material characterisation is being extended to feed data into this stream of research, in particular to the modelling effort. The long term goal is to establish a numerical model to enable further insight into the physiology of blast lung injury development, with validation coming through system experimentation.

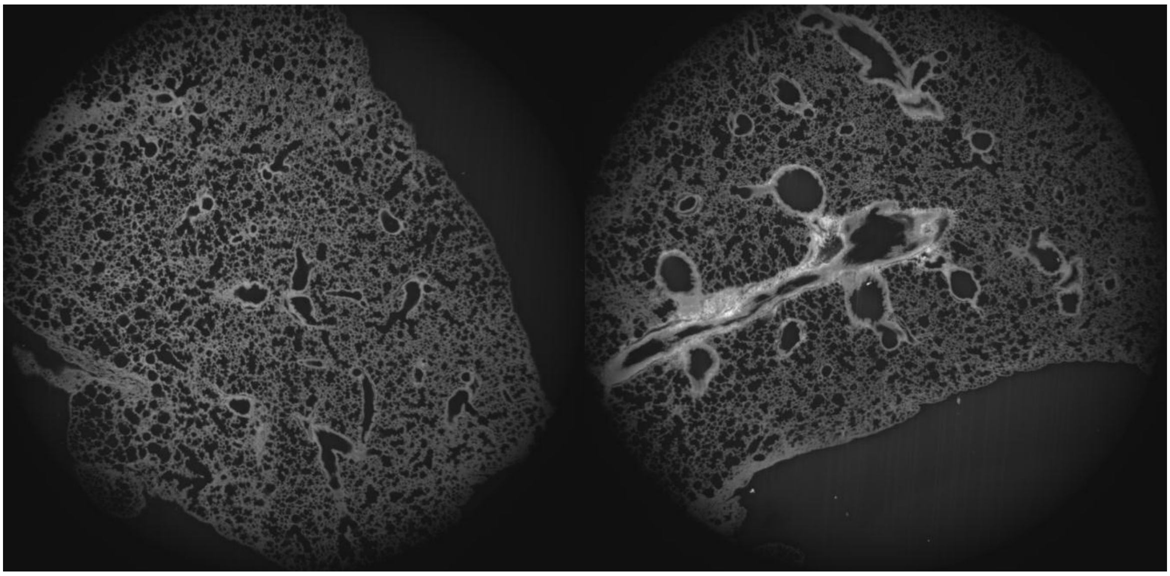


Figure 13: Example images taken of mouse lung using the histocutter technique, highlighting the alveoli and the conducting airways.

Inflammation

Blast injured patients frequently suffer from multiple injuries. Limited understanding exists of the indirect mechanisms that may initiate or exacerbate systemic or pulmonary inflammation in blast injury. These preliminary studies sought to establish a model to investigate systemic and pulmonary damage and inflammation as a result of limb blast trauma in rodents.

Systemic response to blast injury

Work was carried out to investigate the indirect mechanisms that may initiate pulmonary inflammation in blast injury. A purpose-built experimental rig was developed to subject rat hind limbs to a focussed primary blast injury using the shock tube. Blood, broncho-alveolar fluid (BAL) and lungs were harvested 6 hours after blast and analysed for markers of cellular and molecular inflammation, utilising histological, ELISA and Flow Cytometric techniques. High-speed visual technology was utilised to image the trauma.

16 Sprague-Dawley rats (250-350 g) participated in this preliminary study; 8 animals served as controls (anaesthetised only) and 8 animals were anaesthetised and exposed to a simulated blast insult using a compressed gas-driven shock tube with mylar membranes rupturing at a predetermined pressure threshold of 4.5 bar overpressure. In each case the pressure wave was directed only onto the hind-limbs (Figure 14). Blood and tissue samples were collected for analysis 6 hours after blast.

Sample results are presented in Figure 15 demonstrating that under these experimental conditions there is no change in neutrophil numbers in the different tissue compartments, indicating that there is not an inflammatory response.

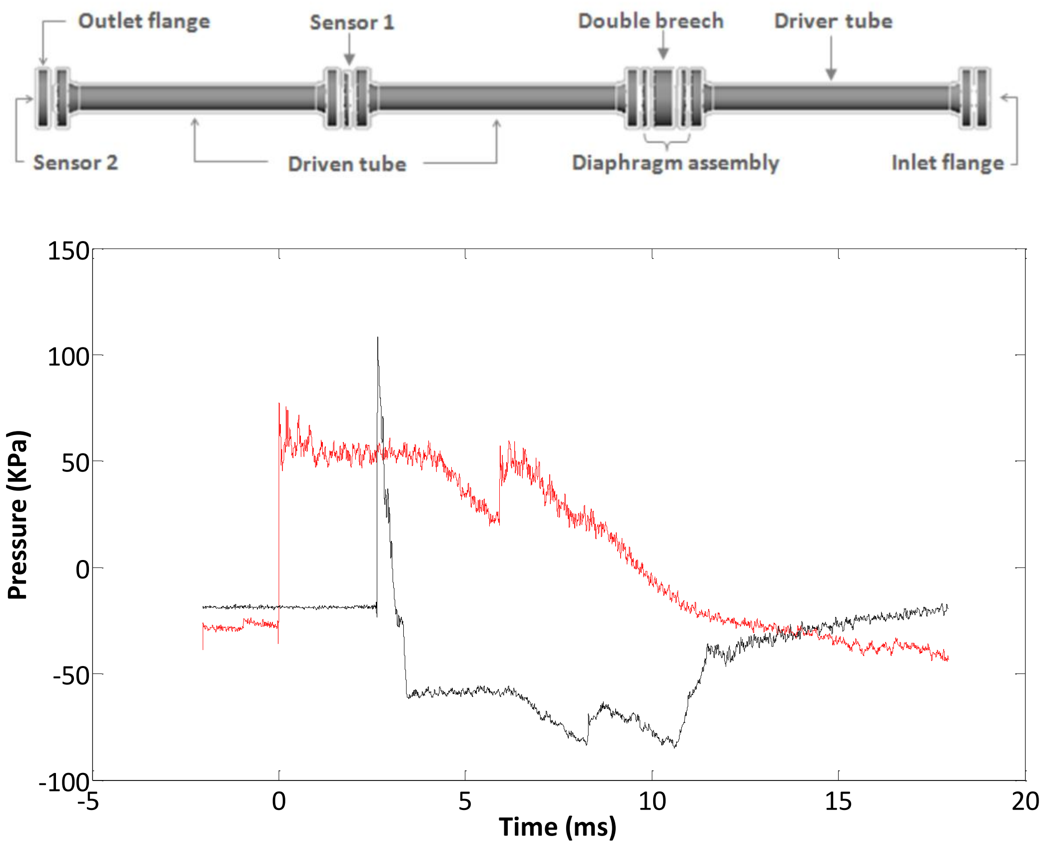


Figure 14: Top: schematic of the shock tube experimental platform; Below: pressure data collected from shock tube tests, the pressure trace in red is recorded from sensor 1 and the black from pressure sensor 2.

