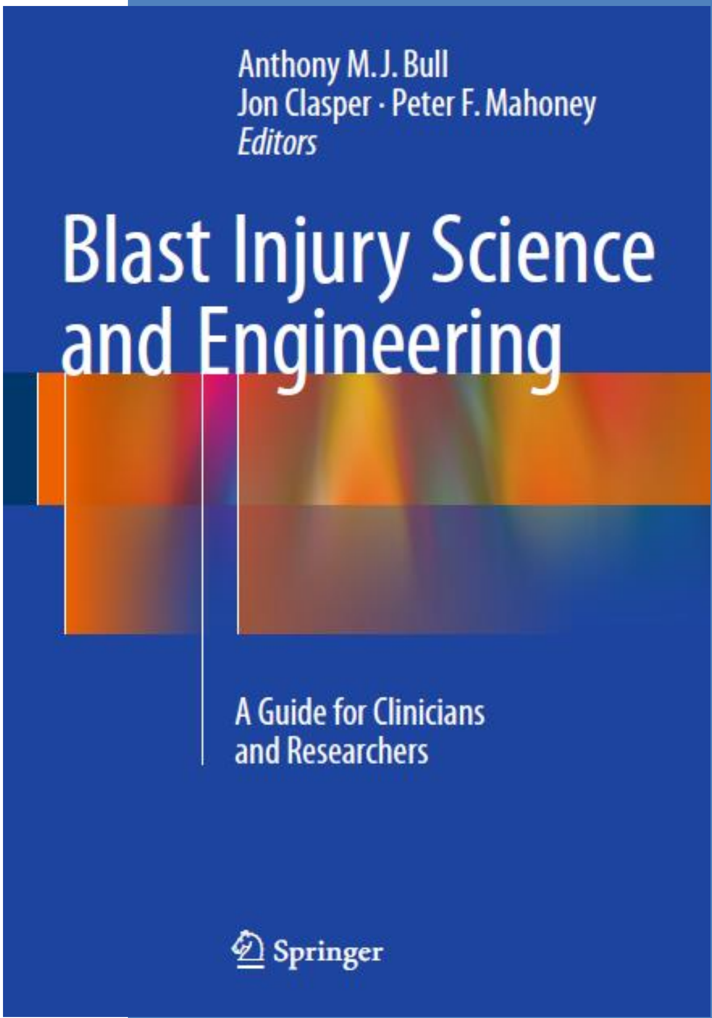
THE ROYAL BRITISH LEGION
CENTRE FOR BLAST INJURY STUDIES
AT IMPERIAL COLLEGE LONDON

# 2015

# CBIS Annual Report




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

April 2016

# 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, April 2016**

Imperial College of Science, Technology and Medicine

# Contents

# Director's Foreword

This fourth Annual Report represents a very successful and very engaging year for the Centre, and with a renewal of funding from The Royal British Legion, the future looks very bright indeed. The commitment of a further 6 years of funding allows us to continue to make bold, long-term decisions regarding our research, and enhance the impact of investments that have been made to date. Given the complexity and novelty of the research conducted at the Centre, bold and long-term decisions made possible by corresponding commitments from its stakeholders are vital to maximise the unique opportunity the Centre has to deliver breakthrough advances in the understanding, mitigation, treatment and rehabilitation of blast injuries.

While a highlight for some earlier this year was seeing me bungee jump during the College's Fundraising Week (*this year on behalf of the Mines Advisory Group*), for me it was the results of the Research Excellence Framework (REF) assessment. Imperial College once again demonstrated that it is the leading technical university in the UK. Its research is internationally leading, has very wide reach and delivers societal impact as assessed by our peers. Success continued in the National Student Survey (NSS) where the Department of Bioengineering received 97% overall student satisfaction. The Centre's clinical lead Professor (Col.) Jon Clasper and Professor (Col.) Peter Mahoney, associated with the Centre through his leadership in anaesthesia and critical care, were both honoured in the Queen's honours list with an appointment to "Commander of the Most Excellent Order of the British Empire" for their services to military medicine. As part of Imperial College's Awards for Excellence in Research, the Centre received the President's Award for Outstanding Research Team; an award given in recognition of "outstanding research that delivers impact, a team's international standing and their beneficial contribution to Imperial College". The Centre also saw a milestone PhD awarded this year. Under the supervision of Professor Sara Rankin, Ashton Barnett-Vanes is the first PhD student directly and solely funded by the Centre. He successfully defended his thesis which investigated the inflammatory response in blast-related lung injury. The MB/PhD programme that Ashton undertook is designed to build on a scientific foundation and equip medical students with the confidence and skills to pursue areas of interest in a clinical, research-based environment. Ashton re-joins his medical school course in 2016 to complete his medical studies before moving into the NHS; another conduit for the lessons learned at the Centre.

Some high profile Government visits this year once again confirmed the relevance of the Centre's research to issues of national and international interest. Minister of State for Universities and Science Jo Johnson, Secretary of State for Defence Michael Fallon, Ashton Carter, the US Secretary of Defense and The Rt Hon Earl Howe, Minister of State for the Ministry of Defence each visited the Centre to meet with researchers and to see first-hand some of the work currently being undertaken. The public launch of the The Bioengineering Trauma Initiative (page 31) in the presence of our colleagues and collaborators from St. Mary's Major Trauma Centre, Barts Health NHS Trust, John Radcliffe Hospital and Aberdeen Royal Infirmary, demonstrates the Centre's leadership in the translation of lessons learned from military research to the civilian domain, in order to improve the outcomes of those suffering trauma. The compilation of our knowledge and experience, together with that of our colleagues at Dstl, the NHS, Met Police and a host of UK academic institutions, in a textbook (page 34) for clinicians, engineers, and scientists, further demonstrates the Centre's commitment to education in the areas of blast injury and trauma.

Finally, I would like to thank all my colleagues and students working in the Centre and our supporters and stakeholders; 2015 has been an exciting and rewarding year for the Centre and we look forward to the years ahead with thanks to the continued commitment of The Royal British Legion, Imperial College London and the Ministry of Defence.

**Professor Anthony M J Bull FREng**

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

**Head, Department of Bioengineering, Imperial College London**

# Funder’s Foreword

The Royal British Legion was established in 1921 to help those returning from the First World War. The purpose was simple and clear; to provide support for those who had suffered as a result of service in the British Armed Forces, whether through their own service, or through that of a husband, father or son. Suffering took many forms and so too did the support of the Legion. It provided financial, social and emotional care. It became involved in housing provision. Legion regional groups brought the military canteen concept into post-war civilian life, providing meals and food parcels.

Throughout the 1920s, the pioneering national network of orthopaedic centres that offered rehabilitation and retraining for amputees disappeared. Its medical staff were returned to general hospital facilities and duties, and the remarkable expertise that had evolved throughout the network was lost. Increasing amounts of the Legion’s resources were allocated to meet these new shortfalls. It paid medical bills, rail fares to metropolitan hospitals, the price of new or repaired prosthetic limbs. It developed institutions where the wounded destitute could find shelter, respite and a home.

By 1930, no other institution in Britain understood the implications or extent of the challenges posed by the plight of the disabled and impoverished ex-servicemen. The Legion became the foremost advocate on their behalf in both the political and public sphere. The annual Remembrance Day commemorations, instituted by the Legion alongside its Poppy Appeal, reminded the entire British population not only of the sacrifices made on their behalf, but also the long-term needs and costs of such sacrifice.

A century on, the Legion is addressing those long term needs via a radical new strategy; one that includes research so that we can better protect our Armed forces and effectively treat its injured. The Royal British Legion Centre for Blast Injury Studies at Imperial College London is making a real difference to the survival and quality of life of those who serve. With 5 years of funding from The Legion, and support from the Ministry of Defence and Imperial College, the Centre was established in 2011 to address the disabling, life-changing effects of blast injuries. It is a unique, world leading research unit where scientists, engineers and clinicians work side by side to resolve the old problems of a new casualty cohort, in the face of fresh and emerging threats.

This annual report, like previously published editions, is not a comprehensive survey of all activities in the Centre, but will give you a taste of the breadth and depth of the current work being undertaken. I am thrilled, not only to have the opportunity to pen its foreword, but to be able to include in it a significant announcement. The Legion has, this year, committed to funding the Centre for a further 6 years, allowing research activities to continue until 2021. The Legion remains committed to supporting the Armed Forces community and sees the Centre for Blast Injury Studies as key to addressing clinical and welfare priorities in order to deliver real effect through its research and translation activities. I encourage you, as you have always done, to continue your support for the benefit of the war wounded.

**John Crisford**

**National Chairman**

**The Royal British Legion**

# Introduction

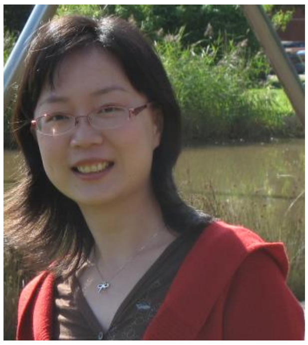
This report, the fourth in series, reminds us of the role and importance of governance and peer review in our work. It summarises the Centre's published work during 2015 and current research activities. It presents two biographical pieces from current researchers in the Centre, and an update on one of our alumni making a difference in another walk of life. We discuss the significance of cohort studies in light of the Centre's leadership role in the Headley Court-led ADVANCE study which looks at the long-term outcomes of seriously injured servicemen from the recent conflict in Afghanistan. We introduce a new feature "In the Spotlight" to highlight other leading work from our collaborators in the areas of blast injury and trauma. The newly established Bioengineering Trauma Initiative is discussed, along with some associated work at Imperial College's Department of Bioengineering. The financial support of other funders is acknowledged. We conclude with a review of our media presence and outreach activities throughout 2015.

# Staffing & Facilities

## Researchers Joining CBIS in 2015

**Phill Pearce** joined the Royal Air Force as a medical cadet. He graduated from medical school in London in 2008 and following a period as a general duties medical officer began training in general surgery. His clinical interests are in emergency, colorectal and trauma surgery. He began a period of out-of-programme research at the Centre in October 2015 and his project involves defining the mechanism of non-compressible torso haemorrhage in mounted blast casualties. Phill is supervised by Professor (Col) Jon Clasper and Professor Anthony Bull.

**Ziyun Ding** joined the Centre as a post-doctoral research associate under the supervision of Professor Anthony Bull. She received her PhD degree in the University of Liverpool, focusing on digital human modelling for ergonomics analysis. At Imperial College London Ziyun's research expertise lies in lower limb musculoskeletal modelling, simulation and analysis. Her current role is to develop an advanced musculoskeletal model for British amputees. Information obtained from computational models can be used to better assist the clinical intervention strategies, rehabilitation, and prosthesis design for amputations.



## Facilities

To investigate the mechanism of under-vehicle explosion, researchers in the Centre designed **AnUBIS**, an Anti-vehicle Underbelly Blast Injury Simulator. The device, capable of recreating the complexities of an explosive event in a controlled, laboratory based environment, has been the subject of much published work over the years[1]. With emerging threats in the civilian domain and a constantly changing battlefield, AnUBIS underwent some modifications this year to increase the Centre's experimental capability. By increasing the achievable velocity in a reduced time frame, researchers are afforded the opportunity to assess the effects of a more expansive range of explosive events. Coupled with a Finite Element modelling competency, results can be replicated and validated in house for a range of conditions.

A falling mass guided by columns, a **drop tower** is used to measure the energy absorbed by a sample, or to apply a set amount of damage to a specimen. This year, researchers in the Centre designed and manufactured a 2.5 m drop tower to enable the dynamic testing of materials at a range of impact velocities up to 7 m/s. Driven by questions about the behaviour of human tissue at high strain rates, but also the suitability of protective equipment such as helmets and gloves (*discussed further at page 32*), the Centre designed the bespoke piece of equipment to enable testing which includes cadaveric specimens.

Other facilities for the Centre are housed in bespoke laboratories in the Bessemer Building on the South Kensington Campus. These laboratories, housed in Department of Bioengineering space, provide the core facilities for use by all researchers in the Centre. Additionally, many other facilities are available within all the host departments including advanced histology, imaging, proteomics, tissue testing and specialist manufacturing.

[1] http://www.imperial.ac.uk/blast-injury/publications/

**White City Campus** is Imperial College's major new campus currently under construction in West London. The College's aim for the £3 billion, 25-acre campus is to provide academics and students with a place to expand its multidisciplinary ethos and collaborate with entrepreneurs, investors and technology experts from across London. At the very heart of the development lies the Michael Uren Biomedical Engineering Research Hub. The 13-storey building will comprise state-of-the-art laboratory and office facilities for translational research initiatives at the interface of biomedical sciences and engineering. In addition, it will house an outpatient clinic, a 150-seat auditorium and a series of social spaces to encourage the informal exchange of ideas. Harnessing the expertise of Imperial College's scientists, engineers and clinicians under one roof, the research hub will drive forward medical technology and bring direct benefit to patients. The Centre for Blast Injury Studies is hosted by the Department of Bioengineering at Imperial College and, as such, will benefit greatly from the opportunities that the Research Hub and indeed, the entire White City Campus, will provide.

