Imperial College London

THE ROYAL BRITISH LEGION

CENTRE FOR BLAST INJURY STUDIES

AT IMPERIAL COLLEGE LONDON

THE ROYAL BRITISH LEGION

2014

CBIS Annual Report


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"Pain is the legacy of all human conflict, whether on the unimaginable scale of World War 1 or today's far smaller yet no less brutal campaigns worldwide."

See Series page 1715

Editorial
The medium and the message of Ebola
See page 1641

Comment
Refugees and health: lessons from World War 1
See page 1644

Articles
TIPPS: Antepartum dalteparin versus no antepartum dalteparin for the prevention of pregnancy complications in pregnant women with thrombophilia
See page [illegible]

Articles
The 3C Study: Alemtuzumab-based induction treatment versus basiliximab-based induction treatment in kidney transplantation
See page 1684

Articles
A genomic analysis of the extant World War 1 dysentery bacillus NCTC1
See page [illegible]

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The Royal British Legion

Centre for Blast Injury Studies

at Imperial College London

March 2015

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, March 2015

Imperial College of Science, Technology and Medicine

Contents

Foreword

The Royal British Legion Centre for Blast Injury Studies at Imperial College London is one of the principal academic institutes engaged in military medical research in the UK. CBIS has a targeted focus on blast injuries in order to understand the injury mechanism, develop mitigation and influence both acute treatment and rehabilitation. This third annual report reports the continued research progress and substantial contribution to new knowledge in this field: it will be welcomed by all those committed to the welfare of our serving armed forces and veterans.

As Medical Director of the Defence Medical Services I am privileged to shape the military medical research strategy. I regard CBIS as a close partner and ally to deliver this broad and complex requirement, and the collegiate relationship enjoyed between the two organisations is highlighted by the opportunity to write this foreword. This annual report specifically demonstrates how medical intelligence can drive research to both prevent and treat injury. CBIS calls this “clinically-led research”. One example is the finding that a certain pattern of heel injury (“blast foot”) cannot be reconstructed even with the most advanced technology and surgery, which has led to a programme of research on mitigation and protection. The results are that new standards for protection of vehicles have been proposed, “blast mats” to provide energy absorption have been tested, and recommendations on in-vehicle posture have been promulgated. Other, more fundamental research is now utilising computational modelling to act as a design tool for new protection against injury. The focus here is about protection against injury, rather than protection against a specific threat. This concept is at the heart of CBIS’ academic enquiries, where research starts with the investigation of the person, the wounding patterns and the treatment; it then looks outwards to the interface with the environment. This ensures that research is clinical-outcome focused, while identifying common protection from injury arising from diverse threats.

A defining characteristic of CBIS is its inter-disciplinary approach. Military medical personnel, biochemists, physicists, engineers and life scientists actively collaborate and it is through these cross-cutting interactions that the truly innovative and disruptive ideas can emerge. History tells us that it is essential to continue to innovate between major campaigns, to avoid accruing an intellectual deficit that is repaid in Servicemen’s lives at the start of the next campaign—following the drawdown from Afghanistan in this reporting year, CBIS has a critical role to play in this continued knowledge development.

My confident expectation, therefore, is that CBIS will continue to play a major role in delivering valuable research to meet the Defence medical requirement and I encourage you, the reader, to support this work and its dissemination for the benefit of the war wounded, their families and society in general.

Brigadier Tim Hodgetts CBE

Royal Centre for Defence Medicine

Birmingham, United Kingdom

Introduction

The 4th of August 1914 was the day that Britain entered the First World War. The Great War, as it was later named, lasted over 4 years and, in its scale and devastation, was one of the costliest conflicts in history. Almost a million British soldiers died and more than double that amount returned home injured. Leg wounds were the most commonly recorded area of injury during the war and amputations, deemed necessary, led to significant new challenges for the medical profession. A century on, Improvised Explosive Devices (IEDs) in conflict have made limb injury and amputation common once more. The Royal British Legion Centre for Blast Injury Studies at Imperial College London (CBIS) is a clinically-led research and translation centre with a mission to improve the mitigation of, and recovery from, blast injuries. Our research themes in biomechanics, rehabilitation, force protection and biology are targetted to deliver the Centre's mission.

This report, the third in series, is not meant as a comprehensive survey of all activities of the Centre, but is meant to give a flavour of the breadth and depth of the current work referring to specific highlights during 2014. Information on the Centre's background, structure, and governance can be found in the 2012 Annual Report or on the Centre's website (www.imperial.ac.uk/blastinjurystudies). Within the Centre's core research themes, we provide a summary of published work this year and current research activities. The report presents two biographical pieces from current researchers in the Centre. There is an update on some of our alumni and a summary of communications and outputs for 2014. We start with a historical note on the relevance for Imperial College London and CBIS of the First World War Centenary.

Figure 1: Some 2014 Centre members outside the CBIS main office.

1914 - 2014

In 2014, Britain began national commemorations to mark the outbreak of the First World War. This centenary has special relevance for Imperial College London and for CBIS in particular. The Centre leads the field nationally and internationally in blast injury research and, with its emphasis on civilian transfer projects, is focused firmly on the future. Less well known is that this extraordinary work is carrying on a century-long tradition of interdisciplinary research and commitment by staff at Imperial College to mitigate the effects of weaponry and complex casualty. There are remarkable parallels between the Great War and Britain's recent conflicts, both in the nature of the wounds themselves, the efforts to treat and understand their consequences, and in the problems that are yet to be resolved despite the passing of a century.

Imperial College's first volunteer for war service in 1914 was the Rector, Sir Alfred Keogh (pictured) who was immediately assigned by Kitchener to direct Britain's Army Medical Services. By Christmas 1914 everyone in the new military medical organisation was aware of the demands of the new, horrifying forms of industrialised mass casualty, in particular the complex wounds caused by heavy artillery shell fragments and shrapnel. With his background from Imperial, Keogh knew that science would have an essential role in providing both protection for the fighting soldier and treatment for the wounded. Keogh's man in the field in France, Sir Arthur Sloggett, agreed with him, and the two men began the first official correspondence in Britain to explore the consequences of blast injury. Sloggett wanted armour for the troops, capable of deflecting "the numerous fragments that are scattered by the explosions of bombs and grenades [which were] the cause of a large number of bomb-wounds." Both men knew it would require a multi-disciplinary effort from both scientists and medics so Imperial was the ideal place to undertake the necessary complex work:

> *"It seems that, with Pilcher* [RAMC Professor of Surgery] *on the spot to speak from the point of view of Military Surgery, with Starling* [Professor of Physiology] *and all his assistants all accustomed to experimental work, and with Lucas* [Department of Chemistry] *and his knowledge of where and how to obtain materials,* ***we might obtain valuable results by experimental work at the College."***

Although the numbers of casualties from today's conflicts are significantly less than those of the Great War, the wounds themselves are surprisingly similar. Whether the delivery mechanism was a roadside IED or a "Jack Johnson" artillery shell fired from a huge gun in Flanders, the principal injury was musculoskeletal trauma with damage to peripheral nerves in the upper and lower limbs, complicated by the effects of blast injury. Many of the injuries resulted in amputation by surgeons in field hospitals close to the fighting, or on returning home. Today CBIS continues to meet the challenge of those "bomb-wounds," first laid down by Keogh and Sloggett, in its 21st century experimental work. CBIS is still working on armour protection (clothing and vehicular) and has developed its research into the physical consequences of the bomb-wound, from prosthetic design and materials, to heterotopic ossification). Keogh and Sloggett would have been astonished by these "valuable results" and greatly satisfied in this remarkable vindication of their faith in scientific research.

Perhaps their satisfaction might be tempered by the understanding that there are still challenges first identified during the Great War that have yet to be resolved. Heterotopic ossification (the formation of bone growth in soft tissues at amputation stump sites) was discovered as a consequence of blast injury in a French military hospital in 1917. Yet research into the causes and treatment of this highly problematic condition ceased in the mid-1920s and only resumed in the 21st century when it was identified as occurring in 64% of military amputees. Today another military surgeon is "on the spot" at CBIS tackling the problem enabled by state of the art scanning and diagnostic technology, analysing the condition at the molecular level and working towards effective treatment for the condition in the military casualty. This will have important ramifications for those suffering from HO in civilian life, in particular after hip replacement surgery – a condition likely to increase as in the global ageing population.

HO is one of a cluster of pain related conditions that have impaired amputee patients from wars a century apart. In a recent article for *The Lancet* [the cover is shown on the front of this report], researchers from within CBIS and Imperial College analysed medical records and testimony concerning post-amputation pain from the Great War, and compared them to similar data sets from today. They found that pain outcomes remain broadly similar, despite the passage of time. Scientists and medics are once again involved in comprehensive research efforts to combat the multiple forms of this debilitating condition, including stump pain, residual limb pain and phantom limb pain.

CBIS has resumed this vital work on casualty conditions that are a century old. Their research has a particular importance that goes beyond its scientific value – one that reflects both the future and the past. History shows that, despite both the scale of Great War casualty and the medical-scientific response to it, research went unfinished, solutions remained out of reach, and lessons were forgotten. As a result, casualties lived out lives blighted by pain and disability, relying in great numbers on organisations such as the Royal British Legion, set up especially to provide welfare for those beyond medical help. Today TRBL is one of the primary funders of CBIS and together they are working towards a better future for today's casualty. Wars end but casualty endures, as should the work to prevent, treat and cure it, for now and for the future.

Staffing & Facilities

2014 saw further expansion to the Centre in terms of personnel and bespoke test facilities. With the recruitment of seven full time PhD students, a full time MD(Res) researcher and research assistant, full- and part-time support staff, as well as associated academics this year, CBIS now boasts over 40 staff and students based at Imperial College. The brief biographies below of some of our new members further highlight the interdisciplinary nature of the Centre's activities and the continued recruitment of highly skilled and experienced personnel.

Researchers Joining CBIS in 2014

Anabela Areias joined the Centre to focus on the "Cellular Biomechanics of Blast". Anabela will investigate how controlled pressure waves directly affect the biological activity of living cells in vitro. Anabela has a BSc in Bioscience and an MSc in Micro and Nano Technology. Her MSc thesis was a study on Chitosan Nanofibres Membranes for Tissue Engineering. Anabela is supervised by Dr Darryl Overby from the Department of Bioengineering, an expert in cellular mechanobiology who has recently committed his research efforts to the Centre's aims.

Octave Etard graduated from the École Centrale de Paris, and holds an MSc. in Biomedical Engineering (Neurotechnology) from Imperial College London. Octave joined Dr. Tobias Reichenbach's "Biophysics of Hearing and Sensory Neuroscience" Group to study the "EEG assessment of central auditory disorder in patients with blast-induced traumatic brain injury".

Under the supervision of Professor Alison McGregor, **Matthew Hopkins** is developing Smart Sockets for Lower Limb Prosthetics in the Department of Surgery and Cancer in collaboration with colleagues in Mechanical Engineering. Matthew has a BEng in Mechanical Engineering from the University of Southampton with specialisation in bioengineering and lower limb prosthetics. His interest in innovative rehabilitative technologies and the multidisciplinary science behind it have drawn Matthew to join CBIS.

Richard Pangonis became involved with CBIS during his MEng degree at Imperial College when he undertook a group project, a summer placement and his final dissertation in the Centre. This commitment to the Centre's activities and his own excellence in biomedical engineering ensured a perfect fit for his PhD that is aimed at investigating injury mechanisms for blast induced traumatic brain injury, with a view to improving diagnosis, treatment and protective equipment. Richard works under the joint supervision of Dr Mazdak Ghajari (Department of Aeronautics) and Professor David Sharp (Department of Medicine).

Due to her interest in post trauma inflammatory response, **Anna Sharrock** has joined CBIS to undertake an MD(Res) investigating the generation and function of Microvesicles in blast injury. Anna is a military General Surgery Registrar who studied Medicine at Imperial College London and, following a period of work in the UK and Germany, was deployed to the Balkans and Afghanistan. Anna will initially focus her research on blast induced endothelial activation under the supervision of Professor Sara Rankin.

Kalpi Vitharana completed a BEng in Medical Engineering at Queen Mary, University of London and then embarked on a fascinating competition-funded MRes project entitled: "Implantable sensor technology to monitor response to chemotherapy in epithelial ovarian cancer". Having completed this, Kalpi is now undertaking a PhD in CBIS which involves looking at "Blast wave transmission through the thorax and the effects on structures within the lung". Kalpi is supervised by Dr Hari Arora.

A qualified doctor in the Royal Air Force, **Claire Webster** joined the Centre under the supervision of Col. Jon Clasper and Dr Spyros Masouros. Claire has interests in vascular and trauma surgery, and genitourinary trauma and reconstruction. Claire will undertake a project entitled "Mapping the Blast Pelvis", establishing the mortal injury in Pelvic Trauma and developing potential mitigating factors.

Dan Zaharie joined the Centre to work on structural finite element modelling of soft and hard tissues of the pelvic region. This follows an MEng degree at Imperial College during which time Dan undertook two Research Placement opportunities in the Centre. Like Richard Pangonis above, Dan is living evidence of the attractiveness of the Centre's activities for the 'brightest and best' at Imperial and the Centre is pleased that he is able to continue as part of CBIS. For his PhD, Dan is working under the supervision of Dr Andrew Phillips in the Department of Civil Engineering.

Dr Dilen Carpanen joined CBIS as a research assistant under the mentorship of Dr Spyros Masouros. He received his first degree in Mechatronics Engineering in 2009 and in 2014 successfully defended his PhD thesis in Computational Biomechanics. Dilen's interests lie mainly in the behaviour of human joints and the design of devices. He has substantial expertise in computer aided engineering (CAE) – primarily finite element analysis (FEA) - and design (CAD). His current role is to support the numerous CAD/CAE research students and projects within the Centre; these projects include models of the human body (lower extremity, spine), and protective and experimental equipment design and evaluation (blast mats, combat boot, surrogates, traumatic injury simulators).

Associate Academics

Dr Emily Mayhew is a military medical historian specialising in the study of severe casualty, its infliction, treatment and long-term outcomes in 20th and 21st century warfare. Emily joined CBIS to undertake work that provides a historical perspective and context to today's medical and scientific research done at the Centre into consequences of blast injury in both military and civilian contexts. Emily is observing the work of the scientists and clinicians at the Centre as part of her ongoing historical analysis of the field, as well as identifying and interpreting relevant historical data for comparison purposes. This comparative work is highlighted in a paper published in the Lancet (summarised later) which Emily co-authored with another member of CBIS, detailing the surgical recognition and treatment of amputation related pain in military casualty.

Support Staff

The high profile and complex nature of the Centre's research requires not only academic leadership but programme management, stakeholder engagement, operational leadership and day-to-day direction. Performing this role for the Centre is **Dr Emma Burke**. After completing a PhD in explosives chemistry at Cranfield University, Emma worked as a design engineer in the defence industry before moving into a management role in academic and medical research at King's College London, home of our sister Centre for Military Health Research. It is from this role that Emma joined CBIS.