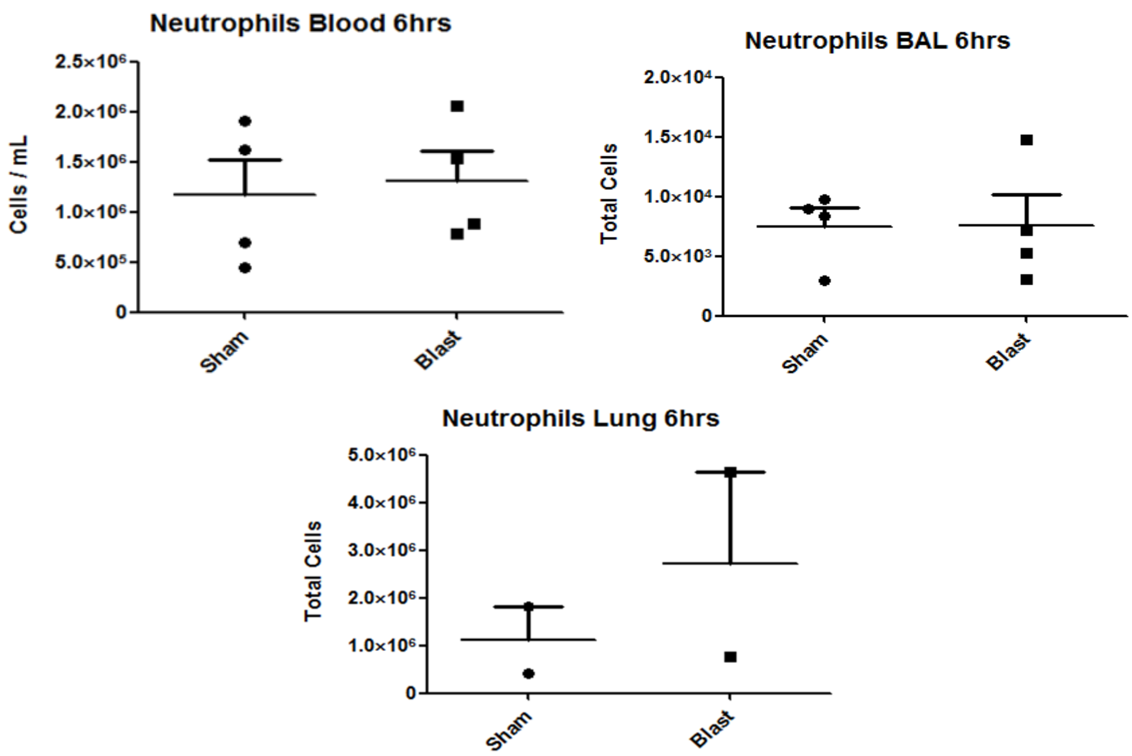


Figure 15: Neutrophil mobilisation occurs after primary blast limb injury, and results in moderate trafficking to the lung at acute and sub-acute time-points.

Having investigated the inflammatory effects of limb trauma with a 4.5 bar overpressure shock wave, we turned our attention to investigating the effect that a higher busrt pressure shockwave of a long duration has on limb injury and inflammation. As illustrated in Figure 16, preliminary data show that blast waves of 6.0 bar burst pressure directed to the hind limbs elicit substantial cellular inflammation, as observed from a rapid neutrophilia in the blood and increased neutrophil numbers in the lung and BAL. This work serves to highlight one of the strengths of CBIS as an interdisciplinary centre as we have been able to integrate the expertise of the physicists and engineers to devlop the platform technologies and design these experiments and the biologists for analysis and interpretation of the biological responses.

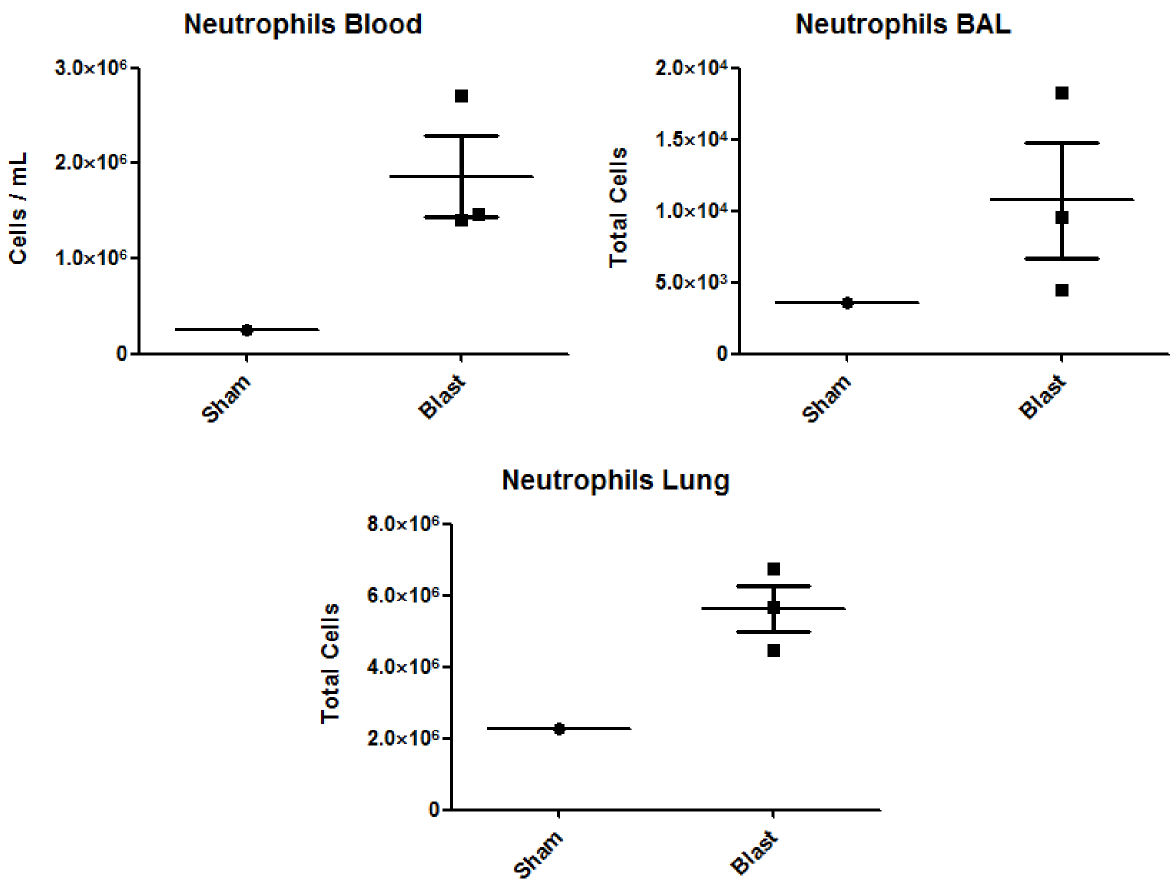


Figure 16: Primary blast limb injury with full driving volume, results in a significant systemic and pulmonary neutrophilia at 6hrs.

The objectives of this preliminary work were: to establish the experimental conditions and protocol for the investigation of blast injury in rats; to integrate biological and mechanical research techniques for blast injury research; and to develop and optimise biological research tools for the investigation of injury and inflammation in rat models of blast injury. Understanding of the mechanisms by which injury to the limbs or head promote systemic inflammation is limited. Blast injured patients are often polytraumatised, with the head, torso and limbs being the most common sites of injury. In polytraumatised blast injured patients, the lungs are most susceptible to the inflammatory sequelae, which can result in pulmonary oedema and poor oxygenation. Understanding of the inflammatory mechanisms that contribute to pulmonary inflammation in blast injury is vital for improved diagnostic and therapeutic interventions.

The studies presented in this section will enable the Centre to investigate in detail how common sites of non-thoracic injury (leg and head) may contribute to or exacerbate pulmonary inflammation in blast injury, alongside direct insult to the thorax ('blast lung injury').

A new experimental protocol has been submitted for approval to the Home Office that will enable the investigation of the physiological effects of directly applied shockwaves to the thorax. The licence will also enable the rigorous interrogation of pulmonary inflammation due to indirect injuries. With this new protocol, animals under general anaesthesia will be subjected to a primary blast wave directed to the chest at preselected overpressure magnitudes. Circulating blood samples will be withdrawn at regular intervals to investigate for an inflammatory response. The chest of the animals will also be imaged using a micro CT or MRI scanner at different stages pre and post insult that will enable the tracking of physiological changes in the lung after blast in a detailed, clinically relevant manner, with the aim to triangulate these observations with other physiological readings. At the end of the investigation multiple tissue samples will be collected for analysis.

Summary and future work

The breadth of the research question within blast lung injury is great. Current work is concentrating on primary blast lung injuries and how the patients, who survive the initial insult (seconds) but not the longer-term lung injury (days), can be saved. The work is focused on identifying mechanisms at play under pure shock wave loading. The performance of the individual materials and structures at strain rates experienced in blast, as well as the whole system performance in shock conditions, is being evaluated.

Future work will examine how varying blast parameters will affect the various tissues in the thorax in terms of both the mechanical and biological responses. Platforms are being developed to allow for work on solid blast (or tertiary blast) to be evaluated later. There is a difference in the way stress builds up and transfers through media hit by solids compared to pressure waves (impedance changes, etc.). Research within each theme is progressing and constantly evolving to give greater depth of insight into this complex problem.