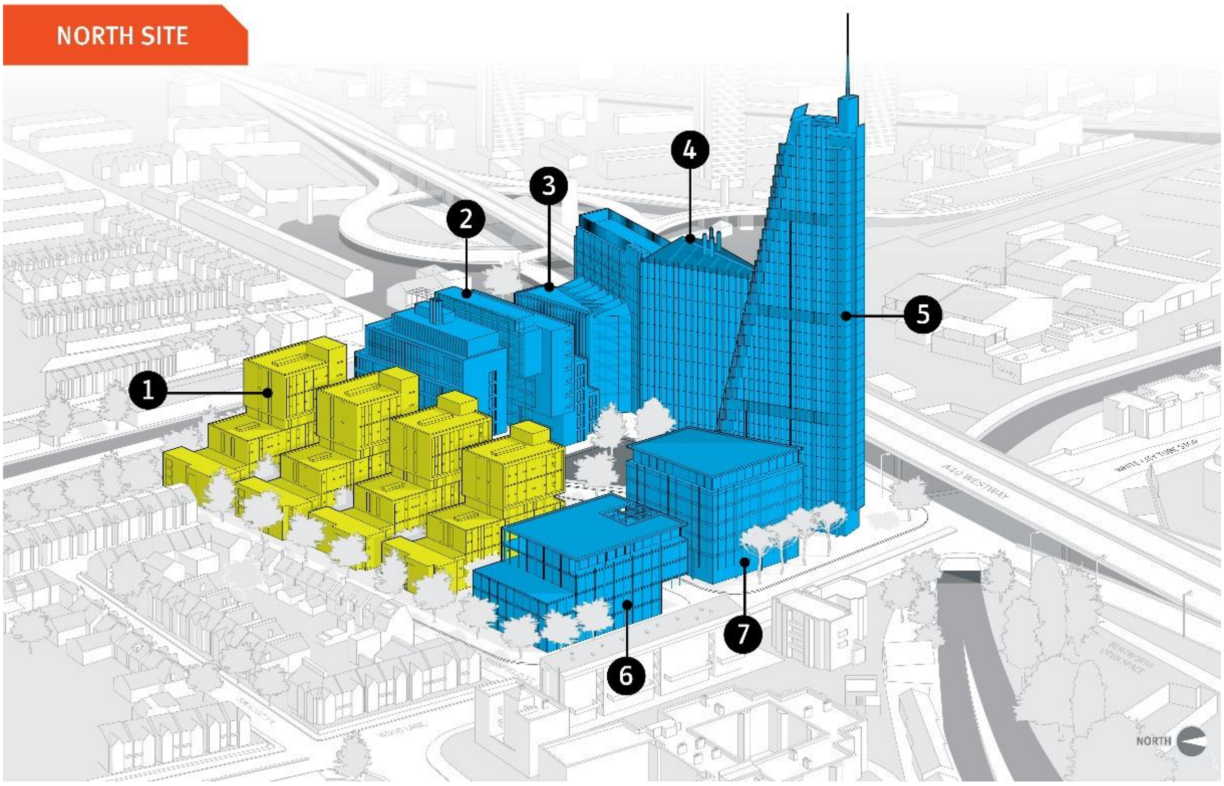



**Figure 1: White City Campus plans - 1. Wood Lane Studios, 2. The Molecular Science Research Hub, 3. The Translation & Innovation Hub, 4. The Michael Uren Biomedical Engineering Research Hub, 5. Residential Tower, 6. Offices & University use, 7. School of Public Health**

# Peer Review

Peer review is a critical and commonly accepted part of the functioning of the scientific community. It is the evaluation of work done in order to maintain standards of quality. This year, the Centre undertook a scientific review of its work to date. The purpose of this review was to provide CBIS with a scientific assessment of, and advice on, all of the programmes it supports, in order to enable the Centre's mission to promote research excellence of blast injuries.

The review was chaired by Professor Sir Anthony Newman Taylor, President's Envoy for Health at Imperial College, London. Anthony is also the Director of Research and Development in the National Heart and Lung Institute at Imperial College. As Chairman of the Independent Medical Expert Group of the Armed Forces Compensation Scheme, Anthony advises Government on medical and scientific matters concerning the welfare of military personnel and veterans. Members of the scientific review panel included the following: Professor Neil Alford, Vice Dean for Research, Faculty of Engineering, Imperial College London, Professor Karim Brohi, Professor of Trauma Sciences Barts and The London School of Medicine and Dentistry, Director of the North East London and Essex Trauma Network, Professor Duane Cronin, Professor of Impact Mechanics and Trauma Biomechanics, University of Waterloo, Canada, Professor Dame Julia Higgins, former Principal Faculty of Engineering, Imperial College London, Mr Mat Philippens, Injury Biomechanics, Explosives, Ballistics and Protection, TNO, Netherlands, and Professor Gavin Screaton, Dean of Faculty of Medicine, Imperial College London.

Director of the Centre, Professor Anthony Bull, provided the panel with an overview of the Centre's structure and position at Imperial College London, its military and industrial links and the accomplishments since its inception. This was followed by a tour of the Centre's facilities within the Department of Bioengineering to demonstrate the bespoke laboratory equipment that has been developed to enable the recreation of blast conditions in a laboratory setting. Subsequently, presentations were delivered by Centre researchers in two main areas: Biology and Platforms, and Trauma Biomechanics. The panel examined each individual research project for its relevance to the Centre's goals. Research aims and methods were assessed for their clarity, scientific merit and innovation. The Centre's research activities, though recognised to be within a niche area of science, engineering and medicine, were assessed like any traditional discipline for adherence to academic standards in the pursuit of research excellence. The working environment and career progression of students and researchers were examined. Academic staff in the Centre were measured against the academic performance metrics expected of all academic staff in Imperial College in relation to scientific publications, grant income, education influence and esteem.

Findings of the review were reported by the panel and included acknowledgement of the strengths of the Centre; its focus, its close working relationship with the Ministry of Defence, its location at one of the leading science, technology and medicine universities in the world and its position globally in the area of blast injury research. The panel made recommendations on the maintenance of national and international collaborations, the importance of publication of findings in the public domain and the value of strong leadership.

# Governance

CBIS has a strong advisory board chaired by former Chief of the Defence Staff, Admiral of the Fleet Lord Michael Boyce KG GCB OBE DL. The board has comprised membership as follows: Zoltan Bozoky, UK Department of Health; chief strategy officer responsible for research which informs health care in England, General Sir Tim Granville Chapman GBE KCB, ex-Vice Chief of the Defence Staff & Programme Director Defence and National Rehabilitation Centre, David Henson MBE, veteran's representative, Professor Sir Anthony Newman Taylor CBE, Chairman of the Independent Medical Expert Group of the Armed Forces Compensation Scheme, Ian Stopps CBE, Chairman of Raytheon UK and Professor (Col) Jon Clasper CBE, ex Defence Professor Trauma and Orthopaedics.

The function of the advisory board is to provide independent and external advice, strategic oversight and monitoring, and an ambassadorial purpose for the Centre. As such, the Centre receives a critical but supportive perspective on the issues confronting it. The varied membership of the board affords CBIS the opportunity to take its discoveries from the laboratory to the military frontline, in terms of protection and healthcare, and in order to improve outcomes for all personnel.

Additions were made to the function of the advisory board during the review of the Centre this year. It was recommended that the strategic and associated spending proposals were validated annually by an informed and independent external body, and that the Advisory Board were the most appropriate for this. Strategic and financial plans are reviewed by the board in line with the set clinical priorities against perceived benefit to the intended beneficiary.

Mr Zoltan Bozoky retired from the Centre's advisory board this year and we would like to take this opportunity to thank him publicly for the invaluable contributions during his time as the Department of Health representative.

# Exemplar Research Findings

The Centre is committed to transparency in its activities and one of its main outputs is publication in the open literature. This section of the report is a collection of published journal articles summarising the Centre's research findings in 2015. It highlights the varied yet focused work being undertaken in the Centre, as well as its wide reaching interdisciplinary audience.

All research activities in the Centre are clinically led. No one study is undertaken without prior assessment of clinical data in order to identify the clinical problem and determine appropriate research questions. The presence of military medical staff in the Centre is key to the interrogation of this data which drives further studies involving physical experimentation and computational modelling. Injuries are recreated in the laboratory and can be computer simulated for a variety of environments and conditions to further the understanding of the injury mechanism. Once the mechanism of injury is determined, protective equipment can be assessed or designed to mitigate its effects. Treatment and rehabilitation options can be examined and varied in order to improve the outcomes of those who have suffered injury. An example of this pathway to innovation is illustrated below when we examine some of the recent studies undertaken by one of the Centre's military medical researchers.

In 2014, Maj DS Edwards published a review of Heterotopic Ossification (HO) (*Heterotopic ossification: a systematic review. JRAMC. Vol 161 Iss 4, pp 315-321, 2014*). As a consequence of recent operations, and the characteristic injury that is blast-related amputations, a renewed interest in HO emerged due to an increased incidence seen in casualties. Edwards' review was a detailed study of the published literature that illustrated the military problem of HO and its management, while also serving as a gap analysis providing detail of the knowledge deficit in the field. From here Edwards examined civilian clinical data for comparison (*Heterotopic ossification in victims of the London 7/7 bombings. JRAMC. Vol 161 Iss 4 pp 345-347, 2015*). It was believed, prior to his study, that the mechanism of injury of HO was influenced by military environmental factors. The analysis of the 7/7 clinical data showed that the risk of HO is valid in the civilian domain devoid of military-established risk factors. Edwards' literature review also identified an incidence of HO in patients of total hip replacement. His examination of this clinical data (*Posterior mini-incision total hip arthroplasty controls the extent of post-operative formation of heterotopic ossification. European Journal of Orthopaedic Surgery & Traumatology. Vol 25, Iss 6, pp 1051-5, 2015*) served well to identify the surgical factors and patient variables which influence HO. Techniques to reduce the extent of HO found in soft tissue were identified. Understanding HO in the civilian population will shed light on the findings in amputees due to blast. Ultimately, knowledge such as this will contribute to identifying the long term needs and the most appropriate treatment for those suffering HO. Indeed, Edwards has described and quantified the extent and nature of traumatic amputations of British service personnel from Afghanistan (*What Is the Magnitude and Long-term Economic Cost of Care of the British Military Afghanistan Amputee Cohort? Clinical Orthopaedics and Related Research, Vol 473, Iss 9, pp 2848-2855, 2015*). This study has been used to identify the long term health needs and costs of this cohort beyond their service in the armed forces. Research into the formation of HO is ongoing at the Centre and is discussed further by post-doctoral research associate Dr Harsh Amin at page 25.

The following pages (15-22) detail our 2015 research findings which can be summarised as follows:

**Heterotopic Ossification** - Military HO research informs and is informed by civilian HO research. The risk of HO is valid in the civilian domain devoid of the (military) environmental factors previously thought to contribute to HO formation. The posterior minimal incision is a safe approach to use during a total hip replacement (THR) with regards to the formation of HO. The minimal incision technique reduces the extent of HO found in the soft tissue.

**Veteran's health care** - The Afghan conflict resulted in high numbers of complex injuries. The long-term cost of care of the UK Afghan lower limb amputee cohort is estimated at £288 million. It is likely that the described cohort will experience chronic health problems suffered by the general population, as well as specific issues as a result of their injuries. It is incumbent upon society to investigate the long-term effect of these significant injuries.

**Computational simulation & modeling -** An innovative method has been developed to derive muscle synergies based on movement kinematics and kinetics, without requiring electromyography or predicted muscle activation data. The method has applications in the rehabilitation of amputees or those with neuromuscular damage due to blast injury. A model whose structure and mechanical behaviour are biofidelic while maintaining the high computational efficiency of a purely structural model is possible. The method has the potential to be extended to include cellular response to blast loading, allowing the long terms effects to be investigated across the skeletal system. Biological materials, such as skin, are highly heterogeneous. Current computational models are limited in their ability to capture fully the complexity of the material responses of living tissues at the high strain rates that occur during blast injury. CBIS work allows the development of more realistic material models that take into account the composite nature of skin and other tissues that are highly vulnerable to blast.

**Spinal injury** - Spinal injury is common in mounted troops due to under vehicle explosions. The transmitted forces are applied anterior (in front) of the spinal column causing it to break at specific locations. The mechanism of injury is complex. Injuries are caused by forces directly through the structure of the vehicle but also due to the legs being thrown up by the deforming floor. Ongoing CBIS work will produce a better injury model of the spine in under-vehicle explosions that can be used to improve assessment of the protective ability of vehicles and personal protective equipment.

## Heterotopic Ossification in Victims of the London 7/7 Bombings

*Edwards DS, Clasper JC, Patel HDL. (2015)*
*Journal of the Royal Army Medical Corps. Vol. 161 Iss. 4 pp 345-347*

Heterotopic ossification (HO), the formation of bone at extra skeletal sites, has been described in the military setting for over 1000 years. Over 60% of amputees injured by improvised explosive devices in the Afghan conflict have developed HO and as such, a renewed interest in its formation has developed. The pre-requisites for bone formation are (i) an agent capable of inducing bone formation, (ii) the presence of bone forming cells and (iii) an environment capable of supporting bone formation. It is hypothesised that a mesenchymal stem cell that experiences a blast wave can be manipulated to differentiate into bone-forming cells.

The London suicide terrorist bombings that occurred in July 2005 resulted in 755 blast-related casualties, 40% of whom were managed by the Royal London Hospital. This study retrospectively analysed the Royal London patients to assess the presence, or absence, of military-established risk factors (age, zone of injury, injury severity score) for the formation of HO. This cohort of severely injured patients whose injuries also included trauma-related amputations shared some, but not all, of the risk factors identified in the military population. Similarities in injury severity score (>16) and local wound management were identified. HO was confirmed as being present by radiographs taken at least 3 months after injury and was classified according to its morphological shape and magnitude, as well as the percentage of total width of the affected limb. Evidence from military and civilian patients has demonstrated that a blast mechanism of injury subjects casualties who sustain amputations to a high risk of forming HO.

**Figure 2: Left lower limb radiograph four months post-traumatic transtibial amputation with subsequent 'beetle carapace' type heterotopic ossification formation [reprinted with permission]**

### HO – a military and civilian problem

HO results in functional impairment.
The exact aetiological process in the formation of HO remains elusive.
The risk of HO is valid in the civilian domain devoid of the (military) environmental factors previously thought to contribute to HO formation.
Thus military HO research informs and is informed by civilian HO research.

## Posterior Mini-Incision Total Hip Arthroplasty Controls the Extent of Post-Operative Formation of Heterotopic Ossification

*Edwards DS, Barbur SA, Bull AMJ, Stranks GJ. (2015)*
*European Journal of Orthopaedic Surgery & Traumatology 25(6): 1051-5*

Heterotopic Ossification (HO) is the formation of bone at extra-skeletal sites. Current literature identifies a range of 8-90% of patients undergoing total hip replacement (THR) in the civilian setting will develop HO of differing levels of severity (Figure 3). Recent research investigating the effect of inflammation and local ischemia on stem cell manipulation and subsequent HO formation has proposed the possibility that HO is likely to be stimulated by local and systemic factors contributing to the pathological picture. In the case of THR, it is surgery itself that indicates the index event leading to HO.

The purpose of this study was to examine which surgical factors and patient variables influence HO rates; incision length, intra-operative measures such as prosthetic fixation type, the use of pulsed lavage and canal brush, component size and material, age, gender and fat depth of the patient.