Facilities

With core facilities for the Centre provided within the various departments that house the researchers, CBIS added to the newly developed laboratories of 2013 with a specialised facility for underbelly blast simulation in the Department of Bioengineering at the South Kensington campus (Figure 2). The £1.1 million laboratory, fully funded and built by Imperial College, houses AnUBIS - the Anti-Vehicle Underbelly Blast Injury Simulator. AnUBIS is a traumatic injury simulator that replicates the response of a vehicle floor pan that has been hit with an explosive blast. Specimens can be tested on this platform, including whole cadaveric lower extremities and spinal columns as well as their equivalent commercial surrogates. Such tests can provide information on the biofidelity of surrogates, the effect of posture and loading on type and severity of injury, as well as assess current and prototype protective systems. The intention is to build upon this facility in 2015, allowing tests to be conducted at higher energy levels and with larger experimental specimens.

Figure 2: New trauma biomechanics laboratory opened in 2014.

Imperial College is building a new facility on its White City Campus ("Imperial West") to develop new engineering and medical research centres and facilities. Professor Anthony Bull and Professor Justin Cobb (Professor of Orthopaedics and Imperial's civilian lead for reconstruction) led the fundraising in 2014 for this new building. To date £40 million has been raised externally, with the full project valued at £120 million. The Michael Uren Biomedical Engineering Research Hub will provide long term security for interdisciplinary activities between engineering and medicine and the opportunity for growth for the Centre beyond the South Kensington footprint.

Exemplar Research Findings

Compressive strength after blast of sandwich composite materials

Arora H, Kelly M, Worley A, Del Linz P, Fergusson A, Hooper PA, Dear JP. (2014)
Philosophical Transactions of the Royal Society A-Mathematical Physical And Engineering Sciences, 372: 20130212.

This paper assesses the performance of structural materials in open-air field explosions. Deformation characteristics were recorded during each blast using digital image correlation (DIC) to highlight relative performance of carbon-fibre reinforced polymer (CFRP) composite-skinned polymer foam-cored sandwich panels to glass fibre-skinned (GFRP) equivalent panels. This work built on previous studies by assessing the residual strength after blast. This has not been previously considered for blast applications, commonplace in ballistic evaluation. The purpose was to give more information regarding the application of these materials in military applications. The information included was not only about 'survival' of the material, but, more importantly, to test the structurally viability in order for them to perform their requirements in terms of service loads, to enable personnel to return for repairs or to withstand further impacts.

Results confirmed that which we expected, which is that the carbon fibre structures resisted a given blast better than glass fibre equivalent targets, due to the superior stiffness and strength of carbon fibre (Figure 3). This paper, however, is concerned with the residual load bearing capacity of these targets. The carbon fibre targets saw a greater reduction in strength compared to the glass fibre targets. This was due to the severity and nature of damage caused by the 100 kg TNT equivalent at a stand-off distance of 14 m blast to each target. The research presented here shows several evaluation techniques that can be used on other materials to be used in blast environments.

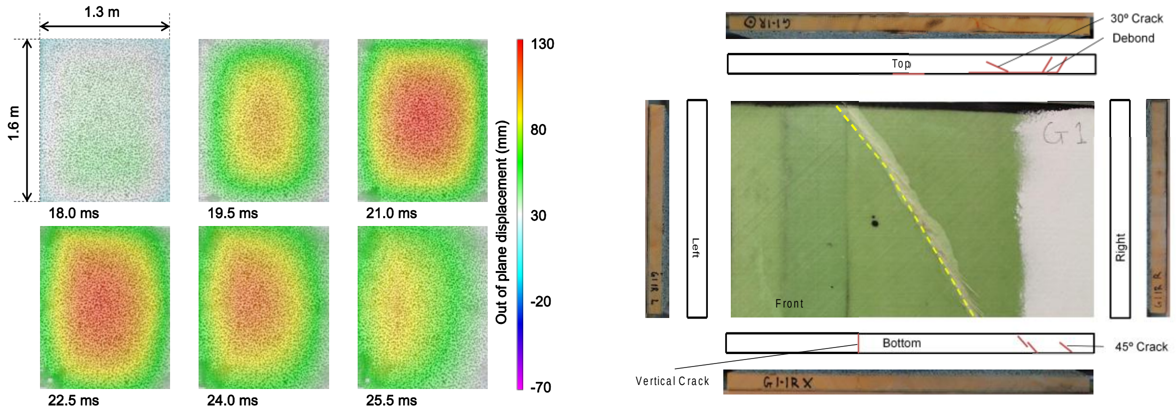


Figure 3: (a) Out-of-plane displacement of the GFRP sandwich panel using DIC; (b) Example damage in GFRP target.

How blast proof is "blast proof"?

Where a large deformation of structures is undesired, carbon fibre is favoured for blast applications. However there can be a trade-off for residual strength which must be fully evaluated for a given application's needs. This is often overlooked in engineering design as the strongest and most rigid components may not always be the optimum solution, particularly during blast when large amounts of energy may need to be absorbed.

This evaluation technique is now a core capacity for CBIS and is being applied to other materials subjected to blast.

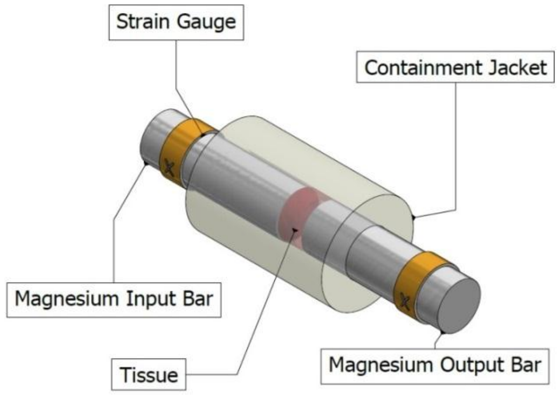
Mechanical and histological characterisation of trachea tissue subjected to blast type pressures

Butler BJ, Bo C, Tucker AW, Jardine AP, Proud WG, Williams A, Brown KA. (2014)
Journal of Physics Conference Series, 500(18),2007.

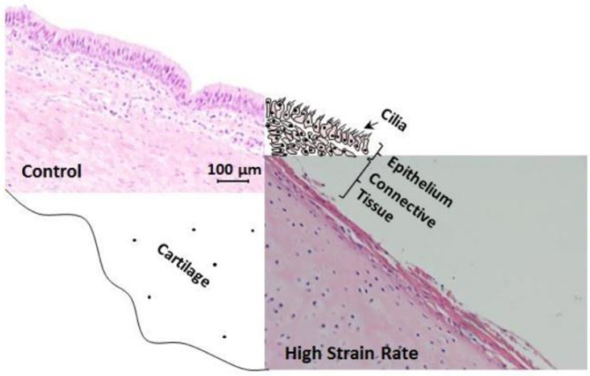
Not all respiratory tissues are equally vulnerable to injury. The purpose of our work is to investigate the material properties of multiple respiratory tissues under a range of strain rates to determine their susceptibility to compression. From this, we will be able to infer the likelihood of individual tissues succumbing to blast-type loading and thereby inform military and clinical practice.

Using a split hopkinson pressure bar system (SHPB) (Figure 4a), a reproducible compressive pulse was sent through fresh biological samples within 7 hours of harvesting. This is the first time such work has been conducted. Using the data recorded it was possible to determine a quantitative measure of the material's resistance to compression. The value obtained differed markedly from those present in the literature. Principally, we believe this reflects the fact that other groups were using samples that had deteriorated in the period between harvesting the sample and testing it. We consider our data to be representative of the response of biological tissues in a real-world scenario.

Additionally, the samples were examined using optical microscopy to highlight any structural changes resulting from high rate compression (Figure 4b). The images suggest that the distinct sub-components of respiratory tissue are not equally vulnerable to compression. The epithelial layer, which is responsible for the principal functionality of the tissue, appears most at risk.



(a)



(b)

Figure 4: (a) Schematic showing the SHPB system used to test the tissue samples. The tissue (red disc) is held between the lubricated end faces of the input and output bars. A hollow polycarbonate jacket is used to ensure biological containment of the sample throughout the test; the sample is unconfined. (b) Light photomicrographs of uncompressed trachea (control) with trachea subjected to a high strain rate (6000s^{-1}).

The response of respiratory tissue under impact

We are merging mechanical, structural and functional information to provide a complete picture of changes to the respiratory system resulting from primary blast.

Distinct sub-components of respiratory tissue are not equally vulnerable to compression.

The epithelial layer, which is responsible for the principal functionality of the tissue, appears most at risk.

A cochlear-bone wave can yield hearing sensation as well as otoacoustic emission

Tchumatchenko T, Reichenbach T. (2014) Nature Communications, 5: 4160.

Humans have two ways of perceiving sound. The first involves the well-known process of sound vibrations travelling through the middle ear to the inner ear, which is where they are transmitted to the brain. The other relies on sound being conducted through the skull bones, a process known as bone conduction, which has been poorly understood until recently.

We have developed a model that explains more clearly how bone conduction works (Figure 5). Specifically, we describe how sound, transmitted as vibrations through the skull, travels to the temporal bone, which is situated at the sides and base of the skull. The temporal bone transmits the vibrations to the basilar membrane in the inner ear and tiny bundles of hair - each finely tuned to detect sounds at different frequencies - transmit the vibrations to the brain for decoding. Understanding this process could pave the way for future clinical and industrial applications involving improvements in a range of technologies that use bone conduction to transmit sound.

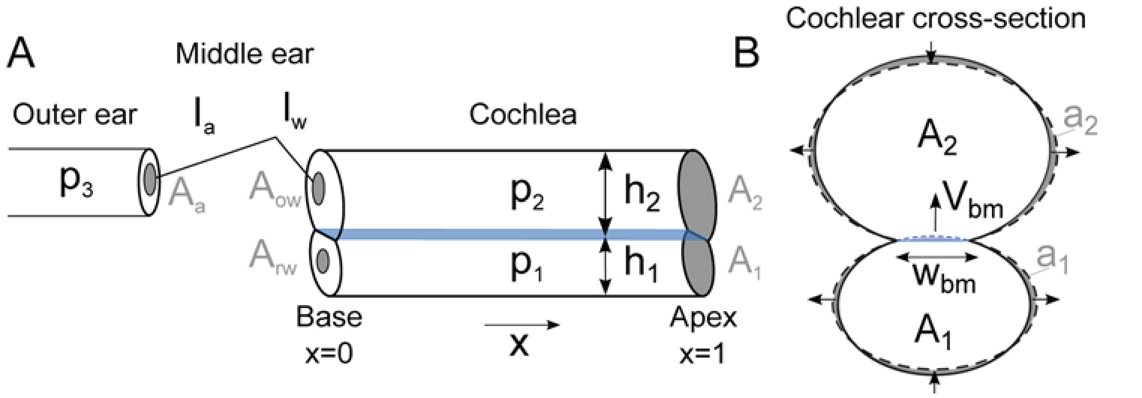


Figure 5: Anatomy of the ear. (A) Sound causes a pressure vibration p_3 in the ear canal and a motion of the ear drum (area A_a). The middle ear's ossicles, namely in the mallus of length l_a incus of length l_w and stapes convey the motion of the inner ear, or cochlea, to vibrate the oval window (area A_{ow}) and the round window (area A_{rw}). The pressures p_1 in the scala tympani and p_2 in the scala vestibule change accordingly. (B) A transverse section of the inner ear shows the basilar membrane separating two chambers of cross-sectional area A_1 and A_2. Vibration of the membrane (velocity V_{bm}) and deformation of the cochlear bone, at constant circumference, lead to area changes a_1 and a_2.

Hearing without the middle ear

Blast exposure often leads to hearing loss that can be partially treated through hearing aids. The middle ear can be impaired through blast.

Current hearing aids require a functional middle ear.

We show how stimulation of the bone around the inner ear can produce a hearing sensation. This pathway does not require the middle ear.

Future hearing aids may soon employ this principle to restore better the hearing in blast victims.

Blast injury in the spine: Dynamic Response Index is not an appropriate model for predicting injury

Spurrier E, Masouros S, Gibb I, Clasper J. Clinical Orthopaedics and Related Research, in press.

Assessment of injury risk to the spine in vehicles subjected to explosions uses a standardised mathematical model, the Dynamic Response Index (DRI). The DRI was intended for evaluating aircraft ejection seats and has not been validated in blast conditions. It has been suggested that the DRI is not suitable for blast as well as ejection injury, because the mechanisms and patterns of injury are significantly different. We compared patterns of injury in blast and ejection to see if there was any similarity. The hypothesis is that if the injury *patterns* are different, then the *mechanisms* are different and a unique injury prediction model should be used for each situation.

We compared the injury patterns in UK victims of blast with the injury patterns in aircraft ejection seen in the literature. The distribution of injuries between blast and ejection was not similar (Figure 6). In the cervical spine, the relative risk of injury is 11.5 times higher in blast; in the lumbar spine the relative risk is 2.9 times higher in blast. In the thoracic spine the relative risk is identical in blast and ejection. At most individual vertebral levels including the upper thoracic spine there is a higher risk of injury in the blast population, but the opposite was true between the T7 and T12 section of the thoracic spine, where the risk is higher in aircraft ejection. The patterns of injury in blast and aircraft are different, suggesting that the two are mechanistically dissimilar. The differences in relative risk at different levels, and the resulting overall different injury patterns, suggest that a single model cannot be used to predict the risk of injury in ejection and blast.

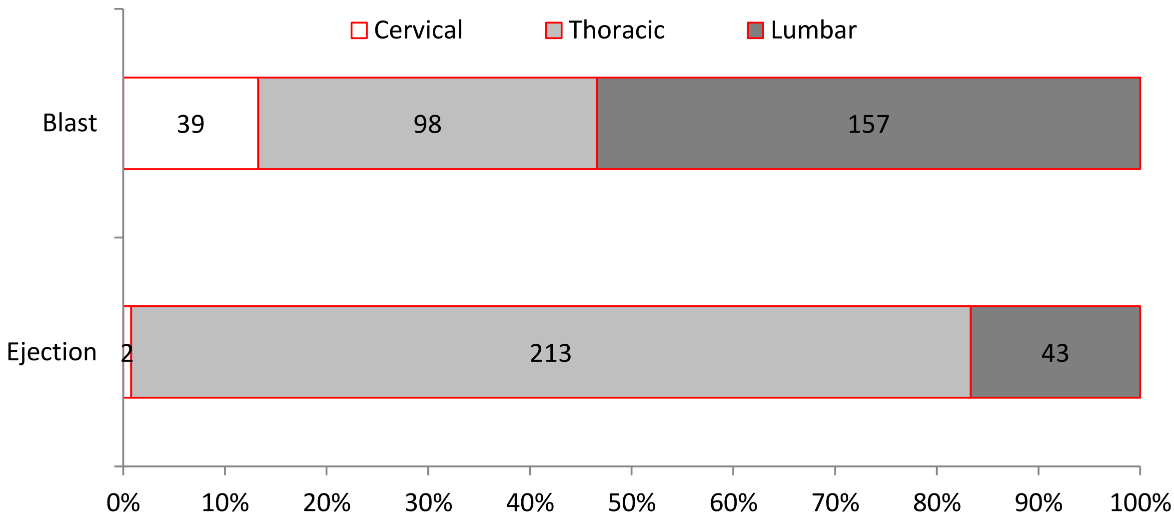


Figure 6: Number of fractures in the spinal column between blast and aircraft ejection casualties.

