Royal College of Surgeons

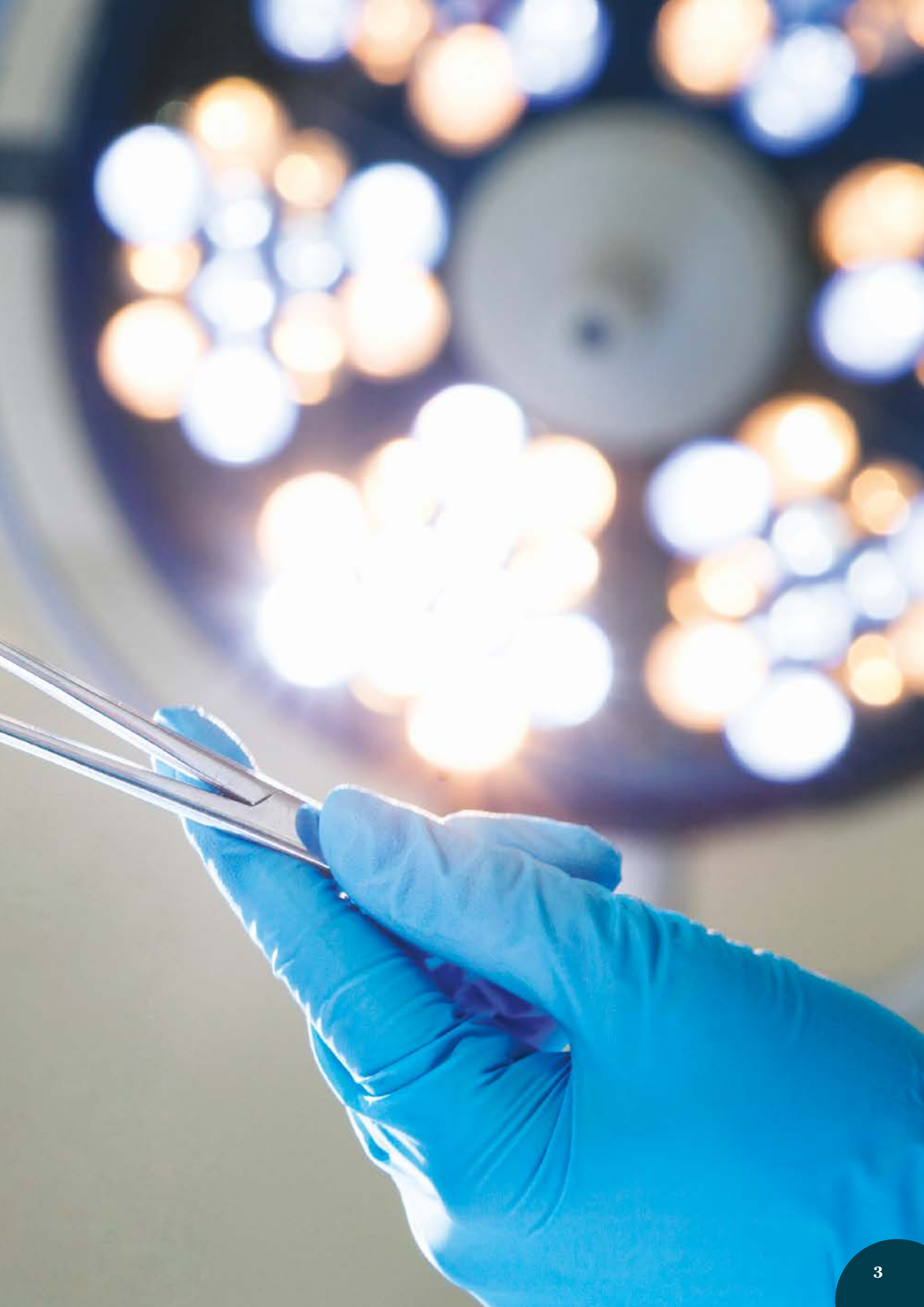
ADVANCING SURGICAL CARE

Surgical Research Report

2017/18

The Royal College of Surgeons of England

Contents



Chairman's introduction

Research is not an optional add-on, it is the very lifeblood of surgery. We need to introduce new technologies safely and effectively, we need to understand basic mechanisms of disease and we need to do the things we are doing now, but better. Most important of all, we need to inspire the surgeons of the future to see this as part of their mission in improving the experience and standards of care for our patients.

Neil Mortensen
Chairman, Research Fellowship and Lectureship Selection Group

The Royal College of Surgeons through its Research Fellowship scheme has committed more than £40million to support over 700 individual trainee members during the past 24 years, and this year we have approved a further £2million funding for some 30 new Research Fellowships. The quality of the applicants has been outstanding and most are either starting or completing a PhD, which now means three years of funding. The College does not undertake the research itself but provides seedcorn funding for start-up projects which then attract funding from such bodies as the Wellcome Trust, CRUK and MRC.

This yearly round of appointments depends on our many donors to whom we remain immensely grateful, but we can always do so much more. We have added to our Research Fellowship partnerships the British Society of Endovascular Therapy (BSET), the Virginia Mason Hospital Seattle, and Addenbrooke's Charitable Trust. Two novel Fellowships in Clinical Leadership have been introduced with the Faculty of Medical Leadership and Management and McKinsey. Our prestigious Fulbright Fellowship to the USA agreement has been renewed.

The Clinical Effectiveness Unit (CEU), a joint programme with the London School of Tropical Medicine and Hygiene, continues to provide a major focus for national audits in oesophagogastric, bowel, breast and prostate cancer, as well as vascular surgery, cleft lip and palate, emergency laparotomy and falls and fractures. These important studies provide the facts on which to base health policy and improve outcomes for our patients.

The Surgical Trials Initiative introduced in 2012 has developed rapidly. There are now seven chosen Surgical Trial Centres in the UK and there are 15 appointed Surgical Specialty Leads with the task of promoting trials and trial recruitment, and providing a link between surgeons, investigators and the trials centres. Some 25,746 patients have been recruited to 85 trials across the surgical specialties. A particular success has been the development of trainee research collaboratives. We are especially grateful to the Rosetrees Trust for their support for these developments.

We need to inspire the surgeons of the future in improving the experience and standards of care for our patients

The Surgical Technology Evaluation Portal (STEP) is run jointly with the NIHR to help with the rapid assessment of new technologies and was launched earlier this year. This will provide technology companies with access to clinical advice and appropriate patient groups to ensure the safe introduction of new procedures.

Over the last 20 years many University Departments of Surgery have been closed or subsumed into larger groupings with a consequent loss of surgical academic leadership. If these exciting new programmes are to be successful this decline needs to be reversed and in 2017/2018 the College is planning to establish new chairs in surgical clinical research. We need to raise some £2.5million.

Professor Sir Peter Morris who with great foresight started the Research Fellowship scheme in 1993 has recently retired as Director of the Centre for Evidence in Transplantation. We are particularly grateful to Claire Large who has retired as CEO of the Dunhill Medical Trust, who have been major supporters of the College research initiatives in research related to the elderly.

Martyn Coomer and Jonathan Fountain and their staff have worked tirelessly to underpin all this activity. Jonathan has moved on to a new job for which we wish him all the best. Professor Derek Alderson has been inspiring our focus on surgical trials and Professor Dion Morton as Director of Clinical Research has with great energy and enthusiasm helped make it happen.

To all our many funders we are most grateful and hope that on seeing our many successes you will continue to help us with our work.

Over the last 20 years many University Departments of Surgery have been closed or subsumed into larger groupings with a consequent loss of surgical academic leadership.

Fellowships are awarded to subscribing members of the College in a training post, or trainees who have passed the MCQ papers and will sit the final MRCS examination at this College. All applications are rigorously assessed by a panel of experts to ensure that the research, surgeon, supervisor and facilities are of a high standard, and that the proposed work will be valid, beneficial and original. The fellowships cover salary, on-costs and some running expenses. Fellows may study any aspect of surgery or surgical care including basic science, diagnosis, treatment, surgical technology, logistics or audit.

Research Fellows' Reports

Zaid Awad
Marc Bailey
Basil Bekdash
James Berry
John Broomfield
Marc Bullock
Andrew Cowie
Helen Cui
Andrew Currie
Praveena Deekonda
Harveer Dev
Nicholas Eastley
Ellie Edlmann
Dafydd Edwards
Jason Fleming
Mathew Gardiner
Katherine Gash
Michelle Griffin
Rachael Harrison
Jasmine Ho
Amel Ibrahim
Zita Jessop
Matthew Kirkman
Kathryn Lynes
Dermot Mallon
Gulraj Matharu
Elizabeth Maughan
David Metcalfe
Anita Mohan
Aadil Mumith
Suzanne Murphy
Sumit Nandi
Liza Osagie
James Paget
Karl Pang
Keval Patel
Henrietta Poon
Jason Powell
Stuart Roberts
Bynvant Sandhu
John Saunders
Annabel Sharkey
James Singleton
Anna Slovick
Peter Szatmary
Tanujan Thangarajah
Peter Vaughan-Shaw
Christopher Wearn
Michelle Wilkinson
Hugh Wright
Rasheed Zakaria

Structured, rigorous and validated assessment which integrates simulation and workplace modules can help deliver better surgical training. Better training equates to better and safer patient care.

A comprehensive evaluation of workplace and simulation-based assessment in otolaryngology training

Zaid Awad

FELLOWSHIP/SPONSOR:
Colledge Family Fund

SUPERVISORS:
Neil S Tolley, Paul Ziprin and Ara Darzi

SITE OF WORK:
Imperial College London

PUBLICATIONS:
1. Construct validity of cadaveric temporal bones for training and assessment in mastoidectomy, Awad Z, Tornanri C, Ahmed S, Tolley NS. Laryngoscope. DOI: 10.1002/lary.25310

2. Utilisation, reliability and validity of Clinical Evaluation Exercise in otolaryngology training. Awad Z, Hayden L, Muthuswamy K, Tolley NS. Clin Otolaryngol. DOI: 10.1111/coa.12400

PRESENTATIONS:
1. Construct validity of cadaveric temporal bone simulation in mastoidectomy training, Annual Meeting of the Faculty of Surgical Trainers, RCSEd, Edinburgh 22 Oct 2014

2. Cold steel tonsillectomy simulator: using silicone to train future trainees, Annual Meeting of the Faculty of Surgical Trainers, RCSEd, Edinburgh 22 Oct 2014

PRIZES:
1. Nan Blofeld Travelling Fellowship, University College London Hospitals Charity, Feb 2015

2. HCA International Traveling Fellowship Grant, HCA International Foundation, Oct 2014

The otolaryngology curriculum requires trainees to show evidence of operative competence before completion of training. The General Medical Council recommended that structured assessment be used throughout training to monitor and guide trainee progression. Despite the reduction in operative exposure and the variation in trainee performance, a 'one size fits all' approach continues to be applied. The number of procedures performed remains the main indicator of competence.

Our objectives were to analyse the utilisation, reliability and validity of workplace-based assessments in otolaryngology training, to identify, develop and validate a series of simulation platforms suitable for incorporation into the otolaryngology curriculum and to develop a model of interchangeable workplace- and simulation-based assessment that reflects the trainee's trajectory, audit the delivery of training and set milestones for modular learning.

We used a detailed review of the literature, identified a list of procedure-specific assessment tools, as well as simulators suitable to be used as assessment platforms. A simulation-integrated training programme was piloted and models were tested for feasibility, face, content and construct validity, before being incorporated into the North London training programme. The outcomes of workplace- and simulation-based assessments of all core and specialty otolaryngology trainees were collated and analysed.

The outcomes of 6,535 workplace-based assessments were analysed. The strengths and weaknesses of four different assessment tools were highlighted. Validated platforms utilising cadavers, animal tissue, synthetic material and virtual reality simulators were incorporated into the curriculum.

Sixty trainees and 40 consultants participated in the process and found it of great educational value.

We concluded that assessment with structured feedback is integral to surgical training. Assessment using validated simulation modules can complement that undertaken in the workplace. The outcomes of structured assessments can be used to monitor and guide trainee trajectory at individual and regional level. The derived learning curves can shape and audit future otolaryngological training.

A group of trainees practicing micro-laryngeal procedures under faculty supervision

Targeting Ca^{2}+ channels to attenuate AAA growth

Marc Aaron Bailey

FELLOWSHIP/SPONSOR:
Joint RCS/Circulation Foundation Fellowship

SUPERVISORS:
Professor David J Beech FMedSci

SITE OF WORK:
LIGHT Building, Leeds Institute of Cardiovascular & Metabolic Medicine, University of Leeds

PUBLICATIONS:
Main paper from the work has been submitted to Nature Communications. Details of the paper remain confidential at present. I am the lead author.

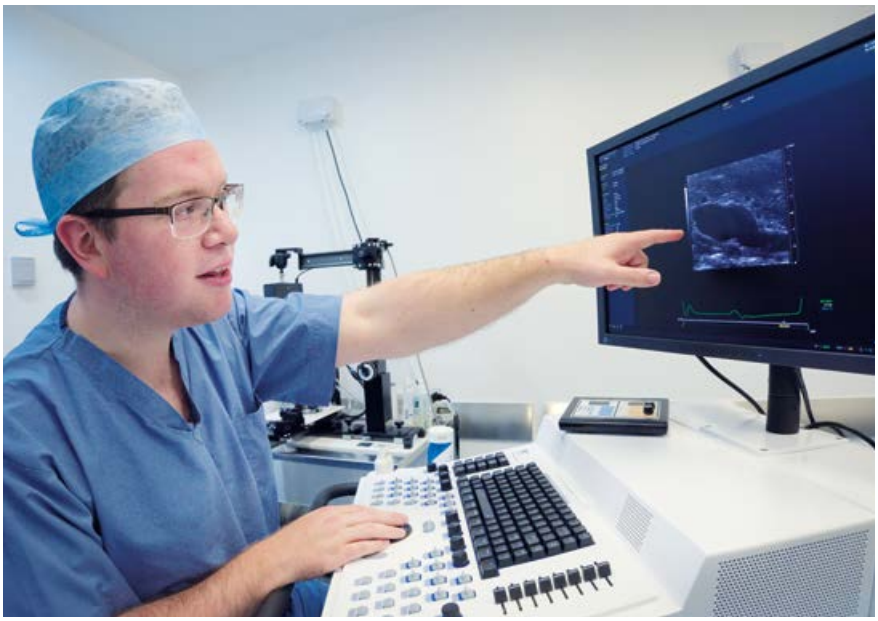
PRESENTATIONS:
1. Inhibition of pathological vascular smooth muscle cell remodelling as a treatment strategy for abdominal aortic aneurysm. International Meeting on Aortic Diseases, Liege Belgium, Sept 2016
2. Assessment of novel therapeutics for AAA with 3D ultrasound in mice. British Medical Ultrasound Society, Cardiff, Wales, Dec 2015

PRIZES:
1. James Ellis Award Sept 2015
2. David Gamble Charitable Trust Award Sept 2015

FURTHER FUNDING:
Medical Research Council, University of Leeds for MRC: 12 months, UoL: five years

An abdominal aortic aneurysm, or AAA, is a ballooning of the aorta – the main blood vessel in the body. The condition is silent but can be deadly if the expanding vessel ruptures. In the UK we have a national screening programme for AAA but can only offer surgical repair when the AAA is large and the risk of rupture greater than the risks associated with surgery. My work centres around developing a medical therapy that could be used to slow the growth of these small aneurysms to prevent progression to surgical intervention or rupture. This will reduce exposure to intervention which is reducing mortality, morbidity and improving quality of life.

The idea of the project is to target a calcium channel in the vascular smooth muscle cells to prevent their dysfunctional remodelling behaviour. Our group previously identified that a calcium channel called Orai1 controls cell function in vascular cells pertinent to disease. In this project I used mouse models of AAA and ultrasound imaging to track disease progression. A potent and specific Orai1 inhibitor was developed and delivered to the animals only after aneurysms had formed – mirroring the human situation.



Marc performing invivo ultrasound of an experimental aneurysm

I discovered that by using this approach, AAA progression could be reduced by 40%. This is a new area of research but there is emerging evidence from other groups around the world that modifying the response of the vascular cells in the aorta might slow disease progression in AAA.

This award helped me to attract funding from the Medical Research Council to continue to develop the small molecule Orai1 inhibitors and the University of Leeds to validate our findings using gene manipulation techniques. I have recruited a team of PhD students from the basic sciences who will continue the project.

Blocking the Orai1 calcium channel slows aneurysm progression by 40%.

The majority of patients who develop type I diabetes will do so in childhood or early adult life but do not have access to an appropriate way to replace the lost insulin producing cells (β-cells).

Pre-conditioning of islets of Langerhans for use in an implantable bioartificial pancreas

FELLOWSHIP/SPONSOR:
Joint BAPS/RCS
Research Fellowship

SUPERVISORS:
Professor Paul RV Johnson
and Dr Daniel Brandhorst

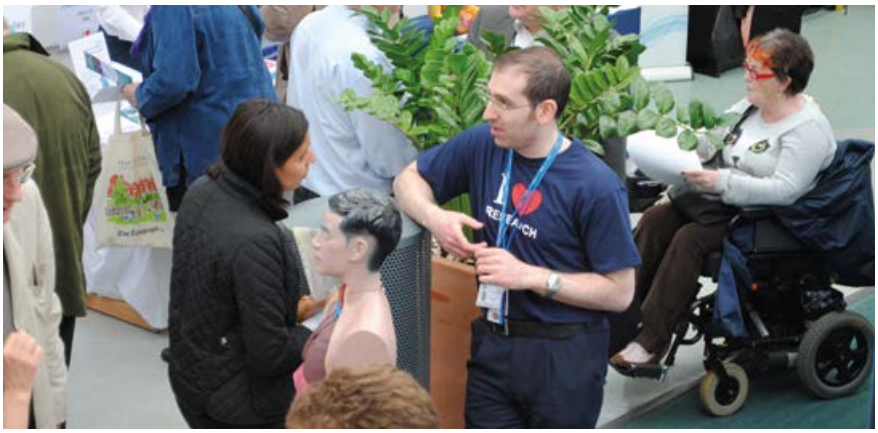
SITE OF WORK:
Nuffield Department of Surgical
Sciences, University of Oxford

Basil Bekdash

There are currently no effective and acceptable treatments to reverse or prevent this lost insulin, meaning patients require a lifetime of monitoring and artificial insulin replacement. Even with the best care and control, this is imperfect and leads to long-term complications. Some patients also experience loss of awareness of low blood sugar with potentially life-threatening consequences. Transplantation of the destroyed cells from another person (pancreatic islet transplantation) is an existing treatment for some patients.

Basil preparing a donor pancreas for islet transplantation

My work has been related to the development of a means of protecting donor cells from destruction by the transplant recipient's immune system. One approach is to physically separate donor and recipient cells by placing the donated cells in an artificial implant. This allows them to monitor sugar levels and produce appropriate levels of insulin but prevents contact with the patient's immune system cells and prevents them destroying the transplant.



Basil meeting members of the public at an open engagement event at OCDEM (Oxford Centre for Diabetes Endocrinology and Metabolism)

If this goal is achieved not only will patients potentially be free of the need to take insulin, they will also avoid the side effects of the drugs necessary for current transplantation treatments. It might also then be suitable for younger patients, including newly diagnosed children and adolescents.

One of the many remaining challenges is producing, selecting and optimising tissue for these purposes and this is the focus of ongoing research.

The islet transplant group and colleagues from OCDEM

The role of visceral peritoneum in inflammatory responses and healing in the injured abdomen

FELLOWSHIP/SPONSOR:
Joint RCS/Military Research Fellowship

SUPERVISORS:
Professors GL Carlson, Midwinter & Warhurst, and Dr Herrick

SITE OF WORK:
Salford Royal Foundation Trust

FURTHER FUNDING:
The National Institute for Health Research Surgical Reconstruction and Microbiology Research Centre (NIHR SRMRC) University Hospital Birmingham, Drummond Foundation Trust and HM Forces

James Berry

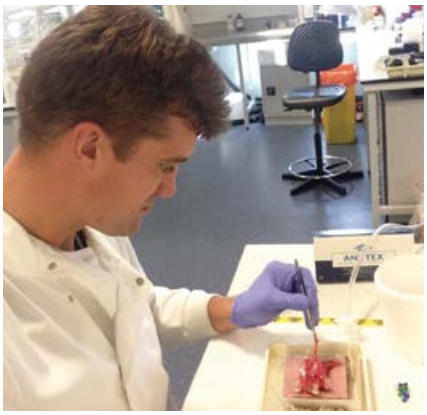
Peritoneal adhesions are bands of fibrous tissue that join abdominal organs to each other or the abdominal wall and occur in over 90% of patients following surgery and may cause significant health problems, such as pain, infertility, intestinal fistulae and bowel obstruction. Adhesion-related small bowel obstruction occurs in 10% of patients following abdominal surgery and is a significant burden on patients and healthcare resources. Adhesions are particularly severe following abdominal infection, trauma and repeated surgery. This increases the risk of unplanned bowel injury, further infection and fistula formation. Reducing adhesions is important to improve the patient's quality of life. However, mechanisms behind adhesion formation are complex and poorly understood and few reliable methods of reducing adhesion formation exist.

James at the Camp Bastion Hospital

The abdominal organs have different tendencies to form adhesions, with the bowel being most likely. The cells lining the abdominal organs and wall – mesothelial cells – are thought to be responsible for controlling inflammation that leads to adhesions.

To date, research has mainly concentrated on animal models and cell lines. The human small bowel lining, visceral peritoneum, has not been investigated and may behave differently to abdominal wall lining, parietal peritoneum, predisposing it to adhesions.

We have created a new model studying inflammation in humans. Using visceral and parietal peritoneum, donated from patients undergoing planned surgery, we are investigating the reaction of each surface to infection with the aim of understanding how adhesions develop and potential targets to reduce formation.



Dissecting peritoneum from the bowel specimen

Our data suggests that visceral peritoneum is capable of producing a pro-inflammatory response to infection which is controlled through a specific receptor, not previously identified in human mesothelial cells. Blocking this receptor may be important in reducing inflammation and adhesions. Further studies are planned comparing visceral and parietal peritoneum, and what effect biological implants, used in abdominal wall reconstruction, have on this response. The project has gained further funding for an additional researcher and investigations are ongoing.

The visceral peritoneum elicits a proinflammatory response to infection that promotes adhesion formation through modification of the fibrinolytic system.

Evidence shows that hip labral tears may be present in up to 55% of patients presenting with hip pain.

Can hip arthroscopy prevent hip arthritis?

FELLOWSHIP/SPONSOR:
Joint RCS/Arthritis Research Trust Fellowship

SUPERVISORS:
Professor S. Glyn-Jones

SITE OF WORK:
Nuffield Orthopaedic Centre, Oxford

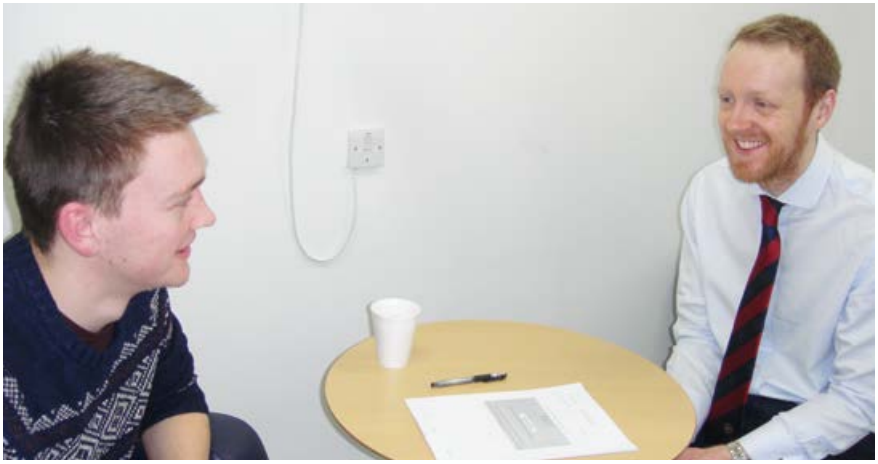
John A. J. Broomfield

This research is a trial to investigate surgical treatments for tears of the labrum of the hip. The labrum is a cartilage structure which encircles the hip socket to provide a 'seal' and contribute to the joint stability. Injuries to this structure may occur as a result of prolonged degeneration or as a consequence of injury to the joint.

There are two common approaches to treating this problem: to repair the labrum or remove the damaged portion. This project aims to identify whether the outcome from one surgery is superior to the other.

This will be achieved by randomly allocating patients to one of the two treatments and subsequently comparing their outcomes both in terms of patient reported measures and appearance of joint tissues using scans. The two treatments being investigated have both been shown to be effective for the treatment of this problem, but they have never been directly compared to each other before and therefore this study is the first to definitively address this problem.

This project will take 18 months to fully recruit sufficient patients to satisfy the requirements to demonstrate reliable results. The trial will have an overall duration of approximately three to four years, meaning there will be a large research team with clearly defined roles to complete this study.



Research patient consultation

Currently patients struggle for many months, and often years, because there is no robust evidence available to clinicians to inform their treatment. The results of the project will provide, for the first time, a clear clinical message as to the best treatment for this problem, which will improve the patients' journey from injury to treatment and through to recovery. This will mean a better, more streamlined, pathway to the most effective treatment for patients, thereby expediting their recovery and return to normal activity.

John undertaking a clinical examination

Identification and characterisation of deregulated long non-coding RNAs during colorectal cancer progression – interplay between tumour stroma and epithelium

Marc David Bullock

FELLOWSHIP/SPONSOR:
RCS Fulbright Scholar Award

SUPERVISORS:
Professor George Calin

SITE OF WORK:
MD Anderson Cancer Centre, Houston, Texas

PUBLICATIONS:
1. Bullock MD, Silva AM., Kanlikilicer-Unaldi P, Filant J, Rashed MH, Sood AK, Lopez-Berestein G, Calin GA. Exosomal non-coding RNAs: Diagnostic, prognostic and therapeutic applications in cancer. Non-coding RNA 2015: 1; 53-68

2. Silva AM, Bullock MD, Calin GA. The clinical relevance of long non-coding RNAs in cancer. Cancers 2015: 7; 2169-2182

PRESENTATIONS:
MD Anderson Cancer Centre Seminar. 'The clinical roles of exosomal non-coding RNAs in cancer' Houston Feb 2015

PRIZES:
1. NIHR Clinical Lectureship Award. July 2015

2. Wessex Medical Research Innovation Award. June 2015

FURTHER FUNDING:
NIHR for four years and Wessex Medical Research for two years

As the 2014-2015 Fulbright-RCS Scholar, I undertook a period of post-doctoral research training in the Department of Experimental Therapeutics at the MD Anderson Cancer Centre in Houston. Under the supervision of Professor George A Calin, a world expert in experimental cancer treatment, I characterised the expression of a class of molecule called long non-coding RNAs in human colorectal cancer using technology purpose-built for the task.

Long non-coding RNAs have only recently been discovered and are generating increasing research interest. Although it is known that they perform important roles in both normal and diseased tissues, relatively little is known about their contribution to cancer spread. By focusing on long non-coding RNAs in the tissues surrounding the tumour, this was an opportunity to better understand the biology of colorectal cancer metastasis and conduct research in a novel field with significant translational promise.

Furthermore, long non-coding RNAs are promising prognostic and diagnostic markers, and they are potentially targetable by drugs. As such, this research may be adapted in future to help improve and extend the lives of patients with colorectal cancer.

The Fulbright experience was overwhelmingly positive. On a professional level, I was able to use technology unavailable to me in the UK to generate highly novel and interesting data, helping me secure a NIHR Clinical Lectureship position at my home institution and additional funding to support my research in the UK. Furthermore, in six months I published two articles as first author and contributed to several other manuscripts published high impact peer-review journals.

In the coming years, this highly productive relationship with the host laboratory will continue to underpin my program of research. I will also have the opportunity to share my new research skills with colleagues at the University of Southampton.

Marc teaching on a surgical skills course in Toamasina in Madagascar. A collaboration between ASGBI and Texas-based charity Mercy Ships

Understanding the role of novel molecules called long non-coding RNAs during colorectal cancer spread – the contribution of cancer cells and the tissues which surround a cancer.

At the time of diagnosis less than 1 out of 3 patients with oesophageal cancer will be able to have curative surgery.

Stromal targeting in oesophageal cancer

Andrew Stuart Cowie

FELLOWSHIP/SPONSOR:
Joint RCS/Arthritis Research Trust Fellowship

SUPERVISORS:
Associate Professor T J Underwood

SITE OF WORK:
Department of Experimental Pathology, Cancer Sciences Division, University of Southampton

PUBLICATIONS:
1. Strategies to improve outcomes in esophageal adenocarcinoma. Cowie A, Noble F, Underwood T. Expert Rev Anticancer Ther. 2014 Jun;14(6):677-87. doi: 10.1586/14737140.2014.895668. Epub 2014 Mar 2013

PRESENTATIONS:
1. Developing model systems to understand the functional and clinical significance of somatic genetic variations in oesophageal cancer – Moynihan Prize Session, ASGBI International Surgical Congress 2014, Harrogate

2. Stromal targeting with phosphodiesterase type 5 inhibitors in oesophageal adenocarcinoma – Moynihan Prize Session, ASGBI International Surgical Congress 2015, Manchester

PRIZES:
1. Developing model systems to understand the functional and clinical significance of somatic genetic variations in oesophageal cancer, Best Poster Prize, 8th National Barrett's Symposium, London, April 2014

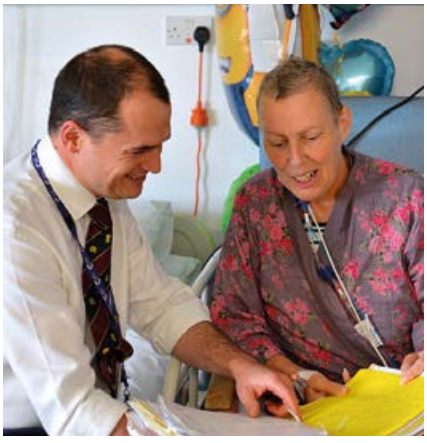
2. Shortlisted for Moynihan Prize session ASGBI International Surgical Congress 2014 & 2015

Oesophageal (gullet/food pipe) cancer is the most rapidly rising cancer in Western males and the UK has the highest incidence of any country in the world. Despite advances in modern surgery and medicines we have failed to significantly impact upon survival from this dreadful cancer with less than one in six people living for five years or more after diagnosis. Research into new treatments for this disease is urgently needed.

Andrew collecting fresh tissue from a resected oesophageal cancer

The major focus of cancer research over the past three decades has been cancer cells themselves. However, cancer cells do not exist in isolation and attention is being increasingly paid to the tumour stroma; this is the 'soil' in which the cancer grows. The major cell type in the stroma is the cancer associated fibroblast (CAF), a 'normal' cell type that has been hijacked by the cancer to support its own development. CAF play a vital role in cancer invasion and spread. A CAF-rich stroma is associated with poor survival in aggressive cancers. We have shown this to be the case in oesophageal cancer. No currently licensed medicines target the cancer stroma and we have been working on this in cancer of the oesophagus.