**Figure 3: Brooker's classification (classes 1–4) of HO after hip replacement with worsening severity (left to right) where Grade 4 is bridging of the joint with HO resulting in joint stiffness [reprinted with permission]**

510 cases of THR were analysed. 10.4 % demonstrated evidence of HO 12 months after surgery. Male patients were statistically more likely to develop HO ($p = 0.027$). Longer operations (greater than 60 min) caused higher grades of HO ($p = 0.047$). Incision length was positively correlated with the extent of HO. HO was limited to areas above the greater trochanter in smaller incisions ($p = 0.007$). Incisions greater than 10 cm resulted in more widespread HO formation ($p = 0.021$).

Results demonstrate that differences in intra-operative practice do not contribute significantly to the factors that initiate HO formation. It is therefore an ''all or nothing'' event where the act of surgery itself, no matter how extensive, is the contributing factor. Inflammation and tissue damage/ischemia are therefore likely to be the key in the formation of HO.

### Inflammation and ischemia are likely to be the key in the formation of HO

The rate of HO in this total hip replacement cohort was 10.4%; this is at the lower end of the range of published rates.
The posterior minimal incision is a safe approach to use with regard to the formation of HO.
The minimal incision technique reduces the extent of HO found in the soft tissue.
Understanding HO in the civilian population will shed light on the unique HO findings in amputees due to blast.

## What is the Magnitude and Long-term Economic Cost of Care of the British Military Afghanistan Amputee Cohort?

*Edwards DS, Phillip RD, Bosanquet N, Bull AMJ, Clasper JC. (2015)*
<u>*Clinical Orthopaedics and Related Research 473(9): 2848-2855*</u>

2014 saw the withdrawal of British troops from Afghanistan as military operations were handed over to the Afghan security forces. It is now well documented that the Afghan conflict is associated with casualties surviving highly complex trauma; attributed to improved personal protection equipment, on the ground medical care and rapid extraction of the casualty. However, one consequence of the complexity of the wounds is illustrated by the resulting multiple amputees. This study was the first to fully quantify and qualify the extent and nature of all trauma related amputations from the 13 year conflict. It aimed to estimate the projected long-term cost of the Afghanistan amputation cohort from the perspective of the healthcare provider, the National Health Service.

A total of 265 casualties sustained a total of 416 amputations. The average number of limbs lost per casualty was 1.6 (SD ± 0.68). The most common level of amputation was transfemoral (above knee) totaling 153 patients. Single amputations were more likely to be associated with transtibial-level (below-knee) injuries (89 patients out of 140 single amputations), whereas transfemoral amputations were most common in double and triple amputees (134 amputations out of 268 limbs lost). Using the Markov mathematical model for health economics, the study generated general and limb associated health outcomes over a 40 year cycle based on an average amputee's profile. Using current cost of care and prosthetic costs, the study estimates the long-term cost of the UK Afghanistan lower limb amputee cohort to be £288 million in today's (2015) currency.

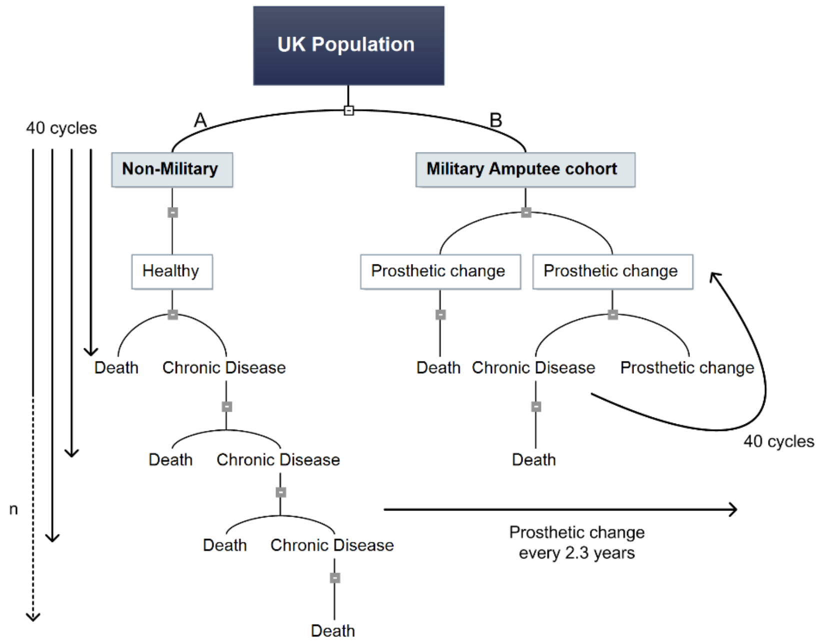



**Figure 4: A Markov decision tree demonstrating the difference in the chronic health profile of (A) the normal population and (B) the military amputee cohort described in this work [reprinted with permission]**

### Society must investigate the long-term effect of injuries on the war-wounded

The Afghan conflict resulted in high numbers of complex injuries.
The long-term cost of medical care of the UK Afghan lower limb amputee cohort is estimated at £288 million.
It is likely that the described cohort will experience chronic health problems experienced by the general population, as well as specific issues as a result of their injuries.
It is incumbent upon society to investigate the long-term effect of these significant injuries.

## A Novel Computational Framework for Deducing Muscle Synergies from Experimental Joint Moments

*Gopalakrishnan A, Modense L, Phillips ATM. (2015)*
<u>*Frontiers in Computational Neuroscience. 3:8 153-168*</u>

This study presents a new synergy based method for predicting muscle forces for a range of activities. Synergies are weighted muscle groupings as illustrated in Figure 5. In previous computational and experimental studies it has been found that similar sets of movements can be achieved through activation of a low number of synergies (around four), presenting a smaller and potentially more physiologically relevant solution space than other musculoskeletal modelling techniques such as static optimisation, when addressing the muscle load sharing problem. This approach is seen to have particular advantages over more common methods including static optimisation with and without electromyography (EMG) measurement. The derivation of synergies (groups of muscles activated to varying degrees for a set of similar movements) has potential application in rehabilitation as well as training in assessing what activities might be completed based on the patient's existing synergies.

An approach is demonstrated whereby muscle synergies are derived from inverse dynamics joint movements computed from movement kinematics and kinetics. This approach does not rely on muscle activation profiles obtained either from EMG measurements, static optimisation using a cost function, or a combination of these. In addition to obtaining 'pure synergies' based on minimising errors compared to recorded joint moments, a modification of the technique was developed to obtain 'optimal synergies' in which muscle activations were also minimised.  This has application in rehabilitation where particular muscles or muscle groups may have been damaged, while retaining some function. The methodology could be applied to assess whether a particular movement sequence is possible based on training to alter synergy groupings.

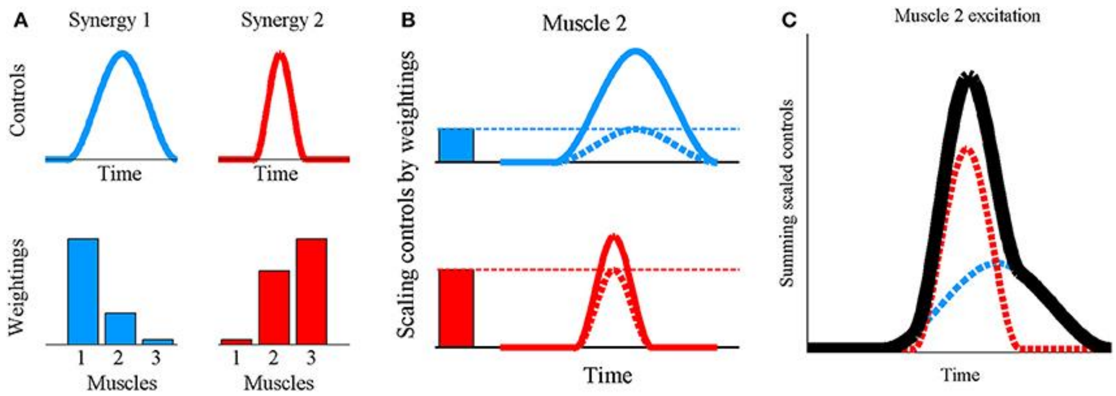



**Figure 5: Simplified schematic showing activation of a single muscle based on derived muscle synergies [reprinted with permission]**

### Predicting muscle forces – a rehabilitation tool

An innovative method has been developed to derive muscle synergies based on movement kinematics and kinetics, without requiring electromyography measures or predicted muscle activation data.
The method has applications in the rehabilitation of amputees or those with neuromuscular damage due to blast injury. It assesses movement sequences that could be achieved based on remaining muscle synergies with and without the assistance of passive or active prosthetics, as well as in training to alter muscle synergies to achieve a family of tasks.

## Informing Phenomenological Structural Bone Remodelling with a Mechanistic Poroelastic Model

*Villette CC, Phillips ATM. (2015)*
*Biomechanics and Modelling in Mechanobiology* *In press DOI 10.1007/s10237-015-073504*

Studies suggest that fluid motion in the extracellular space of the bone matrix may be involved in the cellular mechanosensitivity at play in the bone tissue adaptation process. In the presence and absence of bone fracture due to blast injury long term bone deterioration can occur, thought to be linked either to an altered cellular environment or altered cellular response. Hence, an understanding of the macroscale implications of altered cellular mechanosensitivity is essential to understanding the long term musculoskeletal response following blast injury. The primary goal of this study was to isolate phenomenological drivers based on the results of a mechanistic approach, to be used with a beam element representation of trabecular bone in mesoscale structural modelling.

A single beam model and a microscale poroelastic model of a single trabecula were developed. A mechanistic iterative adaptation algorithm was implemented based on fluid motion velocity through the bone matrix pores to predict the remodelled geometries of the poroelastic trabecula under 42 different loading scenarios. Regression analyses were used to correlate the changes in poroelastic trabecula thickness and orientation to the initial strain outputs of the beam model. Linear ($R^2$ >0.998) and third order polynomial ($R^2$ >0.98) relationships were found between change in cross section and axial strain at the central axis, and between beam reorientation and ratio of bending strain to axial strain, respectively. Implementing these relationships into the phenomenological predictive algorithm for the mesoscale structural femur has the potential to produce a model combining biofidelic structure and mechanical behaviour with computational efficiency.

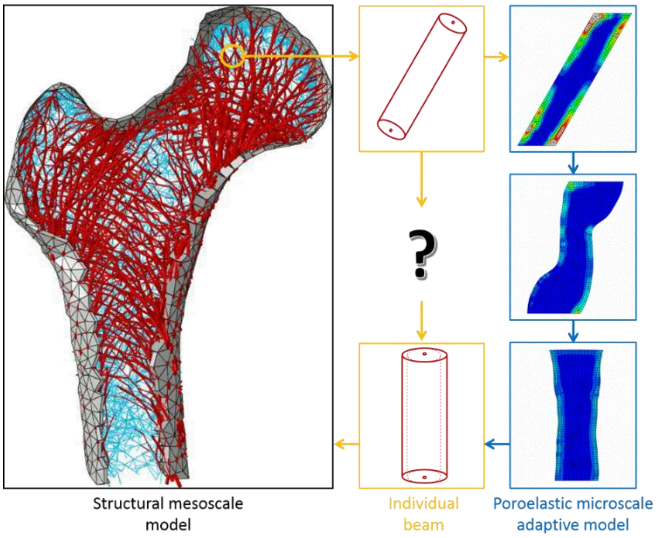



**Figure 6: Overview of the rationale for the present study: a strain-based phenomenological model for a trabecula represented as a single structural beam element is computed using a surrogate microscale poroelastic model iteratively adapted based on its fluid velocity profile under loading. The phenomenological model will be used in the efficient structural mesoscale model of long bones developed by the authors [reprinted with permission - http://creativecommons.org/licenses/by/4.0/]**

### A new computer model to assess the effects of blast injury on bone structure

A model whose structure and mechanical behaviour are biofidelic while maintaining the high computational efficiency of a purely structural model is possible.
The method has the potential to be extended to include cellular response to blast loading, allowing the long terms effects to be investigated across the skeletal system.

## Composite Nature of Fresh Skin Revealed During Compression

*Butler BJ, Boddy RL, Bo C, Arora H, Williams A, Proud WG, Brown KA. (2015)*
*Bioinspired Biomimetic and Nanobiomaterials, 4, 2:133-139.*

A key driver for the Centre is an improved understanding of the nature of the biological response to blast at the cellular and tissue levels. This understanding would be greatly improved by a comprehensive computational model capable of accurately replicating biological responses at high strain rates. In attempting to produce such a model however, difficulties arise due to the complexity of the material under study. Even a seemingly simple tissue, such as porcine skin, is composed of at least four different layers. Each layer is subtly distinct at the molecular and cellular level and from those adjacent to it. Artificial surrogates, such as rubbers or plastics, rarely mimic this level of heterogeneity.

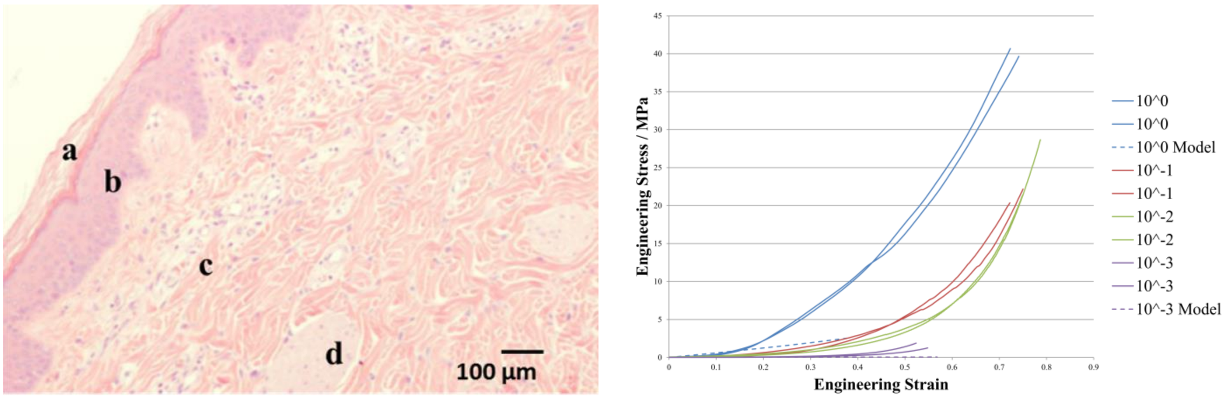



**Figure 7: (L) An optical image highlighting the composite nature of skin. Each of the lowercase letters corresponds to a separate layer comprising a distinct cellular and molecular structure: a) keratin, b) epidermis, c) papillary dermis, d) reticular dermis. (R) Graph of the genuine material response of porcine skin as compared to a computational model. The solid lines represent experimental data, whilst the dotted lines are estimates produced by the model. The different colours signify varying rates of testing. At the lowest rate of testing (purple) the model reasonably approximates empirical data, however, as the rate of testing is incrementally increased up to high rates (blue), the model loses its predictive power [reprinted with permission]**

When we compared empirically derived material data on porcine skin to estimates of dynamic behaviour produced by a simple computational model, the two fits were noticeably different. This discrepancy increases as the skin is compressed at higher rates. As a result, this is a profound challenge to those wishing to computationally model the blast response of biological tissue.