The current predictor for spinal injury in blast is invalid

Ejection and blast injury in the spine have different patterns.

The mechanisms of injury are likely to be different.

A new model of injury risk in blast needs to be developed to aid design of mine-protected vehicles for future conflicts.

UK combat-related pelvic junctional vascular injuries 2008-2011: implications for future intervention

Walker NM, Eardley W, Clasper JC. (2014) Injury, 45(10): 1585-1589.

Haemorrhage is the most common cause of potentially survivable death on the battlefield. Recognition of the importance of haemorrhage as a possible remediable cause of death has led to the development of a paradigm shift in battlefield trauma management. Priority has been given to the control of catastrophic haemorrhage from the limbs with the introduction of tourniquets. However, bleeding may also result from injuries that are deemed too 'high' for a tourniquet; the junctional areas such as the groin or axilla. In a US study, 297 of 6450 (4.6%) military coalition deaths over a ten year period (2001-2010) were reported to be due to junctional bleeding. The authors suggested that some of these deaths could have been avoided with the use of a novel junctional haemorrhage control device to apply pressure in the groin.

We reviewed the UK experience of death related to junctional bleeding (Figure 7). Prospectively collected data on all injuries sustained in Afghanistan by UK military personnel from 1st August 2008 to 31st July 2011 were reviewed using the UK Joint Theatre Trauma Registry. All fatalities with significant pelvic injuries were identified and analysed, and the cause of death established to assess the potential role for a junctional haemorrhage control device.

Significant upper thigh, groin or pelvic injuries were recorded in 125 casualties, of which 93 died. Of these 93, pelvic injury was the cause of death in 37, but only 1 casualty with potentially survivable injuries was identified where death was due to a vascular injury below the inguinal ligament, not controlled by a tourniquet. This represents <1% of all deaths in this period, a lower figure than previously published. We further identified 32 casualties where the cause of death was due to a vascular injury between the aortic bifurcation and the inguinal ligament. Eight of these survived to a medical facility but subsequently died of their wounds. These represent a subset in which vascular control proximal to the inguinal ligament could have altered the outcome.

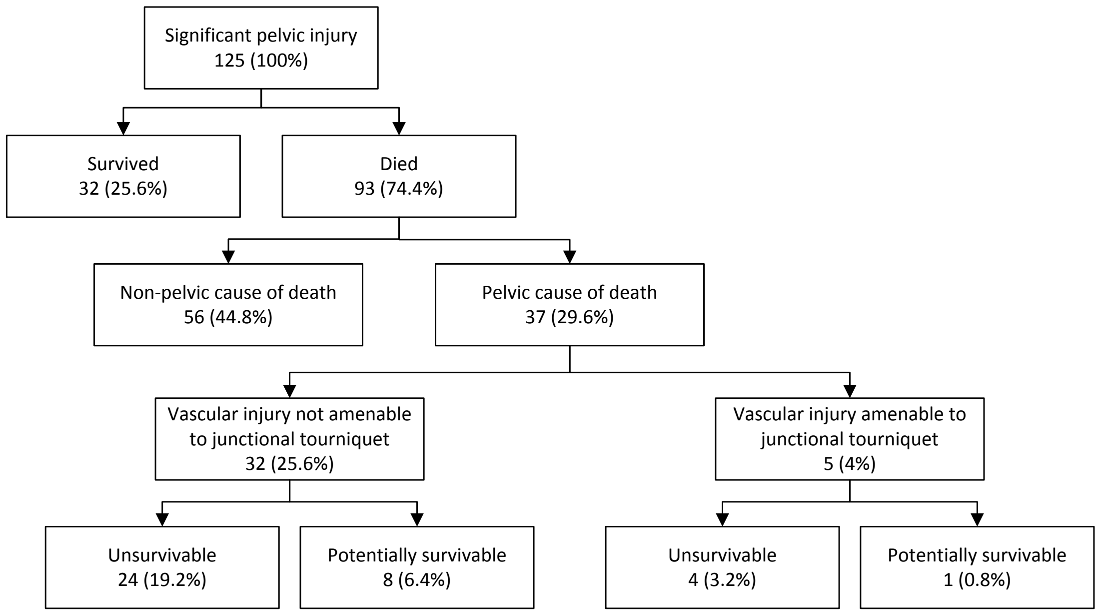


Figure 7: Flowchart of all UK casualties with significant pelvic trauma from Afghanistan over a 2-year period.

Controlling pelvic bleeding

Some deaths due to exsanguination may be amenable to proximal vascular control.

Use of a groin junctional tourniquet is not likely to achieve this.

There may be a role for more proximal vascular control of pelvic bleeding.

Strain-rate sensitivity of the lateral collateral ligament of the knee

Bonner TJ, Newell N, Karunaratne A, Pullen AD, Amis AA, Bull AMJ, Masouros SD. (2014)
Journal of the Mechanical Behavior of Biomedical Materials, 41: 261-270.

Tensile tests on ligament at strain rates from 0.01 to 100/s were conducted. A screw-driven uniaxial testing machine was used for tests at the first two strain rates, a servo-hydraulic uniaxial testing machine was used for the tests at 1/s, and a drop-weight testing machine with a custom-made impact tensile adaptor (Figure 8a) was used for tests at 10 and 100/s. For all tests video extensometry, utilising high speed photography, was employed to calculate strain using multiple dots (Figure 8b) that were made across the ligament with permanent black ink immediately prior to testing. The results demonstrate that ligament tissue is sensitive to strain rate at lower strain rates, and that this effect reaches a threshold at approximately 1/s, beyond which a further increase in strain rate does not affect the material properties (Figure 8c).

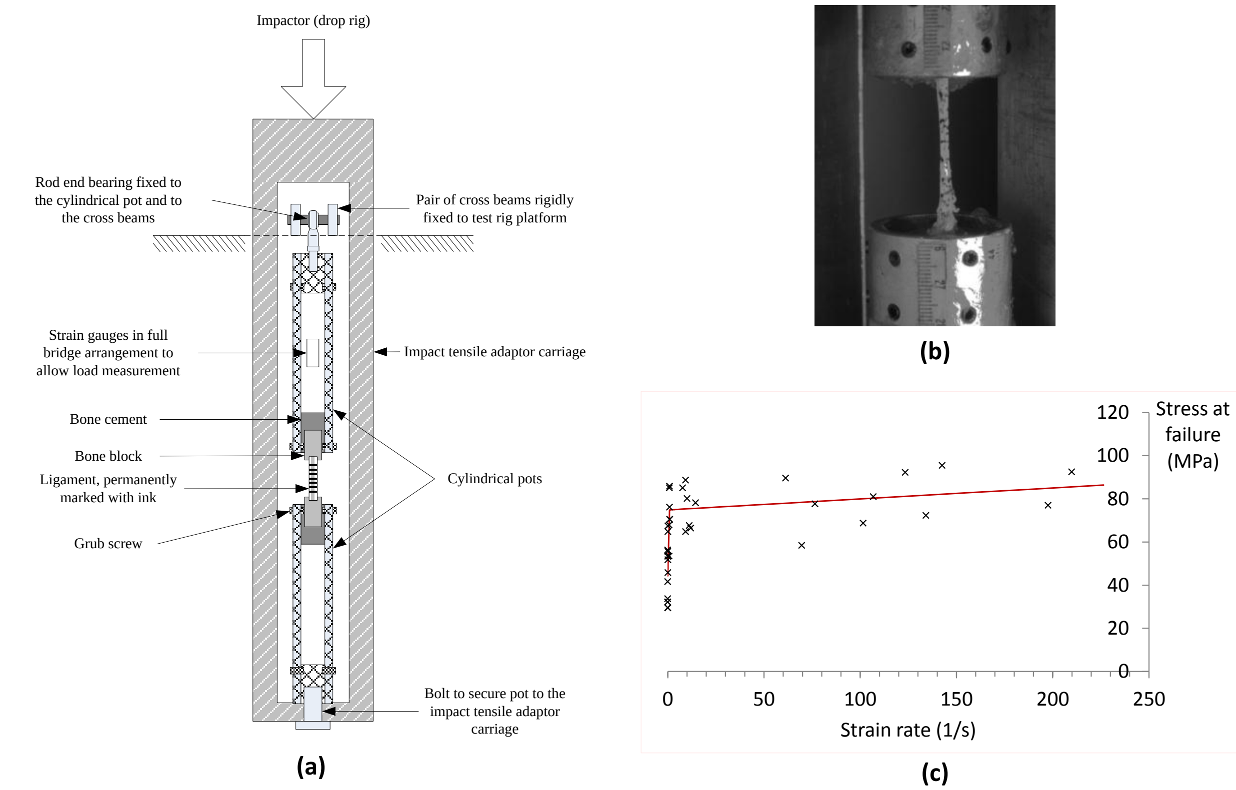


Figure 8: Ligament testing across strain rates. (a) Schematic of the apparatus for the drop-tower tests showing our custom-made impact tensile adaptor. (b) A ligament sample held within pots (top and bottom) and stained with ink to measure strain during testing with a high speed video camera. (c) Stress at failure (or strength) of the ligament across strain rates; the red line through the data points is the line of best fit.

In addition, X-ray diffraction was performed and testing conducted to measure the contribution of collagen-fibre deformation to the overall deformation of the ligament. It was found that this contribution diminishes as the strain rate increases, suggesting intra-fibrillar sliding at high strain rates due to early debonding of the ligament's matrix.

Ligament material behaviour at injurious conditions

Ligaments are sensitive to loading rate up to a threshold.

For rates up to 1/s the stiffness and strength of the ligament increases.

Beyond rates of 1/s, stiffness and strength remain relatively constant.

This information can be used readily into computer models that simulate the behaviour of human joints in blast.

Gait compensations in rats after a temporary nerve palsy, quantified using dynamics and kinematics

Eftaxiopoulou T, Macdonald W, Britzman D, Bull AMJ. (2014) Journal of Neuroscience Methods, 232: 16-23.

About 12.9% of extremity injuries sustained after a blast are associated with peripheral nerve injury, the effects of which can range from motor or sensory disturbance to a painful neuroma. *In vivo* models have been used for investigating neurological insults. Most of these neurological conditions are accompanied by gait changes so a good understanding of the details of the limb movements during locomotion can provide an objective measure for nerve dysfunction and recovery. *In-vivo* systems such as Digigait™ (Mouse Specifics, Boston, MA) have been developed to assess temporo-spatial parameters in animal models. A high-speed digital video camera mounted below a transparent treadmill belt continuously images the underside of the walking animals, interrogates each individual frame for the presence of paw contact and then identifies the portions of the paw in contact with the treadmill belt in the stance (time in which the paw remains in contact with the belt) and swing (time in which the paw is not in contact with the belt) phase of the stride. In addition, angular displacements which describe the motion of the joints are typically measured by filming an animal with markers fixed over chosen bony landmarks during walking. Both temporo-spatial parameters and kinematic analyses are well established individually, however, the two techniques have not previously been used in combination. In this study it was our aim to (a) assess the effect of lower speeds on kinematic angles and (b) to combine kinematic analysis with the simultaneous data provided by DigiGait to give more accurate measures of activity and Peripheral Nervous System function.

The gait of five female Sprague-Dawley rats was assessed at different speeds using an optical motion tracking system (Vicon, Oxford, UK) and the DigiGait™ imaging system during normal locomotion, shortly after temporary nerve block to the left hind limb (30 min post injection) and after recovery (90 min post injection). Results showed that the classification of gait changes due to injury improved using both dynamic and kinematic parameters, providing valuable information about the compensation methods adopted by rats after a nerve injury (Figure 9a). Finally, baseline data of normal rat locomotion were acquired, showing that comparisons across speeds are possible as long as speed variations are small (Figure 9b).

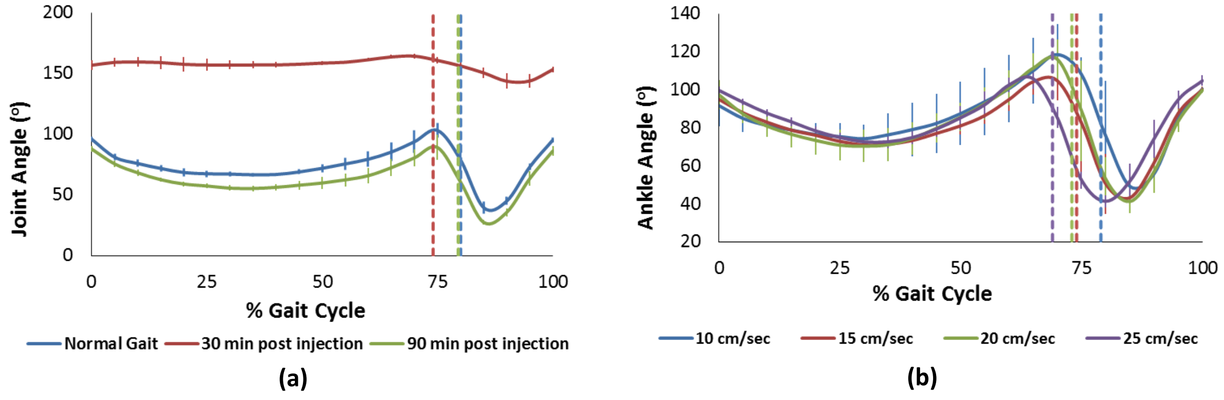


Figure 9: Mean flexion (-ve) / extension (+ve) angles and standard deviations for the left ankle joint during treadmill locomotion of one rat during (a) normal, impaired gait, and recovery and (b) during normal locomotion at different speeds. The vertical dashed line marks the stance-swing transition.

A new method to analyse nerve dysfunction

Using gait dynamic analysis and joint kinematics simultaneously is a more reliable method than using them in isolation for the quantification of healthy and impaired gait.

This method can be used to assess nerve dysfunction and recovery after blast trauma and to develop or improve therapeutic strategies.

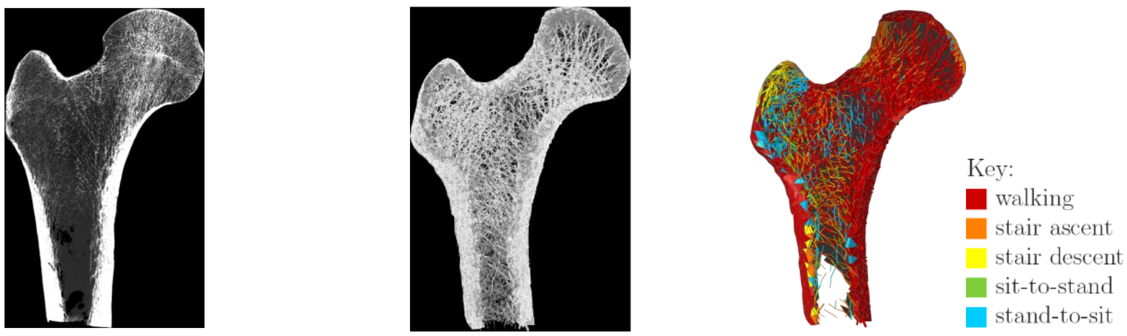
Femoral bone structural architecture prediction using musculoskeletal and finite element modelling

Phillips ATM, Villette CC, Modenese L. International Biomechanics, accepted for publication.