Our work has focused on using drugs from the 'Viagra family' (phosphodiesterase type 5 inhibitors) to target CAF. We have used complex 3D tissue culture techniques to study the potential of these drugs in changing the interaction between the cancer cells and the stroma. We have shown that these drugs can reverse the support of CAF to cancer cells and increase sensitivity to anti-cancer therapies. We are currently working with the Southampton Clinical Trials Unit to design the first human trial of phosphodiesterase type 5 inhibitors for stromal targeting in oesophageal cancer.



Andrew discussing oesophageal cancer research with a patient

Activity monitoring: profiling patient performance

Helen Cui

FELLOWSHIP/SPONSOR:
RCS Research Fellowship supported by the Sorab (Soli) Jamshed Lam Legacy

SUPERVISORS:
Mr Benjamin Turney

SITE OF WORK:
Churchill Hospital, Oxford

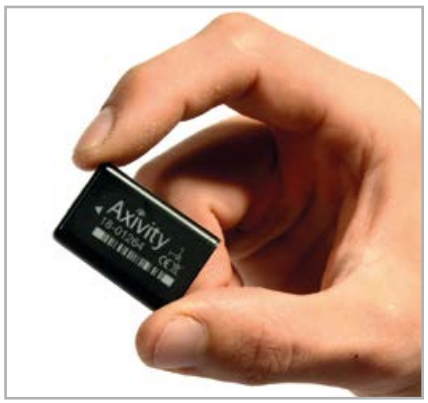
PUBLICATIONS:
1. Can preoperative home activity monitoring help determine cardiorespiratory fitness before major surgery? A study of the feasibility and utility of a wearable accelerometer in the preoperative setting.
Helen W Cui, Georgina S.J. Kirby, Karl Surmacz, John Griffiths, Caroline Hargrove, Benjamin W Turney. Paper in submission to British Journal of Anaesthesia

2. Preoperative home activity monitoring: predicting patient risk for major elective surgery. Georgina S.J. Kirby, Helen W. Cui, Karl Surmacz, John Griffiths, Benjamin W. Turney, Caroline Hargrove, Freddie C. Hamdy Paper in submission to the Annals of Biomedical Engineering

PRESENTATIONS:
1. 'Working towards a personalised surgical pathway', Oxford Innovation Society Technology Showcase, Said Business School, Oxford, July 2016

2. 'How Fit is Your Patient? Using Activity Monitoring to Assess the Surgical Patient' , World Congress of Endourology, ExCel Centre, London, October 2015

The assessment and care of the surgical patient in the period before and after the operation is just as crucial to ensuring a good outcome of surgery for the patient as the operation itself. A key step in the preoperative period is to be able to accurately risk assess a patient so that adequate preparations can be made to optimise patient health and fitness before undergoing surgery. An assessment of the patient's physical fitness, in terms of heart and lung function is a crucial part of this process. Research in this area has investigated a range of methods, from questionnaires asking the patient to report their activity levels, to the more detailed cardiopulmonary exercise test where maximum effort is demonstrated on an exercise bike. With regards to the postoperative period, in order to be able to provide information about a patient's likely recovery and function, we also need to be able to accurately measure progress of recovery after the patient leaves hospital. Research on this is currently centred around asking for patient feedback in the form of Patient Reported Outcomes questionnaires.



Wearable activity monitor

We are building on this area of research by using a novel fitness assessment tool, a small, wearable three-axis accelerometer, to monitor daily activity levels at home in comparison to established methods of fitness assessment. We have shown in our preliminary study of 50 patients wearing the activity monitor for three days before and after surgery, that we can identify key measures of activity level that reflect patient fitness both before and after surgery. The next step is to utilise activity monitoring in trying to improve patient fitness before surgery so that they are better prepared to undergo surgery. The aim is to personalise perioperative care for patients by using targeted intervention based on individual fitness assessment. Further research into continuous home activity monitoring will develop the ability to provide more accurate monitoring techniques and personalised feedback to benefit the care of the surgical patient.

Hub for patient use to transmit live activity data for processing and feedback

Daily activity monitoring of surgical patients at home before their operation reveals new parameters that can be used to predict patient fitness with up to 83% accuracy compared to standard exercise testing.

Around 1000 patients a year need a colectomy for endoscopically-unresectable polyps. Colectomy causes complications in up to 40% of patients, when a local full-thickness resection would suffice.

Developing innovative risk-reducing surgery for colonic polyp excision

Andrew Currie

FELLOWSHIP/SPONSOR:
Joint RCS/Dunhill Medical Trust Fellowship

SUPERVISORS:
Professor Robin Kennedy and Mr Omar Faix

SITE OF WORK:
St Mark's Hospital, London

PUBLICATIONS:
1. Currie A, Burling D, Mainta E, Ilangovan R, Moorghen M, Lung P, Faiz OD & Kennedy RH (2016) An analysis of the accuracy of CT colonography when defining anatomy for novel full thickness colonic excision techniques in early colonic neoplasia. Colorectal Disease. Epub Feb 29 2016

2. Currie A, Brigic A, Blencowe NS, Potter S, Faiz OD, Kennedy RH, Blazeby JM. (2015) Systematic review of surgical innovation reporting in laparoendoscopic colonic polyp resection. British Journal of Surgery. 102: e108-16

PRESENTATIONS:
1.American College of Surgeons Clinical Congress, McCormick Place West Convention Center, Chicago, Illinois, USA. October 2015

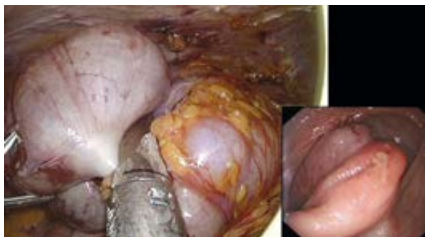
2. Digestive Disorders Federation International Meeting, ExCel Centre, London. June 2015

PRIZES:
1. ACPGBI Poster Prize – Digestive Disorders Federation international meeting, London 2015

2. American College of Surgeons Poster of Exceptional Merit – American College of Surgeons Clinical Congress, Chicago 2015

FURTHER FUNDING:
Pelican Cancer Foundation

Half of 70-year-olds have precancerous bowel polyps, which if left could cause symptoms and shorten life. Bowel cancer screening is diagnosing an increasing number of these benign, but precancerous large bowel (colon) polyps that cannot be managed by telescopic (endoscopy) means.



The combined laparoscopic and endoscopic views of the FLEX procedure in action

The standard surgery for these patients is removal of large sections of bowel (segmental colectomy), resulting in complications in up to one third of patients, some of which can be very serious. Long-term problems, such as increased bowel frequency and diarrhoea, although uncommon, can be disruptive to patients' lives after colectomy.

Recognising these risks, we have developed a new full-thickness laparo-endoscopic excision of the colon (FLEX) procedure using a telescope and 'key-hole' surgery (laparoscopy) to create a folded disc of bowel containing the polyp. If successful, FLEX could allow patients to avoid the risk of major bowel resection.

New surgical approaches need to be measured and gradually introduced by necessity. The current work was developed in conjunction with the RCS Bristol Surgical Trials Unit. We undertook a prospective, protocol-based descriptive cohort in which all participating patients received the FLEX procedure.

We have now undertaken this procedure in ten patients with complex benign polyps that would otherwise need radical surgery and in seven of these patients the lesion has been successfully removed with the FLEX technique – with the other three undergoing standard radical surgery under the same anaesthetic. In all these patients we were able to remove the polyp completely and successfully close the defect without post-operative surgical complications.

Andy undertaking a colonoscopy for a patient with polyps

Importantly, through the award of competitive national funding, we have been able to register the study of FLEX on the National Institute for Health Research (NIHR) Clinical Research Portfolio which will enhance recruitment. By leading a national roll-out of the procedure, around 1000 patients per year will be spared the risks of major surgery for benign polyps in the UK and achieve faster healing and recovery. If we can adapt the technique to treat early bowel cancer, around 4000 more patients a year, with early bowel cancer, could benefit from FLEX.

Assessing damage control after inadvertent vessel injury in the subpial tumour resection trial using the NeuroTouch simulator

FELLOWSHIP/SPONSOR:
RCS Harry Morton Travelling Fellowship

SUPERVISORS:
Dr Rolando Del Maestro

SITE OF WORK:
Neurosurgical Simulation Research and Training Centre at the Montreal Neurological Institute, Canada

FURTHER FUNDING:
Association of Surgeons in Training (ASiT) Surgical Training and Research Grant 2015 and University of Exeter Medical School – Dean's Individual Career Development Fund 2015/16

For the duration of the placement

Praveena Deekonda

I received an RCS Harry Morton Travelling Fellowship to support a seven-week placement at the Neurosurgical Simulation Research and Training Centre at the Montreal Neurological Institute, Canada. The NSRTC, in conjunction with researchers at the National Research Council of Canada developed a virtual reality simulator, capable of simulating neurosurgical operations, including endovascular, spinal and cranial procedures. Deemed to be one of the best neurosurgical simulators currently available, NeuroVR uses stereovision and a range of surgical tools capable of giving force and haptic feedback to simulate a realistic environment for neurosurgical procedures.

Practicing subpial tumour resection using the NeuroVR simulator

The NSRTC developed a series of module scenarios and have run validation studies. Past work has involved measurement of bimanual psychomotor performance, development of novel metrics to assess safe surgical technique and the development of proficiency performance benchmarks.

Group picture of some of the lab members at the NSTRC this summer

The NSRTC recently completed their subpial tumour resection trial, where medical students, senior and junior neurosurgical residents and consultant neurosurgeons were recruited to undertake a tumour debulking task. As part of my placement I worked on the data analysis of this study, and the development of novel metrics to analyse performance during the scenario. In particular I worked with an MSc student on assessing the damage made to a large vessel in the surgical field, and comparing performance amongst groups of participants based on their level of experience. I also worked on assessing the response to the damage and the methods taken to cauterise the bleed and control the damage.

Virtual reality surgical simulation is still a developing field, and as a medical student this was an unparalleled opportunity for me. In addition to the placement, I also got to learn about the rich history of the Montreal Neurological Institute and explore the beautiful city of Montreal.

For more information on the NSTRC and NeuroVR, please visit neurosim.mcgill.ca

The goal of McGill's Neurosimulation Research Centre is to enhance resident training and ultimately increase patient safety through virtual reality simulation.

One in every seven men will receive a diagnosis of prostate cancer. In common 'localised' forms, we still cannot predict who will benefit most from surgery, radiotherapy, or medical treatment.

DNA repair defects in prostate cancer: a pathway to personalised therapy

Harveer S Dev

FELLOWSHIP/SPONSOR:
RCS Fulbright Scholar Award

SUPERVISORS:
Professor Dipanjan Chowdhury

SITE OF WORK:
Harvard Institute of Medicine, Dana Farber Cancer Institute, Harvard University, USA

PUBLICATIONS:
1. D. H. Lee et al, Dephosphorylation enables the recruitment of 53BP1 to double-strand DNA breaks. Molecular cell 54, 512-525 (2014) – Chowdhury Lab (Harvard)

2. C. Z. Zhang et al, Chromothripsis from DNA damage in micronuclei. Nature 522, 179-184 2015 – Pellman Lab (Harvard)

PRESENTATIONS:
1. Dev H. et al. (2014) Targeting DNA repair pathways in prostate cancer BAUS: Academic Meeting, London, UK

2. Dev H. et al. (2014) Paper: Ataxia Telangiectasia Mutated (ATM) inhibition sensitises Castrate Resistant Prostate Cancer to Poly(ADP-ribose) polymerase 1 (PARP1) inhibition Royal Society of Medicine: Surgery, London, UK

PRIZES:
1. Royal Society of Medicine Urology short papers: first prize 2015

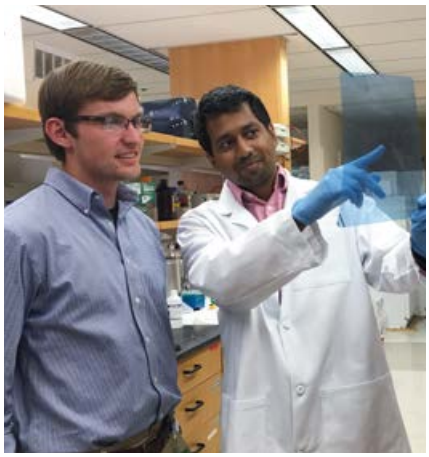
2. Lister Surgical Sciences, Royal College of Surgeons of Edinburgh 2014

FURTHER FUNDING:
Wellcome Trust Clinical PhD Fellowship, University of Cambridge for three years

As we age we accumulate 'mutations' in our DNA, and if enough critical genes are affected these cells will grow uncontrollably and lead to cancer.

Researchers have now established the importance of mutations in the very genes involved in detecting and repairing DNA damage, such as BRCA1, which is defective in many breast and prostate cancers. Cancers with BRCA1 mutations are exquisitely sensitive to drugs (PARP inhibitors) that cause DNA damage and require intact repair pathways to survive. By understanding all the critical factors involved in BRCA1-related DNA repair pathways, we will establish: (1) how mutations in specific repair genes cause widespread chromosomal-instability (CIN), a hallmark of cancer; and (2) whether gene mutations identified from biopsies could predict the successful response to radiotherapy or specific drugs, or their failure and hence need for immediate radical surgery.

I have spent a year working with leading groups at the Dana-Farber Cancer Institute and Harvard University to establish factors that regulate BRCA1



Harveer with a colleague demonstrating the successful genetic manipulation of cancer cells

function. Among these is a key mediator of DNA repair, 53BP1, which antagonises BRCA1. I am looking at how the inappropriate activation of 53BP1 in cells leads to CIN. I have engineered cancer cell models in which we can precisely turn on 53BP1 thus mimicking a potentially aberrant pathway underlying the development of prostate cancer. Using single-cell sequencing we predict that this mechanism will reproduce the complex mutational landscapes seen in prostate cancer. If confirmed, this activity may also reveal 53BP1-related tissue biomarkers as predictors of a response to PARP inhibitors.

Hence, understanding 53BP1 and BRCA1 dysfunction in prostate cancer enables molecular characterisation of a patient's biopsy, in order to guide their optimal management. My aim is to continue to work within surgical and scientific teams to establish personalised therapies in prostate cancer, and minimise treatment failure.

Harveer Dev (left) with Professor Dipanjan Chowdhury (right) at Harvard Medical School, where he conducted cutting-edge cancer research

Telomere characteristics and genetic profile of high-grade soft tissue sarcomas

FELLOWSHIP/SPONSOR:
Freemasons' Fund for Surgical Research with the support of the Arthritis Research Trust

SUPERVISORS:
Mr Robert Ashford

SITE OF WORK:
The East Midlands Sarcoma Service & The University of Leicester

PUBLICATIONS:
1. Soft tissue sarcoma. Eastley N, Green PN, Ashford RU. BMJ. 2016 Feb 24;352:i436

2. Extra-abdominal Desmoid Fibromatosis: A review of management, current guidance and unanswered questions. N Eastley, T McCulloch, C Elser, I Hennig, J Fairbairn, A Gronchi, R Ashford. European Journal of Surgical Oncology, 10.1016/j.ejso.2016.02.012

Nicholas Eastley

Soft tissue sarcomas (STSs) can affect patients at almost every age, and carry a significant morbidity and mortality. Their relative rarity means they have often been neglected compared with other more common cancers in terms of academic research.

STS treatment generally involves surgery to remove the tumour and radiotherapy. Following treatment 50% of STSs return (recur). This either occurs at the same place as the original tumour (local recurrence) or at a different part of the body (metastatic recurrence), and in both cases is a difficult problem to manage. Local recurrence often requires additional surgery, whilst metastatic recurrence almost always proves incurable with a three-year survival of just 25%.

The ability of clinicians to offer curative surgery to patients that recur is dependent on early diagnosis. In cases of local recurrence earlier diagnosis also reduces the likelihood of an amputation being required. This is obviously beneficial to patients individually, and society in general. At present no reliable tests (biomarkers) exist to allow clinicians to diagnose recurrence. This is partly the cause of a lack of standardised follow up in the UK, and the reason why local and distant recurrence is often extensive at the time of diagnosis.

Nick supervising a junior surgeon removing a soft tissue tumour

Data emerging from our research has already identified ctDNA in STS patients for the first time, and may identify specific ctDNA characteristics that may hold a role as future biomarkers of STS recurrence.

Following validation by other groups in larger, multi-centre trials, these results may provide clinical oncologists and surgeons with novel tools to predict or diagnose STS recurrence earlier than current means.

Over 70% of patients with advanced soft tissue sarcomas carry detectable tumour-derived circulating cell free DNA.

On average, every neurosurgical unit in the UK will receive at least one referral a day for a patient suffering from a Chronic Subdural Haematoma (CSDH).

How does dexamethasone alter the inflammatory response in chronic subdural haematoma?

Ellie Edlmann

FELLOWSHIP/SPONSOR:
RCS Rosetrees Surgical Research Fellowship

SUPERVISORS:
Professor P Hutchinson

SITE OF WORK:
Academic Division of Neurosurgery, Department of Neurosurgery, Addenbrooke's Hospital, Cambridge Biomedical Campus

PUBLICATIONS:
1. Edlmann E. et al. Randomised, double blind, placebo-controlled trial of a 2-week course of Dexamethasone for adult patients with a symptomatic Chronic Subdural Haematoma (Dex-CSDH trial) – a progress update. Abstract in: Proceedings of the 2016 Spring Meeting of the Society of British Neurological Surgeons. British Journal of Neurosurgery, April 2016; 30(2): 130-186

2. Chari A, Hocking K, Edlmann E, Turner C, Santarius T, Hutchinson PJ, Kolias AG. Core Outcomes and common data elements in chronic subdural haematoma (CODE-CSDH): A systematic review of the literature focusing on baseline and peri-operative care data elements. J Neurotrauma. 2015 Nov 5. Epub ahead of print

PRESENTATIONS:
1. Oral presentation of work was presented at the SBNS (Society of British Neurological Surgeons) conference, 20th April 2016, Newcastle

2. A poster presentation at the EANS (European Association of Neurological Surgeons) conference, 4th-8th September, Athens, Greece

PRIZES:
First place in poster competition at the National Neurotrauma conference 2015

Chronic subdural haematoma (CSDH) is a neurosurgical condition where layers of blood and fluid build up on the surface of the brain. It typically affects people aged over 65 and is often initiated by minor head trauma. It has become apparent in recent years that following this traumatic injury, there is an abnormal inflammatory reaction that causes a collection overlying the brain to grow over weeks, resulting in compression of the brain. Urgent surgery is often needed, carrying risks, and even after surgery the collection can return in up to 20% of patients. There is a need to investigate why and how this inflammatory reaction occurs and how it can be targeted to develop new treatments for CSDH.
A drug, dexamethasone, has anti-inflammatory effects and I am currently helping to test it in CSDH patients in the Dex-CSDH trial. As part of my research on this drug I also want to understand how it enters the spaces around the brain and what inflammatory cells it targets in this condition. This involves collecting intra-operative fluid and blood samples and testing them in the Neurochemistry laboratory. This is the first time such samples will be tested for dexamethasone, which will increase understanding of how this drug penetrates spaces around the brain and which cells it targets. This information will also be applicable to other brain conditions, such as brain tumours, where dexamethasone is used.

Ellie assessing CSDH images prior to surgery

152 patients have been recruited to the Dex-CSDH trial, which will continue for a further two years. I will be collecting and analysing samples throughout the trial and assessing how well patients recover from their CSDH to understand if dexamethasone treatment confers a significant benefit. CSDH and its complications can be life-threatening, and this risk is highest in patients requiring more than one operation. Therefore, introduction of a drug which either prevents the need for surgery or can be used in combination with surgery to prevent recurrences could have a significant effect on patient survival and long-term outcome.

Ellie reviewing a post-operative patient on the ward

An investigation into the formation of heterotopic ossification in amputees from recent military operations in Afghanistan

Major Dafydd Edwards

FELLOWSHIP/SPONSOR:
Joint RCS/Military Research Fellowship

SUPERVISORS:
Colonel/Professor Jon Clasper

SITE OF WORK:
The Royal British Legion Centre for Blast Injury Studies

PUBLICATIONS:
1. 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. Clin Orthop Relat Res. March 2015; DOI 10.1007/s11999-015-4250-9

2. Heterotopic Ossification In Victims Of The London 7/7 Bombings. Edwards DS, Clasper JC, Patel HD. Journal of the Royal Army Medical Corps. 2015 Feb 2. doi: 10.1136/jramc-2014-000370

PRESENTATIONS:
1. Heterotopic ossification from blast amputees is truly bone: quantitative and qualitative characterisation of its organic and non-organic components. D.S. Edwards, A Karunaratne, .A. Forsberg, T Davis, J.C. Clasper, A.M.J. Bull. BOA Congress (BORS Research Free Paper), Liverpool, 2015

2. Risk stratification for heterotopic ossification in residual limbs of blast related military amputations. D.S. Edwards, J.C. Clasper, A.M.J. Bull. Society of Military Orthopaedic Surgeons, Florida, 2015 and BOA Congress (Trauma Free Papers), Liverpool, 2015

PRIZES:
1. Philip Fulford Prize – Best Research Paper, Combined Services Orthopaedic Society, 2016

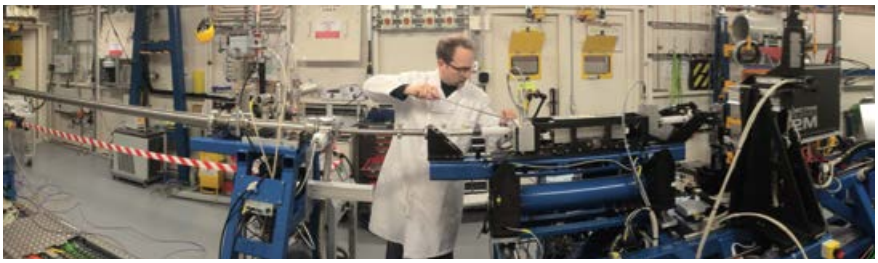
2. Montefiore Memorial Medal, 2014. 'Awarded annually to a surgeon in the RAMC who has by his/her surgical practice, research and application been considered to most have distinguished him/herself in the subject of Military Surgery'

FURTHER FUNDING:
Drummond Committee, Royal Army Medical Corps Charity, the Royal British Legion & the Royal Centre for Defence Medicine

The use of the Improvised Explosive Device and the resultant large cohort of multiple amputees defined the conflict in Afghanistan. Conditions not previously seen in common medical practise have subsequently surfaced. Heterotopic Ossification (HO) is one of those conditions. HO is the formation of bone at sites other than the skeletal system. This causes difficulty to the patient during rehabilitation through pain, pressure sores, and infections requiring surgery to excise the problematic lesion, further delaying recovery.

After the withdrawal of British troops from Afghanistan it was possible to calculate the entire amputee cohort and the HO burden. This was in order to identify risk factors for the formation of HO and calculate the clinical consequence and workload in managing these patients developing HO.

Furthermore this research used novel bio-imaging techniques to analyse the appearance of HO at the microscopic and molecular level. Measured variables were evaluated to examine how HO behaves under mechanical stimulus when compared to normal bone. Imaging techniques used included Backscattered Electron Microscopy and Synchrotron small-angle X-ray scattering imaging. Information on the mineral density and the orientation of the collagen molecules provides clues to its origin and metabolism both of which, it is hypothesised, can be manipulated to benefit the patient. The research is unique and the first of its kind.



Taff experimenting at the Diamond Light Source particle accelerator

The research concludes that formation of HO is systemically driven by the large injury burden and this can be predicted in injuries above a certain threshold. Local factors, such as zone of injury and subsequent amputation, direct us to the location where HO will form.

It is hoped that we can identify patients at risk and manipulate the mechanical drivers in the re-modelling of HO in order to prevent localised wound problems. The research was performed in collaboration with the US Naval Medical Research Center, Silver Spring.

Over 60% of British Military amputees from the conflict in Afghanistan suffer from the formation of Heterotopic Ossification in their wounds.

There are over 600,000 new diagnoses of head and neck cancer every year worldwide yet the five-year survival has remained around 50% for over three decades.

Tensin regulation of tumour cell movement: a link between metabolism and motility

Jason Charles Fleming

FELLOWSHIP/SPONSOR:
RCS Research Fellowship

SUPERVISORS:
Mr Dae Kim, Dr Jeremy Blaydes and Professor Gareth Thomas

SITE OF WORK:
University of Southampton, Academic Cancer Sciences

PRESENTATIONS:
1. CTEN (C-terminal Tensin-like) regulates head and neck cancer invasion and survival; NCRI Cancer Conference 2015

2. The role of Tensin in head and neck squamous cell carcinoma; Faculty of Head & Neck Research Meeting, MD Anderson Cancer Center, 2015

PRIZES
Winner of the Angell James Prize (Otolaryngological Research Society) October 2015

Runner up of the Rosetrees Prize (RCS) December 2015

FURTHER FUNDING:
MRC Clinical Research Training Fellowship

Head and neck cancer is the fifth most common cancer and the sixth most common cause of cancer-related mortality in the world. Existing treatments often result in severe side effects including loss of swallowing or voice, as well as cosmetic problems. New treatment targets are therefore urgently required. Cancer cells have a unique way of producing energy (metabolism) with high glucose uptake and we can visualise this with modern imaging techniques. However, it is becoming clear that rather than being simply a marker for detection, the way that tumour cells use glucose may fundamentally affect their behaviour. Our initial research indicated that head and neck cancer cells demonstrated a unique metabolic signature, and that this profoundly affected the way the cells moved and interacted with their surrounding environment. We therefore proceeded to explore this relationship to further understand what factors affect the invasion and spread of cancer cells around the body, which is ultimately responsible for over 90% of tumour-related deaths.

Our early research into pathways affected by altered metabolism identified changes in a number of proteins important for cell contacts and movement (focal adhesion adaptor proteins). These proteins are therefore important mediators of cancer cell invasion. Further functional experiments showed that through manipulation of the relative amounts of these proteins, tumour cell metabolism was able to influence cell behaviour, including how aggressively it invaded surrounding tissue.

In order to demonstrate the clinical relevance of this new biological finding, we studied the presence of these proteins of interest in a large series of head and neck cancer patients including long-term follow-up data. Interestingly, we were able to demonstrate that high levels of these same proteins that were regulated by metabolism resulted in a reduction in patient survival. The significance of both these laboratory and clinical results offer exciting possibilities for using metabolic markers as both new diagnostic and treatment targets with the potential to reduce side effects.

3D synthetic tumour model helping us to study cancer invasion

Lubrication approaches for articular cartilage regeneration (self-repair) and alleviation of osteoarthritis

Matthew David Gardiner

FELLOWSHIP/SPONSOR:
Joint RCS/Daniel Turnberg UK/ Middle East Travel Fellowship

SUPERVISORS:
Professor Jacob Klein (Weizmann Institute of Science) & Professor Tonia Vincent (University of Oxford)

SITE OF WORK:
Weizmann Institute of Science, Israel

FURTHER FUNDING:
Arthritis Research UK and The Leverhulme Trust, for an artist in residence. She has been working on various aspects of osteoarthritis including our research and the clinical condition – see images

Osteoarthritis (OA) is the most common degenerative joint disease worldwide. Patients with the condition suffer from pain and disability. Unfortunately the treatment options are limited and there are no drugs to treat the disease. Joint replacement surgery is often performed in severe cases.

Osteoarthritis of the base of thumb

OA was once considered a passive disease of 'wear and tear', resulting from joint surfaces grinding against one another. Recent research shows that OA is due to mechanical sensing of the cells within cartilage, causing them to produce enzymes that start its breakdown. Abnormal sideways forces (shear) appear to promote the release of degrading enzymes whereas compressive forces might promote cartilage protection.

Synovial joints (e.g. hip, knee, finger joints) are very well-lubricated. Delivering improved lubrication to the diseased joint may help overcome the increased shear forces experienced by the cartilage cells and promote repair.

The Centre for OA Pathogenesis at the Kennedy Institute of Rheumatology is collaborating with Professor Jacob Klein (Weizmann Institute of Science) to investigate a new form of lubrication. The lubrication uses liposomes, which are small bubbles made of the same material as a cell membrane. The liposomes attract water molecules, creating a 'hydration shell'. When under pressure and exposed to sideways force, surfaces coated with the liposomes have very low friction.

To date the liposomes have been tested in the laboratory. My project is to investigate their treatment potential in a mouse model of OA. I worked with Ronit Goldberg at the Weizmann Institute to develop a method for tracking fluorescently labelled liposomes in the mouse knee joint. This provides information about how long they remain in the joint and whether they are absorbed by the joint tissues.

Our longer-term plan is to investigate whether these unique liposomes offer a potential treatment option for OA. The fellowship has enabled application for further funding to support this project.

A trapeziectomy (Images courtesy of Francesca Corra, Leverhulme Trust Artist in Residence, Kennedy Institute of Rheumatology)

In the UK, 1 in 5 adults aged 50–59 and up to almost 1 in every 2 adults aged 80+ have painful osteoarthritis in one or both knees.

Aspirin enhances the response to radiation treatment in colorectal cancer cells, causing a two-fold increase in cancer cell death.

A novel role for prostaglandins in promoting colorectal cancer stem cells

Katherine Jane Gash

FELLOWSHIP/SPONSOR:
RCS Research Fellowship

SUPERVISORS:
Mr Michael Thomas and Professor Ann Williams

SITE OF WORK:
University of Bristol, School of Cellular and Molecular Medicine

PRESENTATIONS:
1. Aspirin enhances the response to radiation in colorectal cancer cells. Association of Surgeons of Great Britain and Ireland, Manchester, 2015

2. Colorectal cancer and Aspirin: can you teach an old drug new tricks? Royal Society of Medicine Coloproctology Section, Cambridge, 2015

PRIZES:
1. The John of Arderne Medal and a travelling fellowship to the following year's overseas meeting, Royal Society of Medicine, 24 April 2015

2. RCS Rosetrees Essay Prize

FURTHER FUNDING:
The David Telling Charitable Trust Research Grant and the Above and Beyond Charitable Trust Research Grant for one year

Each year in the UK around 40,000 people are diagnosed with colorectal cancer. Regrettably, some patients are resistant to current therapies and many develop recurrent disease or metastases, culminating in an overall five-year survival rate of only 55%. This highlights the urgent need to improve the efficacy of current treatment modalities.

Katherine and supervisor Mr Mike Thomas looking at a rectal cancer endoscopically

Fundamental to this are cells within colorectal cancers, known as cancer stem cells, which trigger cancer cells to multiply and subsequently fuel tumour growth; leading to recurrence or metastatic disease. Chemo-radiotherapy works by targeting cells that it 'sees' as living, but the cancer stem cells are able to become dormant and evade treatment.

My research is focused on developing ways of sensitising colorectal cancer stem cells to chemo-radiotherapy; rendering them less able to survive, and thus unable proliferate and drive tumour growth.

Most colorectal cancers have elevated levels of prostaglandin, which enhances the activity of two pathways (LGR5 and BCL-3), which promote colorectal cancer stem cell function and survival. NSAIDS (such as aspirin) work by reducing prostaglandin levels.