### Physical experiments provide data on biological material reponses

Biological materials, such as skin, are highly heterogeneous. This is rarely true of synthetic proxies, such as rubbers or plastics, used to mimic biomaterials experimentally.
Current computational models are limited in their ability to capture fully the complexity of the material responses of living tissues at the high strain rates that occur during blast injury.
This work allows the development of more realistic material models that take into account the composite nature of skin and other tissues that are highly vulnerable to blast.

## The High-Strain Rate Loading of Structural Biological Materials

*Proud WG, Nguyen TTN, Bo C, Butler BJ, Boddy RL, Williams A, Masouros SD, Brown KA. (2015)*
Metallurgical and Materials Transactions A Vol. 46A 4550-4559

The study of injury to human subjects in a range of civilian and military scenarios is hugely important. To do this, a range of devices operating in the appropriate loading range is required, along with good interaction between physical, biological and medical sciences. This study gives an overview of some of the results of collaborative investigations into blast injury. The requirement for time-resolved data, appropriate mechanical modelling, materials characterisation and biological effects is presented. The use of a range of loading platforms, universal testing machines, drop weights, Hopkinson bars and bespoke traumatic injury simulators are given.

Skin is often damaged by blast. Characterising the material properties of this tissue over a range of loading rates representative of blast injury conditions is an important step towards developing biofidelic models for mitigation applications. Having initiated comparative studies of the heterogenous properties of fresh porcine skin, data obtained at a strain rate of $1.0s^{-1}$ (Figure 8) illustrate variation in the relative stiffness of these skin samples, reflecting differences in their underlying structure and compositions. Results such as these feed the requirement for quantitative data required for mechanical modelling and assessing the medical outcomes of blast injury. Ensuring the correct loading and forces are exerted on materials provides an understanding of how they behave and how they damage. This ensures that clear measurements are made and that damage mechanisms can be addressed in a systematic fashion.

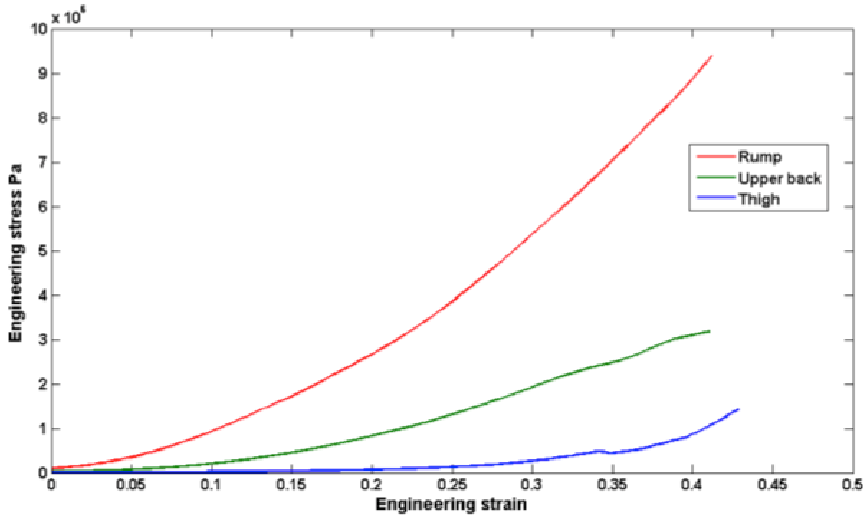



**Figure 8: Comparison of stress-strain curves for skin taken from different anatomical regions. These were obtained on an Instron testing rig at a strain rate of 1 $s^{-1}$ [reprinted with permission]**

### Skin material responses vary greatly; these variations must be taken into account in understanding the effects of blast

The relationship between blast stimulus and the level of injury to specific areas of the body is not well established. In order to study this subject, good interaction between physical, biological and medical sciences is required.

Different experimental techniques, presented herein, are currently being used by multidisciplinary researchers at the Centre to examine the short and long term biological effects of transient mechanical loading to the human body.

Knowledge of the relationship between the stimulus and the level of injury will provide an understanding of the long term clinical manifestations of blast injury.

## Identifying spinal injury patterns in underbody blast to develop mechanistic hypothesis

*Spurrier E, Gibb I, Masouros SD, Clasper JC. (2015)*
<u>*Spine 41(5) 268-275.*</u>

Spinal injuries are common in underbody blast. Despite this, there are few reports in the published literature detailing military spinal injury. While a standard test exists for vehicle designers to improve the systems used to reduce the risk of injury, it is not clear whether this test is realistic or useful. This is because the behaviour of the spine, when it is subject to blast loads, is not well understood. A better understanding of the mechanism of spinal injury in blast is needed in order to begin development of a better injury prediction model. The first step in developing this understanding is to identify the patterns of injury in blast incidents. This study reviewed all British victims of Improvised Explosive Device (IED) strikes on vehicles. A search of the Joint Theatre Trauma Registry (JTTR) yielded 126 casualties of explosion, coded as having spinal injuries. Of these, 48 had minor muscular injuries or back pain, leaving 78 casualties with spinal fractures. Of the 78 casualties, 53 survived. The distribution of spinal fractures is shown in Figure 9. The mean age of the cohort was 26.8 years and each casualty had a mean 3.44 fractured vertebrae. The most common injuries noted were thoracolumbar flexion-compression injuries, along with simple wedge fractures. This suggests that the spine is fracturing because of load in front of the spinal column, and that the spine is flexing at the point of injury. Such injuries may occur as a consequence of the legs being forced upwards by the deforming vehicle floor, combined with the axial load through the pelvis.

Data from this study is being used to inform a series of laboratory experiments in the Centre to enhance our understanding of how the spine fails during blast. Knowledge of this will be invaluable in determining the optimum seated posture within vehicle in order to reduce the risk of thoracolumbar injury as a consequence of under vehicle explosions.

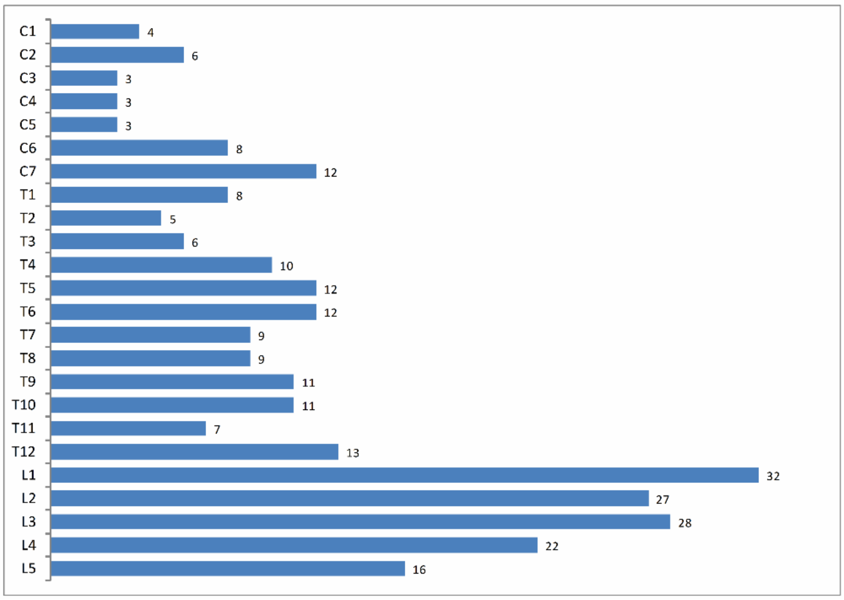



**Figure 9: Number of victims with a fracture at each vertebral level [reprinted with permission]**

### Spinal injury due to under vehicle explosion is not well understood

Spinal injury is common in mounted troops due to under vehicle explosions.
The transmitted forces are applied anterior (in front) of the spinal column causing it to break at specific locations.
The mechanism of injury is complex. Injuries are caused by forces directly through the structure of the vehicle but also due to the legs being thrown up by the deforming floor.
This work will produce a better injury model of the spine in under-vehicle explosions that can be used to improve assessment of the protective ability of vehicles and personal protective equipment.

# In the Spotlight

Introducing a new feature in our annual report, *In the Spotlight* takes a look at significant related work published this year by researchers at key partner institutes who have either built on the output of the Centre, or have generated findings of significant use to its current research goals.

## Vertical accelerator device to apply human loads simulating blast environments in the military to human surrogates

*Yoganandan N, Pintar FA, Schlick M, Humm JR, Voo L, Merkle A, Kleinberger M. (2015)*
*Journal of Biomechanics. Vol. 48 Issue 2 pp 3534-3538*

The objective of this study was to develop a device to apply vertical impact loads to Post Mortem Human Surrogates (PMHS) and dummy surrogates to assess the injuries sustained from underbody blasts. Building on the Centre's previously published work[2] relating to the assessment of cadavers and anthropometric test devices using AnUBIS, the researchers at the Medical College of Wisconsin presented another device (Vertac), capable of applying dynamic loading to different body regions. Acceleration and time data recorded in this study compared well with that of the Centre, and like AnUBIS, the Vertac is capable of accommodating different posture positions for its test specimens. In addition to examining injury to the lower extremity, the Vertac is capable of accommodating a roof structure at a desired height to determine head-neck complex kinetics under contact and or inertial loads. This is of interest to the Centre's work on the performance and design of helmets[3] for protection against traumatic brain injury.

## Make the bleeding stop

*Brohi, K. (2015)*
*Science Translational Medicine. Vol. 7 Issue 277 pp 277-287*

"Trauma haemorrhage is one of the world's biggest killers, responsible for more than 2 million deaths every year… It represents one of the greatest challenges and opportunities in translational medicine". This study highlights the mortality rates in casualties with massive haemorrhage and the effect on survivability when bleeding is controlled, and the physiology and cell integrity can be preserved. Previous work in the Centre examined the positioning of pelvic binders[4] following pelvic fracture and the effect on haemorrhage control. Prior to this, the effect of the position of the pelvic binder in clinical practise had not been described. The results of our study have since changed clinical practise at major trauma centres in the UK, and the technique of positioning the binder identified by CBIS, is now included as part of Military Operations Surgical Training (MOST), a compulsory course for troops being deployed. Brohi's study goes deeper into the haemorrhage problem, or indeed solution, and presents a series of targeted novel therapeutics and diagnostics. The complexities of coagulopathies are identified, together with the challenges of designing appropriate clinical trials. Success, it shows, requires the combined efforts of systems biology, experimental medicine, bioengineering, translational therapeutics and specialist clinical trial units working at the international scale. Through its Bioengineering Trauma Initiative, CBIS hopes to bring together the necessary people to address such issues, and currently has a vascular MD surgeon in the Centre undertaking a 3 years of research into the open pelvis problem. CBIS is currently investigating a formal collaboration with Professor Brohi and his team.

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[2] Newell, N., Masouros, S.D., Ramasamy, A., Bonner, T.J., Hill, A.M., Clasper, J.C., Bull, A.M.J. 2012. *Use of cadavers and anthropometric test devices (ATDs) for assessing lower limb injury outcome from under-vehicle explosions*. Proceedings of IRCOBI. pp. 296–303

[3] Ghajari, M., Peldschus, S., Galvanetto, U., Iannucci, L., *2013 Effects of the presence of the body in helmet oblique impacts.* Accident Analysis and Prevention. Vol. 50 pp263-271

[4] Bonner, TJ., Eardley, WGP., Newell, N., Masouros, S., Matthews, JJ., Gibb, I., Clasper, JC., 2011. *Accurate placement of a pelvic binder improves reduction of unstable fractures of the pelvic ring.* Vol. 93-B No. 11 pp.1524-1528

# 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.

## Matthew Hopkins (Year 2 PhD Student)

My work at the Centre relates to the rehabilitation of the blast injured. Whilst the progression of prosthetic technology has increased dramatically in recent years with the development of powered and bionic limbs, the most fundamental portion of a lower limb prosthetic has been overlooked. The *socket* is responsible for load transfer from the prosthetic limb to the residual limb. Poor fitting sockets or misalignments can lead to instability damaging load transfer and, in combination with temperature build up and moisture from the skin, the breakdown of healthy tissue. Problems resulting from socket fit are not isolated, affecting up to 75% of the amputee population in the form of various skin conditions. To combat this, I aim to produce a device capable of providing prosthetists and patients with real-time feedback to assist in the development of lower-limb prosthesis and to provide an early warning system to limb-users, alerting them to conditions that could compromise the health of their residual limb. This device has been dubbed a 'smart-socket'.

In my time at the Centre to date, I have found that the nature of my research creates cyclic phases of design, evaluation and modification. My project is driven by the production of hardware; an evolutionary process combining elements of circuit design, electronics, biomechanics, programming, modelling, 3D printing and statistical analysis. My time is split between each of these aspects, often with multiple parts developed in unison. Programming phases are the most time consuming. Using a variety of languages – Java, C, C# and BASIC, I need to produce something that is simple for the end user, yet complex in order to manage the extraction and analysis of data. Interspersed with the programming phases is the development of the physical circuitry; bespoke printed circuit boards (PCBs), sensor circuitry and methods of embedding the sensors. PCBs and sensors are designed in computer aided design software (CAD) and manufactured externally or printed in the laboratory. As designs have evolved, processes have become steadily more streamlined as iterative improvements are made. I have completed a number of preliminary tests of my technology which has provided valuable indications as to the technology's capabilities and limitations. Development of the control circuit boards has been undertaken in conjunction with colleague Samuel Wilson, based in Mechatronics in the Faculty of Medicine and his work on upper limb amputees. The combination of pressure sensing capability and room for other peripherals with my circuitry and the mechanomyography (MMG) and inertial units available in his work provide an electronic suite to support a number of projects within the laboratory.