This paper details the development of a structural model of the femur (thigh bone) in which the trabecular (spongy) bone is represented as a network of truss elements (rods) and the cortical bone is represented using shell elements (plates). The model is developed based on the established hypothesis that the bone adapts based on the loading that it is subjected to, with the geometry of the truss and shell elements being altered according to the mechanical environment that they are placed in for a variety of daily living activities; including level walking, walking up and down stairs, sit-to-stand and stand-to-sit. This is done using a computational technique known as finite element analysis, commonly used in structural engineering to assist in understanding the mechanical behaviour of complex structures.

It is not possible to measure directly muscles forces that load bone. It is also not possible to measure directly the joint contact forces that load the bone at the hip and knee joints, without an invasive implantation procedure. Hence, another computational technique known as musculoskeletal modelling is used to predict muscle and joint contact forces force that are required as inputs to the finite element model. This technique uses kinematic and kinetic data recorded for a subject in a specialist gait laboratory. Reflective markers are tracked by a number of infrared cameras to record movement, in a similar set-up to that used to allow actors to interact with computer generated imagery (CGI) in films and games. Force plates, similar to, but more sophisticated and accurate than a Wii-fit board, are used to record the forces acting on the subject through interaction with the environment, for example the forces acting on their feet when walking. These forces are used as inputs to drive the adaptive finite element model, resulting in a structure which compares well to medical images of the internal structure of the bone (Figure 10).

One application of the developed structural model is the additive manufacture (3D printing) of frangible (breakable) bone surrogates for use in testing, as a replacement for human cadaveric material. The structural model is more suited to this than some traditionally-used computational models of bones which treat the structure as a solid mass of material, as predicting the progression of a fracture in a solid model is computationally demanding.



(a) (b) (c)

Figure 10: (a) medical imaging scan of the femur (b) predicted structure using the tools developed here (c) colour map of the activities that are important in determining the bone structure.

Building of geometrically accurate surrogate bones

A technique has been developed to recreate the internal intricate structure of bone on a computer.

These structures can then be physically created using rapid prototyping.

These prototype structures provide geometrically accurate surrogates for the assessment and development of blast protection.

Surgical advances during the First World War: the birth of modern orthopaedics

Ramasamy A, Eardley WG, Edwards DS, Clasper JC, Stewart MP (2014)
<u>Journal of the Royal Army Medical Corps</u>, in press.

The First World War (1914–1918) was the first industrial conflict in history and the first conflict where artillery bombardment was used on a large scale. In 4 years more than 750,000 British troops died and 1.6 million were injured. It is believed that the legacy from WW1 is over 40,000 veteran amputees.

To cope with the new profile of injuries seen, doctors on both sides were required to develop new skills and techniques *in situ*. Many of those techniques and systems formed the foundation of modern orthopaedic trauma management. This study examines the significant advances in wound management, fracture treatment, nerve injury and rehabilitation that occurred during the war.

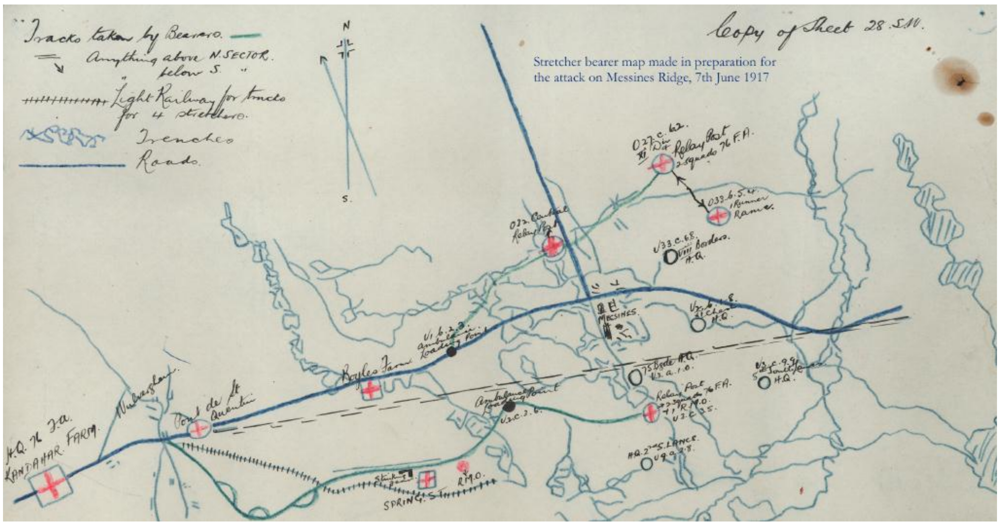


Figure 11: Casualty evacuation map during the First World War.

One hundred years on, strong comparisons can be drawn between the fighting and injuries in the conflicts of Afghanistan, and those sustained during World War 1. This study demonstrates that significant lessons can be learnt; a message which is key to the mission of CBIS. Comparisons to previous wars are an important process to evaluate medical and scientific advances.

20th Century weaponry versus 19th Century surgical principles

The principles of wound debridement and early fracture stabilisations developed during the war remain the cornerstone of modern military surgical practice.

The development of Orthopaedic Centres and Curative Workshops laid the foundations for modern orthopaedic care and rehabilitation.

“Doomed to go in company with miserable pain” A comparative study of post-amputation pain conditions in casualties from the Great War and 21st century conflicts

Edwards DS, Mayhew ER, Rice ASC (2014) Lancet, 384(9955):1715-1719.

The principal feature of injuries from the Great War was musculoskeletal trauma and injury to peripheral nerves as a result of damage to the upper and lower limbs caused by gun-shot wounds and fragments of artillery munitions. Amputation was used as a treatment in field hospitals to save lives; limb conservation was a secondary consideration. A cohort of 41,000 amputee patients was created, the largest ever seen in British medical history. A century later, the principal feature of injuries to soldiers in today’s wars in Iraq and Afghanistan is also musculoskeletal trauma and injury to the peripheral nerves caused by improvised explosive devices. Common to both types of injury is post-amputation pain, both in the residual limb stump and also the phantom pain/sensation experienced in the missing limb.

An interdisciplinary team collaborated during 2014 to research the subject: Professor Andrew Rice (consultant in pain management in the department of Surgery and Cancer, Imperial College/Chelsea and Westminster), Major Daffyd Edwards (TRBL Centre for Blast Injury Studies) and Dr Emily Mayhew (historian in residence, Department of Bioengineering). Their search of *The Lancet’s* own archives revealed the concerted efforts of surgeons in WW1 to understand and treat post-amputation pain in its own right. Yet, despite unprecedented patient numbers and levels of civilian medical expertise, little progress was made in providing relief from this type of pain, a grave concern to the surgeons treating these soldiers.

Today post-amputation pain is understood beyond a surgical context but remains a complex and poorly understood condition with few effective treatments. Pain as the chief legacy of war remains a constant, and should not be forgotten in the 21st century.

Pain is the legacy of all human conflict

Post-amputation pain in all its forms occurs with the same frequency and outcomes in wars a century apart. It remains a significant challenge for patients, medics and scientists.

Modern treatment strategies, advocated for management of postamputation pain in the context of military rehabilitation, focus on comprehensive multidisciplinary assessment and individualised multimodal treatment.

Evidence from robust randomised controlled trials supporting any therapeutic intervention in the treatment of postamputation pain is limited.

High-quality research into interventions for post-amputation pain is urgently needed.

Heterotopic ossification: a systematic review

Edwards DS, Clasper JC. (2014) Journal of the Royal Army Medical Corps, in press.

Heterotopic ossification (HO) is the ectopic formation of mature lamellar bone in non-osseous tissue, such as muscle, tendon and ligament. Its prevalence in the military setting is higher than the civilian setting and it continues to cause problems during rehabilitation and prosthetic use in injured personnel. The heterogeneous nature of a blast related amputation makes it difficult for a single aetiological event to be identified, although it is now accepted that the following are significant factors in HO formation: blast, amputation through the zone of injury, increased injury severity and associated brain injuries. However, the exact cellular event leading to HO has yet to be identified.

Using Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines, a systematic review of the PubMed and Cochrane Databases was undertaken to identify research articles in the last 100 years relating to HO. Initially 7891 articles were identified but were reduced to 637 after refining the search using the primary, secondary and manual exclusion strategies (Figure 12).

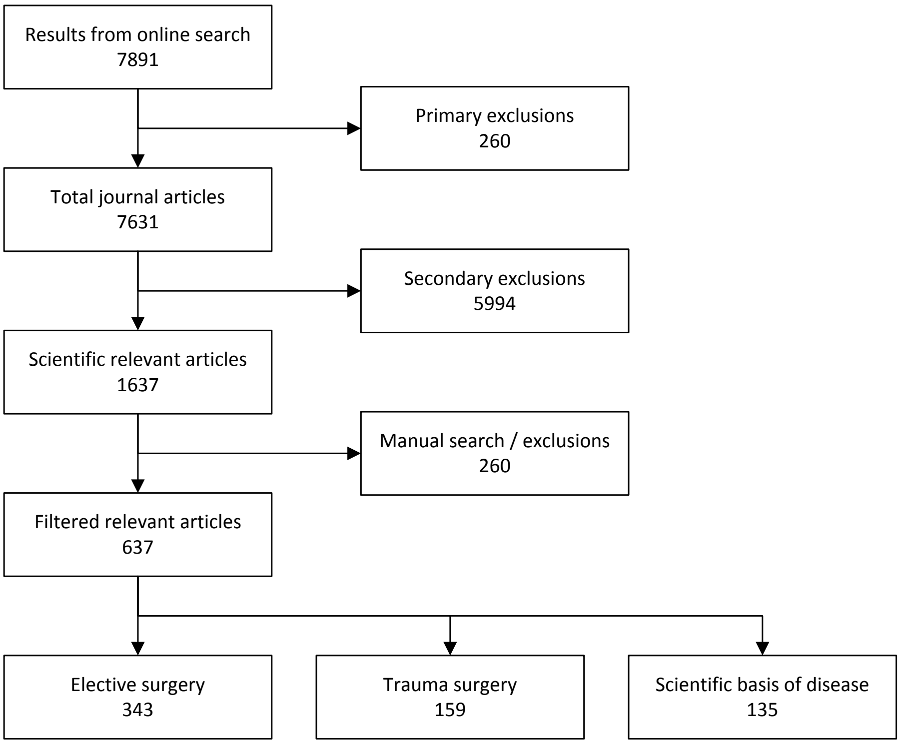


Figure 12: Flow chart of the review process.

Of the articles published, three distinct groups of research were evident: elective surgery, trauma surgery and the scientific basis of disease. These represented 54%, 25% and 21% of the articles, respectively. The most common publication subject was that of HO related to hip arthroplasty (n=218, 34.2%). Only 26 articles were found to be referring to HO in the military trauma setting. A limitation found was a change in nomenclature of HO. Terms such as ectopic bone formation, myositis ossificans and heterotopic ossification have been used interchangeably in history. This review highlighted current research concepts and experimental theories regarding HO which serve as a gap analysis providing detail the knowledge deficit in this field, in particular related to military aspects of HO.

Heterotopic Ossification is ill understood

There are significant gaps in the understanding of Heterotopic Ossification.

Work is required in this field to fully understand HO pathogenesis.

HO will continue to compromise the rehabilitation and long-term outcome of the cohort of traumatic amputees from operations in Afghanistan and Iraq.

Research Updates

Blast Biology and Therapeutics

Heterotopic Ossification

Introduction

The exact trigger of HO remains elusive. Determining mechanisms involved in its onset are pivotal in order to design targeted interventions to treat HO. Although cellular and molecular pathways underlying the onset of HO are not yet fully understood, it has recently been suggested that mesenchymal stem cells (MSCs) might be involved in this process. We have therefore designed experiments to investigate whether primary blast injuries affect the activity of these stem cells. Our research plan for understanding HO is shown in Figure 13.

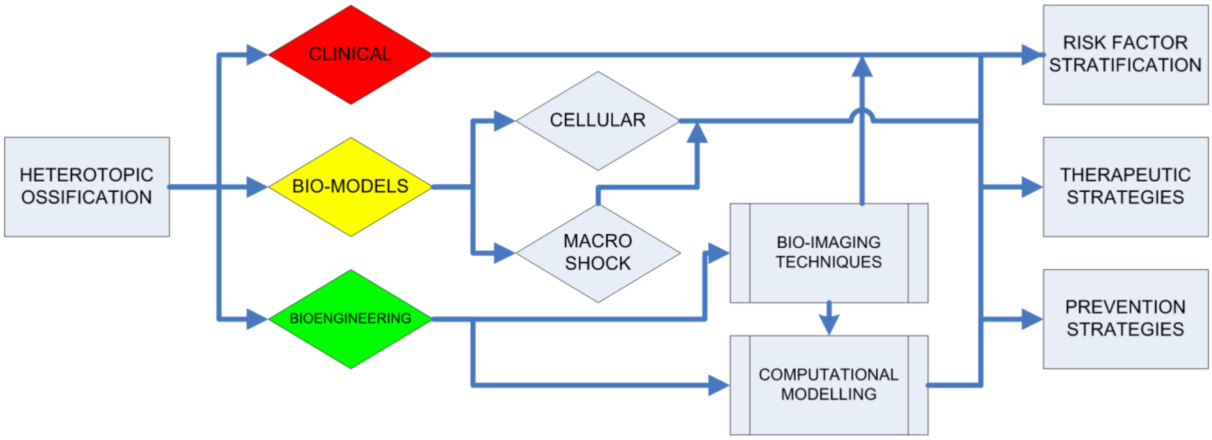


Figure 13: Heterotopic Ossification research process

Clinical data

Edwards D, Clasper JC.

We have undertaken a systematic review of HO detailed in the study described on the previous page. The entire amputee cohort from Afghanistan between 2003 and 2014 is 265 with 416 amputations (average 1.6 limbs per casualty). Compared to previous conflicts this is a greater number of limbs lost. The mechanism of injury in the majority was blast (255 out of 265). Risk factors identified for the formation of HO included blast, high injury severity score, multiple extremity injuries and transfemoral injuries. We have also been able to access clinical data from the small cohort of amputees from the 7/7 bombings. HO is found in 80% of amputees from blast within the tube compartments in London.

Bio-imaging and mechanical analysis

Edwards D, Karunaratne A, Clasper JC, Bull AMJ.

CBIS has established a Cooperative Research and Development Agreement (CRADA) with the Naval Medical Research Centre based in Silver Spring, Maryland. Through this, CBIS researchers have been granted access to HO removed from blast injured US service personnel. We have begun initial assessment and mechanical testing of the samples at the gross, macroscopic, microscopic and nano-scale levels to allow us to identify differences between HO and normal bone.

Cellular analysis in physical models

Amin H, Eftaxiopoulou T, Rankin S.

Sprague-Dawley rats were anaesthetised and exposed to a simulated primary blast insult using the CBIS shock tube at 200 kPa of pressure. The pressure wave was directed only onto the left hind limb while the rest of the body was protected. Two stem-cell compartments, femur bone marrow (both injury/sham and contra-lateral) and blood were collected for analysis 24 hours after trauma. Stromal/stem cells were extracted from the bone marrow and peripheral blood, and the presence of mesenchymal stem cells (MSCs) in bone marrow and blood was assessed by colony-forming unit assays (CFU). The ability of a single cell to form a colony of cells has been recognised as an important characteristic of stem cells, thus the number of CFUs directly represents the number of progenitor/stem cells.