Heterotopic Ossification[8]

Introduction

Heterotopic ossification (HO) is the formation of mature lamellar bone in extra-skeletal soft tissues, usually muscle (Figure 17). It was first described in the literature nearly 100 year ago in relation to military wounded in World War 1. To this day it continues to cause problems to the injured service personnel. The consequences of wound and soft tissues complications in traumatic amputations pose problems to rehabilitation and long term prosthetic use. In the military and civilian setting traumatic amputations are recognised risk factors for HO. Its exact trigger remains elusive. Its prevalence in the military setting is reported to be the increasing. This is thought to be due to a trend of increased extremity injuries seen in recent operations and increased survivorship following major injury and subsequent amputation. In addition to this the characteristic mechanism of injury seen in operations in Afghanistan has been blast secondary to Improvised Explosive Devices (IEDs). Literature published earlier in the conflict describes an occurrence rate of 64% in our service personnel and surgeons report that 50% of these require surgical management of the condition due to adverse symptoms delaying rehabilitation.

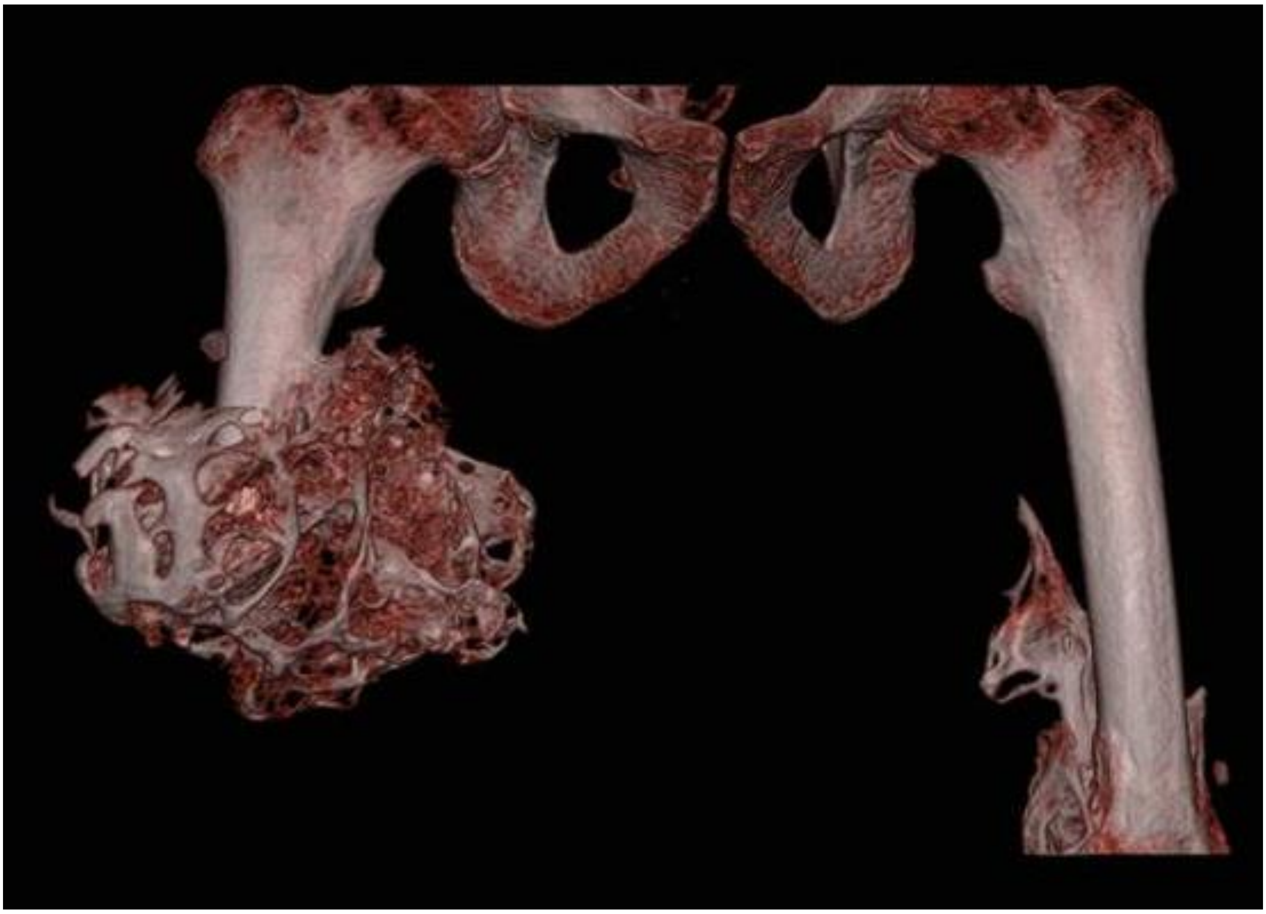


Figure 17: A Computerised Tomography (CT) scan of Heterotopic Ossification (HO) seen in a bilateral lower limb amputee.

[8] This section presents work led primarily by Maj Taff Edwards and Col Jon Clasper with contributions from Professor Bull, Dr Angelo Karunaratne, Miss Naomi Rosenberg, Dr Simin Li and others.

This HO stream at CBIS brings together military surgeons, cellular biologist and bioengineers to tackle the problem by identifying its cause, detailing its structure and biology, and therefore aiming eventually at developing targeted interventions that will prevent its formation (Figure 18).

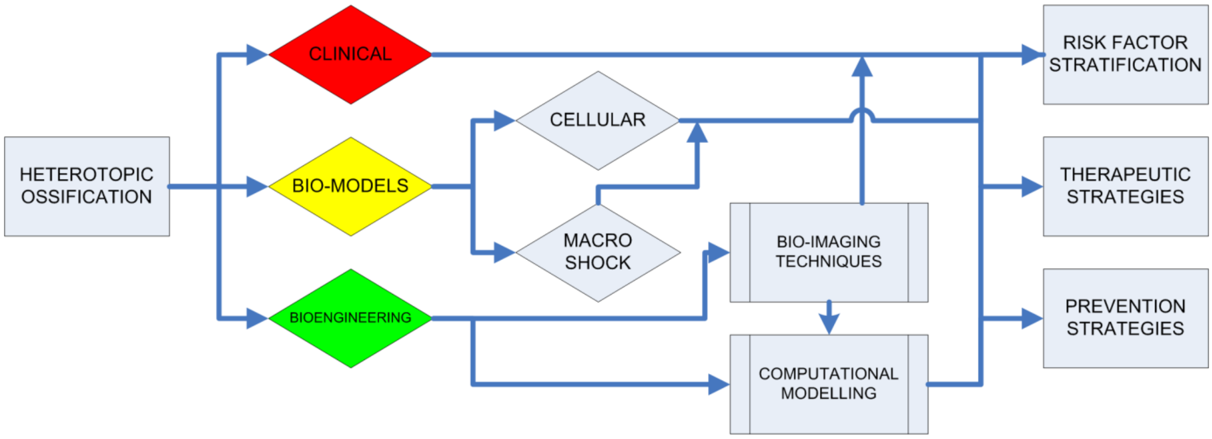


Figure 18: Heterotopic Ossification (HO) research process.

Clinical-based research

Until recently research and evidence concerning HO has been very much led by civilian departments. HO after surgery is commonly seen after total hip arthroplasty (THA). In the civilian trauma setting patients with injuries on the head, the spinal cord and with burns are at particular risk of HO formation. A renewed interest in HO by military academics due to veteran functional outcomes has impressed the need for further work on its aetiological factors, structure, biology, prevention and management. Certainly casualties with blast related amputations are placed at higher risk for formation of HO in their wounds.

This research element will qualify and quantify the entire amputee cohort from Afghanistan. Once complete, the events and care that each casualty experienced will be analysed and compared to identify specific risk factors that contribute to formation of HO. The form that HO takes in individual wounds will also be assessed and classified, allowing early identification of casualties at risk, therefore enabling clinicians to start management expediently.

Cellular research

A prerequisite for bone formation is the presence of bone forming cells, called osteoblasts. Their origin is normally from stem cells found in the bone marrow. The formation of within the muscle HO (ectopic bone), however, also requires the presence of osteoblasts whose cell lineage is not clear.

Our research will focus on examining the onset of heterotopic ossification (HO) in the context of blast injuries. Two strategies will be implemented to study the effects of shock waves on the onset of HO: (i) Rat hind limbs or head will be exposed directly to the shock waves to induce blast trauma-based HO *in vivo*; (ii) Healthy bone marrow stem cells (BMSCs) from rat and human will be seeded into polymer-based scaffolds (hydrogel, polycaprolactone, etc.), and BMSC constructs will be exposed to shock waves to examine mechanotransduction/molecular mechanisms leading to osteogenic differentiation *in vitro*. In addition, *in vivo* studies will investigate whether tissue damage and/or damage-associated molecular pattern molecules stimulate the mobilisation of mesenchymal stem cells/osteogenic progenitors to elucidate the cellular mechanisms underlying blast-induced HO. These findings will enable us to clinically translate our mechanistic findings into therapeutic intervention for treating HO patients, by regulating cellular and molecular pathways responsible for blast injury-associated HO.