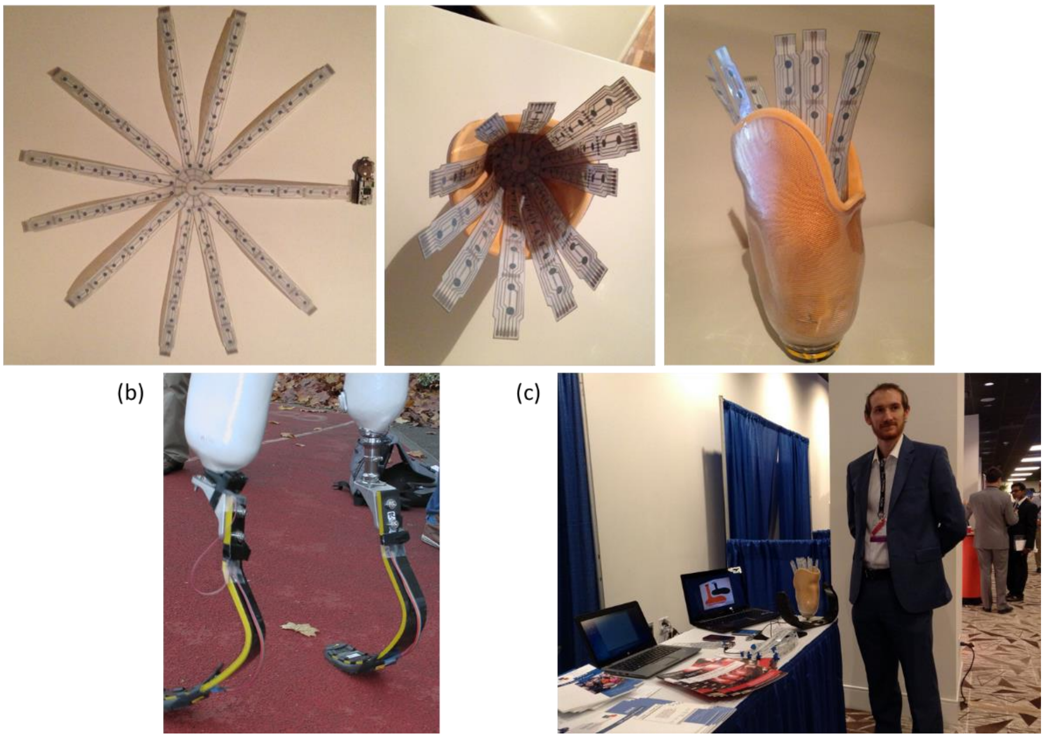
The multidisciplinary nature of my project, much like all the work in the Centre, encourages me to interact with a wide variety of people in both academia and industry. My time is divided between two of Imperial College's campuses – the MSK laboratory in the Department of Surgery and Cancer at Charing Cross Hospital and Mechatronics in Medicine (MiM) at South Kensington. I am frequently in contact with employees of the Blatchford Group, at the Holderness Limb Fitting Centre in Charing Cross Hospital and at Headley Court, each responsible for the development of lower limb prosthetics for the civilian and military populations respectively. Feedback from the prosthetists at Blatchford is invaluable in keeping the project moving in practical directions and ensuring the end product meets user needs.

In addition, I have been involved in representing the University and the Centre at numerous public events in order to raise awareness and interest in our research. Early in 2015, I took part in a two-day demonstration at the British Science Museum, interacting with the public by explaining and demonstrating some of the research conducted within the MiM laboratory at Imperial College. In May, I was involved in the Imperial Festival displaying the varied research conducted at the Centre. A personal highlight this year however was representing the Centre at the Defense Innovation Conference in Austin, Texas. My supervisor Professor Alison McGregor, PhD colleague Samuel Wilson and I manned a stand within the conference to draw attention to the research conducted in the Centre.

I find myself increasingly involved with undergraduate student projects looking to extend the pressure sensing technology to further applications. Such applications include use of pre-existing designs such as the Flexifoot insoles developed by Dr Thomas Burton for gait analysis, to customised designs for the measurement of grip force. I am also involved as a teaching assistant for the module Embedded C for Microcontrollers. This module allows me to make use of skills that I normally implement with the development of the smart-socket in a different environment. I find that the teaching environment, in which I have to explain ideas I am familiar with, reinforces my own knowledge and understanding of the field and can have a beneficial effect on my own work.

As the technology matures, much of my time will move into testing and evaluation through cohort studies using both NHS and military patients. These studies will be invaluable in emphasising the strengths and weaknesses of the prototype and the path to device optimisation. Current work is beginning to branch into the nuances of embedding the sensors with the potential to spread into the realm of 3D printing. I expect both the project and its daily demands to evolve as prototypes follow the cycle of development, evaluation and improvement.

(a)



(b) (c)

**Figure 10: (a) Socket spider showing the extent of coverage within the socket, maximising data collection (b) Preliminary testing of the technology; shows the application of pressure sensors for a lower limb prosthetic running blade for gait pattern and inertial measurement (c) Representing the Centre at the Defense Innovation conference in Austin, Texas earlier this year**

## Dr Harsh Amin (Year 2 Post-Doctoral Research Associate)

We are surrounded by mysterious and mesmerising nature that does not reveal its secrets so easily – instead giving us a sneak-peek through a key-hole. Indeed, dissecting nature's intricacies is challenging, as well as revealing for scientists worldwide. My passion lies in understanding stem cell physiology in the context of musculoskeletal diseases. After finishing a period of postdoctoral training (under the supervision of Professor C Ross Ethier, Department of Bioengineering, Imperial College London), I joined the Centre in June 2014 to pursue a postdoctoral position under the supervision of Professor Sara M Rankin. I am currently elucidating molecular mechanisms involved in trauma injury-led Heterotopic Ossification (HO), specifically in the blast trauma setup.

CBIS is a unique hub of scientists from various backgrounds, including professionals with medical, engineering and scientific qualifications, putting their efforts together to understand blast injuries and subsequently designing therapeutic interventions. Nobel Laureate Frederick Gowland Hopkins noted "It is an old saying, abundantly justified, that where sciences meet, there growth occurs", and rightly so. The driving ethos of CBIS is its multidisciplinary approach to the problem by successful internal and external collaborations.

My daily routine in the Centre is highly dynamic, primarily due to my multiple responsibilities. These include managing/supervising multiple projects of PhD/MDRes students, MRes and undergraduate students and a technician, along with my own laboratory work. Moreover, I spend a reasonable amount of time writing grant applications, research proposals, research articles, reports, giving presentations/talks and correcting theses. In my year and a half as researcher at CBIS, I have successfully developed 2 internal collaborations (with Professor Anthony Bull's and Dr Bill Proud's teams) and 3 external collaborations (Dr Kambiz Alavian, Hammersmith campus, Imperial College; Professor Liam Grover, University of Birmingham; Dr Nicky Mordan, UCL). Collaboration activities range from preparation or providing samples, training PhDs and postdoctoral scientists using protocols we have developed here at the Centre, and out-sourcing out-of-expertise experimental work (such as TEM and patch clamp/membrane potential recordings).

Scientific details of my research work: HO (*discussed earlier; see page 15*) is defined as the ectopic formation of mature lamellar bone in non-osseous tissue, such as muscle, tendon and ligament. HO has been associated in both military and civilian settings with traumatic injuries which include spinal cord injury, elbow and acetabular fractures/limb trauma, amputation, burns and head trauma. However, the high incidence (60-65%) in amputees from recent conflicts in Iraq and Afghanistan, poses a significant clinical problem to the military as this pathology has a direct impact on rehabilitation. HO can cause significant loss of motion/mobility, particularly when it forms in proximity to joints, blood vessels or nerves. Surgical procedures to remove such aberrant pathological bone have been reported to associate with a risk of adjacent neurovascular tissue injury. Thus, determining mechanisms involved in the onset of HO are pivotal in order to design targeted interventions to treat HO. Resident mesenchymal stem cells in the periosteum (PO; highly fibrous and vascular connective tissue membrane surrounding bone) play a critical role in fracture healing, and reduced fracture healing is well recognised in the context of blast injuries. We have therefore carried out a number of experiments to investigate whether primary blast limb injuries affect the activity of PO stem cells.

Our Findings:

1. Primary shock wave (with a specific pressure wave intensity for a specific duration using the shock tube) loading on hind limb femur 'primed' mesenchymal stem cells residing in the PO tissue compartment. Furthermore, there was a notable increase in circulating mesenchymal stem cells in peripheral blood with the ability to spontaneously form bone-like nodules post limb trauma.
2. Naïve PO cells treated with serum from the limb trauma subjects (where there was no mechanical loading) exhibited marked increase in bone-like nodule formation by these cells, compared with control cultures, suggesting a systemic response post traumatic injury.
3. Naïve PO cells exposed to primary shock wave *in vitro* showed a significant increase in mineralized bone nodules compared with control cultures, suggesting that primary shock wave stimulates mechanotransduction which at least in part is responsible for the increase in bone formation. Moreover, we recapitulated *in vivo* effects in this novel *in vitro* trauma model using the shock tube, enabling us to reduce number of *in vivo* experiments.
4. As early as 3h post trauma, PO cells exhibited acutely increased mitochondrial load which was functionally responsible for the trauma-led PO cell osteogenesis.
5. Actin filament network was found to be depolymerised and re-organised 24h post trauma, suggesting a mechanotransduction stimulation.
6. Bcl-XL and ERK1/2 were both found to be phosphorylated within the first 15 min of trauma exposure, suggesting the involvement of MAPK pathway in shock wave-led bone formation.

In addition to the above findings, I have developed a number of techniques within the Centre. These include, mitochondrial dynamics-associated assays, stem cell functional assays, RNA sequencing/Next generation sequencing analysis using Partek software, and computational modelling for mitochondrial and actin dynamics. Our studies are pivotal in pin-pointing 'key' early molecular and cellular changes in the blast trauma-affected servicemen, and concomitantly design early interventions to block biochemical pathways leading to the HO post-blast trauma.

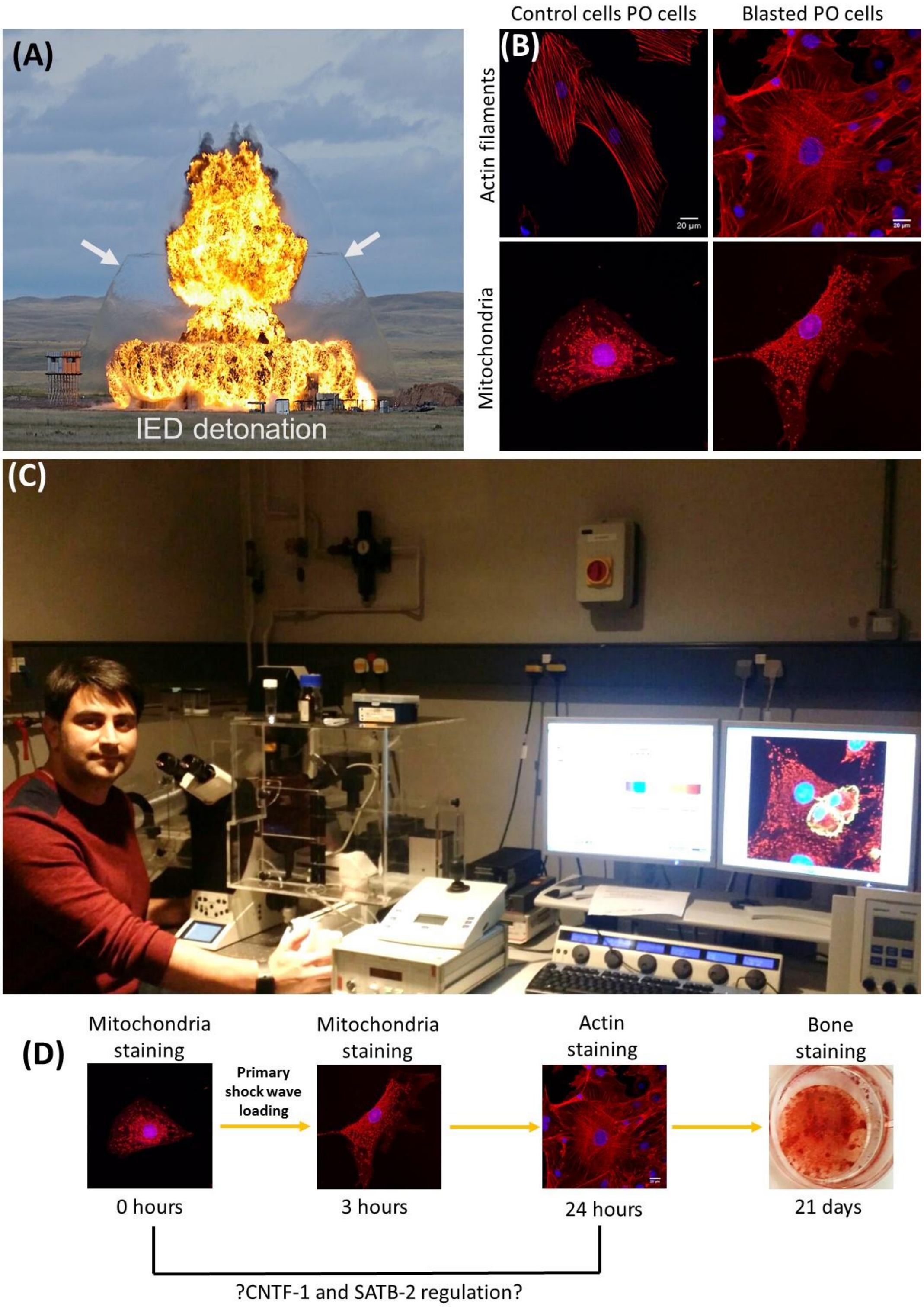



**Figure 11: (a) Representative image of primary shock wave generated from an IED explosion (b) Mitochondrial and actin staining of PO cells subjected to primary shock wave (c) Confocal microscopy for actin and mitochondrial analyses (d) Dissection of molecular mechanisms on hourly bases post primary blast trauma**

# Alumni

This section captures the depth and breadth of the impact of our work by presenting one of our researchers who has gone on to another role in 2015.