Notably, animals subjected to shock wave exhibited significantly increased (1200%; $p<0.05$) levels of MSC in blood (shown as increase in CFU-Fs), compared with control conditions (Figure 14a). In contrast, there was a marked reduction (90%; $p<0.05$) in CFU-Fs from femur bone marrow MSC of injured limb, compared with control/sham subjects. Interestingly, a similar effect was also seen in the contra-lateral site, suggesting an apparent systemic effect of limb trauma (Figure 14b). Stem cells were subsequently grown in culture and then stimulated to turn into osteoblasts using a medium that favours bone formation. As shown in Figure 14c femur bone marrow MSC from the both injury and contra-lateral sites formed more Calcium-rich bone-like mineralised nodules (indicated by red stain), compared with cells isolated from control animals.

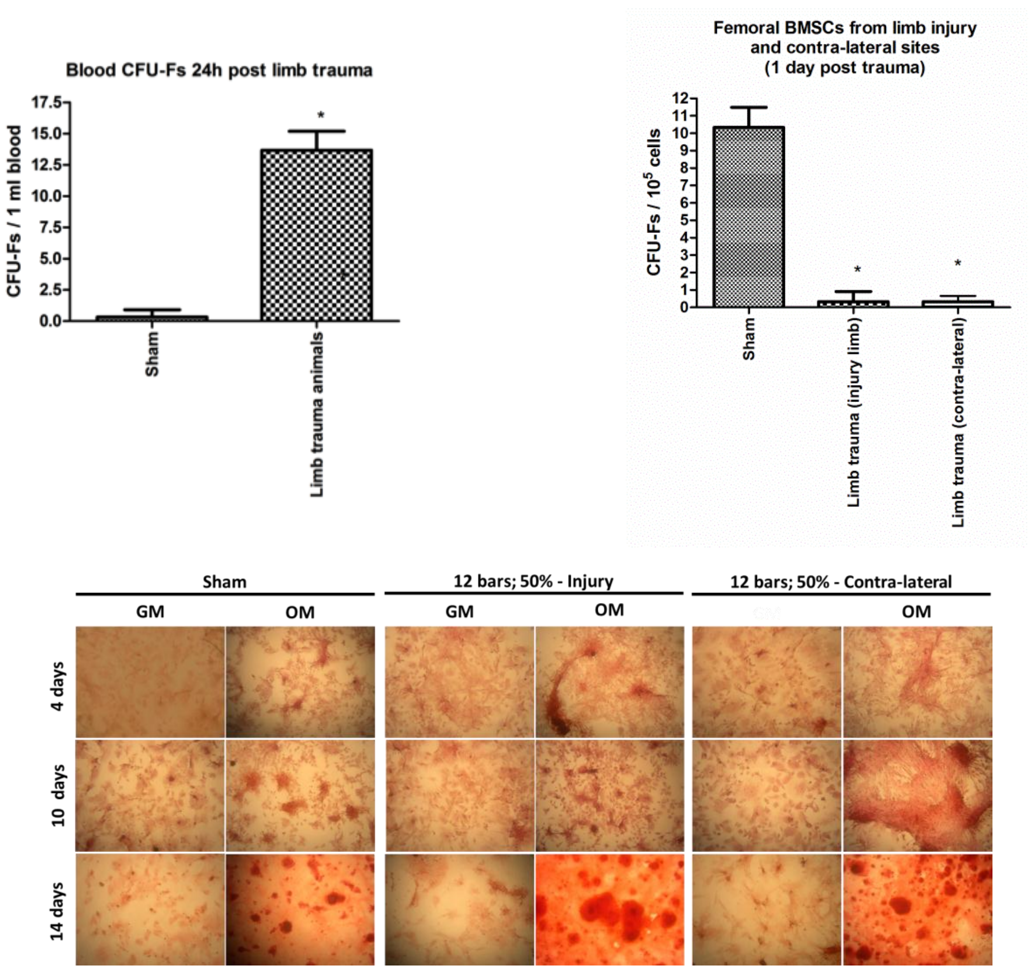


Figure 14: Effects of limb trauma on (a) CFU-Fs from blood, (b) CFU-Fs from bone marrow, and (c) terminal osteogenic differentiation of femur marrow-derived stromal cells. *significant ($p<0.05$)

These results suggest that: (i) traumatic limb injury mobilises MSC/stromal progenitor cells into blood; (ii) MSC numbers are reduced in bone marrow after traumatic injury, possibly by mobilising into the blood stream; (iii) reduction in CFU-Fs from the contra-lateral femur bone marrow suggests a systemic response post limb trauma; (iv) increase in the ability of femur marrow MSC to form mineralised nodules suggests that cells have a higher osteogenic potency after trauma. Further, cells from the contra-lateral sites also showed a similar osteogenic response suggesting a systemic response after trauma.

Blast Lung Injury

Rankin S, Arora H, Eftaxiopoulou T, Barnett-Vanes A.

Introduction

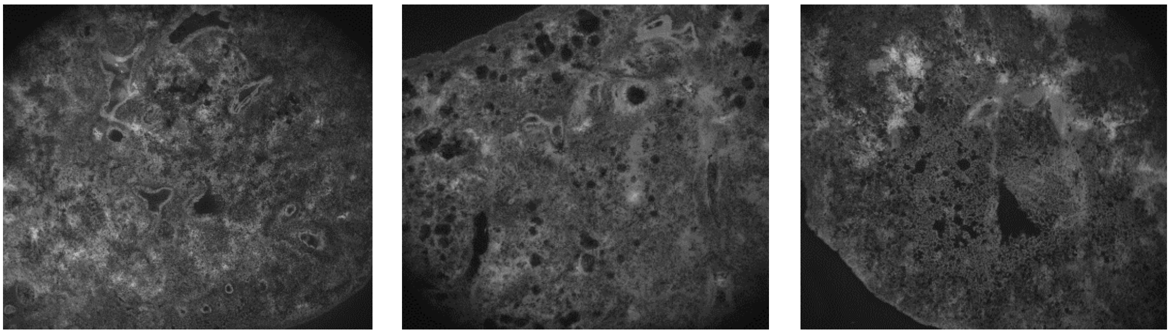
Soft air-filled organs, such as the lungs, are deemed the most vulnerable to blast. Shock wave interactions with the human body can cause significant immediate and long term damage to the lungs. Severe injuries such as alveolar haemorrhage, emphysema, pneumothorax and parenchymal lacerations have been identified as the immediate detectable physical injuries observed in the clinical setting of blast lung. More subtle injuries, however, can develop such as swelling, inflammation and loss of lung function in response to less severe blast exposure, which can go undetected in the immediate assessment of a patient. The aim of the research conducted within CBIS is to determine the exact mechanisms of injury development. A summary is given here of the experiments conducted focussing on structural response of lung architecture to blast and the development of *in vivo* models to investigate inflammation of the lungs due to distal and direct thoracic blast loading.

Imaging studies of blast lung

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 implications for lung injury. Freshly excised lung was taken from Sprague-Dawley rats (250-300 gr). They were then potted in a gel medium to promote homogenised stress state during shock loading and allow for transmitted pressure measurements to be made. The lungs were subject to focussed shock waves produced using the CBIS shock tube. There were also a series of *in situ* studies conducted on the shock tube with the shock isolated to the thorax of cadaveric specimens. The lungs in these cases were recovered for histological studies post-test alongside the excised lung for comparison.

There were clear damage patterns observed from both *in situ* and tissue studies. Whole organ histology imaging was conducted using an in-house optical microscopy slice imaging tool (Figure 15). Sample preparation methods established previously were employed to stain the tissue and embed all samples in wax to create clean images of lung tissue.

The effect of shock wave intensity was shown through the increased volume of damaged tissue present in the sectioned organs. This was observed beyond a threshold of 1 bar incident reflected pressure. This imaging study can allow for new insight into the source of damage within the lung tissue such as capillaries or air-spaces. This work has provided baseline mechanical measurements, which are to be built on in terms of qualitative injury profiling through imaging.

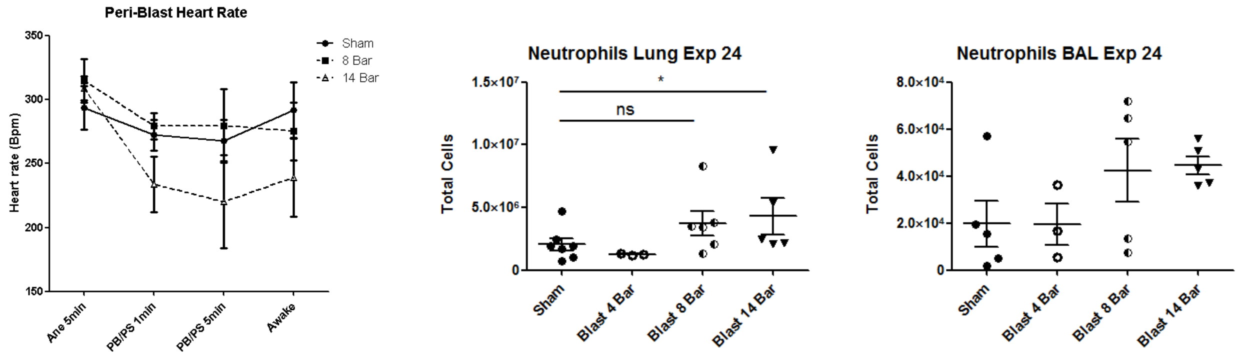


(a) **(b)** **(c)**

Figure 15: Example images taken of: (a) un-blasted lung; (b) blasted excised lung; and (c) blasted in-situ/cadaver lung tissue.

Biological response due to a simulated blast insult to the thorax.

A new experimental apparatus was developed to subject the thorax in isolation to primary blast waves utilising the CBIS shock tube. As lung tissue is particularly sensitive to primary blast injury the effect of escalating the intensity of the blast overpressure was first investigated before longer impulses were trialled. Rats were subjected to 4, 8 and 14 bar operating (burst) pressure. As in the limb model above, a bradycardia was observed in rats subjected to thoracic blast that was directly related to the intensity of blast overpressure (Figure 16). At 24 hours after blast, the lungs were lavaged and a lobe processed for flow cytometry. In both 8 and 14 bar blasts, neutrophils increased in the lung, with the latter reaching significance. Increases were also seen in the broncho-alveolar lavage fluid of rats subjected to 8 and 14 bar at 24 hours.



(a) **(b)** **(c)**

Figure 16: Data summary for direct thoracic simulated blast loading: (a) Changes in heart rate caused by exposure to blast waves; (b) Levels of neutrophils in the lung; (c) Levels of neutrophils in the broncho-alveolar lavage.

Summary

We have developed rodent models of primary blast injury such that we will allow us to investigate the inflammatory response at a cellular and molecular level, with a view to identifying novel biomarkers or therapeutic targets.

Development of a model of primary blast limb trauma

Eftaxiopoulou T, Barnett-Vanes A, Arora H, Nguyen T, Harsh A, Bull AMJ, Rankin S.

Given the clinical burden of lower limb blast injuries, very few experimental models have been reported relating to blast limb trauma. Those that have, have shown that explosive limb injury may lead to systemic inflammatory changes affecting the limbs in addition to sites such as the lungs or kidneys. However, the injury documented in these models is severe, encompassing several blast injury mechanisms. This section summarises the experiments conducted to investigate the response of the peripheral nervous system to mild primary blast waves directed to the hind limbs, specifically investigating the effect of changing the magnitude or duration of the blast wave on this response.

Hind limbs of adult Sprague-Dawley rats were subjected to 3 types of focal isolated primary blast waves of varying overpressure and duration as seen in Table 1 utilising the CBIS shock tube and a purpose built experimental rig (Figure 17).

Burst Pressure (bar)	Driver Volume Used	Peak Pressure (bar)	Plateau Pressure (bar)	Impulse (bar ms)	Duration (ms)
6.0	10%	1.85 ± 0.10	0.55 ± 0.05	0.69 ± 0.10	3.0±0.3
16.0	10%	3.65 ± 0.30	1.68 ± 0.20	2.23 ± 0.20	3.5±0.5
6.0	100%	2.59 ± 0.05	1.17 ± 0.05	10.00 ± 0.60	11.5±0.5

Table 1: Summary of average burst pressure and corresponding peak pressure, plateau pressure and shock impulse (relative to ambient pressure) for three loading scenarios (mean data and standard deviations for each condition are from 3 individual experiments).

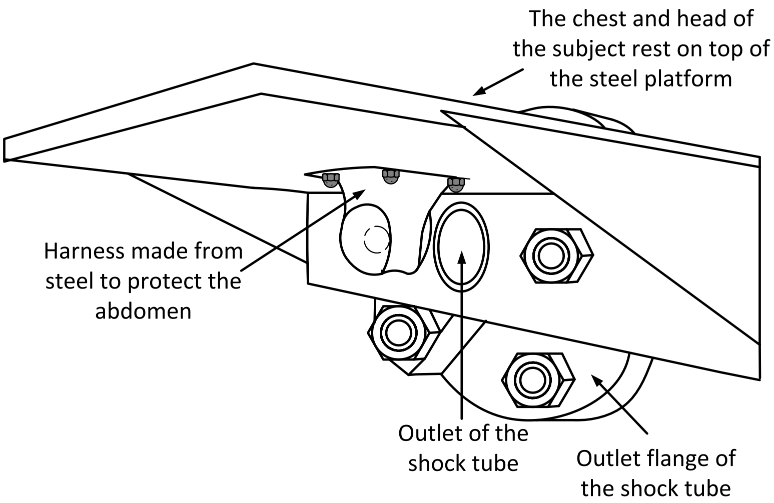


Figure 17: Purpose built rig for rat hind limb primary blast *in vivo* experiments. The rig is bolted in the outlet of the CBIS shock tube to isolate the shock wave to the left hind limb whilst shielding the rest of the animal.

Immediately after blast, a characteristic transient bradycardia was observed in the blast groups that were more notable at the highest overpressure (Figure 18). Systemic inflammation was measured by levels of circulating inflammatory white cells (neutrophils) and the inflammatory cytokine (IL-6) (Figure 19). At 6 hours an increase in both neutrophils and IL-6 was observed in rats subject to 6 bar burst pressure with 100% driver volume. No visible damage was seen in muscle or liver by histology. By 24 hours the inflammatory parameters had normalised.

The normal walking patterns (gait) of the rats were also evaluated 1 week before exposure to a shock wave and on a weekly basis after the exposure, for up to four weeks. Results showed that there were no significant differences between the left and right hind-limbs for any of the gait parameters assessed (Figure 20) suggesting that the selected pressure magnitudes did not elicit an adequate effect on the peripheral nerves. This was further supported by the low levels of Substance P (SP) (Figure 21) measured 24 hours following exposure.