Bioengineering research - local mechanical factors of ectopic bone formation

This element will focus on the possible mechanical influences on HO. Experiments will be performed using finite element computational modelling. The aim is to create a model that will replicate the structure of HO seen in clinical cases. The clinical cases of relevance are therefore those in which mechanical stimulus is isolated from the biological influences. We have selected one such example: HO in the cervical (neck) region. A Department of Bioengineering-funded PhD student is currently developing these models.

Two models are proposed for this study. One will model HO after total cervical disc replacement. It will attempt to produce characteristic HO shapes in response to the suggested boundary conditions applied by the artificial disc on the vertebral body. The other will model ossification of the posterior longitudinal ligament. The initial model will aim to replicate the experimental results seen in previously published work. This data can then be used to define a simple relationship between cyclic stress and bone formation and resorption.

Blast Foot and Bone Failure

Material properties of the fat pad under high strain rates[9]

The first body part in contact with the loading boundary is the heel fat pad whose material behaviour and load-attenuating capacity at high loading rates are ill-understood. The complexity of this material behaviour stems from its unique microstructure. We want to quantify the material behaviour of the human fat pad across loading rates in order to develop more biofidelic computational models and so assess and improve mitigation measures.

An inverse finite element (FE) method was utilised. A cadaveric human foot was dissected leaving the calcaneus (heel bone) intact, with the fat pad attached to it. Quasi-static compressive (displacement rates of 0.01-1 mm/s) and drop (mass of 7 kg, velocities at impact of 0.4-3.5 m/s) tests were performed (Figure 19). An FE model of the cadaveric foot was developed based on MRI and CT scans (Figure 20). A material formulation to describe the complex behaviour of the fat pad was implemented. The material constants of this formulation were obtained through a non-linear optimisation algorithm until numerical and experimental response matched to minimise error (Figure 21) (*the inverse method*). These properties will be implemented in a subject-specific FE model of the foot for under-body blast. This procedure will be repeated with more cadaveric specimens in order to obtain an average material behaviour for the fat pad.

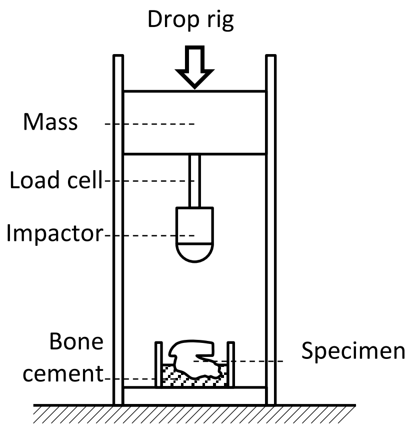


Figure 19: The drop test schematic. The impactor is set at different heights (2-64 cm) and released to hit the specimen while force history is recorded with a load cell.

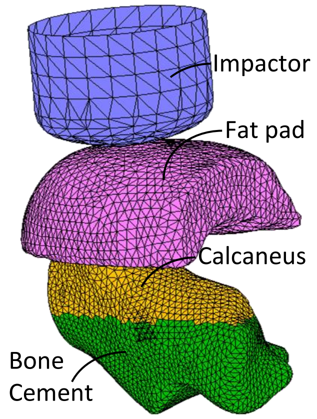


Figure 20: The computational model of the intact calcaneus with fat pad attached to it. It was used to simulate the quasi-static and dynamic tests.

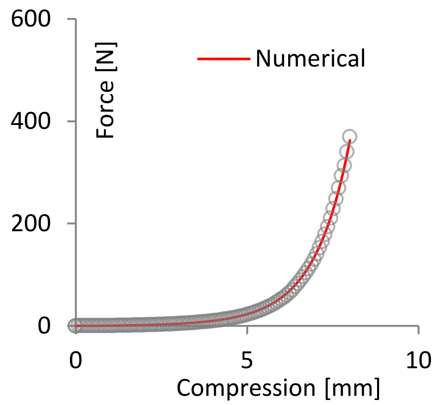


Figure 21: Comparison between numerical and experimental results. The good match indicates that the derived material formulation is correct.

[9] This section presents work from Grigoris Grigoriadis with supervision and contributions from Dr Nic Newell, Dr Spyros Masouros and Professor Anthony Bull

Evaluation of bone mechanical integrity following injury[10]

Casualties of under-body blast with complex musculo-skeletal injuries are likely to have reduced bone toughness proximally to the zone of fracture. Potential alterations in microstructure may result in reduction in fracture toughness, thereby making bone more prone to secondary failure and unable to support surgical fixation. We characterised the mechanical integrity, micro cracks and damage accumulation of human tibiae loaded axially at high loading rates. Cadaveric lower limbs were previously tested using our traumatic injury simulator (AnUBIS) that replicates the response of the vehicle floor-pan that has been attacked by a mine. Different occupant postures (seated, standing – brace, neutral and hyper-extended) tested resulted in diverse injury severities, all concentrated at the hind foot, without gross failure of the tibia. For this study cortical bone specimens were harvested mid-diaphysis and the proximal and distal metaphysis of these tibiae for mechanical testing under three-point bending, scanning electron microscopy (SEM) to investigate micro cracks and histocutter technique to image micro damage accumulation tested them to failure, and compared their response to unimpacted tibiae.

There was an increased spatial variation in the work of fracture of cortical bone along the unimpacted tibiae. Samples from the proximal tibia were found to be tougher than those of the distal and mid-diaphysis regions in unimpacted tibiae specimens (Figure 22) and in specimens that did not sustain any fracture at the foot when tested in the simulator. This spatial variation was absent in the specimens of tibiae that had sustained calcaneal fractures when tested in the simulator. It was revealed from SEM images that microcrack density was greater in lower limbs which were tested in standing hyperextended and neutral postures compared to other postures (Figure 22).

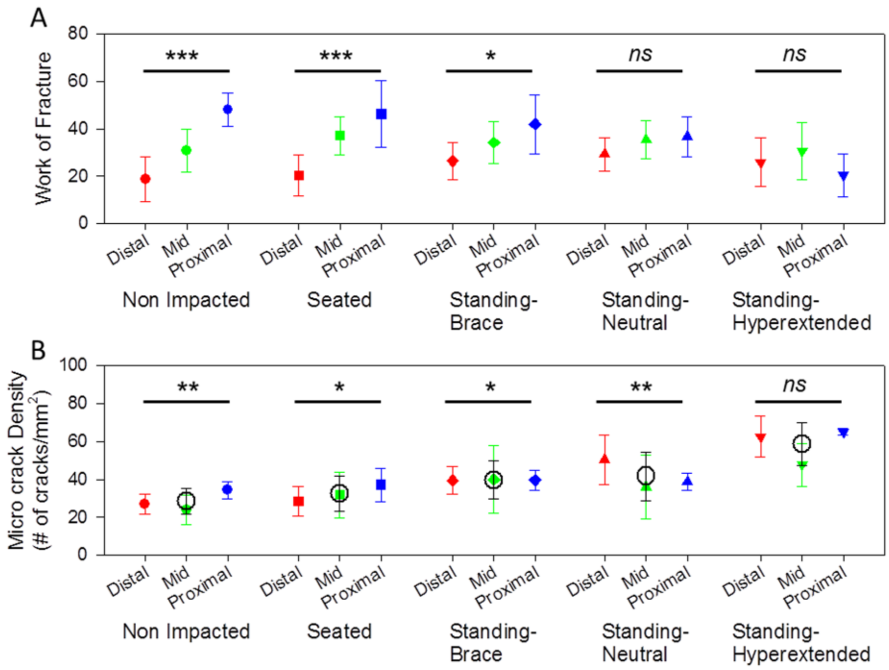


Figure 22 (A) Work of fracture (area under load *vs.* deformation curve) measured using 3 point bending and (B) micro crack density measured using SEM. Cortical bone specimens harvested from distal and proximal metaphysis and mid diaphysis of 4 types of occupant postures and non-impacted tibiae. Pair-wise brackets denote statistical significance (*P<0.05, **P<0.01, ***P<0.001, ns: not significant).