## Dr Angelo Karunaratne

Angelo Karunaratne was one of the first post-doctoral research associates at the Centre, having joined in October 2012. His role was to develop experimental platforms to investigate tissue level mechanical and structural relationships of connective tissues such as bone, ligament and cartilage, especially during blast strain rates. Angelo is an expert in multiscale imaging techniques such as scanning electron microscopy, microCT, confocal imaging and synchrotron X-ray imaging. During his time at the Centre, Angelo designed and manufactured a miniature mechanical testing machine for the high speed, screw driven and hydraulic Instron machines to test biological tissue explants. Using these mechanical testing machines, in conjunction with imaging modalities, Angelo performed in-situ mechanical testing to characterise mechanical properties of connective tissue at cross strain rates and elucidate their structural influence on the strain rate dependent mechanical behaviour. These experimental results (material properties of bone, cartilage and ligament at cross strain rates) can now be used by other researchers at the Centre to develop computational models to predict injury mechanisms in tissues at traumatic incidents.

Angelo was also involved as a co-Investigator in multiple projects that were carried out at the Centre and in collaboration with other departments at Imperial College. These included investigations relating to Heterotrophic Ossification and Blast lung (Department of Bioengineering), Regenerative medicine (Department of Materials) and Bisphosphonates & Osteoporosis (Department of Surgery and Cancer). His strong connections with the UK synchrotron facility Diamond Light Source and expertise in x-ray techniques have provided cutting edge research advancements to the Centre and indeed Imperial College. Angelo has now joined the University of Moratuwa, Sri Lanka as a Senior Lecturer to continue his teaching and research career. In Sri Lanka he is in the process of implementing a research project in collaboration with the Centre and Diamond Light Source to investigate Heterotrophic Ossification in Sri Lankan military amputees.

CBIS looks forward to continuing to work with Dr Karunaratne as his career progresses.

# Cohort Studies

From 2016, Imperial College London will participate in the ADVANCE cohort study. ADVANCE is the largest study ever undertaken of Britain's military casualties and their long-term injury and health outcomes. The idea of a cohort study was first introduced in 1935, and it is defined as the study of a group of individuals distinguished by a single variable – occupation or geographical location for instance – and is one of the most valuable tools for medics and medical scientists. The cohort study offers a rich and varied data set, essential for understanding and progress in the fields of complex physiological and psychological conditions. The goal of the ADVANCE study is to achieve an improved sustained transition into civilian life for British military battlefield casualties, present and future, by providing high level evidence of their long term cardiovascular, musculoskeletal and other physical and mental health and psychosocial related outcomes.

Funded by the MoD, Help for Heroes and Libor, the ADVANCE study will be led by Wing Commander Alex Bennett, Head of Research Defence Medical Research Centre, Professors Paul Cullinan and Anthony Bull (Imperial College London), Professor Nicola Fear (King's College London) and Dr Amarjit Samra (Director of Research, Royal Centre for Defence Medicine). The 20 year study of 600 combat casualties, with matched controls, offers a unique opportunity to describe the long-term outcomes of blast and other military trauma. ADVANCE will influence the development of medical, surgical and rehabilitation care pathways for the future, by filling the knowledge gap related to military combat trauma patients and civilian blast victims. ADVANCE will also provide the means to identify and access the war wounded to facilitate early translation of new therapies when they become available.

The first military-medical cohort study began in 1941, a year since the skies over south-east England quietened after the Battle of Britain. The Guinea Pig Club didn't know it was a cohort study – it thought it was a drinking club – but this was part of a cunning plan by plastic surgeon Archibald McIndoe who frequently smuggled sound medical practice into his military wards disguised as social activities. A large barrel of beer stood at the end of one room and the patients were allowed to refill their own tankards as much as they liked. This was no challenge to military regulations: the beer was so watered-down it was essentially brown fizzy water. For his patients with severe burns injuries, inflicted as a result of their service in the Royal Air Force, keeping properly hydrated was an essential part of the management of their condition and it was a great deal easier to achieve if they thought they were up to mischief.

The Guinea Pig Club's creation was part of the same impulse. Improvised by McIndoe over the next twenty years, it laid the foundations for future effective military medical cohort studies. Although focusing on one particular injury, severe facial and functional burns, the Club's signature casualty has much in common with the current understanding of complex polytrauma. When the first severely burned patients were brought to McIndoe at the Queen Victoria Hospital in East Grinstead, the injury was seen in very much the same terms as blast injury. Both were originally thought to be unsurviveable. Into the late 1930s, burns casualties were given morphine and their families gathered at their bedside for their last hours. But quiet advances in intravenous therapies of plasma and saline meant that the effects of secondary shock became manageable. Suddenly, those young men burned in Spitfires and Hurricanes during the Battle of Britain were now still alive, in RAF hospital wards, needing treatment for wounds the like of which no surgeon, anaesthetist or physiotherapist had ever seen before.

For the remainder of the war, McIndoe, John Hunter (chief anaesthetist) and Edward Blacksell (rehabilitation and welfare officer) worked to reconstruct and rehabilitate a patient cohort of 700 pilots, navigators, weapons operators and ground crew, most in their early twenties. 200 of them would require total facial reconstructions, over many years. Most of the others would need hand surgery, modification of amputation stumps, eye socket and jaw repairs, in addition to their burns treatment. At the time, multiple surgeries were thought to be dangerous, particularly the likely long-term effects of repeated anaesthetics given for procedures regularly taking eight to ten hours. No-one knew how the grafts and repairs would hold up – or how the lives of those who had them would hold up also. The Guinea Pig Club, with its annual post-war meetings and effective club-wide communications via newsletters offered the opportunity to find out.

Every year from 1941, as many members as could travel, met at East Grinstead. There was a club dinner with speeches but quietly the event was about the medical examinations the members went through during the day. McIndoe, and after him the RAF's consultant plastic surgeons, carefully examined hundreds of faces and hands that had been rebuilt, noting where the grafts had been particularly successful and repairing any that had not. Behind them stood the chief anaesthetist, listening for breathing irregularities and monitoring circulatory disorders, although noting that none of the Club members seemed to demonstrate any ill-effects from their frequent and heavy anaesthetics. Blacksell asked chattily about their work and family lives, and along the way found out how their reconstructed limbs worked, designing exercises for joints under heavily scarred tissue that needed to maintain functionality. After the Falkland Islands campaign, Guinea Pig Club members visited burns casualties and taught them the same exercises that they had learned and which continued to work forty years later.

The Club still meets today. At the time of writing there were 21 members living in the UK, and those that can still travel attended the 2015 meeting where there was a dinner with speeches and the discreet medical examinations through the afternoon. Their survival, as demonstrated in the results of those examinations, has defined and consolidated the specialisms of plastic and reconstructive surgery and the reputation of Queen Victoria Hospital in East Grinstead. Above all, the results show the long-term effects of multiple procedures for a severe form of casualty; this is unique, invaluable evidence and there is nothing else like it in modern military medicine.

However, it is not the burns injury itself that makes the operation of the Guinea Pig Club so valuable as a comparative for future cohort studies. The Guinea Pig Club had very particular features that enabled it to function for so long, so effectively. Its members felt very special – it was "the most exclusive club in the world but the entrance fee was something most men would not care to pay…"- and always part of something that represented the cutting edge of medicine and medical science. The newsletter was fundamental to its success also: it appeared regularly, and efficiently kept everyone up to date with personal, military and medical developments that affected them. There is a club tie (Bill Foxley who had a total facial reconstruction, is wearing it in Figure 12) and a strong group identity – branding before the concept was properly understood. The annual check-up monitored not only the long-term physical effects of treatment but also psychological welfare. Employment, relationships and general wellbeing could be followed and interventions recommended where necessary. Club membership maintained morale in a patient group that otherwise could feel isolated, and the annual medical check was a form of intervention in itself. Group welfare was self-sustaining; members were not just RAF veterans, they were Guinea Pig Club RAF veterans, with access to the finest medical care in the land, and success rates to prove it. First among (wounded) equals.

**Figure 12: Bill Foxley (second from left) in 1945 and in 2007**

The Guinea Pig Club is therefore the exemplar for the modern military medical cohort study. Many of the practical questions that will arise with a long-term study of this nature have already been answered back in the 1940s and 1950s. A community was created that consolidated the extraordinary medical developments of the war years, and helped bring surgery and rehabilitation into the modern era. Today, both civilians and military patients still benefit from its vision and its outcomes.

# The Bioengineering Trauma Initiative

Medicine has historically advanced in war. Combat casualty care has progressed in multiple areas in recent years; innovations in pre-hospital care, expedited casualty evacuation and new in-hospital damage control resuscitation protocols optimised for battlefield trauma cases. In making these changes, the field hospital changed the way medics and nurses received and managed casualties. Modern military survival rates now include such severe cases that would previously have been considered unexpected survivors. Valuable lessons learned at British military field hospitals in recent conflicts are now being used to save civilian lives. The Ministry of Defence's placement of medical officers in major trauma centres across the UK ensures the transfer of knowledge and the advancement of medical practise for the benefit of casualties of civilian trauma. The Bioengineering Trauma Initiative at Imperial College London is the Centre's attempt at achieving the same.

Hosted by Imperial College's Institute of Biomedical Engineering[5], the Bioengineering Trauma Initiative represents a cross college programme between the South Kensington Faculties of Engineering and Medicine, and Imperial's own Major Trauma Centre at St. Mary's Hospital, London. Building on research which, to date, has focused on injuries sustained by military personnel, the mission of the Initiative is to translate the lessons learned from this research to the civilian domain, to discover and develop transformative solutions for patients and clinicians of trauma. According to the Trauma Audit and Research Network "every year across England and Wales, 12,500 people die after injury. It is the leading cause of death among children and young adults of 44 years and under. In addition, there are many thousands who are left severely disabled for life".[6]

Current research being undertaken via the Initiative is divided into three research themes reflecting the expertise in CBIS and the most significant injuries treated at the Major Trauma Centre. Leadership is provided clinically by Mr Shehan Hettiaratchy, Chief of Service (Plastics, Orthopaedics & Major Trauma Services), St. Mary's and member of the British Army Reserves serving with Airborne Forces, and academically by Prof (Col) Jon Clasper, former Defence Professor Trauma & Orthopaedics, Royal Centre for Defence Medicine. Key personnel involved in the Initiative include:

**Musculoskeletal**

Professor Anthony Bull – musculoskeletal mechanics

Professor (Col) Jon Clasper – consultant trauma and upper limb surgeon

Surg Cdr Mansoor Khan – consultant trauma surgeon

Lt Col Graham Lawton – consultant reconstructive and plastic surgeon

Dr Spyros Masouros – trauma biomechanics

**Head & Brain**

Professor Martyn Boutelle – deployable sensors on the front line

Dr Mazdak Ghajari – traumatic brain injury

Dr Dan Plant – design consultancy (protective systems)

Professor David Sharp – neurology

Mr Mark Wilson – consultant neurosurgeon St Mary's and London Air Ambulance

**Auditory System**

Dr Andrei Kozlov - sensory neuroscience

Dr Tobias Reichenbach – biophysics of hearing

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[5] http://www.imperial.ac.uk/biomedical-engineering/

[6] https://www.tarn.ac.uk/

# Associated Bioengineering Research

Written by researchers in the Department of Bioengineering, this section highlights some of the ongoing research supported by the Centre, where the staff and students are directly funded by other sources.

## Long bone response to penetrating fragments - Alexander Haley

Funded by the Department of Bioengineering and EPSRC.

One of the new focus areas in Bioengineering is the investigation of the musculoskeletal implications of penetrating injuries from blast fragments. A gas gun facility, recently developed in the Department of Physics will enable us to simulate explosive fragment threats ('shrapnel') in a controlled and reproducible manner. The preliminary set of testing will examine the relationships between fragment properties and the associated risk of fracture in long bones such as the tibia. Ultimately, this work is undertaken with the aim of providing the foundations for accurate injury prediction and will help all Centre researchers by identifying targets for novel mitigation technologies.

## Understanding the musculoskeletal function of through- and above- knee amputees – David Henson

Funded by the Department of Bioengineering.

Amputation, and certainly multiple limb-loss, has unfortunately become the image of our casualties in the last decade, especially following conflicts in the Middle East. The increase in the use of the improvised explosive device (IED) as an offensive weapon by the enemy has resulted in hundreds of young, motivated military lower-limb amputees. Whilst steady-state walking kinematics have largely been replicated through modern prosthetic systems, more complex activities of daily living, such as ambulation on uneven terrain, ascending and descending stairs and slopes, running and cycling remain highly challenging, energy demanding activities. This project aims to analyse, understand and quantify amputee locomotion through the use of advanced musculoskeletal modelling techniques developed at Imperial College. Having created the amputee model, the project then aims to identify and understand deficiencies in the amputee movement strategy. Through the identification of these deficiencies, it becomes possible to design individualised and optimised intervention strategies such as implants, rehabilitation programmes, surgical procedures and prosthetic devices that offer potential for improved performance in sport or activities of daily living, as well as improving amputee comfort and long term health outcome.

## The new generation protective glove - Dr Angela Kedgley

Funded by SBRI / Innovate UK / MoD.

Hand trauma can affect the injured personnel's ability to perform even the simplest of activities, so can have a dramatic effect on the function of a military unit. Statistics from the United States Joint Theatre Trauma Registry (JTTR) indicate that a high prevalence of hand injury persisted in recent conflicts. A collaborative project between Armourgel Ltd. and Angela Kedgley and Spyros Masouros from the Department of Bioengineering, funded by the Ministry of Defence by Innovate UK through SBRI, aims to design, fabricate and evaluate the next generation of protective gloves. The aim is to surpass the protective ability of current technology, while maintaining or increasing levels of dexterity. A new glove is being developed to have targeted protection against blunt trauma for key areas of the hand, which will be achieved by employing Armourgel®, a breathable, energy absorbing material. This will be integrated in a seamless way, providing a comfortable, unobtrusive design. In order to provide the best possible protection, the injury tolerance of the hand is being evaluated. Prototypes of the newly designed glove are being compared against commercially available gloves, designed for a similar purpose, using both current European Standards for testing and additional injury simulation scenarios. This project offers the potential to revolutionise the military field of injury prevention for the hands by increasing both protection and functionality in glove design.

 

## Characterisation of Intervertebral disc material properties across strain rates - Dr Nic Newell

Funded by EPSRC.