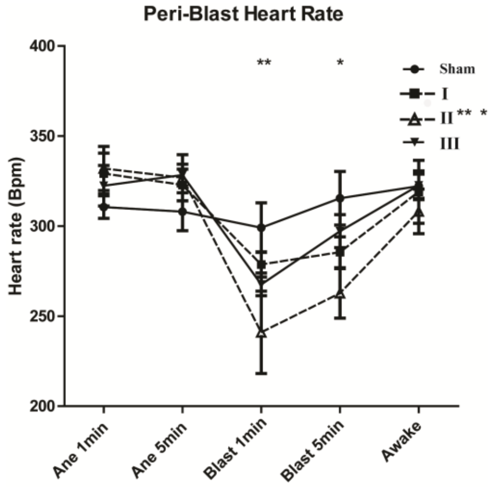


Figure 18: Changes in heart rate caused by exposure to blast waves. Heart rate (bpm) measurements collected at different time points of: 1 and 5 mins after anaesthesia was induced (Ane 1 min and Ane 5 min), immediately after blast (Blast 1 min), 5 min post exposure (Blast 5 min) and once the subjects recovered (10-20 min after the blast).

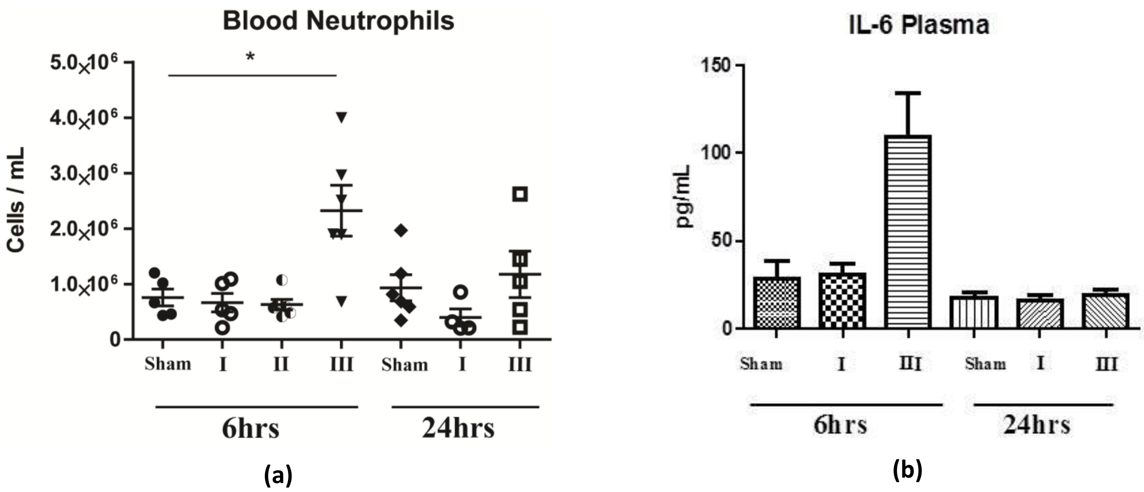


Figure 19: (a) Circulating levels of blood neutrophils and (b) plasma levels of IL-6.

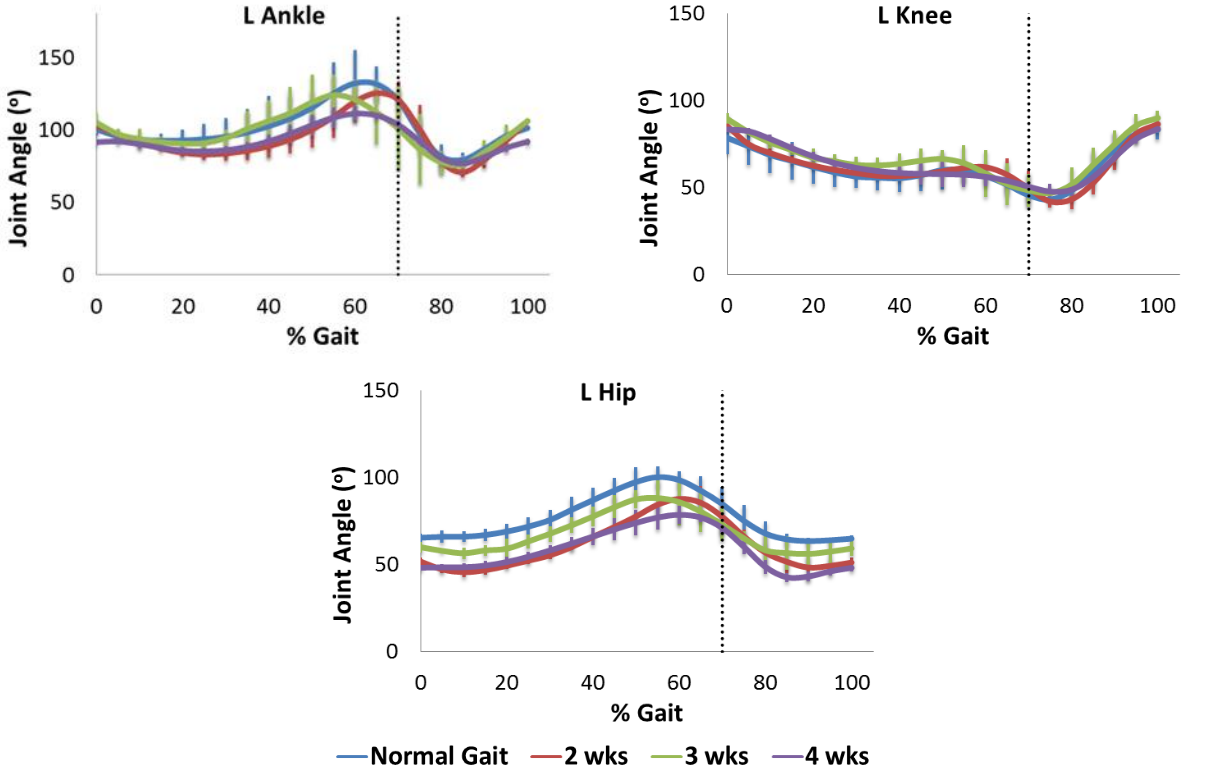


Figure 20: Mean flexion (-ve) / extension (+ve) angles and standard deviations during four consecutive strides for the left ankle, knee and hip joints during treadmill locomotion of one rat before exposure (normal gait) and 2, 3 and 4 weeks post exposure to a shock wave. The vertical dashed line marks the stance-swing transition.

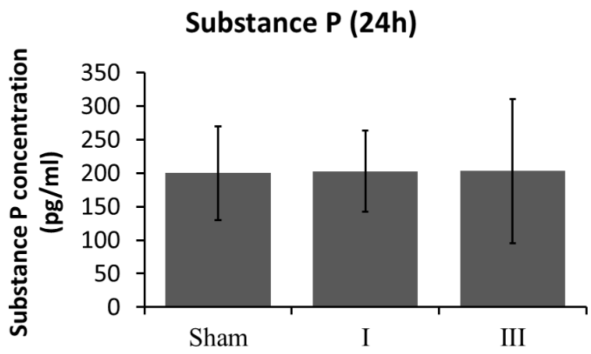


Figure 21: Levels of substance P, a compound released from activated afferent nerves and inflammatory cells, measured 24 hours following exposure to blast.

Summary

This study demonstrates that focal application of blast waves to the limb can elicit a systemic inflammatory response. The changes observed are dependent on the characteristics of the wave, relatively short-lived (normalising by 24 hours), and occur in the absence of other blast wave injury mechanisms. The combined biological and mechanical methods employed in this work aim to further understanding of the complex effect of blast waves in the peripheral nervous system in-vivo.

Blast Injury Rehabilitation

McGregor AH, Vaidyanathan R, Burton T, Hopkins M.

The initial three Centre research themes were extended in 2013 to include Blast Injury Rehabilitation to reflect the priorities of TRBL and the clinical need, to leverage significant activity at Imperial College through the Sports Innovation Challenge (for disabled athletes) and the Medical Engineering Solutions in Osteoarthritis Centre of Excellence (research and translation for bone and joint disease). The Blast Injury Rehabilitation theme develops evidenced based novel approaches for supporting recovery and optimal return to function following a blast injury.

International conflicts in Afghanistan and Iraq involving the deployment of British troops have led to higher numbers of amputee survivors than seen before. CBIS has reported extensively on the burden of injury. Prosthetic limb technology, used to restore some level of amputee functionality, has advanced significantly in recent years with the integration of micro-processor control and powered limb systems. Despite the advances in the technology and function of the limb itself, the socket, a core component of the prosthesis has long been neglected. Loading of the residual limb takes place through the socket interface and problems with misalignment and the build-up of temperature can lead to instability, discomfort and tissue breakdown. The accuracy with which the socket aligns with the residual limb is an important factor in user comfort and satisfaction, as well as limb functionality.

The interaction between the residual limb and the prosthetic socket is not a natural partnership with forces being passed through soft tissue that is not intended to endure significant loading. The skin and soft tissue sustain both axial and shear stresses and in addition the residual limb is known to vary in shape and size through the day and over longer time periods. The combination of poor socket to limb fit and cyclic loading can lead to conditions including, but not limited to, blisters, stump oedema and skin carcinoma. Up to seventy-five-percent of amputees using lower limb prostheses experience some form of skin problem.

A further issue with prosthetic sockets, since lower limb sockets fully encompass a significant portion of the lower limb, is thermal regulation of the limb. The human body naturally attempts to regulate excess temperature through the secretion of sweat, a mechanism that relies heavily on the evaporation of water. The prosthetic socket traps sweat produced by the residual limb by denying it exposure to the environment and heat builds up causing discomfort. The heat and moisture combination compromises hygiene and can cause softening of the tissue or “maceration”, leading to infection and tissue damage.

There is, therefore, demand for a mechanism capable of recording pressure, thermal and inertial properties throughout the socket, to clarify the mechanical properties of the socket-residual limb interaction during normal daily life. In October 2014 Matthew Hopkins was recruited to the first PhD studentship in this research theme, focusing on the development of a smart amputee socket. Matthew is jointly supervised by Professor Alison McGregor (theme lead) Department of Surgery and Cancer and Dr. Ravi Vaidyanathan, Department of Mechanical Engineering. Ravi has supported a range of industrial projects based on his academic research, one of which produced the first ever wheelchair controller for the physically challenged that did not require external bodily movements or invasive insertion. Dr. Thomas Burton of the Musculoskeletal Laboratory, Charing Cross Hospital is also involved in the project as a supervisory post-doctoral researcher. Alan Tanner, a senior prosthetist at the Holderness Limb Fitting Centre at Charing Cross Hospital, in association with Blatchford Group, is providing valuable input to the project, ensuring that valid and safe principals are carried forward when designing the smart sockets, Dr. Alex Bennett, Consultant Rheumatologist at the Defence Medical Rehabilitation Centre, Headley Court is also closely involved in Matthew’s work. The project proposes a portable system, integrated into a socket, such that accurate information regarding core variables of the socket-limb interaction can be gathered without being cumbersome or uncomfortable. The system also has the potential to lead to automatic adjustments of the socket to compensate for volume changes within the residual limb and temperature regulation to counter the low ventilation available in prosthetic sockets.

Being a Researcher in CBIS

Written from the perspectives of a PhD student and a post-doctoral research associate, this section highlights what it is like to be a researcher within the Centre.

Grigorios (Greg) Grigoriadis (Year 3 PhD Student)

As a final year PhD student within CBIS I have realised that the daily routine of a researcher in the Centre is far from mundane; especially when both computational and experimental work is conducted, as is the case with the majority of CBIS projects. My own project focuses on the heel biomechanics under blast conditions, aiming to understand the lower limb injury mechanism that occurs in the case of an under-vehicle explosion and provide better foot and ankle protection. To achieve these goals I am trying to develop a finite element (FE) model of the lower limb able to simulate underbody blast.

The Improvised Explosive Device (IED) has been the weapon of choice by insurgents in recent conflicts and as such the majority of non-fatal injuries to coalition troops in both Iraq and Afghanistan have been to the lower extremities. In the case of an explosion under a vehicle, the floorpan deforms rapidly and transfers a high rate axial load to the lower extremities of the occupants which results in intra-articular calcaneal fractures. As these injuries are very difficult to treat and lead to high rates of amputation, the main priority is to use the FE model of the lower limb I am developing to improve foot and ankle protection. This cost effective computational method will be used to develop and assess mitigation means (boots and blast mats) and to check the effect of different postures without the need to run complicated and time consuming experiments.

The experiments I am involved in are usually high loading rate tests to obtain viscoelastic material properties for complex biological tissues such as the heel fat pad (Figure 22) or tests to validate the FE models I am developing. To validate the response of the FE model of the lower limb I need to compare experimental and computational results for a similar load-case. For this reason I am also participating in large scale tests on AnUBIS while I am running computational simulations for the same loading scenario. AnUBIS was designed by researchers in the Centre and resides in the "Bunker" (basement) at our South Kensington campus. Using pneumatics, it replicates the response of a vehicle floorpan that has been hit with an explosive blast. Without this rig and the tests we undertake on it, we would not have been able to influence such things as the posture and placement of mounted personnel in the field: systematic primary reduction of the risk of injury.

My experiments tend to be a day long task. Specimen preparation, which includes dissection, potting with bone cement and bonding strain gauges occurs in the morning and involves significant input from our military orthopaedic surgeons. Next comes the time consuming part - setting up the data acquisition system and test equipment. We only get one chance at these high loading rate tests so ensuring the correct data is acquired is crucial. This is checked a number of times before we proceed. In the case of an AnUBIS experiment, prior to conducting the test, the specimen is placed and aligned correctly in the rig (Figure 23) to make sure that the posture tested is the appropriate one. Conducting the test itself is usually the quickest part of the experiment as it is very fast and occurs late in the afternoon. Several months of preparation are needed before any kind of experiment in order to design and manufacture parts. Satpal Sangha, the Centre's mechanical technician, gets involved at this stage and is still involved on the day that the experiment is undertaken. Equipment needs to be booked well in advance and preliminary tests are conducted over many weeks in order to help finalise the experimental protocol. The advantage of being a member of CBIS is that we work as a team in the majority of the experiments undertaken so there is always help on hand. Likewise, I always give some of my time to help others with their experiments.

The computational work related to this project is the development of the FE model of the lower limb. To be able to set up and run high rate simulations I need to first obtain the geometry of the tissues from medical imaging scans (MRI and CT). The scans are performed by military radiographers at the Queen Elizabeth Hospital in Birmingham. Often the radiographers come to the Centre and witness our testing to better understand the origins of what they see during scanning. The segmentation process for modelling can last at least a week for complex structures. Then, depending on the complexity of the load-case, running the simulation can take anything from minutes to days. I have also developed an inverse FE method which I am using to compare computational and experimental data in order to get viscoelastic material properties for biological tissues. In order to develop this automated method, programming was required and with it a lot of my time each week.

Preparing presentations, scientific papers and writing reports are also included in my day to day activities and can take up considerable time close to deadlines for conferences or submissions. CBIS prides itself on its research being publicly available so everyone is encouraged to publish and share their research. Depending on the stage of the project, the daily life of a PhD student varies, especially within CBIS which promotes and facilitates the collaboration between people from different fields. As different skills are needed and improved for different tasks, I believe this variety is beneficial while daily routine becomes more interesting.

Figure 22: Testing apparatus for drop tests on a cadaveric human heel fat pad.

Figure 23: The lower limb is placed in the traumatic injury simulator (AnUBIS).