Through a series of laboratory experiments with colorectal cancer cells, I have demonstrated that treatment with Aspirin reduces activity in these pathways (LGR5 and BCL-3), and reduces cancer cell survival.

By replicating the radiotherapy that patients receive, using a laboratory irradiator, I have shown that when colorectal cancer cells are treated with aspirin prior to radiation, there is a two-fold increase in cell death. This is compelling evidence supporting the notion that aspirin has an efficacious role in colorectal cancer treatment.

To translate this clinically I am currently running an NIHR portfolio adopted study at six NHS sites, (ASPIRE: ASPirin & Irradiation in REctal cancer), analysing tumour tissue from patients with rectal cancer and investigating the impact of taking aspirin or NSAIDs during chemo-radiotherapy on tumour response.

This exciting work may further justify the use of aspirin as a novel treatment adjunct in colorectal cancer and has huge potential to improve treatment response, having an immeasurable positive impact on both cancer patients and their families.

Katherine and a patient who has recovered from colorectal cancer discussing the treatment he has undergone

Outcomes of Rectal Cancer Management – Analysis of the US National Cancer Database

FELLOWSHIP/SPONSOR:
RCS Fulbright Scholar Award

SUPERVISORS:
Professor R.P. Kiran

SITE OF WORK:
Columbia University Medical Center/New York Presbyterian Hospital, New York, USA

PUBLICATIONS:
1. K Gash, RP Kiran. Factors associated with response to neo-adjuvant radiotherapy in patients with rectal cancer

2. K Gash, K. Suradkar, RP Kiran. Rectal trauma injuries: outcomes from the U.S. National Trauma Data Bank

PRESENTATIONS:
1. K Gash, K. Suradkar, RP Kiran. Outcomes of Rectal Trauma Injuries: the USA National Trauma Data Bank. Association of Coloproctology of Great Britain and Ireland, Edinburgh, July 2016

2. K Gash, RP Kiran. Formation of Kock Pouch (Continent Ileostomy). Association of Coloproctology of Great Britain and Ireland, Edinburgh, July 2016

The Fulbright/RCS Scholarship enabled me to embark on a six-month period of research at Columbia University Medical Center, New York. This afforded me the fantastic opportunity to carry out a series of epidemiological studies using the largest cancer database in the world, working in an outstanding department, with forward-thinking, innovative academic surgeons. We utilised the US National Cancer Database (NCDB) to address some of the most important clinical questions regarding the optimum treatment for patients with rectal cancer.

Katherine outside New York Presbyterian Hospital/Columbia University Medical Center

Regrettably, colorectal cancer is the second most common cause of cancer death in the UK and 34% of all colorectal cancers arise in the rectum. Patients with advanced rectal tumours often receive pre-operative (neo-adjuvant) chemo-radiotherapy, which has been widely demonstrated to improve oncological outcomes. However, there is significant disparity in how well tumours respond (Tumour Regression Grade), with some demonstrating complete regression (which is associated with better survival rates), while others exhibit no response. The reasons for such varied regression are poorly understood.

Further, tumours that respond well can potentially be removed via 'local excision' i.e. trans-anally, thus avoiding much of the morbidity associated with radical surgery. However, it is essential that local excision does not subsequently compromise oncological outcomes.

Therefore, we identified:

1. Factors predictive of complete response to neo-adjuvant radiotherapy.
2. Adequacy of local excision vs. surgery according to Tumour Regression Grade and T-stage, after neo-adjuvant radiotherapy.
3. Impact on Tumour Regression Grade and patient outcomes, including local excision rates, according to the modality of neo-adjuvant therapy administered.

In addition, I analysed data from the National Trauma Data Bank investigating outcomes from rectal trauma and created videos of innovative surgical techniques, including construction of Kock Pouches and colonoscopy tips and tricks.

Receiving the Fulbright/RCS scholarship has significantly enhanced my research training and established an ongoing international collaboration. It also enabled me to complete a Value-Based Healthcare Course at Harvard University, participate in a Fulbright Seminar in San Diego and volunteer on the medical team at the largest marathon in the world.

Promoting patient and public involvement – 'the walk through colon' at bowel cancer awareness day at New York Presbyterian Hospital

Each year in the UK 16,000 people die from colorectal cancer.

Each year worldwide thousands of surgical operations are required to restore nasal defects caused by cancer, trauma, burns and congenital deformities.

Development of a nasal hybrid construct using nanocomposite material and stem cells

Michelle Griffin

FELLOWSHIP/SPONSOR:
Freemasons' Fund for Surgical Research

SUPERVISORS:
Professors Alexander Seifalian and Peter Butler

SITE OF WORK:
Centre for Nanotechnology & Regenerative Medicine, UCL

PUBLICATIONS:
1. Griffin MF, Butler PE, Seifalian AM, Kalaskar DM Control of stem cell fate by engineering their micro and nanoenvironment. World J Stem Cells. 2015;7:37-50

2. Griffin M, Kalaskar DM, Butler PE, Seifalian AM. The use of adipose stem cells in cranial facial surgery. Stem Cell Rev. 2014;10:671-85

PRESENTATIONS:
1. Characterisation of the Biomechanical Properties of Human Nasal Cartilage – ESPRAS 2014

2. Facial Implants Using Nanocomposite Polymer – ESPRAS 2014

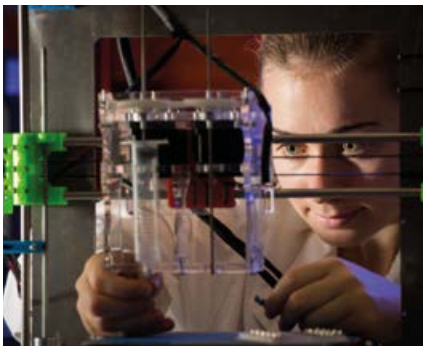
PRIZES:
1. UCL Berkeley Fellowship, 1st October 2014

2. RCS Rosetrees Essay Prize, 23rd March 2015

FURTHER FUNDING:
Medical Research Council, Action Medical Research and Royal Free Charity for two years

The devastating facial disfigurement that results causes huge psychological and physical difficulties for patients. The significant impact on patient's self-esteem affects their social life, interpersonal relationships and their ability to work. Current surgical treatment involves harvesting tissue from elsewhere in the body and using this material to carve a new nose. These techniques cause pain, can fail and are associated with many surgical risks. Artificial materials are available as an alternative but they result in high levels of infection, have an unnatural look and feel and thus are not acceptable alternatives. With current surgical techniques failing to repair nasal defects, there is an urgent need to find an alternative synthetic material.

Our research team develops human organs using a unique man-made material, polyhedral oligomeric silsesquioxane-poly(carbonate-urea) urethane (POSS-PCU). We have already utilised POSS-PCU to replace patient's organs that have failed, including the world's first synthetic windpipe, tear duct and lower leg artery. My fellowship aimed to develop POSS-PCU into a material that restores nasal defects.

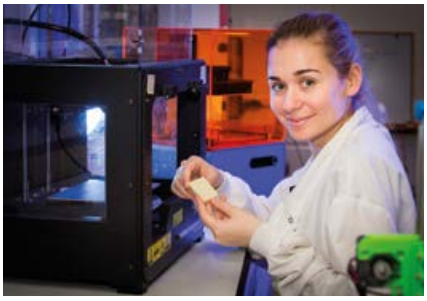


A desktop 3D printer built during the RCS fellowship

My first task was to modify the POSS-PCU material so it had similar properties to natural nose cartilage to minimise failure and infection risks. I changed the structure, mechanical and surface properties to mimic natural nose cartilage. I then developed a desktop 3D printer that could produce POSS-PCU implants that are personalised for each patient undergoing nasal reconstruction. This means I can take a pre-operative CT scan of a patient and design the nose specifically for each patient using POSS-PCU, resulting in fewer postoperative complications and better aesthetic outcomes.

The main risk of placing nasal implants beneath the skin for patients requiring nasal reconstruction is the failure of the implant to integrate with the surrounding tissue and cause infection. I discovered that adding adipose-derived stem cells to my nasal implants could overcome these complications and provide better outcomes for patients.

Due to the successful nasal implant prototypes I created during my fellowship I was able to secure further funding to take the POSS-PCU nose implants to clinical trial.



A 3D printer used to optimise the POSS-PCU nasal implant prototypes

Engineered scaffolds for preservation of gliding tissue interfaces

Rachael Helen Harrison

FELLOWSHIP/SPONSOR:
Blond McIndoe
Research Fellowship

SUPERVISORS:
Professor Molly Stevens

SITE OF WORK:
Imperial College London

PUBLICATIONS:
1. Modular and Versatile Spatial Functionalization of Tissue Engineering Scaffolds through Fiber-Initiated Controlled Radical Polymerisation, RH Harrison, JAM Steele, R Chapman, AJ Gormley, LW Chow, MM Mahat, L Podhorska, RG Palgrave, DJ Payne, SP Hettiaratchy, IE Dunlop, MM Stevens. Advanced Functional Materials (Volume 25, Issue 36 p5748-5757) 2015

2. Free Radical Polymerization for the Controlled and Facile Production of a Cell Repellent and Antifouling Surface in 2 - and 3D Systems, RH Harrison, R Chapman, AJ Gormley, LW Chow, JAM Steele, M Mahat, L Podhorska, SP Hettiaratchy, IE Dunlop, MM Stevens. Tissue Engineering: Part A (Volume 21, Issue S1 pS-307) 2015

PRESENTATIONS:
1. Tissue Engineering and Regenerative Medicine International Symposium World congress (TERMIS-WC), Boston USA, September 2015. Future Investigators of Regenerative Medicine, Girona Spain, September 2014

PRIZES:
1. Best oral presentation at Future Investigators of Regenerative Medicine, Spain, September 2014, 'Engineering Gliding Surfaces; Focusing of the Human Hand', RH Harrison, R Chapman, AJ Gormley, SP Hettiaratchy, IE Dunlop, MM Stevens

2. BAPRAS Travelling Bursary for Presentation Overseas (February 2016) for presentation at TERMIS World Congress, Boston, USA, September 2015

FURTHER FUNDING:
Imperial College Bursary Scheme, funded by the Engineering and Physical Sciences Research Council (EPSRC) for two years

Tendons are tissues that connect muscles to bones: when a muscle contracts, this pulls on the associated tendon and results in bone and joint motion. Tendon continuity and a smooth gliding surface are therefore essential for movement.

In the hand, tendons run close to the skin and are commonly cut as a result of injury. When cut, the tendon ends spring apart leaving a surgical repair essential to restore function. However, these repairs often result in patients being left with reduced hand function due to scar tissue compromising the tendon's gliding surface. Through this fellowship I have designed a bilayer scaffold to offer protection from this scarring to reduce the impact such injuries can have.

Rachael undertaking the plastic's trauma list with a consultant hand surgeon, where patients with injured tendons are typically operated on

Taking into account the high functional demand of the hand, this project has designed and produced a scaffold with a non-stick surface (resistant to cell and protein attachment) and an opposing cell-sticky surface (to promote cell attachment).

The bulk of the scaffold is made using a process called electrospinning. This produces a flat sheet of very fine fibres that is made of two different dissolving materials; one on each surface. One surface has cell-sticky peptides within the material, promoting cell attachment. The opposing surface has a reactive group from which a non-stick surface can be grown using a specialist chemical reaction. This prevents cell and protein attachment to that region of the scaffold.

This scaffold could be used to improve outcomes for patients with tendon injuries, as the non-stick surface will prevent scar tissue tethering the tendon's gliding surface. The opposing cell-sticky surface may support tendon healing; together improving outcomes for patients. The design of the scaffold is extremely versatile and different aspects of the design can be simply modified for different applications. We hope this will allow easy adaption to applications beyond the hand.

Rachael discussing current post-operative management of tendon repair patients with a senior hand therapist

In excess of 30 million tendon injuries occur globally each year; essential surgical repair is often complicated with scarring to the tendon surface resulting in reduced hand function.

Production of functional engineered tissue is currently 100% limited by the lack of adequate vascularisation.

Angiogenesis into tissue engineered decellularised scaffolds

Jasmine Onn Yee Ho

FELLOWSHIP/SPONSOR:
RCS Research Fellowship supported by the Rosetrees Trust

SUPERVISORS:
Professor Martin Birchall

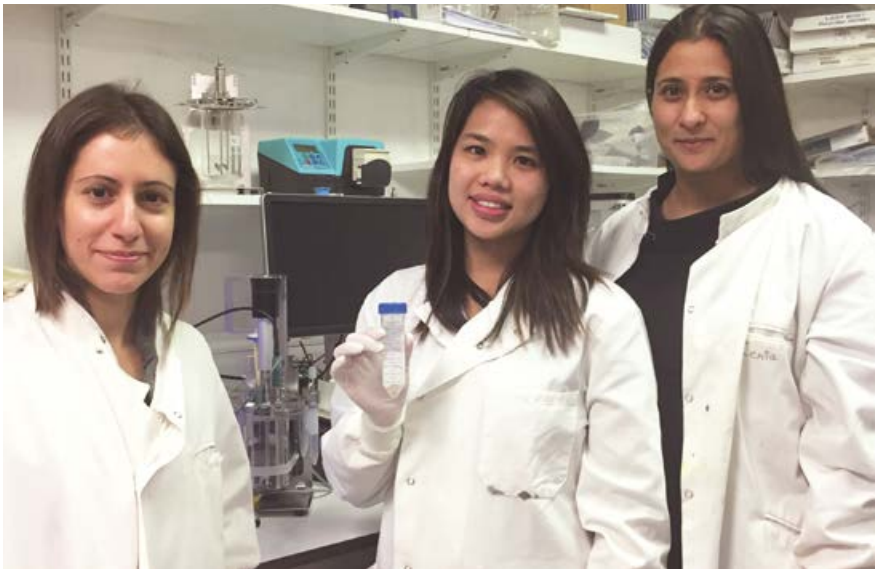
SITE OF WORK:
UCL Stanmore, London

PRESENTATIONS:
Is hypoxic cells the key to angiogenesis of tissue engineered constructs in regenerative medicine research? Ho, Jasmine; Stamati, Katerina; Birchall, Martin; Cheema, Umber. BAPRAS/RBSPS Summer Scientific Meeting, Bruges, June 2015

FURTHER FUNDING:
From MRC for 3 years

One of the major obstacles for growing new artificial organs is the provision of blood supply to the vital cells during the period of initial implantation into a patient. Without adequate blood supply, implant with cells would fail in the body. Hence, the aim of my research is to increase the understanding of how we can improve new blood vessel growth during the crucial time of integration of implanted tissue-engineered constructs by evaluating the ability of these constructs to promote blood vessel growth and identified ways to potentiate this process via the use of cells.

Through my research, I demonstrated that a tissue engineered trachea scaffold had retained the amount of matrix proteins which allowed for the support of new blood vessel growth (angiogenesis). This was confirmed when the scaffold was implanted into a chick embryo model. The addition of cells such as human bone marrow-derived stem cells helped promote new vessel formation in collagen scaffolds. Building on published literature, my research confirmed that placing these cells in a state of low oxygen tension helped enhance the process of angiogenesis by an increased release of necessary growth factors from the cells. This has significance in the field of regenerative medicine, as the processing of cells using such techniques to promote blood vessel growth is still relatively new. In addition, I carried out a pilot study using novel photoacoustic imaging technique on our tissue-engineered scaffolds in a mouse model which showed promising preliminary data. This modality of monitoring blood vessel growth has huge implications to this field of research, with conceivable benefit of translation and integrating such techniques into a clinical setting in the future.



Holding a tissue engineered trachea with UCL collaborators Umber Cheema and Katerina Stamati working on tissue engineered scaffolds using bioreactors

The long-term implication from this research will help the development of next generation tissue engineered constructs which would vastly benefit from the outcome from this ongoing research.

Towards bioengineering personalised facial bone implants for the treatment of congenital midface defects in children

Amel Ibrahim

FELLOWSHIP/SPONSOR:
Blond McIndoe
Research Fellowship

SUPERVISORS:
Professor Patrizia Ferretti,
Mr Neil Bulstrode and
Professor Peter Hammond

SITE OF WORK:
UCL Great Ormond Street
Institute of Child Health

PUBLICATIONS:

1. Combined soft and skeletal tissue modeling of normal and dysmorphic midface postnatal development. Ibrahim A, Suttie M, Bulstrode NW, Britto JA, Dunaway D, Hammond P, Ferretti P. Original research article. Journal of Cranio-Maxillofacial Surgery. In press

2. Adipose regeneration and implications for breast reconstruction: update and the future. Combellack EJ, Jessop ZM, Naderi N, Griffin M, Dobbs T, Ibrahim A, Evans S, Burnell S, Doak SH, Whitaker IS. Gland Surg. 2016 Apr 5. Review. PMID: 27047789

PRESENTATIONS:

1. Relating Bone Structure To Surgical Outcomes In Sagittal Craniosynostosis. Rodriguez-Florez N, Ibrahim A, Jeelani NUO, Ferretti P, Dunaway D. 27th EURAPS Annual Meeting. Bruxelles. 26-28th May 2016

2. Towards Bioengineering Personalised Facial Bone Implants. Ibrahim A, Suttie M, Bulstrode NW, Britto JA, Dunaway D, Hammond P, Ferretti P. 28th Head Group Meeting. Jan 2016. London

This project aims to alleviate the suffering and pain caused by facial deformities by providing a more accurate and less invasive treatment alternative to current surgical reconstruction options.

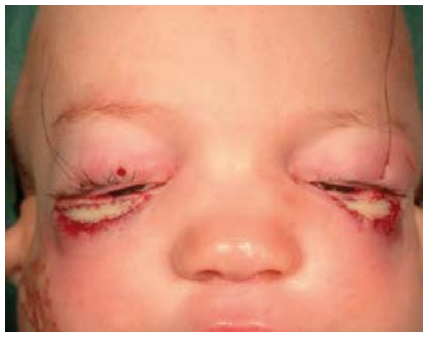
Routine CT scans were used to build a model of the midface in children with and without deformities. Stem cells derived from fat were compared alongside other types of stem cells (from bone) to assess their ability to engineer bone on a biodegradable scaffold. This scaffold was further optimised to improve blood supply and cell growth. Tissue engineered bone samples were tested for safety and survival by implanting in mice for three months.

This work led to the generation of a model that accurately described the difference between children with and without deformities and highlighted the limitations of current reconstructive options. The model was used to 3D-print a mould of a facial bone demonstrating that this can be used to pre-shape tissue engineered implants. This work has also shown that fat-derived stem cells can be grown on a biodegradable scaffold and induced to tissue engineer bone which is capable of survival and establishing its own blood supply when implanted in a mouse.

Previous studies have attempted to model the face although these have usually been in adults or used less sophisticated approaches. This is the first model of the soft tissues and the bone in unaffected children as well as those with Treacher Collins Syndrome and Hemifacial Microsomia. Furthermore, the work on bone tissue engineering using fat derived stem cells utilises a novel scaffold and shows survival in mouse studies that has not been published before. The next stage would be further optimisation of the tissue engineering and modelling protocols in order to generate full-sized pre-shaped facial bones that can eventually be evaluated in clinical trials.

Children born with midface deformities currently need surgery to restore function and harmony to the face. These surgeries are often invasive and require multiple operations to refine the outcome as the child grows. This research combines facial computer modelling technology and tissue engineering techniques to lay the foundations for generating facial bones personalised to the child's needs. This has the potential to provide a lifelong minimally invasive custom-shaped bone implant that grows with the child. Ultimately this would reduce the need for invasive and multiple surgeries enabling normal play, school and life beyond.

Before treatment



After treatment

Children born with Treacher Collins syndrome have malformed or absent facial bones which in the case of the child above can lead to visual loss if untreated. Current treatment options are invasive and involve multiple surgeries throughout childhood

1 in 1000 babies is born with a head or face deformity, which can lead to visual, speech, feeding, hearing or emotional problems and require multiple invasive surgeries to correct.

Ear deformities through trauma (including burns and animal bites) and skin cancer affect more than 1 in 500 people.

Design, biofabrication and characterisation of a new class of durable auricular implants

Zita M Jessop

FELLOWSHIP/SPONSOR:
The Dr Shapurji H Modi Memorial Research Fellowship

SUPERVISORS:
Professors Charles Archer, Iain S Whitaker & Cathy Thornton

SITE OF WORK:
Reconstructive Surgery & Regenerative Medicine Research Group Institute of Life Sciences, Swansea University & The Welsh Centre for Burns & Plastic Surgery

PUBLICATIONS:
1. Jessop ZM, Javed M, Otto IA, Morgan SR, Breugem CC, Archer CW, Khan IM, Kon M, Whitaker IS. Regenerative Medicine in combination with 3D Printing: A paradigm shift in reconstructive surgery. Stem cell research & therapy

2. Jessop ZM, Al-Himdani S, Whitaker IS. Translating Tissue Engineering from Bench to Bedside - Producing "Off the Shelf" Reconstructive Solutions. Frontiers in Surgery

PRESENTATIONS:
1. Jessop ZM, Javed M, Morgan S, Zhang Y, Combellack EJ, Khan I, Whitaker IS. A novel isolation protocol for auricular cartilage derived stem cells (CDSCs) and implications in cartilage tissue engineering. European Association of Plastic Surgeons (EURAPS), 28-30th May 2015, Edinburgh

2. Jessop ZM, Javed M, Morgan S, Zhang Y, Combellack EJ, Khan I, Whitaker IS. A novel isolation protocol for auricular cartilage derived stem cells (CDSCs) and implications in cartilage tissue engineering. British Association of Plastic and Reconstructive Surgeons (BAPRAS) Summer Meeting, 25-27th June 2015, Bruges

PRIZES:
1. RCS Norman Capener Travelling Fellowship

2. GDST Emerging Talent in Technology Award

3. Cutlers' Surgical Prize for Innovation

FURTHER FUNDING:
Medical Research Council Clinical Research Training Fellowship for three years

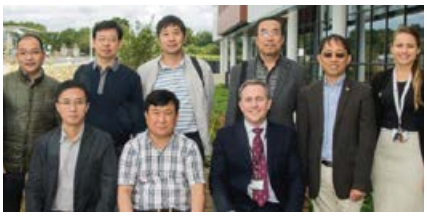
Loss of part, or all, of the ear following trauma or surgery produces disfiguring defects which often have a profound effect on quality of life and associated psychosocial problems. Patient's undergoing ear reconstruction require long-term, stable repair. The current gold standard is to perform surgery by using the patient's own rib cartilage to reconstruct these defects. Donor cartilage however is limited in supply, tends to get reabsorbed over time and its harvest is associated with complications including pain, lung damage, chest contour deformity and scarring. Synthetic materials have been shown to pose the risk of infection, extrusion and foreign body reaction.

The current generation of tissue engineered cartilage, using unrelated cells and materials, tends to be fragile and easily breakable. Once implanted into animals or humans it tends to undergo shrinkage and collapse, resulting in sub-optimal reconstruction.

Zita performing ear reconstructive surgery with supervisor, Professor Iain Whitaker

Our aim is to use the patients' own ear cartilage stem cells in order to tissue engineer durable cartilage for ear reconstruction. We have so far been able to isolate these ear cartilage stem cells from a tiny sample of the patient's own cartilage and grow them in the lab to produce millions of cells. These cells have the ability to produce cartilage pellets and react to tissue-specific developmental cues in order to regulate normal ear growth over the lifetime of the patient.

The next steps will be to optimise the growth of these cells to produce larger three-dimensional pieces of cartilage that can be used in patients. If successful, this research has wide implications in improving the outcomes of facial reconstruction following cancer, trauma or degenerative conditions.



Hosting international collaborators at the Welsh Centre for Burns and Plastic Surgery

Fellowship in healthcare management

FELLOWSHIP/SPONSOR:
RCS/McKinsey Fellowship in Healthcare Management

SUPERVISORS:
Martyn Coomer (RCS) and John Drew (McKinsey)

SITE OF WORK:
McKinsey & Company, London

PUBLICATIONS:
Kirkman MA, 'Developing management skills as a surgical trainee', Bulletin of The Royal College of Surgeons of England 2016; 98(8):364-7. DOI: 10.1308/rcsbull.2016.14

PRESENTATIONS:
1. Leadership and Management. Invited Oral Presentation. International Surgical Training Programme Annual Symposium, Royal College of Surgeons of England, London, 2016

2. Healthcare Management. Invited Oral Presentation. Third National NHS Leadership Meeting, Clinical Leadership Forum, Hammersmith Hospital, London, 2016

Matthew Kirkman

I stepped out of neurosurgical training for 12 months to complete the Healthcare Management Fellowship, based at the management consultancy McKinsey and Company.

My first project involved a comprehensive review of a large teaching hospital's entire operations to understand why they had not achieved the 4 hour A&E target once in the prior 18 months. I was able to subsequently lead in the implementation of several quality improvement initiatives there, contributing to improved performance. In another project, I was able to develop materials for a leadership and development programme for a large Clinical Commissioning Group. A particular highlight of the Fellowship was being able to contribute to the financial turnaround of a large acute NHS Trust that I had worked at myself several years ago.

In every project I completed, my clinical and surgical experience was greatly respected by both my colleagues at McKinsey and also the healthcare organisations we assisted. It genuinely felt like I was making a positive impact on the NHS, although sometimes the routes to success were less tangible than others; in the hospital struggling to meet the four-hour A&E target, I facilitated a board meeting where clinical directors from A&E, medicine and surgery sat down together for the first time and agreed on a set of professional standards to ensure timely review of A&E patients by the medical and surgical specialties. This was something that had not been possible for a long time before McKinsey's involvement.

One of the regular Knowledge Breakfasts arranged by McKinsey's Healthcare Practice. These meetings are frequented by, and offer the opportunity to network with, internal and external experts on various topics relevant to improving healthcare

My experience was both enjoyable and educational, and I learnt much more about the high-level political and financial construct of the NHS than was possible as a surgical trainee. The networking opportunities were also unparalleled. Going forward, I hope to use the skills and knowledge acquired from the fellowship to continue improving performance and quality in the NHS.

Matthew with the Organising Committee and co-speakers at the Third National NHS Leadership Meeting

An exciting and unique opportunity to step out of surgical training and improve healthcare from a different perspective.

Despite recent improvements in treatments for rectal cancer, 20-30% of patients undergoing surgery for rectal cancer are still left with a permanent stoma.

Determinants of sphincter preservation in low rectal surgery for cancer

FELLOWSHIP/SPONSOR:
Joint RCS/David Johnston Research Fellowship

SUPERVISORS:
Mr Mohamed Thaha

SITE OF WORK:
National Centre for Bowel Research & Surgical Innovation, Barts and The London School of Medicine & Dentistry, Queen Mary University London

Kathryn Lynes

Rectal cancer is common, with over 14,000 people diagnosed each year in the UK. Restoration of gastro-intestinal continuity, with preservation of sphincters and avoidance of a permanent colostomy, remains a priority in rectal resection. However, sphincter preservation is currently not achieved in a large proportion of cancer patients (especially those with distal rectal tumours) due to a variety of reasons. These include concerns about cancer recurrence and post-operative function.

Kate analysing ultrasound and manometry data in the GI Physiology lab

The operation that most patients undergo for rectal cancer is an anterior resection. Unfortunately this surgery frequently leads to disrupted bowel function, with patients suffering from incontinence, urgency and unpredictability, a problem known as 'low anterior resection syndrome' (LARS). These problems are believed to be fairly common following surgery but follow-up appointments have traditionally concentrated on ensuring that the cancer has not returned and have not reviewed functional outcomes in sufficient detail. Because of this we are unsure exactly how common the problems described are.

We have carried out an epidemiological study including >1000 patients who have undergone surgery for rectal cancer, allowing us to determine how many patients have ongoing bowel symptoms. In these survivors, who are all more than one year post surgery, over 40% of patients suffer from major LARS, and a further 22% from minor LARS. Ongoing analysis of the results will focus on determining the effect that these problems have on cancer survivors' quality of life.

An appreciation of the impact of these problems on post-operative quality of life will encourage a more careful assessment of functional outcomes during cancer follow-up, allowing identification of patients who may benefit from treatment. A further research project is aiming to identify biomarkers that can help to stratify use of pre-operative radiotherapy, which is known to affect bowel function. Future work will focus on prospective determination of the risk factors for poor post-operative function.

Kate at The Blizard Institute

Computational analysis of HLA alloantibody binding and HLA immunogenicity

Dermot Mallon

FELLOWSHIP/SPONSOR:
RCS Research Fellowship supported by the Rosetrees Trust

SUPERVISORS:
Vasilis Kosmoliaptsis

SITE OF WORK:
Addenbrooke's Hospital, Cambridge

PUBLICATIONS:
1. Mallon DH, Winn PJ, Bradley JA, Taylor CJ, and Kosmoliaptsis V. Three-dimensional structural modelling and calculation of electrostatic potentials of HLA Bw4 and Bw6 epitopes to explain the molecular basis for alloantibody binding: towards predicting HLA antigenicity and immunogenicity. Transplantation. 2015 27;99(2)

2. Mallon DH, Bradley JA, Taylor CJ, and Kosmoliaptsis V. Structural and electrostatic analysis of HLA B-cell epitopes: inference on immunogenicity and prediction of humoral alloresponses. Current Opinion in Organ Transplantation. 2014 19:420-427

PRESENTATIONS:
1. World Transplant Society Congress, July 2014, San Francisco. Tertiary Structure and Electrostatic Potential of HLA B-cell Epitopes Reveal the Molecular Basis for Alloantibody Binding and Epitope Immunogenicity

2. British Society for Histocompatibility and Immunogenetics Annual Conference 2015, Cambridge. HLA immunogenicity can be predicted by quantification of structural and surface electrostatic potential differences between donor and recipient HLA molecules

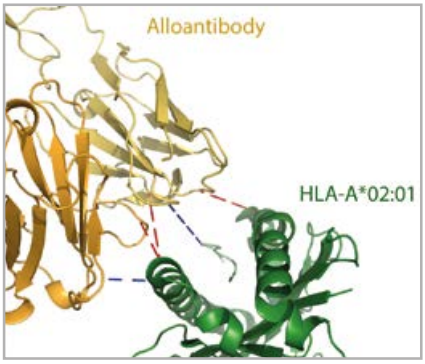
PRIZES:
1. The Kevin Burnand Prize for Translational Science, Society of Academic & Research Surgery (SARS) conference, January 2016

2. Shortlisted for Scientist of the Year from British Society for Histocompatibility and Immunogenetics (BSHI) conference, September 2015

Renal transplantation prolongs and improves quality of life of patients with chronic end-stage renal failure. Approximately 3,200 kidney transplants are performed each year in the UK but despite efforts to increase the availability of donor organs, the size of the kidney transplant waiting list has remained largely unchanged. Although early results after transplantation are excellent, long-term outcomes have remained static and over 30% of kidney transplants fail within ten years. This is due to a process called 'chronic rejection' which occurs mainly due to development of antibodies against the donor organ. The risk of antibody-mediated rejection can be offset by ensuring donor kidneys are allocated to recipients with a good tissue-match but current methods for determining tissue compatibility are inadequate. Another implication of tissue incompatibility and donor-specific antibody development is that they compromise access to future re-transplantation should the first kidney transplant fail.