While a large number of studies have attempted to characterise the mechanical behaviour of the 24 intervertebral discs in the human spine at slow strain rates, few have investigated the high strain rate properties of the disc. The aim of this ongoing project is to characterise the material behaviour of intervertebral discs (IVD) across a range of loading rates using a combination of experimental and computational techniques. The results of this study will be able to be feed into finite element models of the complete spine, which can be used to investigate circumstances in which the spine is exposed to high-rate loading, for example during under-vehicle explosions.

## Biomechanics of the pelvis & sacroiliac joint - Thanyani Pandelani

Funded by the Dept of Bioengineering and CSIR (South Africa).

The traumatic disruption of the pelvic ring is associated with high rates of morbidity and mortality. This has been even more pronounced in the military setting and specifically in recent conflicts, with high mortality rates due to associated injuries to the soft tissues. The mechanism of traumatic injury to the pelvic ring involves transfer of high loads caused by improvised explosive devices, anti-vehicle landmines and falls from heights, thus, these injuries rarely occur in isolation. These high loads also result in vertically and rotationally unstable pelvic injuries and open-book injuries which require a multidisciplinary approach to treatment. The open book injury involves damage to the symphysis pubis and the ligaments. Interestingly, the widening of the sacroiliac joints was present in 60% of casualties sustaining pelvic ring injuries during the Afghan conflict. This suggests that the integrity of the sacroiliac joints is critically associated with disruption of the pelvic ring. The aim of this research focuses on determining the mechanism of injury of sacroiliac joints, and assessing the degree of instability of the pelvic ring. This study will help in improving current mitigation strategies so that the incidence and severity of pelvic ring injuries is reduced, as well as inform surgical treatment and reconstruction for maximising the return to normal function.

## Local mechanical factors of ectopic bone formation – Naomi Rosenberg

Funded by EPSRC.

This project focuses on the possible mechanical influences on ectopic bone, specifically ectopic bone (or heterotopic ossification HO) seen after traumatic leg injury, by using an adaptive finite element analysis of the residual limb of an amputee. The adaptive part of the remodelling considers local and global mechanical forces and adjusts the bone density and material properties accordingly. The addition of a HO modelling factor regulates the increase in stiffness of surrounding soft tissue elements, or hence, the recruitment of soft tissue elements into ectopic bone. The modelling factor considers the level of trauma and the likelihood of each tissue element behaving aberrantly. Adjusting certain parameters alters the final shape of stiffened tissue (or ectopic bone formation). As such, the relationships can be determined between the sensitivity of a given parameter (such as loading) and the effect it has on the morphological appearance of ectopic bone. This work supports the Centre led activities of Maj D Edwards and Dr H Amin in the investigation of HO in blast injuries.

# Other Funder Support

Whilst the core funding for CBIS is from our three main stakeholders The Royal British Legion, Imperial College London and the Ministry of Defence, the Centre receives significant support from other funding bodies. Below is a look at the support the Centre has received to date.

**ABF The Soldiers' Charity** – *the National Charity of the British Army* supported a research fellow for 2 years in the area of trauma biomechanics. The charity also contributed to the costs of designing AnUBIS, the Centre's traumatic injury simulator.

**AO UK** - *existing to promote and support clinical and basic science research in the treatment of patients with musculoskeletal trauma* contributed the costs of undertaking an assessment (questionnaire) or national volunteers to assist with the Centre's work on spinal injury.

**Atomic Weapons Establishment (AWE)** – *the organisation that provides a central role in the defence of the UK* supported a PhD student to develop new experimental techniques to investigate the effect of blast on live biological material.

**Biotechnology and Biological Sciences Research Council (BBSRC)** – *the lead funding agency for academic research and training in the biosciences* supported a PhD student for 3.5 years to examine foot and ankle blast injuries.

**Defence Science Technology Laboratories (Dstl)** – *a Government organisation that ensures that innovative science and technology contributes to the defence and security of the UK* has contributed to the Centre in the analysis of incident data. In addition, it has provided 6 months of funding via its Centre for Defence Enterprise to examine the structural finite element modelling of bone structure.

**Engineering and Physical Sciences Research Council (EPSRC)** – *the UK'S main agency for funding research in engineering and the physical sciences* funded a PhD student in the Department of Bioengineering focused on the mechanical influences on ectopic bone seen after traumatic leg injury. This work lends greatly to the Centre's research efforts in the area of Heterotopic Ossification.

**Medical Research Council (MRC)** – *the research council that works to improve the health of people in the UK* contributed the cost of tuition fees for a PhD student in the Centre working on lower extremity injuries.

**Soldiers, Sailors, Airmen and Families Association (SSAFA)** – *the Charity that provides lifelong support for our Forces* contributed to the costs of producing AnUBIS.

**The F H Muirhead Charitable Trust** – *the Trust who gives grants to research institutions for the purpose of equipment for medical research* contributed to the costs of producing AnUBIS.

**The Drummond Foundation** – *dedicated to providing relief from suffering* contributed to experimental costs for the Centre's work on Heterotopic Ossification.

**Qinetiq** – *in support of the UK MoD and NATO* contributed to the development of capability by funding a short term research contract to examine the blast mitigation properties of dry and dampened sand.

 

# Communication of the Work

Communication with the wider society is seen as a key factor in delivering the Centre's vision to progress understanding of blast injury through research and education. This usually occurs through a variety of media and public engagement activities. In addition to a host of these during 2015, Centre academics and researchers, together with a number of external collaborators, compiled a textbook detailing the science and engineering of blast injury science. Aimed to help the spectrum of researchers from all backgrounds who seek to conduct science and engineering based research on blast injuries, the contents of the book are a consequence of our experience in working in an inter-disciplinary environment. As such, there is something for everyone.


The text is divided into 4 sections. Section A provides a background in blast physics, biomechanics and the behaviour of materials, giving the reader a solid introduction to the underpinning physics of blast transmission through and within materials. Section B characterises blast injuries by the process of explosion and some of the weapons that produce such injuries. Using the London 7/7 suicide bombings as an example, Section C provides information on the principles of forensic investigation and the types of physical and computational models used to improve the understanding of blast and blast mitigation. The effects of blast on the human is further developed in the final Section (D). Published by Springer, the textbook is available for purchase via all major retailers, the proceeds of which will go towards the Royal British Legion. *http://www.amazon.co.uk/Blast-Injury-Science-And-Engineering/dp/3319218662*

## Media Mentions

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

- The Times. *For medical staff, the battle to save stricken soldiers*. March 2015. *Refers to the analysis by Dr Emily Mayhew of the medical history of the Western Front in WW1.*
- Science Daily. *High cost of healthcare for UK military amputees from Afghan conflict*. May 2015.
- Legion magazine. *It's because of the Legion this is happening.* June 2015. *A look at the work of Centre academic, Dr Tobias Reichenbach (pictured right), contributor to the MoDs hearing loss strategy HearWELL.*
- Daily Mail. *£288m bill for injured heroes: experts calculate sum of care, rehabilitation and prosthetics for troops who were injured in Afghan bombings*. June 2015. *Reporting on the study by Edwards et al. summarised at page 17 of this report.*
- Imperial College website. *High cost of healthcare for UK military amputees from Afghan conflict revealed.* June 2015. *Reporting on the study by Edwards et al. summarised at page 17 of this report.*
- Russia Today. *£288m needed for Afghanistan veteran amputees – study.* June 2015. *Reporting on the study by Edwards et al. summarised at page 17 of this report.*
- Medical Xpress. *The costs of conflict: Amputees and the Afghan War.* June 2015. *Reporting on the study by Edwards et al. summarised at page 17 of this report.*
- My Science. *High cost of healthcare for UK military amputees from Afghan conflict revealed.* June 2015. *Reporting on the study by Edwards et al. summarised at page 17 of this report.*

- Medical News Today. *High cost of healthcare for UK military amputees from Afghan conflict revealed in new study.* June 2015. *Reporting on the study by Edwards et al. summarised at page 17 of this report.*
- Before its News. *£288m needed for Afghanistan veteran amputees – study.* June 2015. *Reporting on the study by Edwards et al. summarised at page 17 of this report.*
- The Royal British Legion website. *New study reveals high cost of healthcare for UK military amputees from Afghan conflict.* June 2015. *Reporting on the study by Edwards et al. summarised at page 14 of this report.*
- Science Newsline Medicine. *The Costs of Conflict: Amputees and the Afghan War.* June 2015. *Reporting on the study by Edwards et al. summarised at page 17 of this report.*
- Irwin Mitchell Solicitors website. *Care Following Military Injuries in Afghanistan to cost £288m.* June 2015. *Reporting on the study by Edwards et al. summarised at page 17 of this report.*
- Rehab Management (US). *Researchers Calculate High Lifetime Costs for Amputee Veterans of Afghanistan Conflict.* June 2015. *Reporting on the study by Edwards et al. summarised at page 17 of this report.*
- US Veterans News. *The costs of conflict: Amputees and the Afghan War.* June 2015. *Reporting on the study by Edwards et al. summarised at page 17 of this report.*
- Texas Guardian. *The costs of conflict: Amputees and the Afghan War.* June 2015. *Reporting on the study by Edwards et al. summarised at page 17 of this report.*
- Healio Orthotics/Prosthetics News. *Study: Health care is costly for UK military amputees from Afghanistan.* June 2015. *Reporting on the study by Edwards et al. summarised at page 17 of this report.*
- thenakedscientists.com *BOOM! The bang behind the bomb and how to stop it.* June 2015 Podcast featuring Dr Bill Proud and some of his team talking about experimental work in the Centre.

- The Royal British Legion website. *The Legion's CBIS looks to help veterans suffering from APD*. July 2015. *A look at the work of Centre academic, Dr Tobias Reichenbach, contributor to the MoDs hearing loss strategy HearWELL.*
- @JoJohnsonMP Twitter. *Minister of State for Universities & Science Jo Johnson (pictured right) visits CBIS*. July 2015.
- MSC Software Magazine. *Simulating Reality Contest Winners 2015.* September 2015. *Announcing Dr Dilen Carpanen (post-doctoral research associate in the Centre) as a winner for his work on modelling blast injury.*
- Intima. Writing Patient Diaries: A Century of Skill in the Silence, from the Great War to Afghanistan. September 2015. *Refers to the analysis by Dr Emily Mayhew of the medical history of the Western Front in WW1.*
- Blesma Bulletin Member's Newsletter Autumn 2015. *Improving Assistive Devices.* October 2015. *Blesma work with Centre researchers in the recruitment of veterans for studies concerning assistive devices.*
- Paralympic.org *Former soldier Henson reports for Doha 2015 duty*. October 2015. *Reporting on advisory board member David Henson before his trip to Doha to compete at the IPC Athletics World Championships.*

 

- Imperial College website. *US Defense Secretary (pictured right) sees British and American research ties at Imperial.* October 2015. *Reporting on the Secretary's visit to the Centre.*
- ddc intranet news (MoD defence media blog). Defence Secretary Michael Fallon hosts US Secretary of Defense Ashton Carter. October 2015. *Reporting on the Secretary's visit to the Centre.*
- *The Royal British Legion website.* £5m to rehabilitate wounded, injured and sick service personnel. November 2015. *Referring to the partnership with the Centre at the charity expands its funding portfolio.*
- New Scientist. *Man with no limbs controls robotic hand using muscle whispers.* December 2015. *A look at the bio-mechatronics work of associate academic Dr Ravi Vaidyanathan.*
- Royal Academy of Engineering's Ingenia Magazine. *Blast Mitigation.* December 2015. *An article explaining how the multidisciplinary team at the Centre is helping to protect, treat and rehabilitate people who are exposed to explosive forces.*

## Public Engagement

### Annual Network Event 24th November 2015

The objective of this year's annual networking event was to stimulate research and collaboration in trauma. According to the Trauma Audit and Research Network (TARN), it is already the commonest cause of loss of life under the age of 40, the burden of which is set to increase in the next 20 years. The Royal Society for the Prevention of Accidents (RoSPA) estimates that around 19,000 cyclists are killed or injured each year on UK roads. Terrorist activities ensure that Improvised Explosive Devices (IEDs) are now no longer confined to the battlefield. Norwich, Bosley and Cardiff - 3 industrial explosions in as many months in 2015 that resulted in the loss of life and left numerous people severely injured. Trauma is a serious public health problem.

Open to the public, and with attendees from the defence industry, Pan London Trauma Network, Research councils and various UK academic institutions, the event highlighted the current state of trauma care and research needs in the UK. It began with a welcome from Imperial College's Provost, Professor James Stirling. Speaking of Imperial's core academic mission in the pursuit of excellence in education, research and translation, Prof Stirling drew on some examples of the Centre's impact to date to demonstrate its position at the interfaces of Imperial's core disciplines, epitomising the College's ethos of multidisciplinary research excellence for translational benefit. Two brief talks followed from Prof Anthony Bull and Shehan Hettiaratchy, outlining the Centre's role in The Bioengineering Trauma Initiative (*detailed at page 31 of this report*) and the need for more evidence in major trauma in order to develop and evaluate new treatment to ultimately provide better patient care. Shehan is Chief of Service (Plastics, Orthopaedics & Major Trauma Services) at St Mary's Major Trauma Centre London and specialises in hand and wrist surgery and complex limb reconstruction.

Session one saw presentations from Jan Jansen, Consultant General/Trauma Surgeon Aberdeen/London, Surgeon Captain Rory Rickard, Defence Professor of Surgery, Professor Matt Costa, Professor of Orthopaedic Trauma University of Oxford and Surgeon Captain Sarah Stapley, Defence Professor of Trauma and Orthopaedics. The session concluded with a panel review where audience members quizzed the experts on innovating at pace, bridging the gaps between medical and patient expectations and the routes to translation from the military to civilian domain. Session two was focused on current research efforts in Neurotrauma, Trauma Biomechanics, haemorrhage control and the therapeutic options in trauma care. Talks were given by Professor Karim Brohi, Professor of Trauma Sciences Barts Health NHS Trust, Squadron Leader Claire Webster, Vascular Surgeon/PhD student in CBIS, Mark Wilson, Consultant Neurosurgeon & Pre Hospital Care Specialist, St. Mary's Major Trauma Centre & London's Air Ambulance, Dr Mazdak Ghajari, Lecturer in the Dyson School of Design Engineering, Graham Lawton, Consultant Plastic Surgeon, Imperial College Healthcare NHS Trust and Dr Spyros Masouros, Lecturer in the Department of Bioengineering. The day ended with a poster session and a chance to chat with delegates. It was evident from the day's proceedings that there is much yet to be done in the research and treatment of blast injury and major trauma, and that collaboration is key to its success.