[10] This section presents work from Dr Angelo Karunaratne with supervision and contributions from Professor Anthony Bull, Dr Spyros Masouros and Dr Nic Newell

There was a spatial variation in microcracks in unimpacted tibia that correlated positively with work of fracture measurements from mechanical testing. This suggests that there is a threshold value in microcrack accumulation in bone that provides the maximum toughness. When the number of microcracks is greater than this threshold, the microcracks start to merge and develop zones of microdamage; this can be observed in 3D histology images (Figure 23). This study concludes that a stress pulse transmitted through long bones weakens their mechanical competence by creating damage zones in cortical bone with concomitant clinical sequelae.

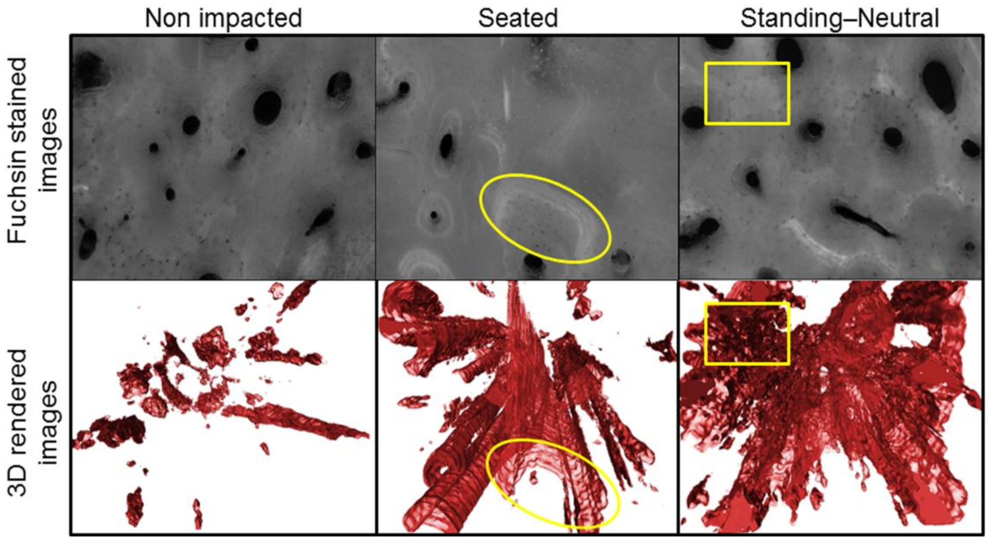


Figure 23 Top row: Bands of arc-shaped circumferential micro damage (oval) and diffuse micro damage accumulation (square). Bottom row: Microdamage accumulation along the length of the specimen.

Alumni

CBIS is focused on *effect* that is delivered through its research and translation activity. Another measure of effect is the work that our alumni have gone on to do, thus widening and deepening the impact of the activities. In order to capture this in some form, we here briefly presents some case studies of those that have been part of the Centre and have now gone on to other roles.

Dr Nic Newell

Nic Newell was a key part of the Centre. Prior to being established with the major funding from the Royal British Legion, the Centre developed much preliminary work through research students such as Nic who were funded through other sources. Nic's PhD funding from the Biotechnology and Biological Sciences Research Council allowed much of the instrumentation associated with our underbelly blast experiments as well as the start of computational modelling in underbelly blast to be conducted.

Having now completed his PhD, Nic has started as a Post-Doctoral Research Fellow in the Paediatric Spine Research Group at Queensland University of Technology in Brisbane, Australia. The aim of his research is to try to develop a better understanding of the aetiology of adolescent scoliosis. As with his work at Imperial this will involve both mechanical and numerical investigations as well as close collaborations with orthopaedic surgeons. Nic has kept close ties with researchers at CBIS since leaving and is sure that this will continue into the future as he seeks to finalise the publications arising from his studies as well as maintain a strong interest and commitment to the *effect* that CBIS seeks to achieve.

Major (Rtd) Martin Dansey

In Martin's own words: "Following two years in the The Royal British Legion Centre for Blast Injury Studies at Imperial College London as the Operations Manager I was fortunate to be offered the position of Chief Executive of Find A Better Way a charity founded by Sir Bobby Charlton aiming to harness technology to rid the world of landmines."

"I came to the attention of Find A Better Way through the work of CBIS as its Director. Professor Anthony Bull, had approached them with some programmes that fitted within the scope of the charity's humanitarian objectives. The programmes ranged from teaching local surgeons the latest techniques in through-knee amputations to producing implants and low cost prosthetics whilst providing rehabilitation in remote areas. Through this interaction in addition to my previous experience of charities as the treasurer and subsequently Director of the Household Cavalry Foundation the Charity considered me for their vacant position with an invitation to attend the opening of the Blast Centre conducted by His Royal Highness Prince Henry of Wales convincing them to make the offer."

[Editorial note: Find A Better Way (FABW) are supporters of CBIS and are currently funding two projects that ensure the transfer of our military related research to the civilian domain.]

"The charity focuses on three objectives to achieve its mission with development of demining technology, education and humanitarian programmes forming its core strategy. As the charity's CEO I am ultimately responsible for the performance across the spectrum of business activities be that strategic planning, governance, finance and fundraising, marketing and communications, operations and risk management. The challenge is varied as we are a multinational organisation with branches in UK and the USA with programmes running in Lebanon, Cambodia, Laos and Jordan with expansion planned into Iraq, Syria, Afghanistan and Colombia. The role is exceptionally rewarding as no two days are the same as one minute I am in the board room of some of the largest corporations in the world, the UN or Parliament and the next I'm in a field in Cambodia.

"It was very difficult to leave such an esteemed organisation as Imperial especially as part of the Blast Centre. I learned an enormous amount during my time taking away ideas to implement in the charity which I hope will significantly benefit those injured by landmines and the wider amputee community. Without my time at CBIS I wouldn't be in my current position and these programmes would not be implemented; therefore I look back fondly whilst focussing on the future and the challenges that lay ahead."

Darshan Shah

Darshan Shah is currently a PhD student in bioengineering at Imperial College. He was part of CBIS during his MSc in Biomedical Engineering where he specialised in biomechanics. Darshan's dissertation was on implants for amputees. The project was closely related to CBIS since the main target population was war veterans who underwent amputations due to blast. A CBIS Advisory Board member and double amputee from Afghanistan, Captain Dave Henson, advised on the work that resulted in the design of a novel lower limb implant that helps transfer the body weight of the amputee from the prosthetic through the bone, thus easing the pressure off the surrounding soft tissues of the stump and providing a comfortable prosthetic fit for the patient.

[Editorial note: Dave Henson is now working on this project himself as part of his MSc dissertation; more of that in the 2014 Report!]

Along with an experience in biomechanical designing, the project gave Darshan a good idea of the facilities and level of research at Imperial College. He states "I started my PhD straight after this project to spend more time on research in musculoskeletal biomechanics, and am currently working on developing a wrist simulator, a project involving hand biomechanics. After my PhD, I plan to continue doing research in this field and become an independent academic in the future."

Civilian Transfer

CBIS has a primary focus on the military and veterans. It is clear, however, that the learning, and the techniques developed to learn, from the military blast environment can be applied widely to civilian healthcare. For example, an estimated 2500 persons each month worldwide, most of them civilians, are victims of blast injury[11]. In addition, the injured Service Personnel that retire from the Forces become the responsibility of the NHS; this cohort is likely to require treatment that is extraordinary in the NHS setting. CBIS addresses this civilian transfer in the following ways:

Strategic Interactions with Stakeholders

The main stakeholder outside of the Centre's primary sponsor, RBL, is the MoD. As guardian of the welfare and wellbeing of service personnel, in addition to their role as provider of protective equipment, it is perhaps the most expeditious route to achieving an effect. In order to identify lessons from civilian and military blast incidents, improve clinical treatment, and influence the protection and rehabilitation of military and civilian personnel, the Centre engages in a number of strategic interactions with additional stakeholders.

A recent partnership with Find A Better Way (FABW) will build on and expand the Centre's current work to the civilian domain. It facilitates the Centre in its mission to "improve the mitigation of injury, develop and advance treatment, rehabilitation and recovery in order to increase lifelong health and quality of life after blast injury". CBIS recognises the link between its own area of specialisation with the broader areas of trauma research. The partnership with FABW provides an additional outlet that will allow for the education of surgeons, the next generation of prosthetics and developments in rehabilitation to benefit the wider society. CBIS Centre Director, Anthony Bull, is a member of the Scientific & Users Advisory Panel of FABW; a panel designed to inform the Charity's Trustees of the research that has been undertaken, to demonstrate how that research will eventually become a working project, and propose strategic future research direction.