The principal aim of my research is to improve the existing method for determining tissue compatibility in kidney transplantation. Our previous studies have shown that the degree of donor and recipient matching can be assessed based on structural and physicochemical differences between their histocompatibility proteins. I have used advanced computational molecular modelling techniques, assisted by laboratory analysis of protein structure, to assess donor-recipient compatibility. This work led to the description of a novel computerised matching algorithm which was then used to predict alloantibody responses and long-term graft outcome following transplantation in a national cohort of kidney transplant recipients in collaboration with NHS Blood and Transplant. My approach was shown to have significant advantages compared to the current histocompatibility strategy.

I anticipate that my research will inform deceased-donor allocation policy in the near future and help improve long-term outcome and access to transplantation for patients undergoing renal transplantation, both nationally and internationally.



Antibody hla interaction figure

One third of all kidney transplants fail after ten years due to chronic rejection.

Approximately 1.5 million metal-on-metal hip replacement patients are at risk of developing abnormal reactions to metal however, current patient follow-up recommendations are not evidence-based or cost-effective.

Optimal follow-up of patients with metal-on-metal hip replacements

Gulraj Singh Matharu

FELLOWSHIP/SPONSOR:
Joint RCS/Arthritis Research Trust Fellowship

SUPERVISORS:
Professor David Murray & Associate Professor Hemant Pandit

SITE OF WORK:
Oxford Orthopaedic Engineering Centre (OOEC), Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences (NDORMS), University of Oxford

PUBLICATIONS:
1. Matharu GS, Berryman F, Brash L, Pynsent PB, Treacy RB, Dunlop DJ. Predicting high blood metal ion concentrations following hip resurfacing. Hip International 2015

2. Matharu GS, Pandit HG, Murray DW, Treacy RBC. The future role of metal-on-metal hip resurfacing. International Orthopaedics 2015

PRESENTATIONS:
1. What are the optimal blood metal ion thresholds for identifying patients with failed metal-on-metal hip replacements? Matharu GS, Berryman F, Brash L, Pynsent PB, Treacy RB, Dunlop DJ. European Federation of National Associations of Orthopaedics and Traumatology (EFORT) 16th Annual Congress, Prague, Czech Republic. May 2015

2. Follow-up of metal-on-metal hip replacement patients is currently not evidence based or cost effective. Matharu GS, Mellon SJ, Murray DW, Pandit HG. British Hip Society Annual Meeting, London. March 2015

PRIZES:
1. Naughton Dunn Club Meeting Podium Presentation Prize (1st place), Birmingham, June 2015

2. The London Hip Meeting Registrar Poster Prize (3rd place), London, April 2015

FURTHER FUNDING:
Arthritis Research UK for 18 months Clinical Research Fellowship

Approximately 1.5 million patients worldwide have metal-on-metal hip replacements for arthritis. Unfortunately many have failed earlier than expected due to abnormal reactions to metal. These reactions can be painful and often require further operations. Little is known about outcomes following further operations; however, observations suggest most patients do poorly.

To identify abnormal reactions to metal earlier, worldwide authorities have published follow-up recommendations for patients. These recommend annual review for most patients with blood tests for metal ion levels and hip scans. However, it remains unclear if this is the best way to follow up patients. Many of these tests may be unnecessary. This research aimed to identify how best to follow up metal-on-metal hip replacement patients.

A critical review of current metal-on-metal follow-up guidance issued by five worldwide authorities demonstrated follow-up did not reflect the best available evidence, nor was it financially sustainable.

A study assessing optimal blood metal ion cut-offs for identifying abnormal reactions to metal in 598 patients observed that the specific cut-off values varied according to implant design. These implant specific cut-offs were more effective than currently proposed fixed cut-off values.

In 40 metal-on-metal hip patients requiring further surgery for problematic hips it was demonstrated that the most effective imaging techniques for identifying abnormal reactions to metal was a combination of ultrasound and magnetic resonance imaging.

After repeating ultrasound scans in 152 patients with pain-free metal-on-metal hips it was concluded that one in three patients did not require any follow-up for at least five years following initial review. Implementing this recommendation in the UK alone could save at least £13,600,000 over five years.

This research proposes an evidence-based approach for the follow-up of metal-on-metal hip replacement patients, which will hopefully improve the clinical and cost-effectiveness of the care delivered to the many patients with these implants.

Discussing the design of a metal-on-metal hip resurfacing with a colleague

A natural-synthetic hybrid scaffold for paediatric tracheal replacement surgery

Elizabeth Maughan

FELLOWSHIP/SPONSOR:
Lady Wolfson One Year Research Fellowship

SUPERVISORS:
Paolo De Coppi and Martin Birchall

SITE OF WORK:
Institute of Child Health, London

PUBLICATIONS:
1. Mesenchymal stem cell homing and immunomodulatory properties in cancer therapies: searching for the perfect balance, Da Silva Lourenco, S, Maughan E, Janes S, Cell & Genne Therapy Insights. 2015; 1(2), 173-192 doi: 10.18609/cgti.2015.024

2. A Polymeric Approach to Airway Tissue Engineering: The Best Biodegradable Material for Paediatric Application, Teoh GZ, Maughan E, Tavakoli M, Birchall M, Seifalian A. Annals of Chemical Research, March 2016

PRESENTATIONS:
1. Quantitation of Residual Detergent in Decellularised Organs for Tissue Engineering with Gas Chromatography-Mass Spectrometry, 28th International Symposium on Pediatric Surgical Research, Dublin September 2015

2. A Tissue-Engineered Rabbit Model for Paediatric Airway Tissue Engineering, presented to the Academic Laryngology Department of UC Davis, USA July 2015

FURTHER FUNDING:
The Wellcome Trust (Research Training Fellowship) for 28 months

PRIZES:
1. The Kevin Burnand Prize for Translational Science, Society of Academic & Research Surgery (SARS) conference, January 2016

2. Shortlisted for Scientist of the Year from British Society for Histocompatibility and Immunogenetics (BSHI) conference, September 2015

Infants born with severe congenital tracheal (windpipe) abnormalities may not survive once separated from their placental blood supply, and will usually require lifesaving interventions as soon as, or even before, they are born. There is also a growing cohort of children who have developed acquired tracheal problems from intubation trauma, oesophageal reconstructions and extrinsic pressure from nearby tumours or infection.

This project aimed to explore the tissue engineering field to manufacture a tracheal scaffold as an alternative to conventional transplantation. Tissue-engineered windpipes do not require immunosuppression, and by sustainably regenerating an organ, the need for serial 'upsizing' re-transplantation as the child grows is avoided. It is well-established that biologically-derived 'decellularised' scaffold materials encourage cell ingrowth and integration, but they are often mechanically weak. Moreover, stents usually need to maintain a patent airway, a strategy which can cause serious morbidity in its own right both in our animal models and in the clinical setting. Synthetic polymeric scaffolds show excellent 'made-to-measure' strength and patency; however, they rarely show significant ingrowth of cells or tissue integration.

The specific aim of this RCS Fellowship was to create a natural-synthetic hybrid scaffold for paediatric tracheal replacement that could combine the advantages, and negate drawbacks, of these two strategies. This builds on a multitude of data from our UCL Airway Tissue Engineering group and other International investigations into the power of hybrid scaffolds.

This Fellowship has generated enough research questions for two postdoctoral researchers to continue parallel work in decellularised gel scaffolds and improved synthetic nanocomposites. I am continuing to work alongside these collaborators as I progress into my Wellcome-funded PhD project, for which the data accrued during this RCS Fellowship has been invaluable.

Elizabeth at the Institute of Child Health, working on decellularised tissue gelation

Congenital anomalies affecting the airway may affect up to 1:1000 pregnancies, but in the rare severe cases where a transplant is required, appropriately-sized donors are almost impossible to come by.

Patients with 'routine' conditions that require prompt treatment (e.g. hip fracture and acute appendicitis) undergo operations later and have worse outcomes in busy US trauma centres. However, there is no evidence that such patients are disadvantaged in UK Major Trauma Centres.

Regionalisation of trauma services in the United Kingdom and United States

David Metcalfe

FELLOWSHIP/SPONSOR:
RCS Fulbright Scholar Award

SUPERVISORS:
Professor Ali Salim

SITE OF WORK:
Center for Surgery and Public Health, Brigham & Women's Hospital, Boston, USA

PUBLICATIONS:
1. Metcalfe D, Olufajo OA, Zogg CK, Gates, JD, Weaver MJ, Harris MB, Rios Diaz AJ, Haider AH, Salim A. Are older adults with hip fractures disadvantaged in level 1 trauma centers? Med Care. In Press

2. Metcalfe D, Gabbe BJ, Perry DC, Harris MB, Ekegren C, Zogg CK, Salim A, Costa ML. Quality of hip fracture care in major trauma centres: a national observational study. Bone Joint J. 98B(3):414-9

PRESENTATIONS:
1. Metcalfe D, Perry DC, Bouamra O, Salim A, Woodford M, Edwards A, Lecky FE, Costa ML. Regionalisation of major trauma services in England: a post-implementation analysis. Academy of Medical Sciences Spring Meeting, London. 25th February 2016. Abstract indexed in The Lancet

2. Metcalfe D, Zogg CK, Scott JW, Olufajo OA, Haider AH, Havens JM, Rios Diaz AJ, Yorkgitis B, Salim A. Disparities in failure to rescue for injured patients. Oral presentation. 11th Annual Academic Surgical Congress, Jacksonville, FL, USA, 2-4th February 2016

PRIZES:
1. Orthopaedic Trauma Society 'Best Paper' Prize 2016

2. Oxford-UCB Prize Fellowship 2016

FURTHER FUNDING:
UCB (Union Chimique Belge) Pharma for three years

It is increasingly recognised that patients with complex needs (e.g. heart attack or severe injuries) are best treated in specialist hospitals. This has driven a trend for one or two large hospitals in each region to deliver the majority of complex services. Although additional resources have been invested in such hospitals, they have become busier and had to restructure to accommodate new services. My aim was to understand how various patient groups have been affected by this trend towards 'regionalisation'.

I used a number of large databases that were based on insurance claims (USA) and submissions by NHS hospitals for performance monitoring (UK).

The results suggested that patients with acute appendicitis and older adults with hip fractures might be disadvantaged by treatment in a regional trauma centre. Both groups spent more time waiting for an operation than those who were treated in non-trauma hospitals. In addition, patients with isolated hip fractures that were treated in trauma centres spent longer in hospital, were more likely to be re-admitted, and had higher rates of blood clots (deep vein thromboses and pulmonary emboli). Patients with appendicitis were more likely to stay in hospital longer and to have infection spreading throughout their abdomen (generalised peritonitis) than those treated in non-trauma hospitals.

Interestingly, this pattern was not seen in the UK. Although Major Trauma Centres (MTCs) were launched across England in 2012, the reconfiguration did not have any measurable impact on the care of older adults with hip fractures. One possible explanation is that UK hospitals are financially incentivised (through the Best Practice Tariff) to ensure that patients with hip fractures receive their operation promptly, whereas there is no equivalent scheme in the US. This research did, however, suggest that the quality of care for patients with severe injuries has improved in new MTCs.

David in theatre during fixation of a hip fracture

Abdominal-based perforator flap breast reconstruction: Evaluation of anatomical studies and contemporary imaging techniques to optimise outcomes

Anita Tanniru Mohan

FELLOWSHIP/SPONSOR:
Blond McIndoe Research Fellowship

SUPERVISORS:
Michel Saint-Cyr

SITE OF WORK:
Mayo Clinic, MN, USA

PUBLICATIONS:
1. Mohan AT, Saint-Cyr M. Advances in ImagingTechnologies for Planning Breast Reconstruction. Gland Surg. 2016 Apr;5(2):242-54. doi: 10.3978/j.issn.2227-684X.2016.01.03

2. Mohan AT, Zhu L, Wang Z, Vijayasekaran A, Saint-Cyr M. Techniques and Perforator Selection in Single Dominant DIEP breast reconstruction: Algorithmic approach to maximize efficiency and safety has been built and requires approval. Plast Reconstr Surg

PRESENTATIONS:
1. Mohan AT, Zhu L, Michalak G, Lachman N, Saint-Cyr M. Quantitative assessment of single dominant perforator territories in bilateral DIEP breast reconstruction using indocyanine green fluorescence angiography and 4D CT imaging. World Society of Reconstructive Microsurgery WSRM, Mumbai, India

2. Mohan AT, Zhu L, Vijaysekaran A, Wang Z, Saint-Cyr M. The Single Dominant Perforator DIEP Breast Reconstruction: A Review of Clinical Outcomes and Risk Factors. Accepted to American Society of Reconstructive Microsurgery ASRM 2016, Arizona, USA

Approximately 18,000 women per year undergo complete removal of the breast tissue, (a mastectomy) and the rate of bilateral operations has tripled over the last decade. Breast reconstruction is an important consideration after mastectomy and can improve the patient's psychosexual wellbeing, and their overall psyche in response to breast cancer management and recovery.

Anita in the anatomy laboratory at Mayo Clinic working on cadaveric specimens

The lower abdomen offers an ideal site for taking tissue that is suitable for breast reconstruction providing long-lasting results, good cosmesis and natural looking appearance. The use of lower abdominal tissue for breast reconstruction is based on transferring skin and fat with its delicate blood supply from small vessels and sparing the underlying rectus muscle.

This study closely examined patterns of blood supply (inflow and outflow) from the single vessels (perforators) of abdominal tissue on which these flaps are based to outline key patterns in their vascular 'roadmap' within the skin and fat that may influence overall flap design. This was achieved through a series of anatomical cadaveric and intraoperative patient studies, combining the use of advanced imaging techniques using 3D and 4D Computed Tomographic (CT) angiography to visualise the distribution and patterns of the small vessels in the skin and fat in detail.

We also reviewed the real-time dynamics of the flap's blood supply using intraoperative imaging in a prospective patient cohort study and correlated this with the underlying anatomy. This study helped to better understand the 'vascular roadmap' of the skin and fat of abdominal flaps and how that roadmap could influence the flow and distribution of blood in and out the tissue.

Preliminary results demonstrated that location and size of perforators alone did not explain the overall extent and distribution of blood flow. It has provisionally highlighted that different patterns seen in blood flow were potentially related to concentration of linking vessels that made up the vascular roadmap.

Examination of these linking vessels on flap vascularity will have pertinent implications in the design of all flaps used in reconstructive surgery. The aim is to advance knowledge to allow surgeons to transplant tissue with a robust and predictable blood supply that will help reduce complications, reduce morbidity, associated healthcare costs and improve patient outcomes.

Anita receiving a prize for best resident oral presentation at the Chang Gung Mayo Clinic Reconstructive Symposium, Taiwan

Around 50,000 women are newly diagnosed with breast cancer per year in the UK and there is a lifetime risk of 1 in 8.

Survivorship of an orthopaedic implant is dictated by its fixation to bone; 30% of massive bone cancer prostheses do not integrate with the surrounding bone, of which 1 in 4 fail.

Enhancing osteointegration using selective laser-sintered porous titanium alloy combined with solution deposited coatings

Aadil Mumith

FELLOWSHIP/SPONSOR:
Enid Linder and the Arthritis Research Trust Fellowship

SUPERVISORS:
Professor Gordon Blunn and Dr Melanie Coathup

SITE OF WORK:
John Scales Centre for Biomedical Engineering, Institute of Orthopaedics and Musculoskeletal Science, Royal National Orthopaedic Hospital

PUBLICATIONS:
1. The use of a novel laser sintered porous collar in optimising osteointegration of endoprostheses, Mumith A, Coathup M, Fromme P, Aston W, Briggs T, Shah A, Blunn G, Combined International Society of Limb Salvage (ISOLS) & Musculoskeletal Tumour Society (MSTS) Meeting October 2015 – Orlando, Florida, USA

2. Optimising osteointegration with 3D printed components: A FEA and histological study, Mumith A, Fromme P, Blunn G, Aston W, Briggs T, Shah A, Coathup M, British Orthopaedic Research Society (BORS) and British Orthopaedic Association (BOA) Annual meeting September 2015 – Liverpool, UK

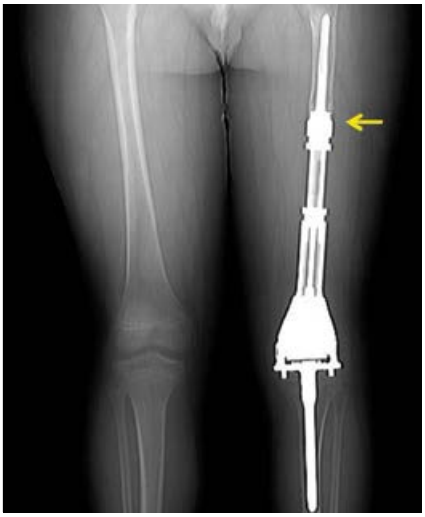
FURTHER FUNDING:
Orthopaedic Research UK, Scat Bone Cancer Trust for one year

Massive bone tumour endoprostheses (synthetic inserts) integrate with the skeleton via a collar sprayed with hydroxyapatite (a major component and essential ingredient of normal bone), which encourages bone to attach onto its surface.

Our research aimed to design and test a new collar covered with an enhanced bone growth boosting coating to improve integration of endoprostheses. We have produced a novel collar that is completely porous and manufactured from 3D-printed titanium allowing us to customise every facet of the collar structure to optimise the design, maximising bone attachment.

Tissue analysis and X-rays of specimens from our study, confirm that these collars allow bone to permeate through the collar, creating fusion between the implant and bone. Our design has integrated to greater than what has been recommended by computer modelling, leading to a more durable implant.

Implants that are coated with hydroxyapatite commercially use a technique that coats the outer surface and not the inner pores. Coating porous



Arrow indicating current solid collar design as part of a distal femoral endoprosthesis in a patient

structures has historically been a challenge. However, our research has enabled us to coat porous structures in full, with a variety of coatings. We have incorporated other elements, most notably strontium, of which its bone growth properties are currently utilised in osteoporosis treatment. This we hope will further augment bone regeneration, attachment and overall integration.

The next phase is to study the effect of our coatings on human stem cells. We predict that our coatings induce greater differentiation of stem cells into bone cells than coatings currently available.

We aim to translate the results of our research to benefit patients who undergo operations using endoprostheses within the next three to five years. We hope to reduce the need for highly complex re-operations needed for implant.

Aadil with his supervisors Professor Gordon Blunn (President of the British Orthopaedic Research Society) and Dr Melanie Coathup (Head of Centre for Cell & Tissue Research, UCL)

Circulating tumour DNA (ctDNA) in melanoma – a non-invasive biomarker of disease

Suzanne Murphy

FELLOWSHIP/SPONSOR:
Jersey H&S Charitable Trust Fund

SUPERVISORS:
Dr Nitzan Rosenfeld,
Dr Pippa Corrie and
Mr Amer Durrani

SITE OF WORK:
Cancer Research UK,
Cambridge Institute, The
University of Cambridge

PRESENTATIONS:
1. Murphy S, Durrani A, Corrie P, Rosenfeld N. 'Liquid biopsy' in melanoma – circulating tumour DNA as a biomarker of disease. British Association of Plastic Reconstructive and Aesthetic Surgeons (BAPRAS), President's Prize Section. Birmingham, November 2015

2. Murphy S, Corrie P, Durrani A. Management of metastatic melanoma; a network perspective on the changing surgical landscape. European Society of Plastic Reconstructive and Aesthetic Surgeons (ESPRAS). Edinburgh, July 2014

PRIZES:
1. Douglas Murray Prize, Eleventh West Midlands Plastic Surgery Meeting. Birmingham, 13th September 2014

2. Health Education East of England Celebration of Success Annual Awards, winner of best Leadership Poster. The Wellcome Trust Conference Centre, Cambridge. 26th September 2013

FURTHER FUNDING:
Addenbrooke's Charitable Trust (12 months) & Cancer Research UK (four months)

Melanoma, a highly invasive form of skin cancer, continues to increase in incidence faster than any other malignancy in the UK. It is the fifth most common cancer in the UK with approximately 37 people being newly diagnosed every day. In 2012 there were in excess of 13,000 new diagnoses and over 2,000 deaths from the disease. The best prognosis is seen when lesions are detected early and surgically removed prior to metastasis.

Metastatic melanoma has been notoriously difficult to treat since it is resistant to conventional chemotherapy and radiotherapy. However, the discovery of hotspot mutations (e.g. BRAF V600E) along with the development of new targeted therapies and immunotherapies, has improved the prognosis for these patients. Nevertheless, most patients develop resistance and eventually succumb to their disease.

Currently there is no blood test which can be used to monitor patients. Therefore, the detection of progression can be delayed. In addition, when a patient develops progressive disease they often require biopsies to check the genetic mutation profile of their tumour to guide any further therapy. Biopsies are invasive, carry risks, and are uncomfortable for the patient. The aim of our study was to look at circulating tumour DNA (ctDNA) in the blood and urine of patients with melanoma as a non-invasive way of tracking the genetic finger-print and burden of disease.

Using 'TAm-Seq', a method developed by the Rosenfeld Group in Cambridge, we successfully tracked multiple mutations in the plasma and urine of melanoma patients during their treatment and follow-up. We have shown that changes in the ctDNA concentration precede progression seen on CT scans as well as elevated LDH levels in the blood. Developing a technique to detect ctDNA in the blood and urine of melanoma patients has the potential to revolutionise the management of this life-threatening disease.

Suzanne working in the laboratory with members of the Rosenfeld Group

Melanoma is the most invasive form of skin cancer, accounts for over 2000 deaths per year in the UK and its incidence continues to rise faster than any other malignancy.

FIve-year survival for pancreatic cancer is 4%. New approaches are required and nanoparticle-based treatment could provide a potential solution.

Treatment of pancreatic cancer using gemcitabine-loaded superparamagnetic nanoparticles [SPIONs]

FELLOWSHIP/SPONSOR:
Freemasons' Fund for Surgical Research with the support of the Jersey H&S Charitable Trust

SUPERVISORS:
Mr Christopher Halloran

SITE OF WORK:
Royal Liverpool University Hospital / University of Liverpool

PRESENTATIONS:
1. European Pancreatic Club Annual Conference, Toledo, Spain 2015
2. National Cancer Research Initiative (NCRI) Cancer Conference, Liverpool 2014

PRIZES:
1. Young Researcher Travel Award (European Pancreatic Club 2015)
2. BASO~ACS Best Poster Prize (NCRI Cancer Conference 2014)

Sumit Nandi

Pancreatic cancer is difficult to diagnose and challenging to treat. Despite advances in surgical and chemotherapy treatments, its survival rates have barely improved since the 1970s, with only around 4% of patients surviving five years. Current chemotherapy agents also have a poor response rate; possibly due to ineffectiveness at penetrating pancreatic cancers as there is an unusually poor blood supply and dense environment surrounding tumours. Consequently, fresh approaches in targeting chemotherapy to these cancers are required.

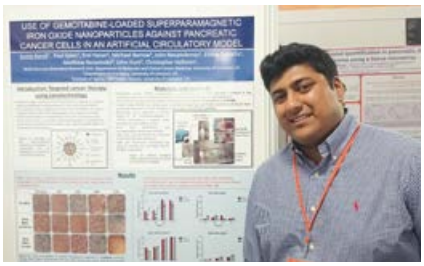
Our project investigates a novel iron core nanoparticle complex loaded with gemcitabine (commonly used chemotherapy agent) to precisely target, deliver its drug and kill pancreatic cancer cells. Previous work has demonstrated successful destruction of cancer cells in a static or 2D environment. During my fellowship, we have developed our knowledge by investigating their cell-killing capabilities in a 3D model and an artificial circulation, attempting to mimic blood circulation.

To investigate the aims, pancreatic cancer cells were grown to form tight, dense spheroids. When chemotherapy-loaded nanoparticles were introduced the architecture of the 'artificial tumour' was successfully disrupted. Furthermore, an artificial circulation model was constructed, which continuously flowed nanoparticles over tumour cells, with some being exposed to a magnetic field. Encouraging results were demonstrated, showing that tumour cells are still destroyed with flowing nanoparticles; but that death is accelerated with the use of a magnet – as the nanoparticles are iron-based.

This is a completely novel project and thorough investigation is required. The project will continue to explore the effects of the nanoparticles and future work is commencing in animal models.

Experimental set-up of the artificial circulation model

Pancreatic cancer outcomes are dismal and urgent attention is needed to attempt to improve this. Nanoparticle-based chemotherapy treatments have huge potential to improve patients' quality of life, by providing a more precise or personalised chemotherapy regime, without the unwanted side effects from delivery of conventional chemotherapy.



Sumit presenting his poster at the 2015 European Pancreatic Club, Spain

Parathyroid hormone enhances osseointegration of a mesenchymal stem cell coated implant

FELLOWSHIP/SPONSOR:
Freemasons' Fund for Surgical Research

SUPERVISORS:
Professors Gordon Blunn & Timothy Briggs

SITE OF WORK:
Institute of Orthopaedics & Musculoskeletal Science, UCL

FURTHER FUNDING:
From Rosetrees Trust and Gwen Fish Trust for two years

Liza Osagie

There are 150,000 hip replacements performed annually in the UK. This number is set to increase 300% by 2030, with a failure rate over 11%. One cause of failure is bone thinning; thus, attention has been turned to methods that can improve bone-implant fixation.

Within our ageing population, osteoporosis leads to one in four suffering an age-related fracture. As such, patients are at an 11% lifetime risk of fracturing around a hip implant.

Treatment of these fractures is often complex, with 10% of patients dying within 30 days of the operation.

Liza listening to Lord Cadogan at the Freemasons' HQ

Liza presenting at a Freemasons' meeting

My work aims to enhance fracture healing and implant fixation using stem cells (MSCs) and parathyroid hormone (PTH) in a rat. I have obtained MSCs from the bone, fat and muscle of adult and osteopenic rats; demonstrating the optimal dose of PTH to turn them into bone forming cells, and the ability for PTH to enhance cell migration to sites of increased bone turnover (i.e. fracture sites or around implants).

I have demonstrated the capacity for PTH to turn fat cells into bone producing cells; this is important in the context of osteoporosis, where patients have a higher concentration of fat cells, thus hindering bone formation.

I have investigated the mechanical characteristics of our fracture fixation device and replicated findings in a computer programme. This allows us to alter the device in a computer model and create the optimum construct to allow bone formation.

Future works will use young and osteoporotic rats, injecting MSCs into the fracture gap, with injections under the skin of PTH to accelerate healing.

My work utilises clinically relevant therapies to answer a growing patient need, with the aim of improving orthopaedic outcomes, and wider implications for bone formation.

Over 150,000 hip replacements are performed in the UK annually; 11% of these will fail, and 11% will fracture around the implant.

Up to 1-in-4 flap breast reconstruction patients that subsequently undergo radiotherapy as part of their cancer treatment develop significant fibrosis.

Optimising a radioprotective gene therapy strategy in free flaps for translation

FELLOWSHIP/SPONSOR:
Joint RCS/BAPRAS Research Fellowship

SUPERVISORS:
Professor Kevin Harrington and Mr Paul Harris

SITE OF WORK:
Royal Marsden Hospital and the Institute of Cancer Research

PUBLICATIONS:
The tumour microenvironment after radiotherapy: mechanisms of resistance and recurrence. Barker HE, Paget JT, Khan AA, Harrington KJ. Nature reviews Cancer 2015;15:409-25

FURTHER FUNDING:
Wellcome Trust Clinical Research Fellow for 33 months

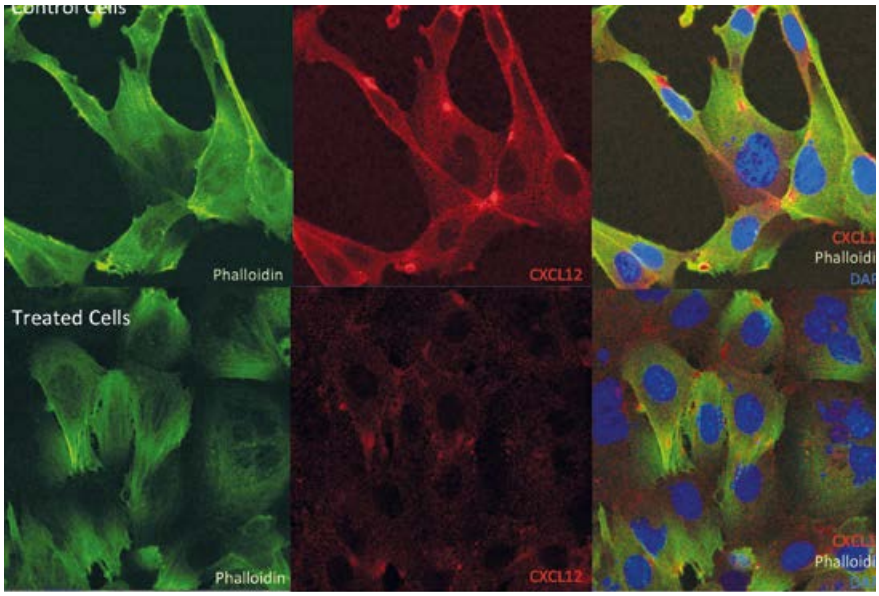
James Paget

Reconstructive surgery plays an important role in the breast cancer care pathway. In particular, reconstruction with the patient's own tissue at the time of cancer surgery has become a standard of care in the UK. 50% of patients have high-risk cancer and undergo subsequent radiotherapy; 25% of these cases develop unwanted fibrotic changes, patient dissatisfaction and the need for revision surgery. The overarching goal of this project was to combine radioprotective gene-therapy with microvascular surgical techniques to give cancer patients a more durable reconstruction.

Using a validated experimental model of radiation fibrosis in reconstructed tissue, we identified that CXCL12 plays an important role in the established post-irradiation biological landscape at six months. It is a secreted signalling protein, called a chemokine, which has a number of functions in immune cell recruitment to damaged tissue and in later fibrotic development. However, a high proportion of immune biology occurs in the first few days to weeks after damage. We therefore explored earlier changes in CXCL12 in our microsurgical model across the first few days to weeks using a combination of messenger RNA and protein assays.

These results demonstrated that the greatest change occurs at one week after irradiation. This time point also correlates with the infiltration of the flap with innate immune cells, particularly macrophages, which are known to play a central role in wound healing and are attracted to CXCL12.

To target this therapeutically, we have developed a modified lentivirus that decreases CXCL12 production, and which will be delivered to the reconstructed tissue in isolation during surgery. Its efficacy at reducing CXCL12 has been confirmed in cell culture (see figure) and we will explore its effects in our model against fibrosis, including the link to macrophage biology, across the remainder of my PhD.