## Imperial Festival & Alumni Weekend 9 – 10$^{th}$ May 2015

Imperial Festival[7] once again broke records with over 12,000 people in attendance, more participants that ever before, and an expansion to new zones and venues across the South Kensington Campus. College neighbours The Band of the Household Cavalry officially opened the Festival with a bit of pomp and ceremony on Saturday afternoon and for the first time, the Festival opened on a Sunday giving thousands of visitors an extra day to soak up the science. CBIS staff and students were involved throughout the weekend, providing an insight to the work of the Centre. Dr Emily Mayhew (Military Medical Historian in Residence) was there to remind everyone of lessons identified from studies of severe casualties of the 20$^{th}$ century and how that knowledge helps shape research today. PhD student Matthew Hopkins (see *page 24 of this report*) demonstrated prototypes from his current work which allowed attendees to capture real time measurements of pressure under foot and see their results on a smart phone application. Recreating some of the Centre's laboratory equipment on the small scale enabled demonstrations of pressure waves and was popular at all ages (*pictured above*). PhD student Kalpi Vitharana used this equipment to explain her current work on the assessment of injuries sustained to the thorax during a blast event. 2016 dates for Imperial Festival have been announced (May 7$^{th}$ & 8$^{th}$) and researchers at the Centre have already begun planning some hands on activities for attendees.

[7] https://www.imperial.ac.uk/be-inspired/festival/

 

# Subject Specific Meetings

## Blast Lung – March 2015

This was the second in the series of new initiatives within the Centre to unite the blast lung injury research communities in the UK. The aim of the meeting is to provide an open forum for discussing aspects of lung injury within a diverse group of researchers. This has already encouraged more people to engage with the research topic, who may not immediately feel relevant. The first meeting held in Queen Elizabeth Hospital, Birmingham in 2014, focused on establishing what military patient data has been collated and what could be learned from x-ray imaging that was conducted during the latest conflicts. This meeting focused on trauma and injury models and involved representatives from Academia, Clinical Care and Military: Professor Sara Rankin, Imperial College London; Dr Tim Scott, ICM and Defence Medical Services; Dr Emrys Kirkman, DSTL; Ashton Barnett-Vanes, Imperial College London; Dr Mainul Haque, University of Nottingham; Dr Zoe Prytherch, Cardiff University; Professor Mark Griffiths, NHLI; Dr Hari Arora, Imperial College London; with others in attendance from these institutions.

This year's meeting covered the current understanding of the injury pathology relayed by those closest to the front line, ensuring as true an understanding of the problem is disseminated to the research community. This facilitated rich discussions during the research presentations from each of the speakers. Such meetings are critical for the development, as well as the refinement, of research efforts in such a challenging interdisciplinary problem. Further to this, keeping an open network on respiratory research in general enables flexibility in our future needs with regard to injury evaluation and treatment development. One valuable lesson learned from the current injury research is that even the smallest change in the threat can result in a very different patient outcome. It is critical therefore to ensure the fundamentals are understood and a broad overview with focused targets is maintained. Presentations, for example, by Dr Prytherch and Professor Griffiths who sit outside the traditional blast injury community add new dimensions to our understanding of respiratory blast injuries. Their work on in-vitro and ex-vivo organ models of inhalation and inflammation are ones, which can be implemented and extended in future work in the Centre.

## Greener and Safer Energetic and Ballistic Systems (GSEBS) – May 2015

The Erasmus + program organised an intensive training course in Bucharest, covering a wide range of multi- and inter-disciplinary topics:

- Environmental impacts of energetics and ballistics systems
- Greener energetic materials and their applications
- Insensitive energetic materials and their applications
- Materials and techniques for ballistic protection
- Modelling and simulation of energetic and ballistic systems and ballistic protective equipment
- Energetic and ballistic systems based technologies for materials processing
- Environmental and toxicology Life-Cycle Impact Assessment

 


The program involved MSc and PhD students, and lecturers from four prestigious institutions across Europe: Imperial College London, University of Coimbra (Portugal), ENSTA Bretagne (France), and Military Technical Academy (Romania) which hosted the event. It provided an opportunity for students from various backgrounds not only to improve their technical knowledge and skills, but also to exchange experiences and opinions with others. Following the two-week-long intensive program was the two-day international conference on the same topics. During this conference, students who attended the training could present their work alongside academics and industrial professionals from other universities, agencies and companies. The conference was a great platform for debates on recent achievements in the use of various systems for civil, defence and space applications, focusing on the safety and environmental aspects. Final year CBIS PhD student Thuy-Tien Nguyen is pictured above receiving the prize for “Best Oral Presentation” for her talk entitled “The Shock Tube System – Blast Waves and Blast Interaction Research”.

## Pressure, Energy, Temperature and Extreme Rates (PETER) – August 2015

The conference was organised by our colleagues at the Institute of Physics and due to popularity, this year introduced research under 8 main themes (Constitutive relations & modelling, Numerical simulations, Perforation & impact, Crashworthiness, Experiments & inverse methods, Friction & interaction, Surface & contact, Blast loading). Chaired by CBIS academic Dr Bill Proud, the 3 day international conference proved a great opportunity to engage with industry and academia both at home and overseas. CBIS PhD student David Sory presented the latest results from his investigation of the cellular response to a wide range of pressure and strain rates. David’s work is key to a number of studies at the Centre in understanding the mechanisms of blast injury. Knowledge such as this will lead to the development of new treatment, diagnosis and preventive measures. Thuy-Tien Nguyen expanded on her work using the shock tube system and presented findings from her investigation of blast mitigation structures. Looking at granular beds and combinations of metal and foam, Thuy-Tien has assessed these materials for their ability to reduce the effects of blast. Such findings are key in the development of personal protective equipment (PPE) for military and civilian applications, as well as protective layers for building and shelters.

## Colt Foundation Research Meeting – December 2015

The Royal Society of Medicine hosted the annual Colt Foundation Research Prize meeting which highlights the work being carried out in the Defence Medical Services. The meeting concludes with the Colt Research Prize, which provides six finalists the opportunity to present their current research from any aspect of Military Medicine. The meeting opened with a presentation from Professor Anthony Bull, who spoke about the past achievements of CBIS and the next five years of research. He emphasised the importance of maintaining communication with military clinicians to ensure that important clinical problems associated with blast injuries are being addressed by CBIS researchers.

Three other presentations followed. Dr. Nick Crombie (Queen Elizabeth Hospital, Birmingham) discussed issues surrounding the delivery of pre-hospital care and the decisions required for administering medical procedures prior to admitting patients into a hospital environment. Dr. Nick Beeching (Liverpool School of Tropical Medicine, Royal Liverpool University Hospital) provided an overview of the issues and methods used for diagnosis of diseases contracted overseas in settings relevant for military personnel. Professor Richard Lilford (Warwick University) followed with an interesting presentation about P-values and the context of their significance in scientific and medical decision-making scenarios.

The final talk of the morning was given by Mr. Joshua Quick (University of Birmingham) describing his experiences with point-of-care diagnostics in the recent Ebola outbreaks in West Africa. In addition to Professor Bull's presentation, CBIS student Anne Sharrock was selected as one of the six finalists for the Colt Research Prize for her work with Professor Sara Rankin, "In-vivo alteration of platelet function following a high energy primary blast wave". Her study explores how primary blast affects the function of platelets; cells that play an important role in coagulation following injury.

## Publications


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Proud WG, Nguyen TTN, Bo C, Butler BJ, Boddy RL, Williams A, Masouros SD, Brown KA (2015). *The high strain rate loading of structural biological materials*. Metallurgical and Materials Transactions A, 46(10): 4559-4566.

Spurrier E, Masouros SD, Gibb I, Clasper JC. *Identifying spinal injury patterns in underbody blast to develop mechanistic hypotheses*. Spine, in press.

Spurrier E, Singleton JAG, Masouros SD, Gibb I, Clasper JC. Blast injury in the spine: dynamic response index is not an appropriate model for predicting injury. Clinical Orthopaedics and Related Research. 2015, 1-7.

Villette C, Phillips ATM., *Informing Phenomenological Structural Bone Remodelling with a Mechanistic Poroelastic Model.* Biomechanics and Modelling in Mechanobiology. In press DOI 10.1007/s10237-015-073504

## Awards

CBIS Team. Winner – Imperial College London Excellence in Research. "President's Award for Outstanding Research Team".

Clasper JC, - Commander of the Most Excellent Order of the British Empire. Queen's birthday honours list 2015.

Mahoney P. - Commander of the Most Excellent Order of the British Empire. Queen's birthday honours list 2015.

Nguyen TT. Winner – Best presentation. "The Shock Tube System – Blast Waves and Blast Interaction Research" GSEBS Conference, Military Technical Academy, Bucharest Romania, May 2015.

Spurrier E. Winner – Peter Templeton prize for best trainee paper. "Spinal Injury Patterns in UK Victims of IED Attacks on Vehicles" Combined Services Orthopaedic Society Annual Meeting, Fenham Barracks Newcastle, May 2015.

## Invited Lectures

Spurrier E. & Mayhew E. *From the Western Front to FHCB.* The Royal College of Surgeons of England. February 2015.

Mayhew E. *Military Medicine in the Great War.* The Friends of RAMC Millbank. February 2015.

Edwards D. & Mayhew E. *From the Western Front to FHCB.* UCL Chemical & Physical Society. February 2015.

Mayhew E. *A Century of Post-Amputation Pain.* Irwin Mitchell Military Rehabilitation Conference, Birmingham. March 2015.

Bull A. *CBIS Achievement and Plans.* The Royal British Legion Research Symposium, RSA House London. May 2015.

Sharrock A. *Research at CBIS.* Women in Surgery Conference, REP Theatre, Birmingham. May 2015.

Masouros S. & Kedgley A. *Injury and MSK Modelling at Imperial College.* UNIFY Meeting, Royal Society of Medicine, London. June 2015.

Bull A. *Centre for Blast Injury Studies*. DSEI Trauma Innovation, ExCel, London. September 2015.

Henson D. *The Hidden Side of Amputation: musculoskeletal wear and tear – arthritis isn't the only concern.* MEIBioEng15 Conference, University of Leeds. September 2015.

Bull A. *Centre for Blast Injury Studies: the next five years*, Colt Foundation Research Meeting. Royal School of Medicine, London. December 2015.

## Conference Presentations

Government Experts on Mitigation Strategies (GEMS) Annual Meeting, London, UK. January 2015.

Arora H. *Primary blast injury: understanding and evaluating shock wave interaction with the body.*

Masouros SD. *Tertiary blast biomechanics in CBIS.*

New Trends in Research of Energetic Materials (NTREM), Pardubice, Czech Republic. April 2015.

Nguyen T-TN, Davey T, Proud WG. *Percolation of gas and attenuation of shock waves through granular beds and perforated sheets*.

Proud WG. *Blast Effects on Large Aggregate Concrete.*

Combined Services Orthopaedic Society (**CSOS**) Annual Conference. Newcastle, UK. May 2015.

Spurrier E, Masouros SD, Clasper JC. *Spinal injury patterns in UK victims of IED attacks on vehicles*.

Edwards DS, Clasper JC, Bull AMJ. *Risk stratification for heterotopic ossification in residual limbs of blast related amputations*.

Edwards DS, Karunaratne A, Forsberg JA, Clasper JC, Bull AMJ. *Quantitative and qualitative characterisation of the organic and non-organic components of heterotopic ossification from blast related amputees*.

Edwards DS, McMenemy L, Stapley S, Clasper JC. *40 years of terrorist bombings - a meta-analysis of 167 incidents*.

McMenemy L, Masouros SD, Stapley S, Clasper JC. *The effect of whole-body vibration and mechanical stress on the lumbar spine of military personnel operating on small marine craft*.

 

Webster CE, Masouros SD, Gibb I, Clasper JC. *The blast pelvis: mechanism of fracture and the potential for mitigation techniques*.

British Association of Plastic Reconstructive and Aesthetic Surgeons and (BAPRAS) & Royal Belgian Society for Plastic Surgery (RBSPS) Combined Summer Scientific Meeting, Bruges, Belgium. June 2015.

Mayhew E. *Forward medicine in the Great War*.

European Society of Biomechanics (ESB), Prague, Czech Republic. July 2015.

Newell N and Masouros SD. *Validation of a computational model for prediction of lower-limb injury in under-vehicle explosions*.

XV International Symposium on Computer Simulation in Biomechanics, Edinburgh, UK. July 2015.

Zaharie DT, Villette CC, Phillips ATM. *Frangible optimised lower limb surrogate for assessing injury caused by underbelly blast*.

Pressure, Energy, Temperature and Extreme Rates (PETER) Annual Meeting, London, UK. August 2015.

Sory D, Proud WG. On the development and validation of in-vitro platform to investigate the response of cells over a wide range of pressure and strain rates.

Nguyen T-T, Proud WG. Investigation of blast mitigation structures using a shock tube system.

Military Health Systems Research Symposium (MHSRS). Fort Lauderdale, Florida, USA. August 2015.

Webster C, Masouros SD, Gibb I, Clasper JC. *Fracture patterns in pelvic blast injury – a retrospective analysis and implications for future preventative strategies*.

International Research Council on the Biomechanics of Injury (IRCOBI), Lyon, France. September 2015.

Christou A, Spurrier E, Grigoriadis G, Masouros SD. *Human cadaveric bi-segment impact experiments at different postures.*

Zaharie DT, Masouros SD. *A multi-body dynamics model of the MiL-Lx surrogate for under-body blast*.

Newell N, Bull AMJ, Masouros SD. *A computational model for prediction of lower-limb injury in under-vehicle explosions*.

Villette C, Zaharie D, Phillips A. *Frangible optimised lower limb surrogate for assessing injury caused by underbelly blast*.

Tri-service Anaesthetic Society Annual Conference, Royal College of Anaesthetists, Red Lion Square, London, UK. December 2015.

Mayhew E. *The Real Meaning of the Anaesthetist in MERT: a century of extraordinary achievement in British Military Medicine.*

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CENTRE FOR BLAST INJURY STUDIES

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