The military aspects of rehabilitation are led by the *Defence Medical Rehabilitation Centre, (Headley Court)*. CBIS supports these activities and addresses rehabilitation from blast injury in the civilian realm by developing technologies to assess the effectiveness of various rehabilitation treatments. This is key particularly for injured Service Personnel that retire from the Forces and become the responsibility of the NHS.

CBIS also collaborates with the NIHR Surgical Reconstruction and Microbiology Centre at Birmingham through our work on heterotopic ossification and blast lung.

Through the Centre's Advisory Board, we can take discoveries from the military frontline to improve outcomes for all patients. Advisory Board member Zoltan Bozoky is the Chief strategy officer supporting teams in the Cabinet Office and Department of Health, working alongside clinical developers, research funders and drug regulators.

[11] Walsh NE1, Walsh WS. Rehabilitation of landmine victims--the ultimate challenge. Bull World Health Organ. 2003; 81(9): 665-70.

In addition to publishing the research, the Centre's principal investigators and some staff often give invited lectures at conferences and other seminars with military and civilian healthcare content and audiences. These, for example, include meetings of the British Orthopaedic Association and the British Trauma Society. PhD students are encouraged to present their work externally at least once in the period of their studies and, as such, CBIS has been represented nationally and internationally at conferences ranging in topic from *Government Experts on Mitigation Strategy* and *Finite Element Methods and Standards* to the *Biomechanics of Injury* and *Bioengineering*. This ensures that the research being conducted in the Centre is disseminated appropriately to a wider audience of stakeholders that can benefit from the research and nurture new, or strengthen existing, collaborations.

Funded Associated Projects

Two grants awarded this year from Find A Better Way mark the beginning of, hopefully, a long-lasting partnership in influencing practices and treatment of injury associated with landmines worldwide. The first project is the dissemination of skills learnt by MoD orthopaedic surgeons in dealing with complex blast-related amputations to civilian orthopaedic and trauma surgeons from developing countries and aid workers from developed countries. Up-to-date evidence based current concepts of surgery in the austere environment will be shared. This is supported and part-funded by Smith & Nephew, a global medical technology business dedicated to improving people's lives through its leadership positions in orthopaedic reconstruction, advanced wound management and trauma extremities and fixation. The second project will launch a pathway to providing affordable prosthetics that will enhance the quality of life for thousands of people and provide value for money solutions in some of the poorest areas in the world.

Professor Alison McGregor has a large programme of funded projects in the use of technology for rehabilitation, including projects funded by the Wellcome Trust, EPSRC, Imperial Confidence in Concept, and Arthritis Research UK.

Personnel Transfer

Another means by which CBIS ensures civilian transfer of the learning is through the skills that its personnel develop and then carry it with them through their career. The military orthopaedic surgeons that work within the Centre for a period of time are embedded within the National Health Service (NHS). Some researchers of the Centre pursue civilian research outside Imperial College, as noted in the case of Dr Nic Newell above, Paediatric Spine Research Group, Queensland University of Technology.

Publication

One of the main outputs from the Centre is publication to the open literature. This aims at disseminating the work to a wide readership that includes clinicians, scientists, and engineers in military, academia, healthcare industry, government and the general public. For example, clinical work that we have published on pelvic injury and follow-up of amputation in the mangled extremity is now being used in guidelines for civilian trauma.

Research Sharing

The Centre fosters a learning cycle with a multitude of civilian establishments ensuring successful knowledge transfer. Through our research we have developed software and methodologies, and progressed understanding and education of blast injuries that is transferable to many other disciplines. Stakeholders of our work are researchers and industry in the wider domains of injury and rehabilitation. Equally, we have gained knowledge of existing medical techniques and procedures being utilised both at home and abroad. A few areas benefiting from this research sharing include the treatment of road traffic casualties, design and manufacture of prosthetics and implants and the treatment of fractures, osteoporosis and osteoarthritis.

Communication of the Work

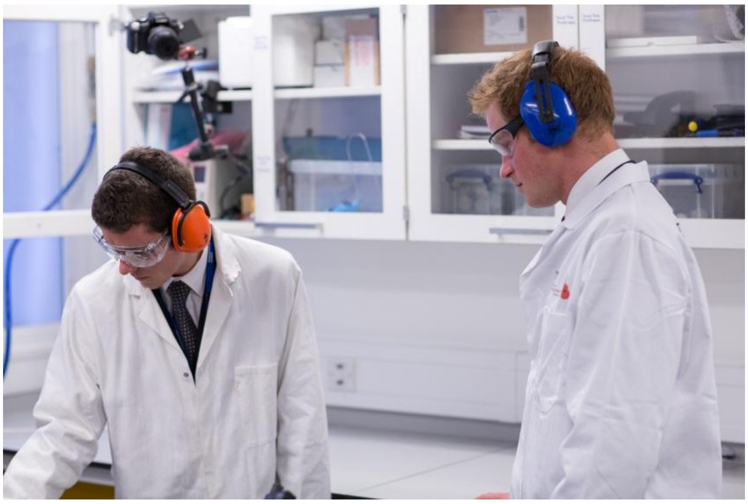
The Centre's strategy document highlights its vision to progress understanding of blast injury through research and education. Collaboration of engineers, scientists and clinicians alongside communication with the wider society are seen as key factors in delivering the Centre's strategy. The Centre openly and transparently publishes its work in the scientific press. We carefully maintain our website, work with our stakeholders and engage positively with the media to ensure dissemination of our output continues to be open and public.

Media and Public Engagement Focus

The Centre continues to generate media attention with visits, articles and interviews. The following represents the external media reports for the year.

Annual Network Event

The 17th October was a momentous day for CBIS, marking both the official opening of the Centre's new laboratories by HRH Prince Harry and also being the day of the Centre's second annual networking event.



Prince Harry was introduced to the Centre by a guided tour of our laboratories. HRH almost managed to blend in with our CBIS researchers apart from the embroidered 'HRH' across the back of his white personalised lab coat.

Dr Theofano Eftaxiopoulou and Dr James Wilgeroth demonstrated the shock tube to HRH and explained how scientists put materials in the way of the shockwave to analyse its effects and thus allow better protective gear to be developed. Prince Harry also met with Professor Sara Rankin, theme leader for biology and therapeutics and Dr William Proud, theme lead of blast force protection who presented to HRH how the split Hopkinson bar is used to simulate damage from IEDs at the cellular level. HRH was also shown the Anti-vehicle, Underbelly, Blast-Injury Simulator (AnUBIS) and how it is used to investigate how roadside bomb blasts impact on the skeletal system.

Before unveiling a plaque to commemorate CBIS's official opening, HRH gave a speech addressing how important the research is at the Centre: *"Today, I have had a brief insight into the work of the Centre including how injured cells are analysed. In the past I've met numerous service men and women injured in operations, many by IEDs and landmines. Their stories are harrowing and inspirational as I am sure you all know. Watching the IED simulation reminded me of the catastrophic trauma experienced by the human body during IED or mine-strikes. To me this makes their extraordinary stories of recovery all the more outstanding. This issue affects people on a global scale and whilst work at the Centre is strongly focussed on military casualties, its findings will no doubt also provide significant humanitarian benefits across the world. The Royal British Legion and Imperial have joined forces to tackle this issue head on. Without this partnership the Centre would quite simply not become a reality."* Prince Harry graciously spent time after his speech to meet with the various luminaries at the event and spoke to many of the Centre's researchers in person. The image on the front page of this report shows HRH meeting Majors Taff Edwards and James Singleton during the event.

The CBIS networking event ran in parallel with the official opening and included an array of exciting lectures about blast injuries and different aspects of the research taking place at the Centre. Professor Anthony Bull opened the event with an introductory talk discussing the aims and intents of the centre followed by a splendid morning of presentations from speakers including Professor Sir Simon Wessely, Dr Mazdak Ghajari and Major James Singleton. The talks ranged from myths of military mental health and traumatic brain injury to battlefield injury clinical research currently conducted at CBIS.

The second half of the event included lectures given by Surgeon Captain Mark Midwinter CBE, Wing Commander Alex Bennett, Dr Tobias Reichenbach and Dr Spyros Masouros on a multitude of intriguing topics including rehabilitation research, blast induced hearing damage and measuring injury burden and outcome parameters in combat trauma.

The poster competition of the networking event was of extremely high standard with first prize being awarded to Scott Armstrong and highly commended awards being given to Ashton Barnett-vanes and Nic Newell.