Confocal microscope images of cultured cells demonstrate our novel therapy working against the target protein

Evaluation of the diagnostic role of a small RNA within PCA3 in prostate cancer

Karl Pang

FELLOWSHIP/SPONSOR:
Freemasons' Fund for Surgical Research with the support of the Rosetrees Trust

SUPERVISORS:
Professor James Catto

SITE OF WORK:
Department of Oncology and Academic Urology Unit, University of Sheffield

PUBLICATIONS:
1. Identification and diagnostic performance of a small RNA within the PCA3 and BMCC1 gene locus that potentially targets mRNA. Cancer Epidemiol Biomarkers Prev. Drayton RM, Rehman I, Clarke R, Zhao Z, Pang K, Miah S, Stoehr R, Hartmann A, Blizard S, Lavin M, Bryant HE, Martens-Uzunova ES, Jenster G, Hamdy FC, Gardiner RA, Catto JW. 2014 Nov 12

2. 'Science made simple'- MicroRNA and Urothelial cell carcinoma. Miah S, Pang K, Catto J. BJU Int. 2014 May:113(5):811-2

PRESENTATIONS:
1. 30th European Urology Association Congress (International), Mar 20-24 2015. IFEMA, Madrid, Spain

2. BAUS Academic Meeting (National), Dec 2 2014. Royal College of Surgeons, London

PRIZES:
European Urology Association 2015, Best Poster of Session (1st Prize)

FURTHER FUNDING:
The Urology Foundation for 12 months

Prostate cancer (PCa) is the most common cancer in men and is the second most common cause of cancer death after lung cancer. In the UK, there were ~42,000 cases diagnosed in 2011 and ~11,000 deaths in 2012.

The investigation of PCa is based on digital rectal examination, blood tests, and a prostate needle biopsy (PBx). However, not all men with abnormal blood tests who undergo a PBx have cancer. This may be due to initially falsely abnormal blood tests, as markers can be raised in infection and benign prostate disease as well. Unnecessary repeat PBx (rPBx) increases healthcare costs and risks of infection/bleeding/pain and patient anxiety. Therefore, better markers are needed to improve patient selection for rPBx.

Prostate Cancer Antigen-3 (PCA3) is an urinary marker used to stratify men for rPBx; however, it is used in selective countries and not in the UK because its biological role is unknown and it's a long molecule that is prone to breakdown by urinary enzymes. Urine is treated chemically to prevent breakdown, which ensures a high cost. We searched the PCA3 molecule using computer analyses to find an alternative shorter form, which may avoid breakdown and potentially replace the current test. We identified a shorter form, which we termed short-PCA3 and showed that its urinary levels are increased in PCa samples.

Reviewing urological patients on a ward round

Analysing a CT scan from a patient with prostate cancer

We explored functions of short-PCA3 and found that it had the ability to interact with other molecules involved in PCa biology. We analysed potential molecule targets and showed that molecule, 'SOX11' was decreased in PCa urinary samples. Unravelling biological mechanisms in PCa would allow further investigation into therapeutic agents.

The discovery of our new marker (termed short-PCA3) may improve selection of patients for prostate biopsy. This marker appears to target other molecules involved in prostate cancer biology.

Less than 1 in 8 men with prostate cancer actually have a form of the disease which requires aggressive treatment, identifying this group is of critical importance.

The translational potential of circulating tumour DNA in urological cancers

Keval M Patel

FELLOWSHIP/SPONSOR:
Jersey DBP Surgical Trust

SUPERVISORS:
Nitzan Rosenfeld

SITE OF WORK:
Cancer Research UK
Cambridge Institute

PUBLICATIONS:
1. Tracking the origins and drivers of subclonal metastatic expansion in prostate cancer. M Hong, G Macintyre, D Wedge, PV Loo, KM Patel, S Lunke, L Alexandrov, C Sloggett, M Cmero, F Marass, D Tsui, S Mangiola, A Lonie, H Naeem, N Sapre, P Phal, N Kurganovs, X Chin, M Kerger, A Warren, D Neal, V Gnanapragasam, N Rosenfeld, J Pedersen, A Ryan, I Haviv, A Costello, N Corcoran, & C Hovens. Nat Comms. 2015.6:6605

2. The translational Potential of Circulating Tumour DNA in Oncology. Patel KM & D.W.Y. Tsui. Clin Biochem. 48(15):957–61

PRESENTATIONS:
1. Circulating tumour DNA as a diagnostic aid in prostate cancer, poster presentation. European Association of Cancer Research, University of Cambridge 2013

2. Academic BAUS conference, podium presentation runners-up prize RCS 2015

PRIZES:
1. Academic BAUS conference. Oral presentation prize (runner up) RCS 2015

2. Rosetrees Essay Award (runner up) RCS 2016

FURTHER FUNDING:
Cambridge Cancer Centre for three years

Prostate cancer is the most common cancer in men and more are being diagnosed each year. Fortunately only about 12% of those diagnosed have an aggressive form that could limit their lifespan, with the majority having a relatively indolent form.

Keval in the laboratory

Current methods do not always accurately differentiate between these aggressive and indolent cancers. Therefore, many patients who actually have indolent disease, are over-treated whilst those harbouring aggressive prostate cancer are not treated aggressively enough.

This project aimed to investigate whether the levels or types of mutations detected non-invasively from blood samples, a method used in other types of cancers, could identify men with aggressive prostate cancer.

During the course of this project we found that a gene called TP53, which plays a pivotal role in other cancers, tends to be mutated in men who have aggressive prostate cancer. Furthermore, we found that in two out of three men (for whom we had historically stored blood prior to their initial attempt at curative surgery) we were able to detect mutations in the TP53 gene directly from the blood sample.

We are continuing to work on this to see if the test results can be reproduced in a larger cohort. If the blood test is able to distinguish between men with aggressive and indolent forms of prostate cancer, we could more accurately target which men need aggressive treatment and which do not.

Keval receiving a pot of jam in thanks for the talk he gave to the Cambridgeshire Prostate Cancer Support Association

Pre-injury statins in early resuscitation of complex battlefield injuries

FELLOWSHIP/SPONSOR:
Joint RCS/Military Research Fellowship

SUPERVISORS:
M Midwinter, E Kirkman, S Watts, P Harrison

SITE OF WORK:
Defence Science and Technology Laboratory, Porton Down, Wiltshire

PUBLICATIONS:
1. Shock: aetiology and pathophysiology, Emrys Kirkman, Henrietta Poon, James D Ross & Sarah Watts Submitted by invitation for inclusion in War Trauma: Principles and Practice of Management (OUP)

2. Intravenous fluids: starches, H Poon, S Watts & E Kirkman. Submitted by invitation for inclusion in Key Topics in Trauma

FURTHER FUNDING:
The project is part of the Combat Casualty Care Programme funded by the MoD

Henrietta Poon

Severe trauma is commonly associated with direct tissue injury and blood loss. As a consequence of excessive bleeding, cardiovascular reflexes in the body reduce blood flow to some organs in order to preserve the delivery of oxygen to other organs that are most critically dependent on oxygen, such as the brain. When blood flow is re-introduced during resuscitation, a secondary injury characterised by inflammation and damage to the lining of blood vessels (the endothelium) occurs. This is known as ischaemia-reperfusion injury (I-R).

I-R is worse at prolonged periods of reduced blood flow and may be worsened by some forms of injury, such as explosive injuries that cause particular damage and inflammation in key organs such as the lungs, reduce the amount of oxygen transferred into the blood and modify cardiovascular reflexes.

This is a particular problem in military medicine where timelines to evacuate casualties to hospitals may be long in the early stages of conflict, and where explosions may be the primary mechanism of injury.

Statins could be beneficial since there is a substantial body of evidence suggesting that they can reduce I-R in other (non-trauma) circumstances, and there is also some evidence that statins may help in models of simple trauma (principally haemorrhage).

Logistic constraints in austere terrain and potentially long evacuation times, especially at entry operations

My study aims to assess the effects of statins on secondary inflammation in two models of complex trauma in terminally anaesthetised rats in a randomised, placebo-controlled, blinded prospective trial. Both models involve tissue injury, haemorrhage and resuscitation phase; but one of the models has an additional blast injury.

Assessment of inflammatory response based on a range of mediators such as cytokines and endothelial damage are ongoing. If we find reduced inflammation in the groups given statin this will provide the proof of principle that statins may be of benefit in complex trauma.

Widespread inflammatory responses, initiated by poor blood flow and subsequent resuscitation in trauma patients, is the cause of significant morbidity and delay in recovery after severe injury.

Cancer of the larynx (voice box) affects several thousand adults in the UK each year and has a poor prognosis; subglottic stenosis affects 1-2% of children admitted to a neonatal intensive care unit and can lead to life threatening breathing difficulties.

Development of a primary subglottic epithelial culture for the study of upper airway host defences

Jason Powell

FELLOWSHIP/SPONSOR:
Shears Northern Research Fellowship

SUPERVISORS:
Professor Jeff Pearson, Dr Chris Ward and Professor Janet A Wilson

SITE OF WORK:
Institute of Cell and Molecular Biosciences, Newcastle University

PUBLICATIONS:
Powell J, Garnett J, Verdon B, Wilson J, Pearson J, Ward C. A human in vitro model of the subglottic airway. Otolaryngol Head Neck Surg. 2015; 153(1s):83

PRESENTATIONS:
1. Powell J, Garnett J, Verdon B, Wilson J, Pearson J, Ward C. A human in vitro model of the subglottic airway. 29th September 2015, American Academy of Otolaryngology - Head and Neck Surgery (AAO-HNS) Annual Meeting, Dallas, USA

2. Powell J, Garnett J, Verdon B, Wilson J, Pearson J, Ward C. A primary in vitro model of the Subglottic Airway. 9th October 2015, ORS Autumn Meeting, Liverpool

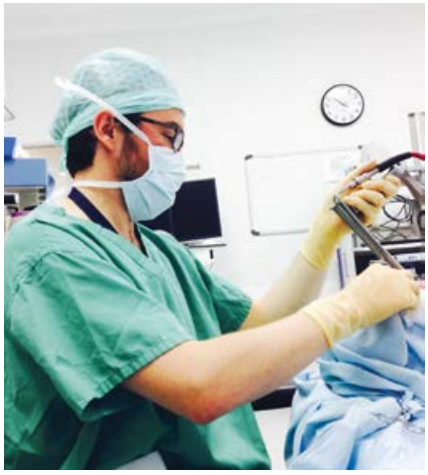
PRIZES:
1. David Howard Prize, British Laryngological Association annual meeting, poster presentation prize, November 2015

2. Munro Black Prize, Northern Deanery Otolaryngology oral presentation prize, November 2015

FURTHER FUNDING:
Wellcome Trust for three years

The subglottis is located in the voice box, in the upper airway. It is a crucial area for the development of certain types of infection, inflammation and cancer. Study of these diseases is limited by the lack of a relevant human model. We aimed to develop a 'living' model of the subglottis using a few thousand human cells, taken from brushings of the throat.

I took brushings from the subglottis of patients undergoing a throat examination. These cells were grown in the laboratory in a special way that makes them behave like they are in the body. In this special culture system the cells are exposed to air above and nutrients below, like in the airway. In these physiological conditions the cells became a 'living' throat lining. The cells specialise into groups with different roles, such as secretory cells. These cells also produced mucus spontaneously which is critical for lining the throat. They also produce small hair cells called cilia that are critical for clearing particles that might be inhaled into the airway.



Jason preparing to take a cell brushing in theatre using a laryngoscope

I have set up reproducible protocols for the collection and growing of subglottic cells, for the first time ever to our knowledge. I have performed multiple assessments to ensure these cells are representative of the area they came from in humans. Therefore this model can be used to study a multitude of diseases in the upper airway.

This is not the end of this work. I have obtained further funding to utilise this unique model in the study of preventing infection in the upper airway. This work aims to prevent critically ill patients in hospital developing serious life threatening infections. This will contribute toward me also completing a PhD.

Jason receiving the David Howard Prize with Professor Janet Wilson

Neuroinflammation and neurodegeneration after blast traumatic brain injury

FELLOWSHIP/SPONSOR:
Joint RCS/Military Research Fellowship

SUPERVISORS:
Professor David Sharp & Surgeon Captain Mark Midwinter

SITE OF WORK:
The Computational, Cognitive and Clinical Neuroimaging Laboratory, The Hammersmith Hospital, London

PUBLICATIONS:
1. Roberts SA. 100 Years of British military neurosurgery: on the shoulders of giants. Journal of the Royal Naval Medical Service. 2015; 101.1: 20-27

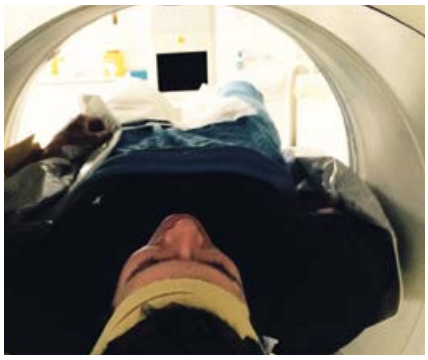
2. Penn-Barwell JG, Roberts SA, Midwinter MJ, Bishop JR. Improved survival in UK combat casualties from Iraq and Afghanistan: 2003-2012. The journal of trauma and acute care surgery 2015; 78(5): 1014-20

FURTHER FUNDING:
Ministry of Defence for completion of PhD

Stuart Alexander Gordon Roberts

Over 400 UK and 2,000 US soldiers have been fatally wounded by blast injuries since 2001. Figures show 70% of injuries resulted from explosive weapons such as Improvised Explosive Devices (IEDs) or Rocket Propelled Grenades (RPGs). The most common mechanism of Traumatic Brain Injury (TBI) was also exposure to blast; and TBI has been described as the 'signature injury' of recent conflicts.

The aim of this research is to investigate if blast TBI causes chronic inflammation and degeneration of the brain. We envisage improved understanding of long-term consequences of blast TBI, allowing for targeted follow-up of soldiers, mitigation therapies and improved battlefield resuscitation strategies.



Moving the soldier into the PET scanner looking for neuroinflammation

This study involves 20 soldiers with blast TBI. Positron Emission Tomography (PET) imaging measures activated microglia, which are markers of neuroinflammation. Magnetic Resonance Imaging (MRI) measures structure and function. We use this to assess haemorrhage, white matter damage and metabolites indicative of neuroinflammation. Sampling Cerebrospinal Fluid (CSF) permits analysis of neurodegenerative markers (such as tau). Genotyping investigates if particular genes (i.e. APOE4) lead to poor outcomes, assessing whether metabolic syndrome, a condition causing inflammation in the body, influences neuroinflammation and neurodegeneration.

Initial findings show extensive white matter injury after blast. We will explore the relationship between this and neuroinflammation. PET has shown neuroinflammation persists many years after non-blast TBI in civilians. This is the first study of neuroinflammation and neurodegeneration in military TBI.

Soldiers are young, so long-term physical, cognitive, behavioural and psychological effects are devastating and under-recognised. TBI has resulted in a 'silent epidemic' of disability, and can lead to neurodegenerative conditions, including Alzheimer's disease. Improving the understanding of these effects represents an aspect of our duty of care to our service personnel, so that they may be afforded the best prevention and treatment strategies into the future.

Performing a lumbar puncture looking for neurodegeneration in an injured soldier

70% of head injuries in Iraq and Afghanistan were as a result of blast injury.

1 out of 5 pancreas transplants are complicated by clot formation in the organ, potentially resulting in failure of the transplant or a second operation for the patient.

Reduction of allograft thrombosis in pancreas transplantation

FELLOWSHIP/SPONSOR:
Frances and Augustus Newman Foundation Fellowship

SUPERVISORS:
Professors Vassilios Papalois and Charles Pusey

SITE OF WORK:
Chelsea & Westminster Hospital

Bynvant Sandhu

Pancreas transplantation offers a life changing treatment for patients with aggressive diabetes by allowing them to become insulin independent. This means no longer requiring multiple daily injections and importantly, reduces the risk of cardiovascular disease associated with diabetes.

Pancreas transplantation does however carry significant risks, including clot formation within the organ. This poses a significant threat to the pancreas and may result in patients requiring a second operation or ultimately losing the transplant.

Bynvant helping a colleague to prepare a pancreas prior to transplantation

My research involved investigation of injurious clotting pathways during storage of the organ prior to transplant and immediately upon transplantation of the organ into the recipient.

We tested a unique anti-coagulant compound with the ability to bind to blood vessels in the organ and therefore act specifically at the site of injury. Using cellular models, we were able to demonstrate effective binding of the drug and reduction of clot formation.

Our research also demonstrated that blocking clotting pathways had the additional beneficial effect of reducing inflammation in the organ. Inflammation in a transplanted organ triggers an immune response in the patient, ultimately damaging the organ. Therefore, targeting clotting pathways provides a potentially critical strategy for improving outcomes in organ transplantation. Testing of the anticoagulant drug in the whole organ is ongoing.

By reducing the degree of injury incurred by the organ during storage and at the time of transplantation we hope to improve both short and longer term outcomes for pancreas transplant recipients.

The problem of clot formation in the transplanted organ is not confined to pancreas transplants. This methodology will be applicable to research involving other organs also, such as liver and kidney transplants.

Bynvant speaking to a young patient after a successful pancreas transplant

Using 3D in vitro tumour models to develop personalised treatment of oesophago-gastric cancer

John Saunders

FELLOWSHIP/SPONSOR:
Frances and Augustus Newman Foundation Fellowship

SUPERVISORS:
Dr Anna Grabowska (Associate Professor)

SITE OF WORK:
Division of Pre-Clinical Oncology, Cancer Biology, University of Nottingham, Queens Medical Centre, Nottingham

PRESENTATIONS:
1. Developing personalised treatment for oesophago-gastric cancer using 3D in vitro tumour models. Saunders JH, Onion D, Parsons S, Grabowska A. European Association of Cancer Research (Goodbye Flat Biology: 3D Models and the Tumour Microenvironment). Berlin, Germany. Nov 2014

2. The value of adjuvant chemotherapy in oesophago-gastric cancer Saunders JH, Bowman CR, Soomro I, Madhusudan S, Parsons SL ASGBI 2015 International Surgical Congress. April 2015

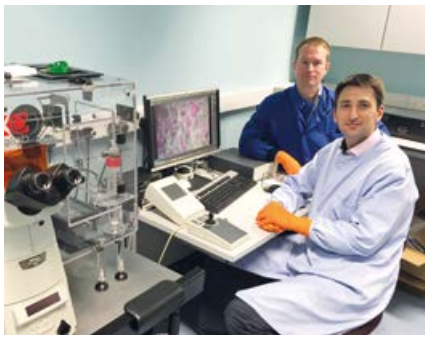
PRIZES:
1. Leonardo Da Vinci Prize, Royal Society of Medicine for the Rotary Societies of Europe, 2015

2. The Sue Watson Postgraduate Research Prize, University of Nottingham, 2015

FURTHER FUNDING:
University of Nottingham for one year

Patients with oesophago-gastric cancer (OG cancer) routinely undergo pre-operative chemotherapy; however, half will not respond and so suffer from chemotherapy side effects as well as experiencing further tumour progression. We have developed 3D in vitro tumour models to study the mechanisms of drug resistance in tumours. We hypothesise that these models will more closely reflect the behaviour of individual human cancer chemotherapy responses, and be able to predict each patient's individual chemotherapy response, thus providing personalised treatment for OG cancer.

Cancers grown in the laboratory have been used to try to predict chemotherapy response without success. It is now clear that human cancer cells, if grown in a laboratory without the local environment and support from other cancer associated cell types found in patients, respond differently to chemotherapy from those same cancer cells grown in a complex microenvironment more closely resembling their original surroundings.



Analysing the growth of the patient's individual 3D cancer clusters

We have developed a laboratory method to grow the patient's own cells (both cancer cells and other supporting cells) directly from patient tumours. We have used these to establish novel 3D tumour growth assays (3D-TGA) that provide a humanised tumour micro-environment for individual patient's cancer cells. Importantly this assay is rapid, requires only small amounts of cancer tissue, and allows numerous drugs and combinations to be tested simultaneously, unlike traditional laboratory models. Our results (in multiple cancer types) have shown that with this 3D humanised tumour micro environment, the cancer cells' sensitivity to the chemotherapy drugs more accurately reflects the high level of chemotherapy resistance seen in patients.

This study aims to determine whether the OG cancer chemo-sensitivity demonstrated in the laboratory 3D-TGA matches with the clinical response to chemotherapy. If this can be demonstrated, we can use this data to support a large clinical trial that will enable delivery of personalised chemotherapy for patients with OG cancer, within the next five years.

Consenting a patient for endoscopy and study participation

There are 15,000 new diagnoses of oesophago-gastric cancer per year in the UK, but less than half of these will respond to chemotherapy.

Despite the global asbestos ban in 1999, the incidence of malignant pleural mesothelioma continues to increase; the UK currently has the world's highest incidence with 65,000 expected deaths by 2050.

Interrogating mesothelioma genomics for personalised radical surgery and secondary prevention

Annabel Sharkey

FELLOWSHIP/SPONSOR:
Jersey H&S Charitable Trust Fund

SUPERVISORS:
Professor Dean Fennell

SITE OF WORK:
University of Leicester and University Hospitals of Leicester

PUBLICATIONS:
1. Sharkey AJ, Tenconi S, Nakas A, Waller DA. The Effects of An Intentional Transition From Extrapleural Pneumonectomy To Extended Pleurectomy-Decortication. Eur J Cardiothorac Surg June 2016
2. Bilancia R, Sharkey AJ, Waller DA. 2015. Thoracoscopy in the diagnosis and treatment of MPM. In: Malignant Pleural Mesothelioma: Present Status and Future Directions. Bentham Science Publishers 2016 Pp. 399-411 (13)

PRESENTATIONS:
1. What Are the Risks and Benefits of Extended Pleurectomy Decortication for Mesothelioma? A Review of the Largest Institutional Series in the UK. 16th IASLC World Conference on Lung Cancer. Denver, USA. September 2015
2. Does the Timing of Chemotherapy Affect Outcome following Radical Surgery for MPM? 12th International Mesothelioma Interest Group Conference. Cape Town, South Africa. October 2014

Malignant pleural mesothelioma is a relatively rare but almost invariably fatal cancer affecting the membrane lining of the lungs and abdomen, often associated with prior exposure to asbestos. The use of radical surgery in the treatment of this disease remains controversial, as this major operation shows markedly differing outcomes. As no clinical reason for this has been found, we assume it is due to genetic differences within the tumours. For patients to benefit from a high-risk surgical resection, we needed to find a way to determine which have the best prognosis tumours, prior to selection for surgery.

To allow the accurate development of a prognostic tool I needed to determine the amount of genetic variation between different areas of the tumour. For this I recruited 60 patients for complex genetic analysis of multiple regions of the tumour. This ongoing work has allowed me to determine the genetic evolution of mesothelioma and therefore the potential variability within tumours.

I will also be able to identify new targets for chemotherapy treatments for patients in the adjuvant setting, or who have relapsed following surgery or first line therapy. I now have data for six patients have identified at least one new possible treatment target which I am currently testing in the laboratory.

Annabel in the laboratory

Using data from patients who have undergone radical surgery, I identified two cohorts of matched patients with good or poor survival and disease recurrence outcomes. Analysis of these cohorts identified the overall number of CNVs (copy number variations) can predict outcome following surgery and several specific CNVs correlate with survival or recurrence outcomes.

Along with my new knowledge of the genetic evolution of these tumours, and therefore the degree of variability within them, these results have allowed me to start developing a tool which should predict prognosis from a single biopsy.

The Leicester Thoracic Surgical team performing a radical resection for mesothelioma

Blast-mediated traumatic amputation: underlying mechanisms and associated injuries

James Singleton

FELLOWSHIP/SPONSOR:
Joint RCS/Military Research Fellowship

SUPERVISORS:
Colonel Jon Clasper MBA DPhil DM FRCSEd(Orth) L/RAMC & Professor Anthony Bull PhD DIC ACGI BEng CEng FIMechE

SITE OF WORK:
Centre for Blast Injury Studies, Imperial College London

PUBLICATIONS:
1. Singleton JAG, Gibb IE, Hunt NCA, Bull AMJ, Clasper JC. Identifying future 'unexpected' survivors: a retrospective cohort study of fatal injury patterns in victims of improvised explosive devices. BMJ Open. 3.8 2013. PMID: 23906957

2. Singleton JAG, Gibb IE, Bull AMJ, Clasper JC. Blast-mediated traumatic amputation: evidence for a revised, multiple injury mechanism theory. J Royal Army Med Corps (2014), jramc-2014. PMID: 24408908

PRESENTATIONS:
1. Battlefield injury clinical research. NATO Symposium, Human Injury Assessment in Vehicle Explosions, ICL, London, Jun 2013

2. Blast-mediated traumatic amputation: evidence for a new injury mechanism. Orthopaedic Trauma Association Annual Scientific Meeting, Phoenix, Arizona, USA Oct 2013

PRIZES:
1. Combined Services Orthopaedic Society 2014: Peter Templeton memorial prize (best presentation)

2. Defence Medical Services Awards 2013: Montefiore memorial prize (best military surgical trainee)

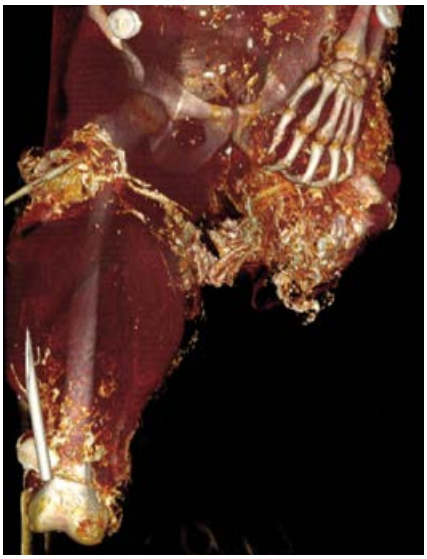
FURTHER FUNDING:
The Ministry of Defence for the duration of the project

Improvised explosive devices (IEDs) came to prominence in Iraq in the 1990s and early 2000s, and became the main weapon used against British troops and vehicles in the more recent conflict in Afghanistan. IEDs caused over 50% of all recent UK combat deaths with 61% of casualties sustaining at least one traumatic amputation (TA). Until recently there was little high quality clinical data to aid understanding of how explosions cause TAs.

An IED strike on a foot patrol in Afghanistan, showing the size of blast involved

Analysis of battle casualty's post mortem CT scans was a crucial part of this clinical research. From November 2007, such scans became part of the Coroners' inquest that happens for every combat death. Before this, simple X-ray images were used, if available. The CT scans were carried out in the British Military Hospital, Camp Bastion, Afghanistan, within hours of the soldier dying. These scans provided never before available detail of the exact injury patterns of these traumatic amputations, along with information on other injuries such as to the lungs. With such sensitive data, much work was required to gain permission to access this data, and to satisfy the necessary military oversight that all data would be kept anonymised whilst also forming the basis of presentations, publications and a research doctorate. Scrutinising the imaging and associated data took several months.

Analysis of these scans along with other post mortem and incident data showed 21.9% of all TAs occurred through joints, far more common than the previously reported rate of 1.3%. There was also no link found between blast lung injury and traumatic amputation, which was previously thought to be the case. This fundamentally changed our knowledge of what components of the blast were capable of causing TAs and by better understanding how these devastating injuries occur, we can use that knowledge to find ways to try to prevent these injuries or decrease their severity to save limbs and lives.



3D Reconstruction of post mortem CT of an IED casualty showing right through knee amputation and left high above-knee amputation

1 in 4 traumatic amputations occurred through joints, showing explosion-mediated flail to be a valid injury mechanism.

1 in 4 of the UK population are affected by hay fever (allergic rhinitis) caused by grass pollen.

Low dose intradermal allergen immunotherapy in the treatment of seasonal allergic rhinitis (hayfever): a double-blind randomised control trial

Anna Slovick

FELLOWSHIP/SPONSOR:
The Dr Shapurji H Modi Memorial Research Fellowship

SUPERVISORS:
Dr Stephen Till & Professor Stephen Durham

SITE OF WORK:
King's College London, Guy's hospital

PUBLICATIONS:
1. Slovick A, Durham S, Till S. 'Grass Pollen Immunotherapy for the treatment of Allergic Rhinitis.' BMJ Nov 2014; 349: g6586

2. Slovick A. Abdel Douiri, Joanna Kelly Andrea Guerra, Rachel Muir, Konstantinos Tsioulos, Caroline Murphy, Mohamed H Shamji, Sun Ying, Stephen R Durham and Stephen J Till. 'Protocol for a double-blind randomized controlled trial of low dose intradermal grass pollen immunotherapy versus a histamine control on symptoms and medication use in adults with seasonal allergic rhinitis (PollenLITE).' Clinical and Translational Allergy 2013, 3:27

PRESENTATIONS:
1. 'Efficient Clinical Trial Recruitment using integrated website and media-based strategy: experience from 2 randomised controlled trials' & 'A randomized placebo-controlled trial of intradermal allergen immunotherapy for seasonal grass pollen allergy' European Rhinology Society Congress, Stockholm, Jul 2016

2. 'Pollen low dose intradermal therapy evaluation (PollenLITE): a double-blind randomised placebo-controlled trial of low-dose intradermal grass pollen immunotherapy in seasonal allergic rhinitis' European Academy of Allergy and Clinical Immunology Congress, Vienna, June 2016

PRIZES:
1. Barry Kay Award: First prize, for oral presentation in adult allergy section, British Society of Allergy & Clinical Immunology, Sep 2015

2. Royal Society of Medicine Allergy Section, 'President's Prize day presentation' runner-up, Mar 2015

Five million people in the UK have hay fever, which significantly affects their quality of life, such as their sleep, ability to work or attend school. In such people, an allergy vaccine (called 'immunotherapy') may reduce the allergic response to grass pollen. Although current vaccines are effective they are expensive and involve frequent visits to specialist clinics for injections or daily self-dosing with tablets or drops for several years.

Based on encouraging results from a pilot study, we undertook a clinical trial of a potentially new and very different form of grass pollen immunotherapy. The new approach involved giving very small grass pollen doses (thousands of times less than existing methods) by injections directly into the top most skin layer (called the dermis). We recruited 93 participants who were randomly selected to receive seven such injections every two weeks before the 2013 summer grass pollen season, or seven dummy injections.

The severity of hay fever symptoms and usage of allergy medications was then recorded. We also performed experiments to see the effect of the new vaccine on the immune system.

The results of the study conclusively showed that the new approach had no benefit in reducing hay fever symptoms or need for medications. Unexpectedly, symptoms in the nose were actually modestly worse in those who had the grass pollen injections. Our experiments also indicated a small stimulation effect on the immune system.

These results have implications for other future research in this area, as there are many trials and companies developing intradermal and epidermal immunotherapies, which may prove detrimental to those with allergies. These results also make an important scientific contribution to our understanding of mechanisms that can drive allergies.

Poster to attract participants to PollenLITE clinical trial

The role of neutrophil extracellular traps in the management of acute pancreatitis

Peter Szatmary

FELLOWSHIP/SPONSOR:
Freemason's Fund for Surgical Research

SUPERVISORS:
Professor Robert Sutton

SITE OF WORK:
The National Institute for Health Research Liverpool Pancreas Biomedical Research Unit

PUBLICATIONS:
1. Xiong J, Szatmary P, Huang W, de la Iglesia-Garcia D, Nunes QM, Xia Q, Hu W, Sutton R, Liu X, Raraty MG; 'Enhanced Recovery After Surgery Program in Patients Undergoing Pancreaticoduodenectomy: A PRISMA-Compliant Systematic Review and Meta-Analysis.' Medicine 2016; 95(18):e3497

2. Ke N, Su A, Huang W, Szatmary P, Zhang Z; 'Regulating the expression of CD80/CD86 on dentritic cells to induce immune tolerance after xeno-islet transplantation.' Immunobiology 2016; 221(7):803-12

PRESENTATIONS:
1. International Association of Pancreatologists Annual Meeting 2015, Shanghai, China

2. American Pancreatology Association Annual Conference 2015, San Diego, USA

PRIZES:
1. International Association of Pancreatologists Young Investigator Award, 2015

2. European Pancreas Club Young Investigator Award, 2015

Acute pancreatitis is a potentially severe, debilitating inflammatory condition of the pancreas. It may result in prolonged hospitalisation with numerous surgical interventions, leaving those who survive with crippling complications. Current best treatment aims to support failing organs allowing them to recover, but no specific and effective therapy is available.