Dr Angelo Karunaratne (Year 2 Post-Doctoral Research Associate)

This is my first position since completing my PhD in December 2012. After spending almost 2 years in my current role at CBIS I have realised that my daily routine is always changing; mainly due to my multiple responsibilities. Within the Centre I play the role of an imaging experimentalist within a team of computational modellers. I provide significant advice and help on designing sample preparation techniques and experimental protocols for other CBIS members. I am also responsible for overseeing the research activities of the Trauma and Blast Research Group and organise a number of research update meetings throughout the year. To date, I have supervised more than ten undergraduate and postgraduate students working on their final year projects in CBIS. Furthermore I manage the Tissue Testing Laboratory in the Department of Bioengineering which hosts the Centre for Blast Injury Studies. With these multiple research and management responsibilities, my daily tasks consist of meetings with research groups, writing and delivering presentations, guided tours for CBIS visitors, supervision of student research projects, sample preparation and performing experiments, conducting lab inductions for new lab users, assisting with experiments in the tissue testing lab and writing research papers, proposals, and grants.

Improvements to protective equipment have ensured greater survivability in recent years and as such, there is a current need to investigate, more robustly, non-fatal injury mitigation. In order to realise this, it is important to understand the structure-function relationship of connective tissues under extreme blast conditions. There is a requirement for physical and computational models to be developed that will allow us to understand, simulate, and predict connective tissue injuries of mild, severe, and poly-trauma casualties. I currently investigate the effects of high strain rate loading scenarios such as those seen in blast explosions on connective tissues such as bone, cartilage and ligaments. I investigate the structure and mechanics of these tissues and how this links to fracture and deformation mechanics by conducting mechanical tests on biological tissues at different loading rates ranging from quasi static (walking) to blast. I combine high resolution imaging techniques to capture as much data as possible from each test. As these experiments require considerable time to prepare and execute, the majority of my day is spent in the lab. My most recent research findings are as follows:

1. *in-situ* mechanical testing combined with synchrotron X-ray scattering experiments reveals that enhancement of modulus of ligaments with increasing strain rates are mainly due to the stiffening of collagen fibrils at high strain rates (Figure 24d);
2. in human cortical bone, the slope of stress vs tissue strain curves increase with strain rates. My nanoscale results demonstrate stiffening of the collagen at dynamic strain rates and make bone more predisposed to catastrophic fracture simply by overloading the mineral phase (Figure 24e); and
3. multiscale imaging methods combined with compact tension fracture experiments of bone demonstrate crack deflection, microdamage accumulation and collagen fibrillar stretching specifically at slow strain rates. Their adverse relation to strain rate leads to the decreasing fracture toughness at 1/s to 1000/s (Figure 24f).

I also actively collaborate with other CBIS and non CBIS research projects in Imperial College. As such, I am applying my experimental techniques to research areas such as heterotropic ossification (Figure 24g-i), peripheral nerve injuries due to primary blast, blast lung and health conditions such as osteoporosis, osteoarthritis and heart valve disease. In addition to my lab based experiments at South Kensington, I spend lengthy days (all 24 hours for 2 to 3 days) at the UK synchrotron X-ray facility at Diamond Light Source, Didcot. For these experiments I design micro mechanical testing machines to test bone, ligament, cartilage and lung tissue with high intense synchrotron light in order to elucidate ultrastructure and mechanics simultaneously. Gaining insight into biological tissue mechanics across a range of strain rates using various techniques pertaining to a range of dimensions will lead to the advancement of existing computer models. The consequence of this is an improvement of safety precautions for preventing bone fracture during impact injuries. This information will also be used to develop new drug therapies, improve mitigation techniques and provide better clinical interventions on skeletal fixations for injured service men and women.

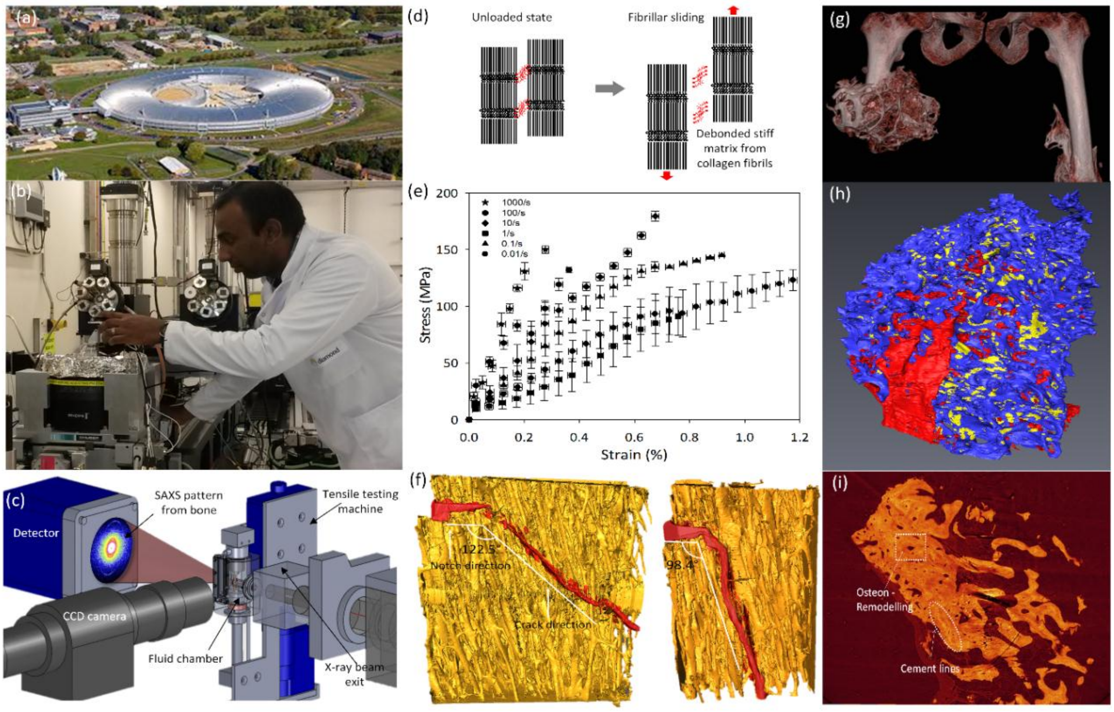


Figure 24: (a) Diamond Light Source Ltd. (DLS) Didcot, Oxfordshire, UK. (b) At I13 beam line, at DLS. (c) The experimental setup for the in situ micro-tensile testing with synchrotron X-rays at DLS. (d) Proposed ligament fibrillar sliding model for high strain rates. (e) Typical stress – strain curves for human cortical bone, each being an order of magnitude apart in strain rate. (f) MicroCT of bone samples tested at 0.001/s and 1000/s loading rates show 3D images of the crack (red) growth from a razor-sharpened notch (Yellow tubes – Haversian canals) (g) 3D rendered image of reconstructed CT scan of HO. (h) Synchrotron microCT of HO specimen (red – muscle, blue - low and high mineralised bone and yellow – high mineralised bone). (i) Osteon remodelling and cement lines in HO specimen.

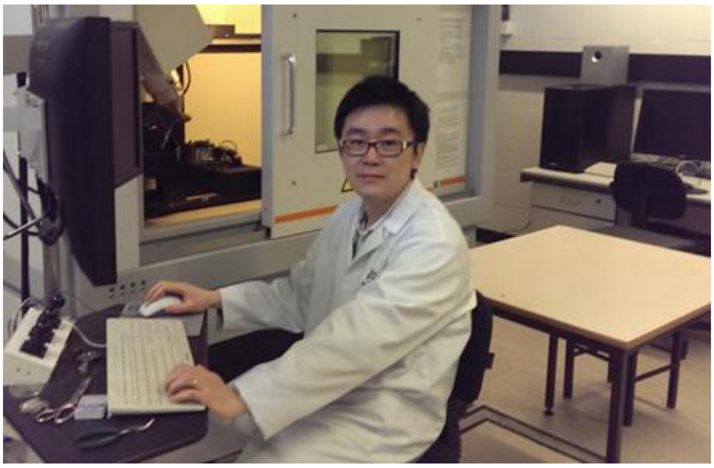
Alumni

This section captures the depth and breadth of the impact of our work by presenting some case studies of those that have been part of the Centre and have now gone on to other roles.

Dr Chiara Bo

Chiara Bo was one of the first students at 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 Chiara who were funded through other sources. Chiara's PhD, funded by the Atomic Weapons Establishment (AWE), focused on developing new experimental techniques to investigate the effects of blast on live biological samples. Along with her colleagues, Chiara developed a bio-compatible chamber to be used in high pressure experiments on cell cultures and tissues and analysed the effects of these shocks using diverse biological techniques. Chiara presented her research at various international conferences and was awarded the AWE Thesis Prize for the best PhD in the field of high energy density shock regimes and plasma physics. After completing her PhD, Chiara joined the Risk Analytics team at Deloitte where she now works as a consultant.

Dr Simin Li



Simin Li was a Post-doctoral research associate at the Centre whose role was to develop advanced computational models to assist the understanding of the effect of under-vehicle blast in human tissues. Simin's research expertise lies in advanced computational modelling of damage and fracture in heterogeneous medium and tissues. During his time at the Centre, Simin initiated a multi-scale modelling project which includes several finite element based models at different length-scales to investigate the failure mechanisms of tissues subject to high strain rate loading. His statistical based microstructural model realised the random distribution of the microstructural constituents of cortical bone at submicron-scale, and further enabled parametric studies on the damage initiation and accumulation of bone tissue in various loading conditions. Information obtained from his models can be used to assist the development of better blast mitigation techniques and clinical intervention strategies.

Simin has now taken a Lectureship at Loughborough University to continue his research in the area of mechanics of biomaterials. He maintains a close liaison with colleagues at the Centre to publish his research outcomes and promote the effect of the Centre to a wider community.

Dr James Wilgeroth

James Wilgeroth's work largely focused on novel experimental design for CBIS research projects using the Split-Hopkinson Pressure Bar (SHPB) and Shock Tube apparatus. Examples of his work include shock-loading of cell cultures and tissues within a sterile, instrumented, and bio-compatible capsule; research into the suitability of foams as protection against blast-induced hearing loss and barotrauma; and the design of a wave-capture system capable of imparting tailored stress-profiles to samples using the SHPB. James also led in the design of a 32mm gas-gun, suitable for the dynamic loading of biological tissues and materials offering protection against shock waves and ballistic threats. James is now the Laboratory Manager for Cella Energy, an advanced materials and technologies company specialising in hydrogen storage at the Rutherford Appleton Laboratory. Accordingly, James is involved in projects focused around the aerospace, defence, and automotive industries. Cella has recently partnered with Safran® - an international leader in engineering and aerospace - and is running projects on unmanned aerial vehicles and hydrogen solutions for cars.

Communication of the Work

Media

The Centre continues to generate media attention and as we learned this year, not all of it is positive. On 2nd November CBIS was the subject of an insensitive and misleading article that appeared in the Mail on Sunday. The journalist reported that the Centre was importing “body parts” and “destroying them in gruesome experiments”. In addition to this, it was reported that the tests were funded “from the sale of Remembrance Sunday poppies”. The same day, TRBL and Imperial College released statements on their websites highlighting the important partnership in the undertaking of vital scientific research aimed at developing protection for British Armed Forces personnel in current and future conflicts and improving outcomes and treatment for those who are injured.

CBIS openly stated that all human tissue used in the course of research at the Centre, whether from the UK or overseas, has been donated to medical science with full informed consent, by either the donor or their relatives. CBIS recognises that these are very valuable donations, without which the Centre would not be able to understand and reduce the injuries sustained by serviceman and women, and are hugely grateful to all the donors.

The use of human tissue in studies at the Centre is subject to regulation by the Human Tissue Act 2004. As provided for in this Act, and depending on the nature of the research, organisations other than the Human Tissue Authority regulate the actual research on human tissue. In the case of the Centre, this has been via an NHS Research Ethics Committee.

Media Mentions

- Defence Codex. *A Roadmap for Innovation.* February 2014. *Brigadier Tim Hodgetts, Royal Centre for Defence Medicine describes the three principal agencies (CBIS, RCDM & Dstl) engaged in military medical research in the UK while outlining the future of the Defence Medical Services.*
- engineering.com Simulation Strategies to Limit Injuries Caused by Explosions. February 2014. *The role of simulation software in mitigating blast injuries.*
- Diamond News Magazine. Pride and joy: Diamond’s award-winning former PhD student. April 2014. *Dr. Angelo Karunaratne is a current post-doctoral research associate in CBIS.*
- Imperial College Website. The Incredible Journey of Captain Dave Henson. September 2014. *Captain Henson is the Veteran’s Representative on the CBIS Advisory Board.*
- Twitter. Alex Cunningham MP sharing a photo of his visit to CBIS. October 2014. *Following a visit to the Centre, the MP shared a photo of the team he met with.*
- BBC Breakfast. Interview with Sir Bobby Charlton and Prof Anthony Bull. October 2014. *Highlighting the plight of civilians injured by explosive devices*
- BBC News Health. Study aims to re-grow lost limbs. October 2014. *CBIS launches an associated regenerative medicine research and translation activity.*
- Northern Echo. More to Legion that I realised. November 2014. *Following a visit to the Centre, Alex Cunningham MP highlights work being done in CBIS with support from the Royal British Legion.*
- Mail on Sunday. How your poppy money funds macabre trade in human legs and feet: £5 million British Legion opened by Prince Harry imports body parts for bomb blast tests. November 2014. *Scurrilous article that was lambasted by the newspaper’s own readers.*
- Imperial College Website. Statement on the use and sources of human tissue in experiments at Imperial. November 2014. *In response to the Mail on Sunday.*
- CBIS Website. Statement on the use and sources of human tissue in experiments at Imperial. November 2014. *In response to the Mail on Sunday.*
- TRBL Website. Centre for Blast Injury Studies. November 2014. *In response to the Mail on Sunday.*

- RTI Surgical Website. RTI Surgical Responds to Mail on Sunday Article. November 2014. *In response to the Mail on Sunday.*
- sciencedaily.com WWI Surgeons could do little for amputees' pain; treatment remains a challenge. November 2014. *High profile media coverage of the Lancet article shown on the front page of this report.*
- The Times. Amputees' agony 'as bad as in 1914'. November 2014. *Referring to the Lancet article.*
- Imperial College Website, WWI surgeons could do little for amputees' pain. November 2014. *Referring to the Lancet article.*
- BBC News Health. Amputation pain 'still a challenge' for medics. November 2014. *Referring to the Lancet article.*
- Imperial College Website (Home page). Imperial researchers examine how amputation pain was managed by doctors in WWI. November 2014. *Referring to the Lancet article.*
- Today Programme. Amputation pain in war casualties. November 2014. *Referring to the Lancet article.*
- Sky 3D/Discovery Channel, Tony Robinson's Great War. *Medical History.* November 2014. *Highest rated programme to be shown on Sky 3D. Dr Emily Mayhew tells the story of medical advances of the First World War.*
- Counter IED Report. *New Centre Manager at CBIS.* November 2014. *Announcing new Centre Manager.*
- Explosives Engineering Magazine. *New Centre Manager at CBIS.* December 2014. *Announcing new Centre Manager.*
- BBC Click. Motion capture technology improving prosthetics. December 2014. *The use of motion capture technology to analyse bone and muscle function in order to improve prosthetics.*
- Reporter Magazine. Blast injury research vital to saving lives. December 2014. *In response to the Mail on Sunday.*
- Radio 4 Science Unit. *Trauma care in Great War.* December 2014. *Historical interview with Dr Emily Mayhew in a discussion about 21st Century trauma care.*
- Radio 4 Front Row. *Great war in culture.* December 2014. *Historical interview with Dr Emily Mayhew regarding the Christmas Truce of 1914 and its depiction in a TRBL sponsored TV commercial.*
- Blesma Magazine. *Will we really be able to grow new limbs by 2039?* And will that make prosthetics a thing of the past? December 2014. *Announcing a £60 million campaign for regenerative medicine funded by charity Find A Better Way.*

Public Engagement

Annual Network Event

The 6th November saw the Centre open its doors to the public once again with the third of its annual networking events. 12 months on from the momentous official opening of some of our new laboratories by Prince Harry, the annual networking event of 2014 included a moving tribute to the First World War as part of Imperial College's Centenary Commemorations. This also coincided with the opening of our new blast lab in the basement of the Bessemer building, home to many of the Centre staff and students.