Website

Our main face to the external world remains our website, which attracted over 12,000 page loads in 2013. *www3.imperial.ac.uk/blastinjurystudies*. Embedded in the main Imperial College website with links from the Royal British Legion's own pages *www.britishlegion.org.uk/can-we-help/other-ways-we-help/centre-for-blast-injury-studies* ensures that what we do is open to the world 24 hours a day, 7 days a week.

Other Media Mentions

Engineering & Technology. *How to … diffuse a bomb.* Jan 2013

Pennant Magazine. *Blast Injury Centre.* May 2013

NAM. *The Unseen Enemy.* May 2013

Elements. *A Look Inside the Centre for Blast Injury Studies.* Interview with Centre Director, Professor Anthony Bull. Jun 2013

Sunday Times. *600 Veterans of Afghanistan left with Brain Injury.* Aug 2013

Numerous newspaper articles, online & TV news coverage detailing the opening of the Centre by HRH Wales. Oct 2013

BBC Radio Essex. Interview with Centre Director, Professor Anthony Bull. Nov 2013

Public Engagement Activities

Imperial Festival

An annual hands-on public science demonstration attracting over 10,000 people of all ages, Imperial Festival aims to celebrate the best on offer from the College's staff and students. This year CBIS provided balloon bursting and smoke ring thrusting demonstrations to grab the attention of adults and children alike. A mini shock tube was created to show the initiation of a shock wave with an industrial sized Air Zooka providing the air blast to prove the point. A rolling video and posters detailed the science behind the toys, which gave a good overall feel for the subject of blast when brought together. *www3.imperial.ac.uk/festival/previousfestivals/imperialfestival2013*

Exscitec event

Through an Excitec programme, a group of eight 11-17 year-old pupils spent four exciting days working with Dr William Proud and Dr James Wilgeroth to develop, calibrate and use a shock tube.

Exscitec is an organization specialising in educational outreach. In the summer of 2013 it organised a series of events in Imperial College London to allow 11-17 year olds the opportunity to experience life at University. There was a strong STEM (Science Technology Engineering Mathematics) component to the programme and in one theme twelve groups, each of eight students, dedicated four days to a project. One of the projects was to develop, calibrate then use a Shock Tube, which they made from sections of (new) drainpipe, balloons and cardboard. The volume of balloon containing the driving gas, the volume of the tube and the cross-section of the tube were all varied. Output was measured using the swing of a pendulum made from cardboard and a small metal frame. The results showed that with this simple apparatus it was possible to achieve exit velocities of over 8 m s-1 (25 km per hr). The final day was devoted to presenting results both orally and on posters. Finally all students were presented with badges and certificates to recognise their achievements. More details on Exscitec can be found at *www.exscitec.com/index.asp*.

This project was supervised Dr James Wilgeroth and Dr Bill Proud.

Royal Institution Engineering Masterclass

Dr Phillips has developed and delivers a Royal Institution Engineering Masterclass, where school children get to build a working model of the musculoskeletal system around the hip joint, before calculating what muscle forces are required to allow us to stand up and move around. As part of the discussion in the Masterclass the role of engineers in understanding how the human body works, and how it can be protected against injury is investigated. Following on from the Masterclasses, Dr Phillips has delivered a Summer School workshop at the Royal Institution which explores bone as an optimised structure, as well as looking at how optimised structural components could be used in preventing bone fracture caused by impact and blast insult. Dr Phillips has also given several talks for the Royal Institution and the Institute of Physics relating to his research.

National Science Museum lates

Dr. Bill Proud, assisted by Dr. David Chapman, both of the Institute of Shock Physics and CBIS, gave three talks at the National Science Museum as part of the 'Lates' events (*www.sciencemuseum.org.uk*). The talk centred on the origins and uses of high-speed photography featuring personalities, crimes and patent—challenging early pioneers as well as current developments in the field of shock waves and blast studies. About 300 people attended these talks, one of 28 themes addressed at the event.

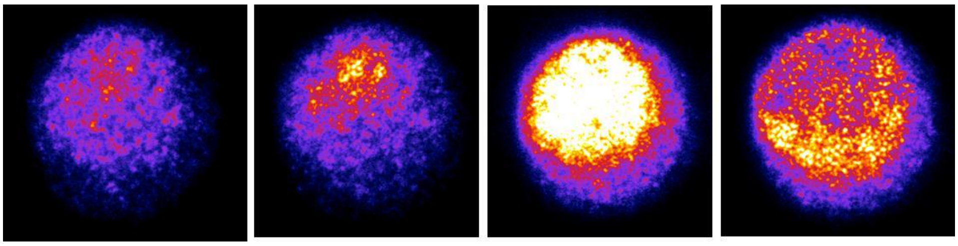


Figure 24: Bed of Ammonium Nitrate, impact initiated 30 ns exposure time and 0 ns interframe time

Awards

Bo C. AWE (Atomic Weapons Establishment) Thesis Prize

Clasper JC. Defence Medical Service Gold Clinical Excellence Award

Singleton JAG. Montefiore memorial prize (Best Military Surgical Trainee), Army Medical Services

Ramasamy A. Naughton Dunn Prize for best presentation, Naughton Dunn Scientific Meeting

Invited Lectures

Proud WG. The Physical basis of explosion and blast injury processes. Royal Society of Medicine, Current Concepts in perineal pelvic blast injury. Dec 2013

Reichenbach T. *Mathematical Neurobiology of Hearing.* IST Seminar, Institute of Science and Technology, Austria, Feb 2013

Reichenbach T. *Mathematical Neurobiology of the Inner Ear and Beyond.* Seminar, Ear Institute, University College London, Sep 2013

Reichenbach T. *Physics of Hearing.* Seminar, Institute of Sound and Vibration Research, University of Southampton Nov 2013

Reichenbach T. *Processing of Auditory Signals: From the Inner Ear to Neural Networks.* Seminar, School of Mathematical Sciences, Queen Mary University of London, Nov 2013

Brown KA. *Military Medicine Challenges of Blast Injury: Visible Reminders of Invisible Light*. University of Houston, Cullen College of Engineering, Houston, TX, USA. Nov 2013

Brown KA. *Military Medicine Challenges of Blast Injury: Visible Reminders of Invisible Light*. University of Texas at Austin, Centre for Systems Biology, Austin, TX, USA. Nov 2013

Clasper JC. *Blast Studies at Imperial*. Presentation to Israeli Military Delegation. Birmingham, May 2013

Clasper JC. *Blasted Limbs*: Combat and Orthopaedic Surgery National Army Museum, London, Sep 2013

Clasper JC. *Blasted Bones*. Travelling Surgical Society, Birmingham, Sep 2013

Clasper JC. Orthopaedic lessons learned from casualties in Afghanistan. Colt Foundation, Royal Society of Medicine, London, Dec 2013

Masouros SD. *Extremity blast injury and its mitigation.* Departmental seminar, Department of Bioengineering, Imperial College London, Nov 2013

Masouros SD. *Use of medical imaging to understand blast injury*. Tri-service radiology conference, Cosford UK, Nov 2013

Singleton JAG. *Identifying future 'unexpected' survivors: fatal injury pattern analysis in IED victims*.

Royal College of Surgeons of Edinburgh Symposium, Research on Injury in Conflict, Edinburgh, Nov 2013

Ramasamy A. *Military blast research*. RCS England Freemasons Research Fund Presentation, Cranfield UK, Oct 2013

Ramasamy A. *Understanding lower limb blast injuries*. RCS England Freemasons Research Fund Presentation, Northampton UK, Sep 2013

Recent Publications

List of documents produced by the Centre in 2013:

Publications in Peer-Review Journals

Brown KV, Clasper JC. *The changing pattern of amputations* J R Army Med Corps. 2013, 000103.

Breeze J, Clasper JC. Ergonomic assessment of future methods of ballistic neck protection. Military Medicine. 2013, 178(8): 899-903.

Breeze J, Leason J, Gibb I, Hunt NC, Hepper A, Clasper JC. *Computed tomography can improve the selection of fragment simulating projectiles from which to test future body armor materials*. Military Medicine. 2013, 178(6): 690-695.

Breeze J, Midwinter M, Pope D, Porter K, Hepper AE, Clasper JC. *Developmental framework to validate future designs of ballistic neck protection*. British Journal of Oral and Maxillofacial Surgery. 2013, 51(1): 47-51.

Breeze J, Clasper JC. *Determining the velocity required for skin perforation by fragment simulating projectiles: a systematic review*. J R Army Med Corps. 2013, 159(4): 265-270.