Newly identified functions of neutrophils – first responder cells of the immune system – that protect from infection and injury in others diseases appear to contribute to injury to the pancreas and other organs. Modulation of these functions could lead to the development of novel therapies. This project aimed to assess the role of these novel pathways in the management of acute pancreatitis.

Patients admitted with acute pancreatitis today are routinely assessed whether their disease is a mild, self-limiting form or a much more severe variety. If severe, they face a one in five chance of death, or the prospect of multiple surgical procedures, months of hospitalisation and a future of chronic pain, malnutrition and diabetes severely limiting their quality of life. Current assessment strategies are highly effective in predicting severe disease from 48 hours after admission, but much less so early on in the presentation.

Peter providing a clinical perspective for patient-driven service improvements at the National Pancreas Patient Forum 2015 in Liverpool

By measuring novel inflammation pathway-specific markers in patient's blood, this project was able to demonstrate similar effectiveness to current strategies 24 hours earlier, widening the window for potential therapy. It further demonstrated that modulating these pathways is effective in reducing severity of the disease in experimental models, paving the way for future clinical trials.

Treatment strategies resulting from this work may therefore, not only lead to better and earlier disease stratification, but may allow treating physicians to alter the course of the disease, reduce many of the long-term complications and greatly improve patients quality of life.

Peter presenting RCS-funded research at the first meeting of the International Association of Pancreatologists hosted by China in Shanghai in 2015

1 in 5 patients admitted with acute pancreatitis develop the severe form of the disease; 1 in 5 of those die, without effective treatment being available.

Rotator cuff tears affect 30-50% of patients over the age of 50 years and are a common cause of function-limiting pain and weakness of the shoulder.

Tendon reattachment using demineralised bone matrix and mesenchymal stem cells

Tanujan Thangarajah

FELLOWSHIP/SPONSOR:
Joint RCS/Arthritis Research Trust Fellowship

SUPERVISORS:
Professor GW Blunn

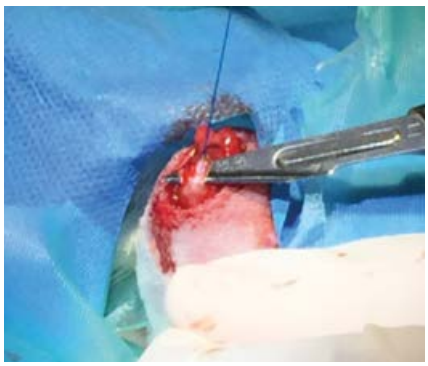
SITE OF WORK:
John Scales Centre for Biomedical Engineering, Institute of Orthopaedics and Musculoskeletal Science (IOMS), Royal National Orthopaedic Hospital, University College London

PUBLICATIONS:
1. Thangarajah T, Pendegrass C, Shahbazi S, Lambert SM, Alexander S, Blunn GW. Tendon Reattachment to Bone in an Ovine Model of Tendon Retraction Using Allogenic and Xenogenic Demineralized Bone Matrix Incorporated with Mesenchymal Stem Cells. PLoS ONE 2016

2. Thangarajah T, Pendegrass C, Shahbazi S, Lambert SM, Alexander S, Blunn GW. Augmentation of Rotator Cuff Repair with Soft Tissue Scaffolds. Orthopaedic Journal of Sports Medicine 2015 June;3(6):2325967115587495

PRESENTATIONS:
1. Thangarajah T, Pendegrass C, Shahbazi S, Lambert S, Alexander S, Blunn GW. Tendon Reattachment to Bone in an In Vivo Ovine Model Using Allogenic and Xenogenic Demineralized Bone Matrix. 26th Congress of the European Society for Shoulder and Elbow Surgery (SECEC/ESSSE), Italy-Milan, September 16th-19th 2015

2. Thangarajah T (speaker), Pendegrass C, Shahbazi S, Lambert S, Alexander S, Blunn GW. Tendon Reattachment to Bone in an In Vivo Ovine Model Using Allogenic and Xenogenic Demineralized Bone Matrix. European Orthopaedic Research Society's 23rd Annual Meeting, Bristol, September 2nd-4th 2015



Tanujan detaching the supraspinatus tendon from its bony insertion in a rat's shoulder

Shoulder pain causes approximately 1% of adults in the UK to present to their General Practitioner annually and costs the NHS £310 million per year. Rotator cuff disease accounts for the majority of these and is found in 54% of those over the age of 60 years. Patients typically present with severe pain, which can negatively impact quality of life and lead to surgery. In the UK there has been a 500% rise in the rate of rotator cuff repair since 2001; however, failure of tendon-bone fixation occurs in up to 90% of cases. This results in poor functional outcomes, revision surgery, and further costs to the NHS. To address this high failure rate, several scaffolds have been developed in order to enhance healing by 'bridging the gap' between tendon and bone. None though have been able to produce a strong interface with a similar structure to the uninjured tissue, and so failure rates are still high.

The tendon biology group at the IOMS have developed a novel biological scaffold made from demineralised bone matrix (DBM). Previous studies have demonstrated that DBM can successfully regenerate a damaged tendon and withstand the high forces normally borne by it. My Fellowship expanded upon this work in order to examine DBM in conditions akin to those observed in the clinical setting following a rotator cuff tear. The initial stages involved the development of a rat model, which was then used to evaluate the effect of DBM and stem cells. This showed that the combination of DBM and stem cells could regenerate 'normal tissue', and therefore presents an exciting prospect for the future.

We hope that this work is a prelude to clinical translation with the ultimate goal of reducing the failure rate following rotator cuff repair and improving surgical outcomes.

The New Royal National Orthopaedic Hospital (RNOH)

Investigation of gene-environment interactions between Vitamin D and colorectal cancer susceptibility genetic variants in large bowel epithelium

Peter Vaughan-Shaw

FELLOWSHIP/SPONSOR:
RCS Research Fellowship supported by the Harold Bridges Bequest

SUPERVISORS:
Professor Malcolm Dunlop and Dr Susan M Farrington

SITE OF WORK:
Colon Cancer Genetics Group and Academic Coloproctology, Institute of Genetics and Molecular Medicine, Western General Hospital

PUBLICATIONS:
1. Vaughan-Shaw PG, Walker M, Ooi LY, Farrington SM, Gilber N, Dunlop MG. A simple method to overcome the inhibitory effect of heparin on DNA amplification. Cellular Oncology 2015, DOI: 10.1007/s13402-015-0250-8

2. Vaughan-Shaw PG, Wheeler JMD, Borley NR. The impact of a dedicated multidisciplinary team on the management of early rectal cancer. Colorectal Disease 2015, 17(8):704-709

PRESENTATIONS:
1. Timofeeva M, Zgaga L, Ooi LY, Vaughan-Shaw PG, Theodoratou E, Walker M, Tenesa A, Farrington SM, Campbell H, Dunlop MG. Susceptibility to colorectal cancer is influenced by interaction between genetic variants and plasma Vitamin D level. European Society of Human Genetics meeting, Glasgow June 2015

2. Vaughan-Shaw PG, Fitzpatrick D, Farrington SMF, Dunlop MG. Investigation into the in vitro and ex vivo effects of Vitamin D treatment on selective gene expression. Presented at Academy of Medical Sciences Meeting for Clinician Scientists in Training, London, February 2015

FURTHER FUNDING:
From MRC Clinical Research Training Fellowship for two years

Recent studies have shown that Vitamin D level may combine with genetic factors to influence risk of bowel cancer. This project investigates the effect of Vitamin D on certain important genes. Ultimately, Vitamin D may be used to prevent bowel cancer in patients with the highest genetic risk.

The first part of my project involved the treatment of several bowel cancer cell lines with Vitamin D. These experiments showed that Vitamin D increased the expression of CDH1 in a number of bowel cancer cell lines. This gene codes for the protein E-cadherin which has several anti-tumour properties.

Next I undertook a clinical study of the effect of Vitamin D level on gene activity. I have recruited over 150 patients, both with and without bowel cancer. Analysis to date shows that a quarter of those sampled are Vitamin D deficient, while the activity of the CDH1 gene appears to be associated with Vitamin D level in blood but not bowel tissue samples.

Data analysis involving thousands of other genes and genetic mutations are ongoing.

The final part of my project investigates the effect of a 12-week course of high-dose Vitamin D on gene activity. I have recruited 40 patients and shown that on average we can double Vitamin D level with supplementation. I have also shown an increase in the expression of the Vitamin D receptor in bowel tissue with analysis of other genes ongoing.

To date I have shown that Vitamin D treatment increases the activity of a gene relevant to cancer prevention in bowel cancer cell lines, while Vitamin D supplementation improves Vitamin D status in study participants. Further analysis aims to determine the effect of Vitamin D supplementation on gene activity and ultimately support a randomised study of Vitamin D supplementation on bowel cancer prevention.

Research nurse sampling blood from study patient for Vitamin D level

There are over 40,000 new cases of bowel cancer in the UK each year, with significant associated death and disability.

Annually in the UK 13,000 people sustain burn injuries requiring hospital admission with an estimated annual NHS cost of £140 million.

Metabolomics as an approach to the prediction and diagnosis of sepsis following thermal injury

Christopher Wearn

FELLOWSHIP/SPONSOR:
The Lord Leonard and Lady Estelle Wolfson Research Fellowship supported by the Rosetrees Trust

SUPERVISORS:
Mr Naiem Moiemen (Clinical Supervisor) and Dr Warwick Dunn (Academic Supervisor)

SITE OF WORK:
Healing Foundation Centre for Burns Research, Queen Elizabeth Hospital Birmingham and Centre for Translational Inflammation Research (CTIR), University of Birmingham

PRESENTATIONS:
1. Severe burn injuries: Applying metabolomics to study longitudinal changes and prediction of clinical outcomes. W. Dunn, C.M Wearn, P. Hampson, J. Allwood, R. DiGuida, J. Hazeldine, M Fitzpatrick, N. Moiemen and J.M. Lord. Metabolomics, San Francisco, July 2015

2. A non-targeted metabolomics analysis of urine and plasma to study longitudinal metabolic changes following a burn injury in adults. W. Dunn, C.M Wearn, P. Hampson, J. Allwood, R. DiGuida, J. Hazeldine, M Fitzpatrick, N. Moiemen and J.M. Lord. Awarded Best Oral Presentation. British Burn Association 47th Annual Meeting, Birmingham, May 2015

PRIZES:
1. Jackson Prize for Best Burns Research Paper, SARS Annual Meeting, January 2015

2. Mercian Travelling Fellowship Prize, National Plastic and Reconstructive Surgery (NPRAS) Meeting, September 2014

FURTHER FUNDING:
There is continued funding for the overarching observational study (SIFTI study) from The Healing Foundation

Patients with severe burns are at increased risk of complications during their recovery. The severity of injury in these patients results in system-wide activation of the immune and endocrine systems. These responses contribute to the development of significant metabolic dysfunction, termed 'hypermetabolism'.

Giving a presentation about the WHO Surgical Safety Checklist to a group of surgical residents as part of an Introduction to Surgical Skills Workshop in Lima, Peru

The consequences of hypermetabolism for the patient include persistently elevated blood glucose levels, increased metabolic rate, elevated heart rate, hyperthermia, muscle wasting and loss of lean body mass. These responses result in immune system dysfunction, which in combination with major skin loss, leaves patients at risk of infections and sepsis with high mortality.

Compared to other populations of critically ill patients, burn injured patients experience a higher incidence of sepsis and poorer outcomes with mortality rates in the range 28-65%. The diagnosis of sepsis in patients with severe burns is challenging, owing to the systemic responses masking the normal clinical signs used to diagnose infection and sepsis.

We developed a prospective multi-centre observational study to investigate these key responses to severe burn injury in adults and children (SIFTI study). Blood and urine samples from a cohort of 48 patients were analysed using a technique called metabolomics, which analyses the majority of small products of metabolism simultaneously. This untargeted approach has led us to identify novel changes in a number of metabolite classes not previously studied in burns which are occurring over the first six months post injury.

Additionally the data has enabled us to identify a number of potential biomarkers that could be measured routinely to diagnose and monitor sepsis. We are currently preparing a grant application to analyse biological samples from the entire SIFTI cohort of 150 patients to validate our findings, with a view to developing a personalised healthcare approach to burns, nutritional support, and for the diagnosis and treatment of sepsis.

Christopher presenting research findings at the American Burn Association 47th Annual Meeting, Chicago

Pre-clinical evaluation of oncolytic virotherapy delivered by isolated limb perfusion, alone and in combination with chemotherapy, radiotherapy and surgical resection

Michelle Jennifer Wilkinson

FELLOWSHIP/SPONSOR:
The Lord Leonard and Lady Estelle Wolfson Research Fellowship

SUPERVISORS:
Professor Kevin Harrington

SITE OF WORK:
The Institute of Cancer Research and The Royal Marsden Hospital

PUBLICATIONS:
Wilkinson MJ*, Pencavel T*, Mansfield DC, Khan AA, Seth R, Karapanagiotou EM, Roulstone V, Aguilar RJ, Chen NG, Szalay AA, Hayes AJ, Harrington KJ. Isolated limb perfusion with melphalan, tumour necrosis factor-alpha and oncolytic vaccinia virus improves tumour targeting and prolongs survival in a rat model of advanced extremity sarcoma. Int J Cancer. 2015 Feb 15;136(4):965-76. doi: 10.1002/ijc.29059. Epub 2014 Jul 22. PMID:24978211

PRESENTATIONS:
1. Wilkinson MJ, Pencavel T, Khan AA, Mansfield DC, Kyula J, Roulstone V, Yu YA, Szalay AA, Hayes AJ, Harrington KJ. A pre-clinical model of isolated limb perfusion to assess the efficacy of oncolytic virotherapy, alone and in combination with radiotherapy, to treat extremity melanoma and soft tissue sarcoma. June 2013, Quebec City, Canada – 7th International Meeting on Replicating Oncolytic Virus Therapeutics. Oral Presentation

2. Wilkinson MJ, Pencavel T, Khan AA, Mansfield DC, Kyula J, RoulstoneV, Yu YA, Szalay AA, Hayes AJ, Harrington KJ. The addition of oncolytic vaccinia virus to standard isolated limb perfusion chemotherapeutics delays tumour growth in a rat model of aggressive extremity sarcoma. September 2013, Amsterdam, European Cancer Congress Poster Presentation

PRIZES:
Sponsored Travel Award: Wuxi APPTEC, 7th International Meeting on Replicating Oncolytic Virus Therapeutics, Quebec City, Canada for oral and poster presentations on the delivery of oncolytic virotherapy by isolated limb perfusion to improve the efficacy of both therapeutic strategies

FURTHER FUNDING:
Dr Lucy M Bull Lectureship and Research Fund for two years

Advanced melanoma and sarcoma carries a poor prognosis because of rapid spread and poor response to standard therapy. Isolated limb perfusion (ILP) is a specialist surgical procedure that delivers high doses of chemotherapy directly to the cancer without side-effects in the rest of the body.

The aim of this research was to evaluate the therapeutic efficacy of using isolated limb perfusion (ILP) to deliver a new cancer treatment called oncolytic virotherapy, which are viruses that naturally target and kill cancer cells, alone and in combination with radiotherapy and surgery.

We found that the combination of oncolytic vaccinia virus and radiotherapy increased cancer cell killing both in bench side laboratory experiments and in an animal model of ILP. The delivery of oncolytic virotherapy by ILP resulted in significantly improved survival compared to current standard therapies, which was further enhanced with the addition of radiotherapy, without any increase in side effects.

This research has progressed from a previous RCS fellowship sponsored project which developed the current animal model of ILP, providing an excellent model for testing new therapies to improve ILP. This model is currently being used to investigate the new anti-cancer immune therapies (ipilimumab and nivolumab) that are currently showing great promise as a novel line of cancer therapy.

Whilst ILP dramatically improves patient symptoms and saves the limb in up to 80% of patients, the disease often relapses and it does not improve survival. Testing new cancer therapies in this laboratory model of ILP is an excellent way of finding new potential therapies to improve outcomes for patients.

The promising results from these experiments, testing oncolytic vaccinia virus delivered by ILP, have already led to NHS ethics and MHRA approval for a phase I clinical trial with the potential for patient benefit.

Targeted Therapy Team, ICR scientific retreat to York to discuss work on the oncolytic virus clinical trials. From left PhD supervisor, team leader Professor Kevin Harrington, Victoria Roulstone – scientific officer, David Mansfield – scientific officer, Michelle, Aadil Khan previous RCS fellow and another PhD student in the lab and Joan Kyula – post-doctoral researcher

In the UK there are over 1,500 deaths a year from melanoma and it is a significant cause of cancer deaths in the 15–39 age group. Despite current expert multimodality treatment, advanced sarcoma and melanoma still have 5 year survival rates of less than 50%.

There are 5,000 hospital admissions and 300 deaths from burns in the UK each year.

Investigation of the molecular effects of cooling human burns

Edmund Hugh Wright

FELLOWSHIP/SPONSOR:
Enid Linder Research Fellowship

SUPERVISORS:
Professors Dominic Furniss and Adrian Harris

SITE OF WORK:
Weatherall Institute of Molecular Medicine and Stoke Mandeville Hospital, Buckinghamshire

PUBLICATIONS:
1. Cooling of Burn Injuries: Mechanisms and Models, EH Wright, AL Harris, D Furniss. Burns, 41(5), 882-889

2. Guidelines for the excision of cutaneous squamous cell cancers in the United Kingdom: the best cut is the deepest, AA Khan, M Potter, JJ Cubitt, BJ Khoda, J Smith, EH Wright, G Scerri, A Crick, OC Cassell, PG Budny. JPRAS 2013; 66, 467-71

PRESENTATIONS:
1. A validated human model for cooling partial thickness burns, EH Wright, D Furniss, AL Harris, Winter Scientific Meeting of the British Association of Plastic, Reconstructive, and Aesthetic Surgeons, Birmingham 25-27th November 2015

2. A validated human model for cooling partial thickness burns, EH Wright, D Furniss, AL Harris, Society of Academic Research Surgery (SARS) Royal College of Surgeons of England, 6-7th January 2016

PRIZES:
Paton Masser prize by BAPRAS in May 2016

FURTHER FUNDING:
Restore Burn and Wound Research Charity for 1 year

Each year in the UK 250,000 people sustain a burn, 175,000 attend A&E, 13,000 are admitted to hospital, 1,000 with life-threatening injuries, and 300 die of burns. While the majority require little treatment, and suffer no long-term problems, a significant number require surgery, intensive care treatment, and protracted rehabilitation and further surgery.

People have been treating burns with cold water for over 2,000 years, and it is effective in reducing burn damage to the skin, scarring, and the need for skin-grafting. Its mechanism is not fully understood, and has been investigated almost entirely in animals.

Hugh discussing the project with HRH the Duke of Kent, who is the patron of Restore, who funded part of the project

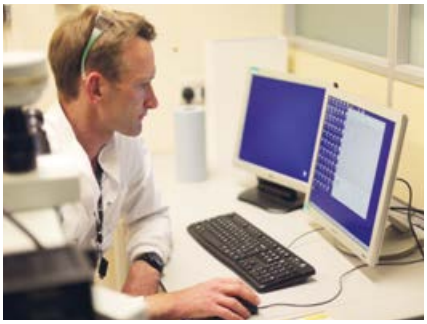
We want to understand burning, and how cooling benefits burns, and to do so using live human skin normally discarded during reconstructive breast surgery in volunteers. We have necessary ethical approval.

The burns are created after anaesthesia, and half the burns are cooled. Both steps use novel, purpose-built apparatus, giving paired burns from the same volunteer in which we can compare the effects of burning and cooling. This has never been done before.

Cooling reduced the clinical severity of the burns, but we were also able to demonstrate a significant reduction in the amount of damage seen in cooled burns, compared to untreated counterparts, with less blockage of the microscopic blood vessels in the skin.

Comparison of gene activation in normal skin, burns, and cooled burns, showed genes related to heat damage, blood clotting, and wounding were significantly activated in burns, while those related to normal skin function significantly deactivated. Cooling significantly reversed some of these burning-related changes.

For the first time we have an insight into the gene activation in the first few hours after burning, and how cooling changes them. Pharmacological targeting these processes could improve healing and outcomes for the thousands of burn patients every year, who require hospital admission, surgery, or even die from their injuries.



Hugh examining a photograph of a microscope section showing a burn blister at three hours after injury. (This has never been seen in a human subject before, and represents the basis for the entire project)

Invasiveness of brain metastases and implications for clinical management

Rasheed Zakaria

FELLOWSHIP/SPONSOR:
RCS Research Fellowship

SUPERVISORS:
Professor Philip Rudland &
Mr MD Jenkinson

SITE OF WORK:
University of Liverpool &
The Walton Centre NHS Foundation Trust

PUBLICATIONS:
1. Zakaria R, Jenkinson MD. Diffusion weighted MRI is a promising imaging biomarker in brain metastases. J Neurooncol 2015 Jan;121(2):421-2. doi: 10.1007/s11060-014-1642-8. Epub 2014 Oct 30. PubMed PMID: 25351580; PubMed Central PMCID: PMC4311059

2. Zakaria R, Jenkinson MD. Using ADC Maps with Structural Scans to Improve Intraoperative Biopsy Specimens in Brain Metastases. Neuroradiol J. 2014 Sep;27(4):422-4. doi: 10.15274/NRJ-2014-10075. Epub 2014 Aug 29. PubMed PMID: 25196614; PubMed Central PMCID: PMC4236864

PRESENTATIONS:
1. World Federation of Neurosurgical Societies. Rome, 2015

2. National Cancer Research Institute. Liverpool, 2015

PRIZES:
Society of British Neurological Surgeons, Sir Hugh Cairns' Essay Prize 2014

FURTHER FUNDING:
The Medical Research Council, Clinical Research Training Fellowship for two years

The brain is a major site of secondary spread for some of the most common cancers like breast, lung and melanoma. The number of people with this spread of cancer to the brain, so-called metastases, is rising and the symptoms, such as weakness, headache and fits have a devastating effect on patients and their carers. Currently there is great uncertainty for patients suffering from brain metastases because we do not have any good markers of prognosis or response to the main treatments: surgery and radiotherapy. Doctors have to estimate how long an individual patient might survive using crude information like age and how many metastases are present. We use these estimates to come to a decision about how aggressively to treat our patients, with huge implications for their length and quality of survival.

Rasheed at a brain metastases planning workstation theatre

Rasheed at a meeting of the Liverpool neuro-oncology patient group – discussing the planned research and getting feedback on what issues affect patients and their carers

Since almost all patients with metastases undergo an MRI scan of the brain, we are trying to develop markers of prognosis using data from these scans. Next, we want to understand what is actually happening in the tumour and surrounding brain tissue that is being measured on those scans, so we will need to look at samples of brain metastases removed during neurosurgery.

We have some promising results suggesting that changes at the boundary between the metastasis and the brain on particular types of MRI scans, called diffusion-weighted scans, are strongly linked to how aggressively the tumour behaves and how long a patient survives after neurosurgery. Confirmation of such markers would greatly improve the quality of life for our patients because we could give them a clearer idea – just from that first MRI scan – of their estimated survival and then make better decisions about who should undergo aggressive treatments like surgery and radiotherapy and who may not benefit from this.

Up to 40% of patients with cancer may develop brain metastases causing significant morbidity and mortality.

The Pump Priming award is given to assist newly appointed consultants and senior lecturers (appointed since 2006) in surgery, who are working at hospitals and universities within the UK, in the early stages of their independent research careers. Awards are used exclusively to support the award holder's own research and not for personal salaries. They may be used, amongst other things, for small items of equipment, for consumables or for technical assistance. All award winners are members or fellows of The Royal College of Surgeons of England.

Pump Priming Reports

Aina Greig
Siong Seng Liau
Sam Oussedik
Chris Peach
Stuart Smith

Over 10,000 children undergo surgery to repair a nail bed injury in the UK every year and this is the commonest hand injury in children.

Nail bed INJury Analysis (NINJA) Pilot Study: Should the nail plate be replaced or discarded after nail bed repair in children?

Aina Greig

SPECIALTY:
Plastic Surgery

CURRENT POSITION:
Consultant Plastic Surgeon

SITE OF WORK:
Evelina London Children's Hospital, Guy's and St Thomas' NHS Foundation Trust, London

PUBLICATIONS:

1. Nail bed INJury Assessment Pilot (NINJA-P) Study: Should the nail plate be replaced or discarded after nail bed repair in children? Study protocol for a pilot randomised controlled trial. Abhilash Jain, Adam Sierakowski, Matthew Gardiner, David Beard, Jonathan Cook, Cushla Cooper, Aina Greig. Pilot and Feasibility Studies. 2015, 1:29. DOI: 10.1186/s40814-015-0025-z URL: http://www.pilotfeasibilitystudies.com/content/1/1/29

2. Surgical treatment of paediatric nail bed injuries in the United Kingdom: Surgeon and patient priorities for future research. Adam Sierakowski A, Matthew Gardiner, Abhilash Jain, Aina Greig; Nail bed INJury Analysis (NINJA) Collaborative Group. J Plast Reconstr Aesthet Surg. 2016 Feb;69(2):286-8. doi: 10.1016/j.bjps.2015.10.025. [Epub 2015 Oct 30]

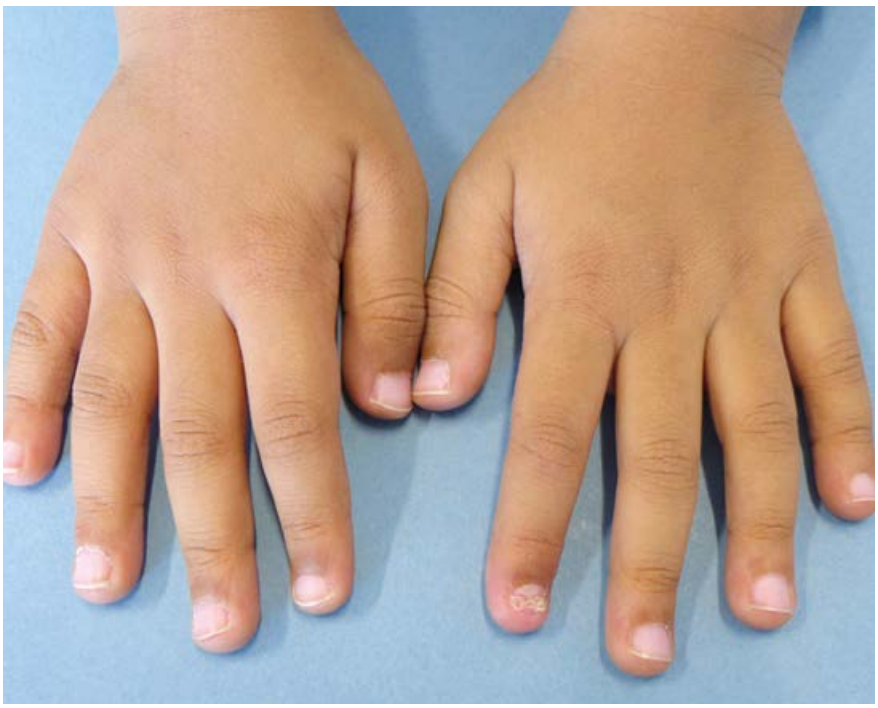
PRESENTATIONS:

1. Update on the NINJA trial – the first Reconstructive Surgery Trials Network trial. Aina Greig, Abhilash Jain, Dominic Furniss, Claire Zweifel, Richard Pinder, David Beard, Jonathan Cook, Adam Sierakowski, Matt Gardiner RSTN Session, BAPRAS, Royal College of Surgeons, London, 26 November 2014

2. Update on the NINJA trial – follow up. Aina Greig, Abhilash Jain, Dominic Furniss, Claire Zweifel, Richard Pinder, David Beard, Jonathan Cook, Adam Sierakowski, Matt Gardiner RSTN Session, BAPRAS, Birmingham, 26 November 2015

The nail bed is the soft area beneath the hard fingernail, and is commonly injured in children. During surgery, the nail is taken off and the cut stitched up. The nail can either be replaced or discarded. Some doctors think that the replaced nail acts as a splint to hold open the nail fold while a new nail grows. Others think that it may cause infections, leading to pain and abnormal nail growth, requiring extra general practice and hospital visits. From our research, children, their parents and carers value most the long-term cosmetic appearance.

A consensus meeting with the British Society for Surgery of the Hand, Royal College of Surgeon, and British Association of Plastic, Reconstructive and Aesthetic Surgeons recognised that the management of nail bed injuries lacked strong clinical evidence. We obtained funding from the BSSH in May 2014 and from the RCS in December 2014, to perform a Pilot Multicentre



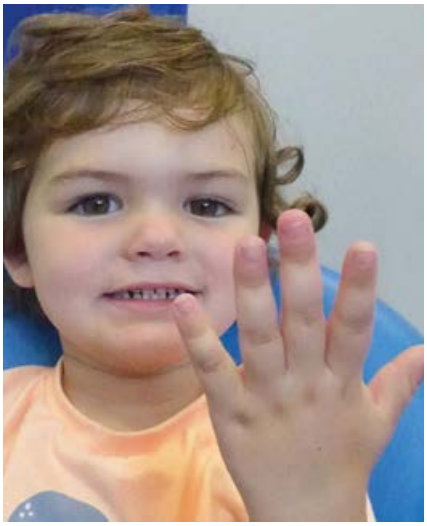
The nail is regrowing after nail bed repair

Aina assessing a child's finger after nail bed repair in clinic

Randomised Controlled Trial, to assess the practicalities of running a trial that addresses the question 'Should the nail plate be replaced or discarded after nail bed repair in children?' (NINJA-P).
The Co-Chief Investigators (Aina Greig and Abhilash Jain) engaged with Oxford Surgical Intervention Trials Unit to undertake project management.
The NINJA-P trial:

- Was the first trial chosen to be supported by the Reconstructive Surgery Trials Network (RSTN)
- Was adopted onto the NIHR Clinical Research Network Portfolio
- Recruited 60 patients in three months
- Across four centres (GSTT, Hull, Oxford, Chelmsford)
- Followed-up patients up for four months

The pilot trial showed the feasibility of timely recruitment to a larger study.
A definitive trial is required to confirm a possible benefit from replacing the nail plate, specifically whether there is any difference in appearance or infection rate. We have worked with the Research Design Service to host a focus group (six parents, one toddler) to discuss the full study plan with Patient and Public Involvement. Two 'lay applicants' have been included on the grant application to perform a definitive trial with a larger study population. An application for funding for a NIHR Research for Patient Benefit Grant has been submitted March 2016.