Sqn Ldr Edward Spurrier welcomed attendees and introduced Prof (Col) Jon Clasper who opened the event with a presentation entitled *The CBIS Edge*. Reflecting on improved survivability, Jon highlighted the problems that led to the establishing of CBIS in 2011 and the strategy of the Centre as it strives to progress understanding of blast injury through research and education. A Consultant Orthopaedic Surgeon in the army, Jon was able to give an insight into his experience of front line traumatic amputations and the many debilitating injuries seen in the field. Outlining the future research challenges and opportunities for the Centre, Jon concluded with a stark reminder that while the conflict in Afghanistan may be ending, the research was really just starting and the work at CBIS needed to continue.

A series of technical presentations followed with Maj Taff Edwards, an MD(Res) student in the Centre, explaining the physics of explosion and the resultant blast injuries. Dr Hari Arora, a research fellow, outlined the interaction of shock waves with the body in relation to primary blast injuries. Detailing the Centre's bespoke equipment used for testing shock wave effects, Hari ensured the audience were well informed of the Split Hopkinson Pressure Bar and shock tube in advance of the Centre tour. Our host, Edward Spurrier, another MD(Res) student in the Centre, showed an array of images and videos in his presentation on spinal injuries due to blast. Illustrating the test rigs used in the research of tertiary blast, Dr Spyros Masouros, lecturer in Trauma Biomechanics, detailed the Centre's work on the role of posture in fracture patterns and certainly whetted the attendees' appetite for a tour of the new AnUBIS facility. Spyros showed the great FE modelling work that has been undertaken in relation to Traumatic Brain Injury. From Diffusion MRI images, Dr Mazdaq Ghajari has recreated a 3D multi scale brain model containing axonal tracts which is being used by fellow researchers to investigate oblique helmeted impact. Representing the Defence Medical Services, Surgeon Captain Sarah Stapley of the Royal Navy outlined the Medical Directorate's innovation road map with CBIS playing a key role in the quest for fundamental understanding. She highlighted that without research, force protection, product innovation and clinical doctrine development could not be improved or sustained.

Concluding the presentations session was Centre Director, Prof Anthony Bull outlining the achievements of CBIS to date and its future plans. The take home message from Anthony's talk was one of effect and impact, and the difficulty in measuring these in a long journey in a changing landscape. He added that CBIS would continue to deliver societal impact for the benefit of the war wounded, their families and society in general.

After refreshments and an array of posters displaying more detailed work of the Centre, the attendees were invited on a tour of the new and existing facilities. Dr Theofano Eftaxiopoulou, Dr Angelo Karunaratne and David Sory each explained how researchers use the specific equipment in various test regimes and the importance of such facilities in understanding the nature and effect of blast. The event concluded with a poignant narrative reflecting on the past, present and future of trauma research and care in a commemoration of the First World War Centenary. The talk, *Battle to Blighty*, was written by Maj Taff Edwards and Dr Emily Mayhew, directed by Hannah Eidinow (London and New York theatre director) and starred Alan Cox (London based Hollywood actor).

Website

Attracting hundreds of first time and returning page loads each week, our website continues to be our main face to the external world (*www.imperial.ac.uk/blastinjurystudies*). Hosting descriptions of CBIS members, their projects and publications, the CBIS website also provides links to TRBL and Imperial College news ensuring its visitors are constantly informed.

Imperial Festival 9th – 10th May 2014

Once again CBIS staff and students joined colleagues from Imperial College to celebrate the best science and arts on offer from the College. The event was bigger than ever with three new venues housing more activities, performances and workshops to entertain and inform the thousands of people in attendance at South Kensington. CBIS built on last year's shock waves and smoke rings with a hugely successful impact demonstration called "Protect Your Head". Using a dummy head/neck assembly mounted to the base on an impact pendulum, audience members were able to control the pendulum imparting a force to the dummy. Experiments were conducted with and without helmets on the dummy and high speed video cameras were set up so that the audience could review what had occurred on a large TV screen. They were then asked to describe whether they saw any difference between wearing and not wearing a helmet before Dr Mazdak Ghajari explained the difference in terms of inertial force sustained by the brain during the impact. This was measured with a miniature accelerometer installed inside the headform which the audience could see. Participants were amazed that even with mild impact, which some might sustain falling from a bicycle, that the force was reduced by over 20% when a helmet was worn (*www.imperial.ac.uk/festival*).

Royal Institution Engineering Masterclass

Dr Andrew Phillips continues to deliver one of the Royal Institution Engineering Masterclasses in which 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, with the latest research work on additive manufacturing of frangible surrogates highlighted. Dr Phillips was also invited to deliver a Summer

School workshop at the Royal Institution, which explored optimisation in structural design, inspired by natural structures such as bone.

Subject Specific Meetings

Trauma and Blast Inflammation Symposium (TABIS) – March 2014

Prof Sara Rankin convened the symposium at the Queen Elizabeth Hospital, Birmingham. The event brought together some of the world's leading experts to share ideas and develop new partnerships as well as examine the current state of research into inflammation following trauma and blast injury. Aimed at clinicians, academics and industry, the focus of the interactive forum was to facilitate potential collaborations and engagement with industry. The symposium covered four areas: Platelets and Inflammation; Blast Lung Injury; Sterile Immunity; and Brain Trauma Inflammation. Keynote speakers included: Prof Ian Roberts (London School of Tropical Medicine and Hygiene, UK) whose main research interests are the prevention and treatment of trauma and the links between energy and health; Prof Leo Koendermann (University of Utrecht, Netherlands) whose research group focuses on improving our understanding of the innate immune system; Prof Carl Hauser (Beth Israel Deconess Medical Centre, USA), a surgeon with particular expertise in advanced treatments for complications of trauma, shock and sepsis, and inflammatory responses to injury; and Prof Michal Schwartz (Weizmann Institute of Science, Israel) whose work focuses on the role of innate and adaptive immunity in central nervous system (CNS) plasticity in health and disease. Two CBIS members, Dr. Katherine (Kate) Brown and Mr. Ashton Barnett-Vanes (a PhD student supervised by Prof Sara Rankin) also contributed presentations at the meeting, describing the various experimental platforms within CBIS and how they are adapted to understanding local and systemic effect of blast injury on tissues susceptible to blast wave damage. The focused meeting provided an excellent forum for new and experienced researchers to share their interests in blast injury and support the development of collaborative projects between clinical and basic sciences.

Annual Heterotopic Ossification (HO) Research Group Meeting – November 2014

CBIS hosted the second meeting of its kind, organised by Maj Taff Edwards (MDRes). The meeting involved key civilian and military researchers from CBIS, the wider Imperial College Faculties of Engineering, Medicine and Natural Sciences, the Royal College of Defence Medicine, the University of Birmingham and Loughborough University. The annual meeting is an opportunity for senior academics and researchers from around the UK to present current work and explore theories relating to HO. This develops cross academic relationships and has resulted in collaborative research to accelerate the progress of research in this field. Discussion points at this year's meeting were the clinical perspective (Maj Taff Edwards, CBIS), biomaterial science (Prof Liam Grover, University of Birmingham), in vitro models (Loughborough University), cellular/stem cell research (Prof Sara Rankin, CBIS), and computational modelling (Naomi Rosenberg, Imperial College). It is anticipated that the third meeting in the series will be an international one which will further extend the opportunities for collaboration.

Publications

Arora H, Kelly M, Warley A, Del Linz P, Fergusson A, Hooper PA, Dear JP. *Compressive strength after blast of sandwich composite materials.* Philosophical Transactions of the Royal Society A – Mathematical Physical and Engineering Sciences. 2014, 372:20130212.

Bonner TJ, Newell N, Karunaratne A, Pullen AD, Amis AA, Bull AMJ, Masouros SD., *Strain-rate sensitivity of the lateral collateral ligament of the knee.* Journal of the Mechanical Behavior of Biomedical Materials. 2014, 41:261-270.

Butler BJ, Bo C, Tucker AW, Jardine AP, Proud WG, Williams A, Brown KA. *Mechanical and histological characterisation of trachea tissue subjected to blast type pressures.* Journal of Physics Conference Series. 2014, 500(18): 2007.

Edwards DS, Mayhew ER, Rice AS. "*Doomed to go in company with miserable pain", surgical recognition and treatment of amputation related pain on the Western Front during World War 1.* Lancet. 2014, 384(9955): 1715-19.

Edwards DS, Clasper JC. *Heterotopic Ossification: a systematic review.* Journal of the Royal Army Medical Corps. 2014, *in press*.

Edwards DS, Clasper JC, Patel HDL. *Heterotopic Ossification in victims of the London 7/7 bombings.* Journal of the Royal Army Medical Corps. 2014, *in press*.

Eftaxiopoulou T, MacDonald W, Britzman D, Bull AMJ. *Gait compensation in rats after a temporary nerve palsy quantified using temporo-spatial and kinematic parameters*. Journal of Neuroscience Methods. 2014, 232:16-23.

Gopalakrishnan A, Modense L, Phillips AT. *A computational framework for deducing muscle synergies from experimental joine moments.* Frontiers in Computational Neuroscience. 2014, 8:153.

Ramasamy A, Eardley WG, Edwards DS, Clasper JC, Stewart MP. *Surgical advances during the First World War: the birth of modern orthopaedics.* Journal of the Royal Army Medical Corps. 2014, *in press*.

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.* Journal of the Royal Army Medical Corps. 2014, 160(2): 117-20.

Singleton JA, Gibb IE, Bull AMJ, Clasper JC. *Blast-mediated traumatic amputation: evidence for a revised multiple injury mechanism theory.* Journal of the Royal Army Medical Corps. 2014, 160(2): 175-9.

Singleton JA, Gibb IE, Bull AMJ, Clasper JC. *Case suitability for definitive through knee amputation following lower extremity blast trauma analysis of 146 casualties, 2008-2010.* Journal of the Royal Army Medical Corps. 2014, 160(2): 187-90.

Tchumatchenko T, Reichenbach T. *A cochlear-bone wave can yield hearing sensation as well as ostacoustic emission.* Nature Communications. 2014, 5:4160.

Walker NM, Eardley W, Clasper JC. *UK combat-related pelvic junctional vascular injuries 2008-2011: Implications for future intervention.* Injury. 2014, 45(10):1585-9.

Awards

Barnett-Vanes A. Winner – Best oral presentation. 3rd annual MD/PhD Conference, Switzerland.

Edwards D. Winner - Montefiore Memorial Medal (Best Military Surgical Trainee). Army Medical Services.

Spurrier E. Winner - Phillip Fulford Memorial Prize (Best research paper) Combined Services Orthopaedic Society.

Spurrier E. Runner up - Colt Foundation Prize. Royal Society of Medicine.

Spurrier E. Winner – Research Grant Award. AOUK.

Invited Lectures

Barnett Vanes A. *Establishing an experimental system to investigate indirect mechanisms of pulmonary inflammation in blast trauma: a rat hindlimb model of primary blast injury.* Queen Elizabeth Hospital, Birmingham. March 2014.

Bull AMJ. *Clinical drivers for research into brain injury in the military research management for maximum effect.* Radcliffe Observatory Quarter, Oxford. January 2014.

Bull AMJ. *One of the eight great technologies.* The Royal Institution, London. June 2014.

Bull AMJ. *Biomedical engineering: advancing UK healthcare.* Institution of Mechanical Engineers, London. July 2014.

Bull AMJ. *Battlefield to South Kensington.* Consort Club, London. November 2014.

Brown K. *Experimental platforms for studying blast damage in respiratory tissues.* Queen Elizabeth Hospital, Birmingham. March 2014.

Clasper J. *Effects of blast on the human.* Pressure, Energy, Temperature and Extreme Rates (PETER) Annual Meeting, London. April 2014.

Clasper J. *Future Military Medical Research*. Ministry of Defence Hospital Unit, Camberley. November 2014.

Clasper J. *Developments in the Mechanics, Physiology and Treatment of Blast Injury, The Clinical Problem.* Austere Medical Environments, London. October 2014.

Edwards D. & Mayhew E. *Great War Medical History*. Army Medical Services, Aldershot. November 2014.

Mahoney P. *Blast injury: clinical issues and research questions*. Queen Elizabeth Hospital, Birmingham. March 2014.

Masouros S. *Understanding Human Injury from Under Vehicle Explosions*. Cavendish Laboratory, Cambridge University. November 2014.
Mayhew E. *War & Psychology.* Royal Institution, London. September 2014.
Mayhew E. *Great War Trauma.* Army Medical Services, Glasgow. September 2014.
Mayhew E. *First World War First Responders*. Liverpool Medical Institution. October 2014.
Mayhew E. *Great War Medical History*. Cheltenham Literary Festival. October 2014.
Mayhew E. *Nursing in the Great War*. Florence Nightingale Museum, London. October 2014.
Mayhew E. *Medicine and the Great War*. Bath Literary and Scientific Institution. October 2014.
Mayhew E. *RAMC Archives Digitisation Project*. Wellcome Collection Library, London. November 2014.
Mayhew E. *First World War First Responders.* Birmingham Library. December 2014.
Sharp D. Inflammation and neurodegeneration after traumatic brain injury. Queen Elizabeth Hospital, Birmingham. March 2014.
Proud WG. *Understanding the Effects of Blast on Biological Systems.* Royal Engineers Crowborough Camp, East Sussex. October 2014.
Proud B. *Activities of the IOP Shock Physics and Extreme Conditions Group.* Pressure, Energy, Temperature and Extreme Rates (PETER) Annual Meeting, London. April 2014.
Proud WG. *Shock and Blast waves*: Natural, Accidental and Scientific. King's College London. December 2014.
Proud WG. *Understanding the Effects of Blast on Biological and Protection Systems*. Nanyang Technological University, Singapore. November 2014
Proud WG. *Explosives – Diagnostics and Time*. Queen Mary University, London. December 2014.
Ramasamy A. *Clinical drivers for blast mitigation*. Wayne State University Biomedical Engineering 75th anniversary symposium. Detroit, MI, USA. August 2014.

Conference Presentations

Government Experts on Mitigation Strategies (GEMS) Annual Meeting, London. UK. January 2014.

Spurrier E, Edwards D. *Heterotopic Ossification in Traumatic Amputations*.

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