Clasper JC, Ramasamy A. *Traumatic amputations*. British Journal of Pain. 2013, 7(2): 67-73.

Clarke SG, Phillips ATM, Bull AMJ. *Evaluating a suitable level of model complexity for finite element analysis of the intact acetabulum*. Computer Methods in Biomechanics and Biomedical Engineering. 2013, 16(7): 717-724.

Durrant JJ, Ramasamy A, Salmon MS, Watkin N, Sargeant I. *Pelvic fracture-related urethral and bladder injury*. J R Army Med Corps. 2013, 159(suppl 1): i32-i39.

Eardley WGP, Watts SA, Clasper JC. *Modelling for conflict: the legacy of ballistic research and current extremity in vivo modelling*. J R Army Med Corps. 2013, 159: 73-83.

Masouros SD, Newell N, Ramasamy A, Bonner TJ, West ATJ, Hill AM, Clasper JC, Bull AMJ. *Design of a traumatic injury simulator for assessing lower limb response to high loading rates*. Annals of Biomedical Engineering. 2013, 41(9): 1957-1967.

Masouros SD, Brown K, Clasper JC, Proud WG. *Briefing: blast effects on biological systems*. Proceedings of the ICE – Engineering and Computational Mechanics. 2013, 166(3): 113-118.

Modenese L, Gopalakrishnan A, Phillips ATM. *Application of a falsification strategy to a musculoskeletal model of the lower limb and accuracy of the predicted hip contact force vector*. Journal of Biomechanics. 2013, 46(6): 1193-1200.

Proud WG. *The physical basis of explosion and blast injury processes*. J R Army Med Corps. 2013, 159(suppl 1): i4-i9.

Proud WG. *Future research areas*. Propellants, Explosives, Pyrotechnics. 2013, 38(2): 197.

Poon H, Morisson JJ, Clasper JC, Midwinter MJ, Jansen JO. *Use and complications of operative control of arterial inflow in combat casualties with traumatic lower-extremity amputations caused by improvised explosive devices*. Journal of Trauma and Acute Care Surgery. 2013, 75(2): S233-237.

Ramasamy A, Newell N, Masouros SD. *From the battlefield to the laboratory: the use of clinical data analysis in developing models of lower limb blast injury*. J R Army Med Corps. 2013, 0000202.

Ramasamy A, Hughes A, Carter N, Kendrew J. *The effects of explosion on the musculoskeletal system*. Trauma. 2013, 15(2): 128-139.

Ramasamy A, Hill AM, Masouros SD, Gibb I, Phillip R, Bull AMJ, Clasper JC. *Outcomes of IED foot and ankle blast injuries*. Journal of Bone and Joint Surgery. 2013, 95(5): e25 1-7.

Ramasamy A, Hill AM, Phillip R, Gibb I, Bull AMJ, Clasper JC. *FASS is a better predictor of poor outcome in lower limb blast injury than AIS: implications for blast research*. Journal of Orthopaedic Trauma. 2013, 27(1): 49-55.

Ramasamy A, Cooper GA, Sargeant ID, Evriviades D, Porter K, Kendrew JM. *(i) An overview of the pathophysiology of blast injury with management guidelines*. Orthopaedics and Trauma. 2013, 27(1): 1-8.

Singleton JAG, Gibb I, Hunt NCA, Bull AMJ, Clasper JC. *Identifying future 'unexpected' survivors: a retrospective cohort study of fatal injury patterns in victims of improvised explosive devices.* BMJ Open. 2013, 3(8): e003130.

Singleton JAG, Gibb I, Bull AMJ, Mahoney PF, Clasper JC. *Primary blast lung injury prevalence and fatal injuries from explosions: Insights from post-mortem computed tomographic analysis of 121 improvised explosive device fatalities.* Journal of Trauma. 2013, 75: S269-S274.

Chapters in Books

Clasper JC. The Management of Military Wounds in the Middle Ages. In: Wounds in the Middle Ages. Ashgate

Government Reports

IB/DSTL/250113/01. Evaluation of lower limb injury risk – Part 1.

IB/DSTL/151013/01. Evaluation of lower limb injury risk – Part 2.

Presentations at Conferences

Government Experts on Mitigation Strategies (**GEMS**) Annual Meeting, Shrivenham, UK. Jan 2013.

Singleton JAG, Hunt N, Gibb I, Bull AMJ, Clasper JC. *Future 'unexpected' survivors: causes of death and injury patterns in IED fatalities*.

Masouros SD, Newell N. *Assessing in-vehicle mitigation systems with different anthropometric test devices (ATDs).*

Pressure, Energy, Temperature and Extreme Rates (**PETER**) Annual Meeting, London, UK. Feb 2013.

Butler BJ, Bo C, Jardine AP, Williams A, Brown KA. *Development of porcine tissue models for blast injury.* Pressure, Energy, Temperature and Extreme Rates (PETER) Conference.

Bo C, Williams A, Rankin S, Proud WG, Brown KA. An experimental platform to study blast injuries: a *bottom-up approach.*

New Trends in Research of Energetic Materials (**NTREM**), Czech Republic. Apr 2013.

Bo C, Newell N, Nguyen T-TN, Butler B, Wilgeroth J, Balzer J, Masouros SD, Bull AMJ, Phillips ATM, Jardine AP, Williams A, Rankin S, Brown KA, Proud WG. *Understanding the Effects of Blast on Biological Systems*

Combined Services Orthopaedic Society (**CSOS**) Annual Conference, Portsmouth, UK. May 2013.

Bonner TJ, Newell N, Pullen AD, Amis AA, Bull AMJ, Masouros SD. *Strain rate sensitivity of porcine stifle joint LCL.*

Singleton JAG, Walker NM, Bull AMJ, Clasper JC. *Case suitability for definitive through knee amputation following lower limb blast trauma: analysis of 146 UK combat casualties 2008-2010.*

American Physical Society - Shock Compression of Condensed Matter (**APS-SCCM**). July 2013.

Bo C, Williams A, Rankin S, Proud WG, Brown KA. *Integrated experimental platforms to study blast injuries: a bottom-up approach.*

Orthopaedic Trauma Society (**OTS**) Research Meeting. Edinburgh, UK. Aug 2013.

Ramasamy A, Evans S, Deshmukh SC. *Distal radius volar locking plates: how anatomical are they?*

International Research Council on the Biomechanics of Injury (**IRCOBI**) 2013 Conference, Gothenburg, Sweden, Sep 2013.

Newell N, Masouros SD, Ramasamy A, Bonner TJ, Hill AM, Clasper JC, Bull AMJ. *A comparison of MiL-Lx and Hybrid-III responses in seated and standing postures with blast mats in simulated under-vehicle explosions*.

Bonner TJ, Newell N, Pullen AD, Amis AA, Bull AMJ, Masouros SD. *Sensitivity of the material properties of the lateral collateral ligament of the porcine stifle joint to strain rate*.

Bioengineering 13. Glasgow, UK. Sep 2013.

Haley A, Zaharie D, Masouros SD. *Breaking ribs: development of torso surrogate to investigate blunt trauma*.

British Orthopaedic Association (**BOA**) Annual Scientific Congress. Birmingham, UK. Oct 2013.

Singleton JAG, Walker N, Gibb I, Bull AMJ, Clasper JC. *Case suitability for definitive through knee amputation following lower extremity blast trauma: analysis of 146 combat casualties 2008-2010.*

Orhtopaedic Trauma Association (**OTA**) Annual Meeting. Phoenix, Arizona USA. Oct 2013.

Singleton JAG, Gibb I, Bull AMJ, Clasper JC. *Blast-mediated traumatic amputation: evidence for a new injury mechanism.*

International Conference on Biomedical Engineering (**ICBME**), Singapore. Dec 2013.

Karunaratne A, Undheim M, Masouros SD, Bull AMJ. *Evaluation of bone fracture mechanisms and load transfer of lower limb injuries from under-vehicle explosions*.

Society of Military Orthopaedic Surgeons (**SOMOS**) Annual Meeting. Vail, Colorado USA. Dec 2013.

Singleton JAG, Gibb I, Bull AMJ, Clasper JC. *Blast mediated traumatic amputation: evidence for a new injury mechanism.*

Imperial College London

THE ROYAL BRITISH LEGION

LEGION

THE ROYAL BRITISH LEGION

CENTRE FOR BLAST INJURY STUDIES

AT IMPERIAL COLLEGE LONDON