Successful nail bed repair in a child

Pancreatic cancer (UK incidence ~9000 per year) urgently requires new therapies as <10% of these patients survive for five years.

A novel model of familial pancreatic cancer to explore genomic instability as a mechanism for pancreatic tumourigenesis

SPECIALTY:
HPB (Hepatopancreatobiliary) Surgery

CURRENT POSITION:
Honorary Consultant Hepatobiliary and Pancreatic Surgeon

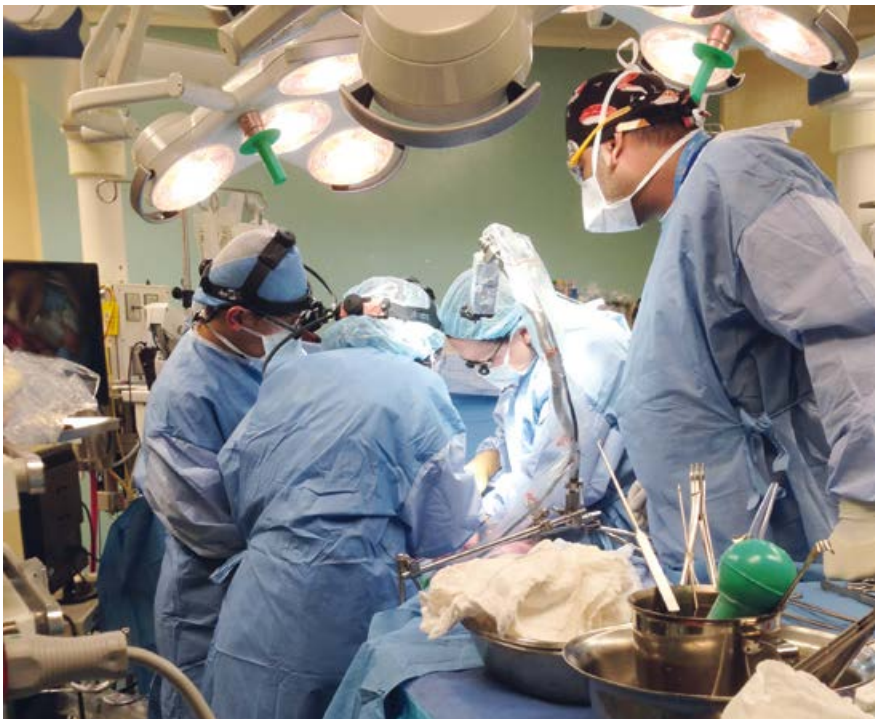
SITE OF WORK:
University Department of Surgery, University of Cambridge, Addenbrooke's Hospital

Siong S. Liau

Pancreatic ductal adenocarcinoma (PDA) is a uniformly lethal disease with the overall five-year survival rate of less than 5%. There is an urgent need for better treatment and this is unlikely to come from surgical treatment alone.

The aggressive biology coupled with the genetic complexity of PDA makes this disease difficult to treat. It is clear that approximately 10-15% of patients with PDAs have a hereditary component (i.e. inherited a defective gene). One of these potential genes is the partner and localiser of BRCA2 (PALB2) gene, which is a gene involved in DNA repair process. In this study, we have successfully developed novel genetically-engineered mouse models (GEMMs) of PALB2 in pancreatic ductal adenocarcinoma.

Our results have shown that PALB2 is a gene critical in the development of PDA. These GEMMs develop PDA with a similar disease spectrum to humans. The impact of the findings of this model is obvious as for the first time we are able to understand the biological impact of such a genetic mutation on pancreatic cancer development. More importantly, we will be able to test and personalise therapy for PDA with specific PALB2 mutations.



Siong performing a Whipple's pancreaticoduodenectomy

PALB2 GEMMs will provide unequivocal evidence for the roles of PALB2 as a major genetic player in PDA formation, speed up the process of personalised drug discovery for PALB2-mutated PDAs and finally, the GEMM will represent an efficient resource for future testing of identified PALB2-related targeted therapies.

Can adipose derived vascular fraction, extracted from adipose tissue prevent osteoarthritis of the knee?

SPECIALTY:
Trauma and Orthopaedics

CURRENT POSITION:
Consultant Orthopaedic Surgeon

SITE OF WORK:
University College Hospital, London

Sam Oussedik

Knee osteoarthritis has a colossal disease burden. The evidence describes the lifetime risk of developing symptomatic knee osteoarthritis is 50%, with 50% developing before age 55. The corresponding burden on knee replacement surgery is equally massive with estimates suggesting the incidence of total knee replacement will rise to 1.2 and 3.4 million patients in the UK and the US respectively by the year 2030.

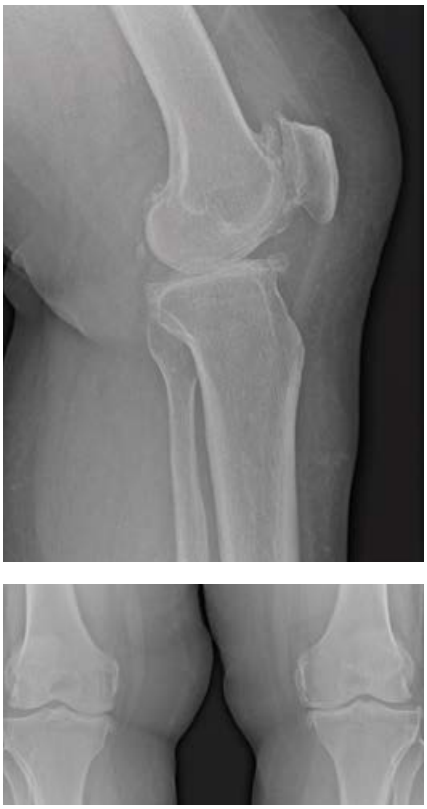
Treatment options at present are limited, advising activity avoidance, analgesia or locally acting steroid injections whilst those with symptomatic osteoarthritis are counselled regarding surgery.

Many patients may have pain which cannot be controlled by medication but unfortunately they are not suitable for surgery owing to a myriad of reasons.

Our study evaluates the use of stem cells, harvested from the fat cells of the patient's body. After preparation, these stem cells are injected into the patient's affected knee on a one-off basis. Our aim is to establish whether there are any clinical or radiological improvements, evaluated according to patient's outcome questionnaires over the course of 12 months. The study seeks to take advantage of DGEMRIC technology, a distinctive form of an MRI scan. In the ADVENT study, DGEMRIC will be used to establish cartilage loss and osteoarthritis progression and whether the stem cells can arrest or reverse progression of osteoarthritis.

We have identified our patient cohort for the study and have submitted an ethics application for review, for which we await a decision. We have also sought an additional research grant to cover some of the study costs. Additionally, we are also seeking to set up a randomised controlled trial in which we will compare the stem cell treatment to a placebo in patients with arthritis of both knees.

The research concerns a very novel therapy, with the use of innovative MRI imaging, which can have far reaching implications for the significant problem of the treatment of knee osteoarthritis, addressing the problem of young people with knee arthritis, whilst also relieving the burden on the knee replacement surgeon and hospital services.



X-rays demonstrating arthritis of the knee, in two views, characterised by joint space narrowing and the formation of bony spurs

The lifetime risk of developing symptomatic knee osteoarthritis is 50%, with 50% developing before age 55.

15% of planned orthopaedic operations are for removal of metallic implants which can be associated with significant side effects. Bioresorbable implants will prevent the need for further surgical procedures.

OsteoFix: novel bioresorbable composite implants for osteoporotic bone fixation

Chris Peach

SPECIALTY:
Trauma and Orthopaedic Surgery

CURRENT POSITION:
Consultant Trauma and Orthopaedic Surgeon

SITE OF WORK:
Manchester Biomanufacturing Centre, School of Mechanical, Aerospace and Civil Engineering, University of Manchester

PUBLICATIONS:
1. Altamimi, A.A, Peach C., Domingos, M., Bartolo, P.J. The evaluation of Poly(e-caprolactone) degradation kinetics in an accelerated environment for bone fixation application. Proceedings of the 2016 Industrial and Systems Engineering Research Conference, edited by Y. Guan and H. Liao, Anaheim, USA, 2016

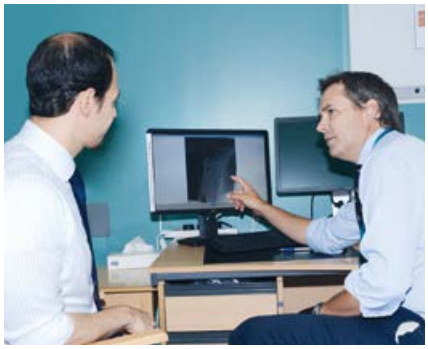
2. Altamimi, A.A., Peach, C., Domingos, M., Bartolo, P.J. Degradable vs. non-degradable bone fixation implants: a computational study. Proceedings of the 2nd International Conference on Progress in Additive Manufacturing (PRO-AM 2016). Edited by C.C. Kai et al. Research Publishing, 2016

PRESENTATIONS:
1. Novel biodegradable and bioactive implants for fracture fixation. Altamimi, A.A, Peach C., Domingos, M., Bartolo, P.J. Industrial & Systems Engineering Research Conference (ISERC) 2016, Anaheim, California, USA

2. Novel biodegradable and bioactive implants for fracture fixation. Altamimi, A.A, Peach C., Domingos, M., Bartolo, P.J. International Conference on Biofabrication. Utrecht, Netherlands. Nov 7-9th 2015

The aim of this research was to develop a customised, biocompatible, bioresorbable and bioactive bone fracture fixation implant that is capable of replacing current metallic implants.

It is estimated that 27.5 million people in the European Union have osteoporosis, a condition that resulting in low-density bones with poor mechanical properties leading to fractures. The annual cost of treating these fractures in the EU will rise to an estimated £60 billion per year by 2025.

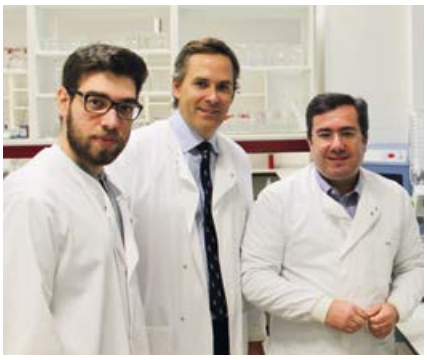


Mr Chris Peach discussing the need for removal of metalwork from the shoulder after fracture treatment with patient at the University Hospital of South Manchester

A common surgical procedure inserts metallic plates which act as fracture stabilisers to enable bone healing. There is substantial evidence of implant failure in osteoporotic patients as well as implants frequently needing removal. Approximately 15% of planned orthopaedic operations are for removal of metallic implants. Over 80% of patients, when questioned, would like to be considered for a bioresorbable implant or be involved in a trial to evaluate one. However, surgeons have had concerns over the potential inferior biomechanical characteristics, consequences of implant degradation in addition to higher implant costs with bioabsorbable materials.

Therefore our research focuses on the development of bioresorbable implants for fracture fixation surgery which would prevent the need for implant removal and develop technology to make these plates bioactive, being capable of delivering osteoporosis treating medications to the immediate area.

Our main investigations to date have evaluated the biomechanical and biological characteristics of Poly (ε-CaproLactone) (PCL), Hydroxyapatite and Magnesium as novel materials for implant manufacturing. Based on these initial studies we have been able to select a suitable material and plate design for further evaluation and testing. These preliminary studies have enabled us to apply for larger grants to allow us to continue these exciting investigations which will hopefully culminate in clinical testing. Further work includes topological optimisation of current implants to develop design parameters, finite element models of degradation and biomechanical characteristics of new material designs.



From right to left: Professor Paulo Bartolo, Chris Peach and Abdulsalam Abdulaziz Al-Tamimi with new equipment purchased for research projects from pump priming grant from the RCS

Evaluating the efficacy of PLGA/PEG chemotherapy delivery into the surgical cavity using an orthotopic brain tumour resection model

Stuart Smith

SPECIALTY:
Neurosurgery

CURRENT POSITION:
Clinical Associate Professor of Neurosurgery

SITE OF WORK:
Children's Brain Tumour Research Centre, University of Nottingham

PUBLICATIONS:
Surgical delivery of drug releasing poly(lactic-co-glycolic acid)/ poly(ethylene glycol) paste with in vivo effects against glioblastoma Annals of the Royal College of Surgeons 2014;96:495-50

PRESENTATIONS:
1. Smith SJ, Gould TW, Barrett DA, Shakesheff KM, Grundy RG, Rahman R Delivery of multiple chemotherapeutic agents into rodent brain using a biodegradable and self-sintering PLGA/PEG neurosurgical system Poster SCIDOT San Antonio, USA 2015

2. Smith SJ, Kelly JC, Gould T, Rahman R Incorporation of nanoparticle conjugated peptides into a moldable neurosurgcially applied polymer paste as a localised dual-layered therapeutic strategy for malignant glioma Poster SCIDOT San Antonio, USA 2015

FURTHER FUNDING:
Hermes Enterprise Fellowship for one year

Malignant brain cancer kills 3500 people per year in the UK, of all ages, causing the highest number of cancer-related deaths in the under 40s. Neurosurgery augmented by radiotherapy and chemotherapy is only partially effective and most patients die within 18 months of diagnosis.

Neurosurgical resection of a malignant brain tumour

Chemotherapy drugs penetrate poorly into the brain because of a natural block called the blood brain barrier. Direct implantation of chemotherapy releasing material at surgery can bypass the blockade, allowing the drugs to better kill tumour cells, whilst minimising side effects for the patient. This project has aimed to further the development of a biodegradable paste that can be surgically implanted by the neurosurgeon during resection of a brain tumour. The paste then gradually dissolves, releasing chemotherapy directly into the brain where it can act to kill cancer cells, whilst also avoiding toxic side effects from the drug in other parts of the body e.g. the bowel or bone marrow.

The funding provided has allowed us to use the paste within a tumour model of the malignant brain cancer. Initial results have been very promising and we have seen significant reductions in the speed of tumour growth. This is an ongoing project that involves collaborations between many different scientific and clinical teams, including the surgical research group, which I lead. We continue to fine tune the paste to achieve the maximal release of drug and to study which might be the best drugs to deliver to the brain using this technology. Preparations are underway to develop the paste to a point where it can be used in a trial in brain tumour patients, where we hope it will extend life for those suffering from this terrible disease.

Stuart in the laboratory placing tumour cell samples into liquid nitrogen for storage

Malignant brain tumour survival is poor, surgical delivery of drugs to the brain will help by getting. chemotherapy to the growing tumour.

Surgical Trials Initiative

Surgical Trials Initiative

The programme has far exceeded expectations in the four years since it was launched, with seven Surgical Trials Centres (STC) and ten Surgical Specialty Leads (SSL) now working on developing and delivering high-quality randomised trials across all specialties. The work of STCs and SSLs in conjunction with regional research collaboratives means support is provided for feasibility, pilot and safety studies, which often lead to randomised clinical trials.

The success of the initiative is down to the hard work of the STCs and SSLs as well as the generous support received from Rosetrees Trust, as well as other charities and surgical societies.

Jane Blazeby (Bristol STC director) training trainees on how to recruit patients on to trials, as part of the BOSTIC workshops run jointly by Oxford and Bristol

Update

- The joint trials portfolio of the seven Surgical Trials Centres has a total of 85 clinical trials, of these 42 are open and recruiting patients, 34 are in follow-up and a further nine trials have completed follow-up. The STCs also have 35 trials which are currently in 'set-up' and are being developed.
- A total of over 25,000 patients have been recruited to this joint portfolio for trials in the ten different specialties. On average patients are being recruited from 14 hospitals, with an average of 15 investigators (surgeons, trainees) working on each trial.
- The RCS/NIHR Surgical Technology Evaluation Portal completed a successful pilot where eight applications from SMEs were processed. The portal was launched by George Freeman MP at the NIHR ten-year anniversary event in May 2016.
- The first RCS International Surgical Trials Network meeting was held in June 2016, with 50 surgical researchers attending from across the globe and work is under way to launch an international network across three globes; Europe, America and Australasia.
- Joint RCS/Royal College of Anaesthetists applications to carry out perioperative systematic reviews were advertised and four successful teams, led by trainees, were selected. These teams have joined the already existing evidence synthesis groups who are working with the Clinical Effectiveness Unit at the RCS, to carry out these reviews.

Plans

- To further encourage the development of clinical trials and the initiative as a whole, the RCS is raising funds to recruit professorial chairs in surgical clinical research at Universities hosting RCS Surgical Trials Centres. These posts will be jointly funded for a period of four years, after this period the funding will be covered by the University partner, alone. The first of these chairs will be advertised and appointed in the first half of 2017.
- The Surgical Technology Evaluation Portal will be further promoted and targeted communications to UK-based SMEs will be distributed. Plans for specialty-specific events between SMEs and clinical researchers from RCS/NIHR infrastructures are being developed, to assist SMEs in developing their ideas efficiently for patient benefit.
- Following the first meeting to discuss launching an RCS International Surgical Trials Network in June, further meetings with the American and Australasian Colleges have taken place and plans are progressing.
- There is grEeat interest from surgical specialty associations regarding the creation of new SSL posts in specialties not currently represented in the initiative. Following further discussions, an advertisement will be placed for the roles in 2017.

The views of a Surgical Trials Centre Director – Professor David Beard

In its fourth year since inception The Royal College of Surgeons clinical trials initiative is enjoying developmental stability alongside sustainable growth. The initiative's impact on surgical research is becoming ever-more evident and important.

In times of evidence-based medicine, limited resources and the increasing demand to show value for money, let alone efficacy, the field of surgery was in clear need of a strong policy on evaluation. The surgical community sadly still lags well behind pharmacological intervention in terms of formal and rigorous assessment of the treatments provided. The RCS Surgical Research Committee has stepped up to the plate and laudably (and audibly, cf. Professor D Morton) grasped this thorn. It has set about putting real effort into promoting and facilitating surgical research. The response, including the initiation and continued support of the five original Surgical Trials Centres, now joined by York and Leeds, has been hugely successful.

In the last few years we have seen exceptional output from all centres. Success in funding trials has risen and the original quizzical looks generated from submissions involving surgical intervention have been replaced by understanding and respect. The advent and success of several new training courses for surgical trainees (including our own BOSTIC course with our close colleagues in Bristol) is changing the face of how surgical trials are viewed. In the near future this teaching package (and the RCS badge) will be projected onto the international stage. New consultants are coming through with a knowledge and thirst for evaluation. Imparting this knowledge has been rewarding and fun, especially to the many and varied surgical speciality groups.

On that note the role of the RCS Surgical Specialty Leads (SSLs) has consolidated and they are effectively prioritising the best projects to portal through to the surgical centres. This increased maturity has created efficiencies within the system. Only the best and truly fundable trials attract attention and resources. The linkages have also facilitated the growth of a national surgical trials network that is both active and influential. We hope the enthusiasm and effective SSL input will continue.

With regard to specific topics, there have been advances in many areas, especially in methodology and design; how to deal with waiting lists; the ethical and design challenges of placebo control groups; the utilisation of qualitative research; standardisation of treatment and the further efforts into delineating the need and positioning of pilot and feasibility studies.

There is more collaboration at higher levels and the surgical research community has substantial visibility at the international and national clinical trials conferences. The suggestion that the UK is currently an international leader of surgical trial research would be not be outlandish. The international push has resulted in several new international collaborations and trials being funded, all evidenced at the recent International Trials Day at the Royal College.

What comes next?

We need to sustain the new culture throughout the whole of surgical sciences and begin to consider sub speciality division. Some specialities already enjoy an established research and trials platform. Others will benefit from further support and attention. There are several sub specialities that are only just setting out on their journey of evaluation. The incorporation of corollary initiatives such as IDEAL, COMET and the increasing importance of qualitative research will help the cause. We hope no stone of surgical practice will remain unturned.

The Oxford Surgical Interventional Trials Unit (SITU) maintains a spearheading and innovative role in the RCS initiative. With our registered trial unit partnerships (with OCTRU and CSM) and continued collaboration with other units, we hope to make a substantial impact on the world of surgical evaluation. The focus has changed from development to output and sustainability. The vision is that within ten years surgical trials will have caught up (and perhaps exceeded in some ways) our pharmacological counterparts. There has never been a more exciting time to be involved in surgical science and the evaluation of surgical treatment.

1. Use of a modified Delphi approach to develop research priorities for the Association of Coloproctology of Great Britain and Ireland. Tiernan J, Cook A, Geh I, et al. Colorectal Disease. 2014;16(12):965-970. doi:10.1111/codi.12790
2. A national patient and public colorectal research agenda: Integration of consumer perspectives in bowel disease through early consultation. McNair AGK, Heywood N, Tiernan J, Verjee A, Bach SP, Fearnhead NS. On behalf of ORACLE Collaboration. Colorectal Disease Accepted Author Manuscript. doi:10.1111/codi.13564

Why we do research

The views of a Surgical Specialty Lead – Mr Simon Bach.

The first Surgical Sandpit, Sheffield 2013

Three years ago, possibly four, I sat down with colleagues and discussed how we might do more to promote high-quality, patient-centred research in our subspecialty. We contemplated a framework that would help promote the latent talent of fellow clinicians, trainees and students, identify new strategies to improve patient care, and assemble teams capable of delivering this work. These discussions coincided with my appointment as RCS colorectal subspecialty lead and the provision of flexible funding to launch the initiative. Key alliances were formed with our professional association the ACPGBI (Nicola Fearnhead), trainee collaborative networks (so many inspiring individuals) and the Bowel Disease Research Foundation Charity (Azmina Verjee, John Northover and Asha Senapati). The RCS became an excellent base for our subsequent exploits.

The Oracle of Delphi deep discussion, RCS 2015

Our first meeting took place in Oct 2013 in Sheffield. We christened it the 'Surgical Sandpit' a euphemism for stripping away inhibitions and playing with new ideas. I was attracted to the notion of holding meetings where attendees were charged with providing all content while facilitators kept proceedings on track. I also thought that research should be inspiring, even fun. We devised an iterative programme of group working that began by brainstorming, followed by prioritisation of ideas, through to development and presentation of fledgling research schemes. The event was supported by experienced surgical trialists (David Jayne and Dion Morton) as well as enthusiastic methodologists from the Birmingham Clinical Trials Unit (Laura Magill). It is perhaps poignant that I am writing this review while travelling back from the NIHR HTA, PREPARE ABC launch meeting, hosted by James Hernon at RCS. This prehabilitation study was conceived at the very first 'Surgical Sandpit' event and grew from there.

Buoyed by the feedback received from our first outing, and convinced that this was a winning formula, we set about delivering an ambitious plan to promote wider engagement in surgical research amongst clinicians and patients. The Delphi format was born or rather borrowed. We conducted a Delphi Exercise of the ACPGBI membership to determine research priorities, created the Oracle of Delphi to learn what patients thought, appointed over 70 Delphi Champions, and held the RCS Delphi Games, which were themed trials workshops similar in format to the original 'sandpit' event where our Champions met to formulate and grow their plans. In two years, we have run three patient and public events capturing the views of over 400 participants, and six themed trials workshops at RCS with 170 delegates drawn from diverse backgrounds including patients, charity representatives, patient associations, clinical academics, NHS clinicians and nursing staff. The response from the community has been tremendous and I thank all of those who have taken part, especially the trainees who have worked hard to support patient events. Hopefully they have enjoyed the experience as much as I have.

The Bowel Disease Research foundation have been utterly fantastic and trustees have attended every Delphi event.

Delphi Games icebreaker, RCS 2016

They were quick to recognise the research mandate provided by this initiative and have focused their funding strategy for 2016 upon answering Delphi questions. This year nine Delphi projects received pump priming funding from the BDRF, while more substantial funds were allocated to run the HiP study (Dale Vimalchandran). BDRF have also supported GRANULE (Aneel Bhangu and Simon Bach) a practical workshop for medical students that teaches how to approach recruitment of patients into randomised trials; expertly supported by

Jane Blazeby and staff from the MRC Methodology Hub in Bristol. The NIHR have already funded three major Delphi initiatives, PREPARE ABC (James Hernon), CIPER (Neil Smart) and LEGO (Hugh Paterson). Cancer Research UK have funded the international STAR-TREC study exploring organ-sparing treatment for early rectal cancer (Simon Bach and David Sebag-Montefiore).

I will end by saying how much I have enjoyed this process, meeting patients and having them help design studies from the ground up has been a revelation. Similarly, the practical training for medical students will hopefully signpost surgery as a forward looking and creative career choice. I thank all of you who have taken part and encourage those of you who have not to come along in 2017.

GlobalSurg: building a platform for high quality global research in surgery

By Aneel Bhangu & James Glaseby

Supported by the RCS, GlobalSurg is an international collaboration of surgical researchers aiming to give grass-root surgeons in low and middle income countries (LMIC) the opportunity to participate in major projects. The wider research network now includes over 3000 clinicians in more than 60 countries. The project is continuing its efforts to develop international surgical research, relevant to low and middle-income countries, by establishing sustainable overseas research Hubs.

GlobalSurg is extending its platform to deliver prioritisation cycles and clinical research for surgical innovation in low and middle income countries. This will enable leadership of GlobalSurg to be transferred from the UK into a sustainable low-middle income country-(LMIC) led structure, capable of delivering high-quality interventional, observational and health service delivery research.

In an effort to build capacity, GlobalSurg will develop a range of overseas 'Hubs' that will coordinate local project delivery and scientific strategy through smaller and rural 'Spoke' hospitals. The Hubs will vary in size and capacity according to need, with some running within their own country and some into neighbouring countries. A Global Surgery Policy Consortium will be convened by our External Advisory Board, supported by the Royal College of Surgeons of England, to create guidelines and guide policy. These will be used to impact on the wider collaborative of over 400 LMIC hospitals.

The GlobalSurg scientific strategy is centred around a four-step Prioritisation Cycle. These cycles will be led by LMIC Hubs:

1. Workshops, to identify and plan research to be conducted across the network.
2. Information Gathering, including feasibility studies and analysis of 'big data.'
3. Evidence Generation, through randomised trials.
4. Sustainability, through long-term funding, training, and policy formation.

Want to read more?
Visit www.globalsurg.org, or contact us at enquiry@globalsurg.org

Research fellowships and opportunities now available.

GlobalSurg launch meeting in Birmingham attended by 60 medical professionals including 25 surgeons from 12 countries. (Right) Professor Chris Lavy and Murat Akkulak at the launch of the meeting. (Left) Group sessions at the meeting

Clinical Effectiveness Unit

David Cromwell

Professor David Cromwell
Director of the CEU

The Clinical Effectiveness Unit (CEU) is an academic collaboration between the College and the Department of Health Services Research and Policy within the London School of Hygiene and Tropical Medicine (LSHTM). Since its creation in 1998, it has become a national centre of expertise on conducting large-scale studies into the quality of surgical care, something that has been built on its multi-disciplinary approach and its close relationship with the College and Specialty Associations. Another key element of its success has been its ability to give opportunities to surgical trainees to work on national studies and enrol in higher research degrees. The CEU currently has four trainees among its 20 staff members.

Kate Walker and Angela Kuryba from CEU with Professor Ian Bissett, a colorectal surgeon visiting from the University of Auckland to discuss bowel cancer research

Audit and research

The core activity of the CEU is to conduct national clinical audits and research projects. Many of the national audits form part of the Government's National Clinical Audit and Patient Outcomes Programme (NCAPOP), which is playing an increasingly important role in the Government's strategy to improve the outcome of secondary care. The CEU is conducting national clinical audits in bowel cancer, oesophago-gastric cancer, prostate cancer, and vascular surgery, as well as supporting others such as the national emergency laparotomy audit.

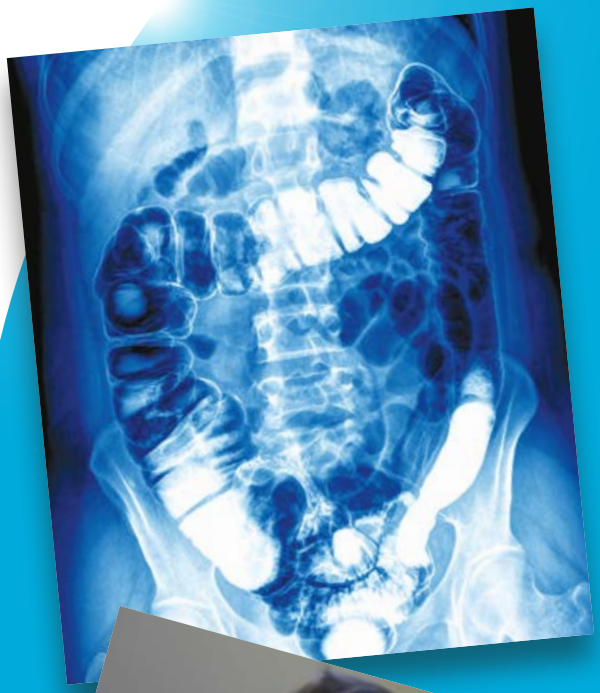
The CEU has also been undertaking work on the quality of surgical care delivered to breast cancer patients. The 'Breast Cancer Outcomes project' uses data on activity within English NHS hospitals to examine the patterns and outcomes of surgery among women having breast conserving surgery, mastectomy, and breast reconstruction procedures. The majority of the research was carried out by Ms Jo Mennie, a surgical trainee, with support from the Association of Breast Surgery, British Association of Plastic, Reconstructive and Aesthetic Surgeons (BAPRAS) and was part-funded by Johnson & Johnson.

A particular focus of this work has been to develop ways of describing the care pathway followed by women with breast cancer, given the multiple potential options women have in breast cancer treatment. As part of this, Jo identified that current studies have tended to examine one type of surgical procedure, which leads to only a partial understanding of this complex clinical practice. Consequently, she aimed to describe the patterns of breast cancer surgery using a more comprehensive approach, and proposed as a new measure the proportion of women who have retained a breast (either through conserving surgery or reconstruction) four years from the date of initial breast cancer surgery.

This novel measure provided a fresh insight into the patterns of breast cancer surgery. Using data from 2008 and 2009, the project revealed that the proportion of women with a breast at four years was strongly related to their characteristics. Among women under 70 years who had no medical conditions apart from their breast cancer, the proportion was 79.3%. But, for women aged 70 or over, it was only 52.6%. If women had other conditions, the figures in each age group were lower again. The proportion with a breast at four years was 64.0% in women under 70 years with comorbid conditions and 38.2% in women aged 70 and over. These differences did not seem to be solely a reflection of a woman's fitness for surgery or her preferences because the proportions within each group varied across regions within England (the highest and lowest regions differed by at least 15% for all four groups) and regions tended to have high or low proportions consistently across all four patient groups.

This breast cancer project was stimulated by the work that the CEU undertook on the Mastectomy and Breast Reconstruction Audit between 2007 and 2011. It also played an important role in us successfully bidding for the new national clinical audit of breast cancer in older patients with the Association of Breast Surgery. This clinical audit began in April 2016. Jo Mennie gained her PhD in October 2016.

A brief description of other major CEU projects undertaken in 2015-16 is given in Box 1.



Box 1: Major CEU projects undertaken in 2015-16

National Bowel Cancer Audit

The audit has been reporting on the care delivered to patients with bowel cancer, and the outcomes of treatment, since 2002. The audit is delivered with the Association of Coloproctology of Great Britain and Ireland and NHS Digital.

National Prostate Cancer Audit

This is the first national clinical audit of the care that men receive following a diagnosis of prostate cancer. The audit is managed as a partnership between a team of clinical, cancer information and audit experts from the British Association of Urological Surgeons, the British Uro-oncology Group, the National Cancer Registration Service and the CEU.

National Oesophago-Gastric Cancer Audit

This audit has been running since 2011 providing information on the care delivered to patients with cancer of the oesophagus or stomach. It is being carried out in partnership with the Association of Upper Gastrointestinal Surgeons, the British Society of Gastroenterology, the Royal College of Radiology, and NHS Digital.

National Audit of Breast Cancer in Older Patients

The CEU, in collaboration with the Association of Breast Surgery, began this audit in April 2016. It will investigate why older women with breast cancer appear to have worse outcomes than younger women. The patterns of breast cancer care received by women aged 70 years and over will be compared with the care given to women diagnosed aged 50-69 years.

CRANE Database

This is a registry of all children born with cleft lips and palates in England, Wales and Northern Ireland, their treatment and the outcomes. The CEU has been the host organisation for this registry since April 2005.

National Vascular Registry

The National Vascular Registry reports on the process of care and outcomes among patients who undergoing major vascular surgery, including the repair of abdominal aortic aneurysm, and lower limb bypass and amputation. It is run in partnership with the Vascular Society of Great Britain and Ireland.

20 years of the RCS Surgical Research Fellowship Scheme

The RCS Research Fellowship scheme was established in 1993 to give medical trainees an opportunity to undertake research on a surgical topic. Since then, between 20 and 30 one-year Fellowships have been offered annually, with the addition of a small number of two to three-year awards that have tended to be awarded jointly with other research funding bodies.

In 2015, the CEU and Research Department surveyed the 502 surgeons who had received awards between 1993 and 2013, to discover what the Fellowships had enabled the trainees to achieve and how their career had then developed.

The Fellowships were typically awarded to trainees in their late 20s/early 30s. The majority of those aged under 30 had not started Specialty Training when they began their Fellowship, whereas most responders aged 32 or over had.

The survey responders had undertaken a broad array of research topics: 62% of Fellowship recipients had undertaken laboratory-based basic research, while another 17% had focused their research on new surgical techniques or practice that directly involved patients. During the fellowship, almost all respondents had enrolled in a higher degree (MD or PHD) and the completion rate has been very high. Among those who had a Fellowship in the first 15 years of the Scheme, 91% of responders had successfully obtained their degree.

The research undertaken during the Fellowships had led to numerous peer-reviewed publications and conference presentations, with a typical recipient publishing between two to five peer-reviewed articles during their Fellowship and presenting three to six times at national or international conferences. The survey respondents supplied information on 527 scientific articles (limited to a maximum of three citations per respondent), many of which had been published in journals with high impact factors. The three most common journals were the British Journal of Surgery (38 articles), British Journal of Cancer (22), and the Journal of Bone and Joint Surgery (14). A small number of articles had appeared in major international journals, including Science, the Lancet and British Medical Journal.

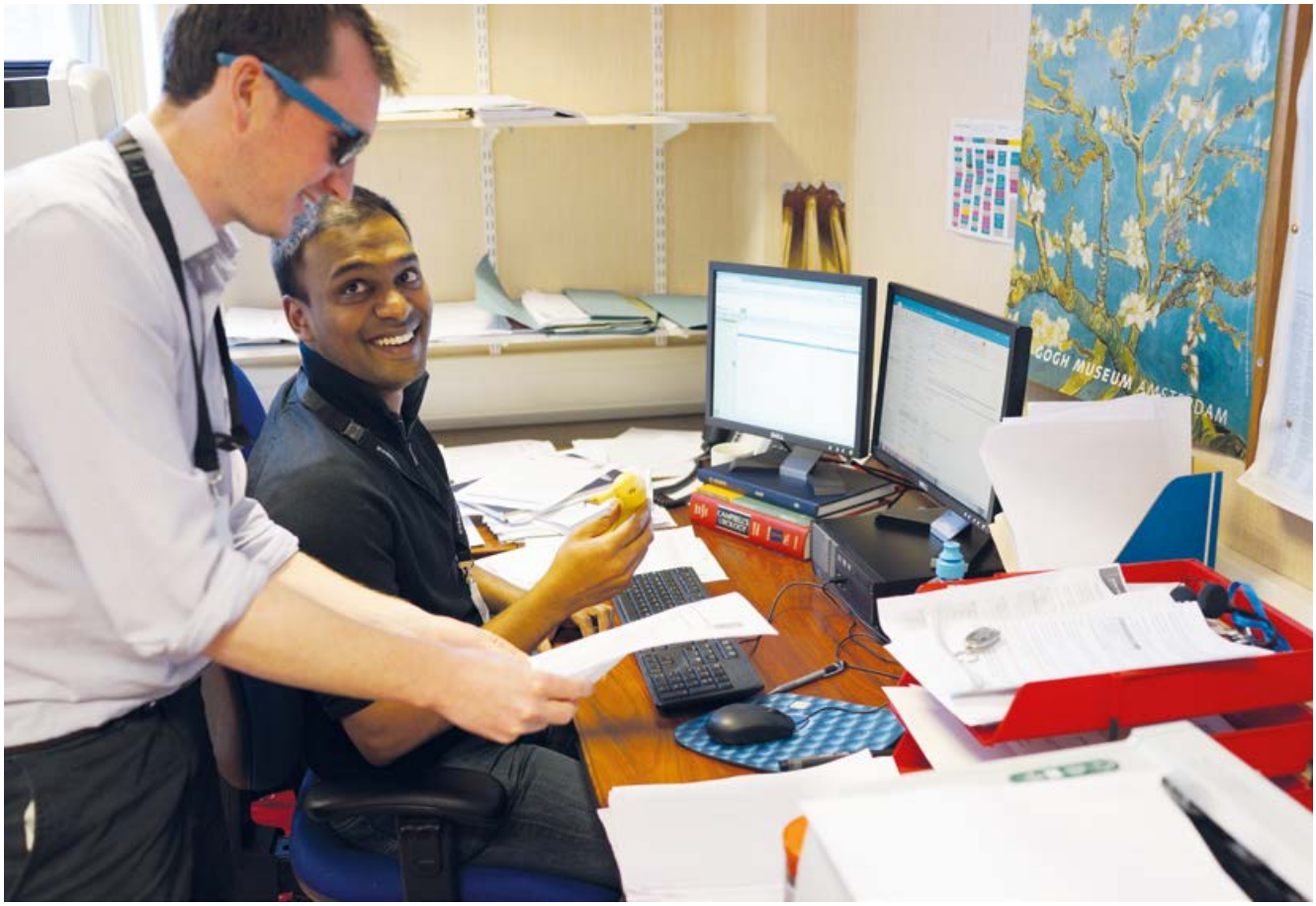
Respondents were also positive about the Fellowship scheme had facilitated both their clinical and academic career, with 60% going on to secure further funding for ongoing research. Among trainees who received their award between 1993 and 2003, over 90% have become consultants, and a quarter of respondents are currently in academic posts.

The RCS Fellowship scheme has played a significant role in the funding and delivery of surgical research. It needs to be remembered that an article in 2008 described the UK academic cancer surgeon as ‘an endangered species’, and in recent years, less than 2% of the UK’s medical research funding was awarded to surgery-based projects. The positive responses from Fellowship recipients shows that the value of the Scheme to trainees and how it supports the development of clinicians with the necessary skills to support medical research in this country.

Teaching

The CEU runs a number of courses for surgeons and other health care professionals on statistics, clinical research methods and evidence-based surgery. The courses use a mixture of teaching methods ranging from lectures to interactive seminars and hands-on computer practicals. Course faculty often includes methodologists recruited from CEU staff as well as senior clinicians with a strong interest in research and audit.

David Cromwell with Anne Jones and Kate Lyons of the Clinical Audit and Effectiveness Dept, Kingston Hospital, who spoke to staff in CEU about how they manage the national clinical audit programme in an acute trust



Mathew Parry and Arun Sujenthiran, Research Fellows at the CEU office

Selected publications by CEU staff in 2015 and 2016

1. Neuburger, J. ; Currie, C. ; Wakeman, R. ; Tsang, C. ; Plant, F. ; De Stavola, B. ; Cromwell, D.A. ; van der Meulen, J. ; The Impact of a National Clinician-led Audit Initiative on Care and Mortality after Hip Fracture in England: An External Evaluation using Time Trends in Non-audit Data. Med Care (2015) 53(8):686-691
2. Tovikkai, C. ; Charman, S.C. ; Praseedom, R.K. ; Gimson, A.E. ; van der Meulen, J. ; Time-varying impact of comorbidities on mortality after liver transplantation: a national cohort study using linked clinical and administrative data. BMJ Open (2015) 5(5):e006971
3. Chadwick, G.; Groene, O.; Riley, S.; Hardwick, R.; Crosby, T.; Hoare, J.; Hanna, G.B.; Greenaway, K.; Cromwell, D.A.; Gastric Cancers Missed During Endoscopy in England. Clin Gastroenterol Hepatol (2015) 13(7):1264-1270.e1
4. Walker, K.; Kuryba, A.; Scott, N.; van der Meulen, J. Regional variation in length of hospital stay after major surgery for colorectal cancer European Journal of Cancer Care (2015) 24:19-20
5. Aggarwal A, Cathcart P, Payne H, Neal D, Rashbass J, Nossiter J, van der Meulen J. The National Prostate Cancer Audit - introducing a new generation of cancer audit. Clin Oncol (R Coll Radiol). 2014 Feb;26(2):90-3
6. Loftus IM, Paraskevas KI, Johal A, Waton S, Heikkila K, Naylor AR, Cromwell DA. Delays to Surgery and Procedural Risks Following Carotid Endarterectomy in the UK National Vascular Registry. Eur J Vasc Endovasc Surg. 2016; 52(4):438-443
7. Mennie JC, Mohanna PN, O'Donoghue JM, Rainsbury R, Cromwell DA. The Proportion of Women Who Have a Breast 4 Years after Breast Cancer Surgery: A Population-Based Cohort Study. PLoS One. 2016; 11(5): e0153704
8. Shalhoub J, Cromwell D, Coomer M, Alderson D. The impact of The Royal College of Surgeons of England research fellowship scheme. Ann R Coll Surg Engl. 2016 Jul; 98(6):431-5

Research in the Faculty of Dental Surgery

By Professor Paul Speight, FDS Research Chair

Throughout our history the Faculty of Dental Surgery has been active in research into the causes and management of oral and dental diseases. In the early days this was carried out in the College in the Department of Dental Science. This included seminal and pioneering research into the development of a caries vaccine, which was carried out at Buckston Browne Farm at Downe in Kent. In 1996, when the College sold the farm the Department closed and research was no longer conducted at the College. However, the endowed funds were still available and the Faculty decided to use these to promote oral and dental research through the award of grants and fellowships.

Since 2008 the Faculty has distributed almost £1.5 million to support research across the country. There have been nine recipients of research fellowships and 31 small grants have been awarded. Two PhD fellowships have also been awarded in partnership with the Wellcome Trust. Our awards primarily support clinical trainees to obtain research experience and the fellowships allow them to take time out of clinical training to study towards a PhD. Among our recipients, 15 have now obtained senior positions in Universities or the NHS and at least three have become professors in their clinical specialties.

Projects supported by the Faculty have covered all areas of oral and dental research including oral cancer, craniofacial abnormalities, periodontal diseases and facial pain. Recently the Faculty has debated the concerns around the poor oral health of children and to this end we have formed partnerships with the British Orthodontic Society, British Society of Paediatric Dentistry and British Association for the Study of Community Dentistry and the British Society of Periodontology. Together we have awarded a number of grants to help improve the status of children's oral health in the UK. This has included studies to explore how children and their families can become more involved in their own care, investigations of the outcomes and acceptability of orthodontic treatments and studies of tissue engineering in the management of facial deformities.

Case studies of some of our successful Fellows:

Projects supported by the Faculty have covered all areas of oral and dental research including oral cancer, craniofacial abnormalities, periodontal diseases and facial pain.

Development of a web-based version of the Children's Experience of Dental Anxiety Measure for clinical assessment

Annie Morgan – Sheffield

Annie held a Faculty Fellowship in 2015, whilst she was in her first year as a substantive consultant in Paediatric Dentistry in Sheffield. As part of her PhD research Annie had interviewed children to explore their experiences of dental anxiety and, with a team of experts that included psychologists, contributed to the development of a new Patient Reported Outcome Measure for childhood dental anxiety called the Children's Experience of Dental Anxiety Measure (CEDAM). The award of the Fellowship allowed Annie to take time out of her consultant role to develop and test an electronic version of the CEDAM (eCEDAM), foruse as a web-based application that children could use in a clinical setting on a tablet device. With software engineers, she pilot tested the eCEDAM with children, using their opinions and ideas to guide its development. The validity and usability of the eCEDAM has also been evaluated in a randomised trial of 100 children comparing the eCEDAM to conventional paper-based questionnaires. This important work gives children a voice in their own care, allows clinicians to properly assess and manage dental anxiety in their young patients, and will have uses in research to evaluate treatment approaches and to inform the development of similar measures in other dental specialties.

The epigenetics of HPV16- mediated oral & oropharyngeal squamous cell carcinoma

Andrew Schache – Liverpool

Andrew was awarded the inaugural FDS-Wellcome Trust Fellowship in 2010, allowing him to take time out from his higher surgical training in Oral and Maxillofacial Surgery. This allowed him to work full time as a Clinical Research Fellow at the University of Liverpool and to study for his PhD in molecular oncology. His research was focused on oropharyngeal cancer (OPC), and its association with human papillomavirus (HPV). The main aim of his work was to clarify the epigenetic alterations that occur in HPV-positive OPC, and the potential mechanisms through which the virus may cause this disease. First, he evaluated the prevalence of HPV infection in OPC and developed valid diagnostic tests for HPV detection in lesions. He then undertook an analysis of the epigenetic changes found in HPV-driven cancer samples and cell lines.

Andrew received several prizes during his Fellowship, including the Richard Hambro Student Prize Award awarded by the National Cancer Research Institute (NCRI) and the Paul Toller Research Prize on two separate occasions from the British Association of Oral & Maxillofacial Surgeons (BAOMS).

Andrew completed his research and was awarded his PhD in 2013 and has subsequently presented his work at several national and international conferences and has published widely, including six peer-reviewed publications resulting directly from this Fellowship.

Andrew also completed his clinical training in 2013, and was awarded the Gold Medal for his performance in the Intercollegiate FRCS Examination. He is currently a Senior Clinical Lecturer in Head & Neck Surgery at the University of Liverpool and is a Consultant Oral and Maxillofacial Surgeon in the internationally renowned Head & Neck Unit at Aintree University Hospital.

Expression analysis of candidate genes regulating successional tooth formation in the human embryo

Ryan Olley – London

Ryan was awarded a Faculty small grant in 2013. This enabled him to carry out research in craniofacial science as part of his Academic Clinical Lectureship. This work was undertaken following his PhD, which he completed at King's College London in 2012 in tooth wear and dentine hypersensitivity. Ryan also had previous experience in craniofacial science having studied for an intercalated Bsc during his undergraduate dental degree. He was awarded the UK and Ireland BDA/ Denstply student clinician prize.

His faculty-funded research project focused on understanding the molecular regulation of human successional tooth formation. The primary aim was to investigate expression analysis of candidate genes identified in human embryos during early embryonic development (8-14 weeks). Using three-dimensional histology and in situ hybridisation, he found that SPROUTY2, GAS1 and RUNX2 are all expressed during human tooth development. The domains of GAS1 and RUNX2 were consistent with a role influencing the function of the primary lamina, but only GAS1 transcripts were identifiable in the successional lamina at early stages of human development. His work was published in a leading physiology journal (Olley, RC, Xavier G, Seppala M, Volponi AA, Geoghegan F, Sharpe PT, Cobourne MT. (2014) Expression analysis of candidate genes regulating successional tooth formation in the human embryo. Frontiers in Physiology 21(5):445).

As part of his Academic Clinical Lectureship, Ryan also completed his specialist clinical training in fixed, removable and implant prosthodontics at Kings College London, and has recently been appointed Senior Lecturer and Consultant in Prosthodontics at Dundee University and Hospitals.

Innate immune responses in patients with inflammatory bowel diseases

Helen Petersen – Manchester

Helen was awarded a small grant in 2014. This allowed her to develop her post-doctoral research investigating innate immune responses in patients with oral mucosal disease, specifically inflammatory bowel diseases. The oral cavity is an often forgotten part of the gastrointestinal tract and can be the first site of presentation of disease. Using patient blood samples, Helen characterised patient neutrophil function and macrophage cytokine release profiles, opening up interesting new avenues of further research on this subject.

This grant allowed Helen to successfully gain further grant funding from the Academy of Medical Sciences to continue her research. Helen has published her work in peer review journals and presented both nationally and internationally, all made possible by this grant from FDS.

Helen is currently a Consultant Senior Lecturer in Oral Surgery at the University Dental Hospital of Manchester, where she combines both clinical practice with research, plus teaching of undergraduate and postgraduate students.

Biological effects of Titanium products on oral epithelial cells

Joanna Batt

UNIVERSITY OF BIRMINGHAM
CLINICAL LECTURER IN |
RESTORATIVE DENTISTRY

MENTOR:
Prof Owen Addison –
University of Birmingham

Professor of Applied Biomaterials –
Consultant (Hon) in Restorative Dentistry

Over the past five years the focus of our research group has been to develop a better understanding of peri-implant disease. Dental implants are an increasingly common treatment modality use to replace individual teeth or secure dentures. However, the development of peri-implant disease (inflammation around the implant) can result in implant loss or the need for revision surgeries.

The pathogenesis of peri-implant disease is poorly understood but oral microbes which colonise the implant surface and the patient's immune response are known to be involved. Increasingly however, implant material derivatives characterised as nanoscale Titanium (Ti) particles and Ti-biomolecule associations have been additionally implicated as a modulating factor in the progression of peri-implant inflammation.

Our group using synchrotron X-ray measurements were one of the first to characterise this accumulation of implant debris and demonstrated that it accumulated in close proximity to epithelial cells. Accordingly the objectives of this project were to model interactions between oral epithelium (adjacent to the implant surface) and Ti implant products.

Confocal microscopy was used with complementary X-ray and electron microscopy techniques to demonstrate that oral epithelial cells can take up (intracellularise) clinically representative Ti products with little impact on cell viability.

A variety of genomic and cellular and molecular biological approaches were applied to study which biological pathways were influenced by this interaction. Key findings include that pre-exposure to Ti can subsequently modify which cytokines are expressed by the cells when challenged with a periodontal microbial pathogens and the presence of extra-cellular Ti, modified chemical gradients of cell signalling molecules (chemokines) which are essential for the host to mount an adequate inflammatory response.

These findings form part of an increasing portfolio of evidence generated by the group which support the overall hypothesis that 'free' Ti in peri-implant tissues can increase the risk of for progression of peri-implant inflammation.

Prizes & Travelling Awards

Travelling Awards

The College is pleased to be able to offer a variety of awards as a result of the generous support of companies and individuals. These awards give surgeons the opportunity to work in an overseas institution to learn more about a particular surgical technique or area. The main benefit of the travelling awards is that the surgeon who benefits can translate the experience and know-how gained during the overseas fellowship to his or her own knowledge base, to benefit future patients in this country. The committees that decide the recipients of the travelling awards always include leading surgeons.

Rex and Jean Lawrie Fellowship and Stefan and Anna Galeski Fellowship

Each year the families of Rex and Jean Lawrie, and Stefan and Anna Galeski, fund a number of surgeons to undertake various surgical skills workshops, and other such activities, to help improve surgical skills, and thus surgical care, for people in low and middle income countries throughout the world. Such generosity is deeply appreciated by the College, the numerous UK surgeons who receive the fellowships' support and most importantly the surgeons who learn various surgical skills in the host countries. Of late, these two fellowships have supported surgeons going to Malaysia, Borneo, Mongolia, Ethiopia, Mexico and Guatemala.

Recipients up to May 2017

- Abigail Vallance
- Victoria Twigg
- Ellie Edlmann
- Michelle Wilkinson
- Bynvant Sandhu
- Anna Sharrock
- Johnny Mathews
- Rhiannon Harries
- Naomi Wright
- Tom Pinkney

Ethicon Foundation Fund

The Ethicon Foundation Fund was established by the generosity of Ethicon Limited. The Fund provides financial assistance towards the cost of the travel to and from a research or training fellowship, thereby promoting international goodwill in surgery. Applicants should be sufficiently advanced in their training to benefit from such an experience or be within one year of their appointment as consultant surgeon.

Recipients May 2015

- Peter Domos – Lyon, at the Clinique Orthopaedic Santy the University Hospital Centre of Toulouse
- Charles Jowett – The Alfred Hospital, Melbourne
- Stella Smith – Groote Schuur Hospital, Cape Town
- Thet Win – Brigham Hospital, Boston
- Riaz Agha – University Hospital, Brussels
- Rafid Al-Mahfoudh – The Weill Cornell Brain and Spine Center, New York
- Siong-Seng Liau – Department of Gastrointestinal Surgery, L'Institut Mutualiste Montsouris, Paris
- Ibrar Majid – International Centre for Limb Lengthening, Baltimore

Recipients December 2015

- Catherine Bradshaw – Red Cross Children's Hospital, Cape Town
- William Lo – Hospital for Sick Children, Toronto
- Charlotte Bendon – O'Brien Institute of Regenerative Surgery, St Vincent's Hospital, Melbourne
- Rebecca Mills – The Children's Hospital at Westmeade, Sydney
- Sherif El-Tawil – Royal North Shaw Hospital, Sydney & Sydney Orthopaedic Research Institute
- Rahul Kotwal – Australian Institute of Musculo-skeletal Research (AIMS)
- Ben Spiegelberg – London Health Sciences Centre, Ontario, Canada
- Fateh Ahmad – Memorial Sloan Kettering Cancer Centre & NYU Langone Medical Centre
- Anthony Barabas – Foothills Medical Centre, Calgary, Canada

Recipients May 2016

- Nadia Ashraf – Sydney Cochlear Implant Centre
- Jemma Bhoday – Toronto, Canada
- Nikolaos Chatzizacharias - Medical College of Wisconsin
- Andrew Chetwood – Royal Adelaide Hospital, Adelaide
- Nil De Zoysa – The Princess Alexandra Hospital, Brisbane
- Jonathan Dunne – Queen Elizabeth Central Hospital, Blantyre, Malawi
- Navin Mani – Memorial Sloan Kettering Cancer Centre, New York
- Daniel Marsland – Mater Hospital Foot and Ankle Unit, Brisbane
- Sid Nagala – Memorial Sloan Kettering Cancer Center, New York
- Graham Sleat – University of British Columbia and Vancouver General Hospital
- Misha Verkerk – Hearing Centre, Ivano-Frankivsk, Ukraine

Recipients December 2016

- Muneer Ahmed – University of Tokyo, Japan
- Neil Barua – Institute for Neurosciences Montpellier, France
- Jack Broadhurst – Catharina Ziekenhuis, Eindhoven, The Netherlands
- James Brousil – Radboud University Medical Center, Netherlands
- Charlotte Brown – Bishop Caeser Asiili Hospital, Luwero District, Uganda

- Thomas Goff – Australian Institute of Musculo-skeletal Research postgraduate fellowship, Sydney
- Thomas Hester – Foothills Medical Centre, Calagary, Canada
- Christopher Hill – The Hospital for Sick Children, Toronto, Canada
- Zita Jessop – Royal Melbourne Hospital, Australia
- Milap Rughani – Princess Alexandra Hospital, Brisbane, Australia
- Shankar Thiagarajah – Mount Sinai, Hospital, Toronto, Canada
- Jim Tiernan – Cleveland Clinic, Cleveland, Ohio, USA
- Emily Young – St Paul's Hospital, Vancouver, BC, Canada

Colledge Family Memorial Fellowship Fund

The Colledge Memorial Travelling Fellowship was established by Miss Cecilia Colledge in 1979 in memory of her father, the distinguished surgeon Lionel Colledge and her brother Maule who died in active service during the Second World War. The Fellowship was founded to promote and advance the study and knowledge of surgery, in particular head and neck surgery, for the benefit of patients. Applicants must be senior trainees or new consultants and plan to a study for a period overseas.

Recipient 2015

- Asit Arora

Recipients 2016

- Mahmoud F Bhutta
- Abhijit Ricky Pal
- Navin Mani

Sir Ratanji Dalal Research Scholarship

This research scholarship was founded under the will of Sir Ratanji Dinshaw Dalal. It is awarded jointly by The Royal College of Surgeons of England and the Royal College of Physicians of London. Applications are invited for this research scholarship, which is intended to support a project in either tropical surgery or tropical medicine. The scholarship is tenable for one year and is open to all medical practitioners registered in any part of the Commonwealth. It may be held in any institution in Britain or overseas that is approved by The Royal College of Surgeons of England and the Royal College of Physicians of London.

Recipient 2015

- Madji Osman

Recipient 2016

- Amitava Banerjee

H J Windsor Prize

The H J Windsor Prize was established in 1975 with a gift of £2,500 from the late Dr H J Windsor KSG CBE FRCS of Brisbane, Australia. The Prize is intended to "assist in the advancement of surgery by an annual prize or by such other means as the Council shall from time to time determine"

Recipients 2015

- Rebecca Mills
- Matthew Sewell

Recipient 2016

- Michelle Griffin

The Rosetrees Trust Prize

The Rosetrees Trust Prize was established in 2009 and applicants are asked to write an essay to "describe how your research project will contribute to improvements in patient care within the next five years".

2015 Winner

- Hew Torrance 'Modulating the immune response to trauma to prevent life-threatening infectious complications'

2015 Runners-up

- Jason Fleming 'Metabolism – a master regulator of cancer cell behaviour'
- Keval Patel 'The Potential of Circulating Nucleic Acids to Improve Outcomes for Patients with Urological Cancers'

2016 Winner

- Muneer Ahmed 'Magnetic technique for Breast Cancer Treatment'

2016 Runners-up

- Pankaj Chandak 'Novel strategies in overcoming barriers in transplantation using 3D printing and ex-vivo normothermic (bypass machine) perfusion of human kidneys.'
- Peter Szatmary 'Rediscovering inflammation in acute pancreatitis'

Galeski winner Michelle Wilkinson in Mongolia with the locals

Higher Degrees for Intercalated Medical Students

Medical students' grants are awarded to medical students wishing to undertake an intercalated Bachelor of Science degree related to surgery. Owing to the variation in the ways students are funded or not funded for such degrees, students require additional support in areas such as bench fees, consumables or subsistence. Each award is worth up to £5,000.

Halimat Afolabi
Oliver Baker
Eilidh Bruce
Charmilie Chandrakumar
Rachel Dbeis
Simon Erridge
Robert Geraghty
Lysander Gourbault
Alexandra Griffiths
Kit Wing Lam
Choong Ngan Lou
Simon McElligott
Toby Murray
Ahmed Shafi
Tittu Thomas
Lauren Wallace

3D printed TPU and collagen incorporated scaffold for the application of wound healing invitro

HALIMAT AFOLABI

MEDICAL SCHOOL:
University College London

SITE OF WORK:
Royal Free Hospital, London

I am grateful to have received the RCS award as it helped me to participate in laboratory based regenerative medicine, which is an area of research I have been very interested in but have not had the opportunity to pursue. My project was on wound healing, and involved creating a 3D printed patch with collagen gel incorporated in it in order to promote the proliferation of dermal fibroblasts and endothelial progenitor cells as a model for wound healing. In all I learnt a wide range of skills including 3D design and printing, cell culture and immunofluorescent microscopy. I hope to continue doing translational research in regenerative medicine and I believe this opportunity provided an excellent foundation for future research.

Cell culture work under a sterile hood

The identification of frailty in colorectal surgical patients

OLIVER BAKER

MEDICAL SCHOOL:
University of Leeds Medical School

SITE OF WORK:
St James University Hospital, Leeds

This award helped me to conduct a research project looking at the identification of frailty in colorectal surgery patients at a university hospital. Frailty is the loss of resilience to stressors, such as illnesses or surgery, and is seen among both young and elderly patients. It is strongly associated with poor post-operative outcomes but is currently not routinely assessed. In our pilot study we found considerable frailty among adult colorectal surgery patients and the proportion increased among elderly patients. We plan to publish this work and hope that we will be able to present it at the international conference of sarcopenia and frailty next year. We hope this study will form the basis of future research into frailty and may aid clinicians incorporate frailty into pre-operative assessment. My thanks are given to the RCS for their generous grant, without which this research project wouldn't be possible.

Oliver with his supervisors; Mr Dermot Burke and Thomas Dale-Maclaine, the senior research nurse and members of the pre-assessment team

Development and validation of the Robot-Assisted Partial Nephrectomy (RAPN) assessment tool

EILIDH SUMMERS BRUCE

MEDICAL SCHOOL:
King's College London

SITE OF WORK:
Guy's Hospital, London

In receiving the College's generous award, I was presented with the opportunity to undertake research in the field of surgical education as part of my intercalated BSc. I have since graduated with a first class honours in anatomy from KCL.

We developed a scoring system to be used in the training and assessment of surgeons undertaking RAPN. In robotics, the requirement for a different skills set from open surgery has implications for patient safety, and this has called for the development of safety-checklists such as this.

Although based at Guy's Hospital, I carried out this research in association with a variety of experts on an international level, and it is with the generosity of the RCS that I have been able to travel to these centres. I travelled to Belgium to observe RAPN and to Madrid as a conference delegate. I am incredibly grateful for the support of the RCS.

Eilidh at the EAU 2015 Congress in Madrid, with the da Vinci Xi Surgical Robot

The role of the primary cilium in the regulation of hedgehog signalling and mechanotransduction in alkaptonuria

CHARMILIE CHANDRAKUMAR

MEDICAL SCHOOL:
Barts and The London School of Medicine and Dentistry, Queen Mary University of London

SITE OF WORK:
The School of Engineering and Materials Science Queen Mary, University of London

Alkaptonuria is a rare genetic disorder that causes the destruction of joints, similar to osteoarthritis. Currently, not much is known about the mechanisms of the disease. The research that we conducted was to explore the role of primary cilia, a component of cartilage, that is known to be involved in cell signalling pathways such as mechanotransduction and hedgehog signalling, which are key pathways in cartilage health. The results of this project show that these pathways are abnormal in alkaptonuria, thus, allowing us to further understand the nature of the disease and opening new avenues in research.

Charmilie with colleagues from the Institute of Bioengineering

I am extremely grateful to the Royal College of Surgeons of England for their generosity. I truly appreciate their support, as it has enabled me to learn about an array of experimental techniques as well as different aspects of research. This year has further inspired me to pursue a career in academic surgery. Thank you very much!

The epigenetics of rectal cancer: clinical implications

RACHEL DBEIS

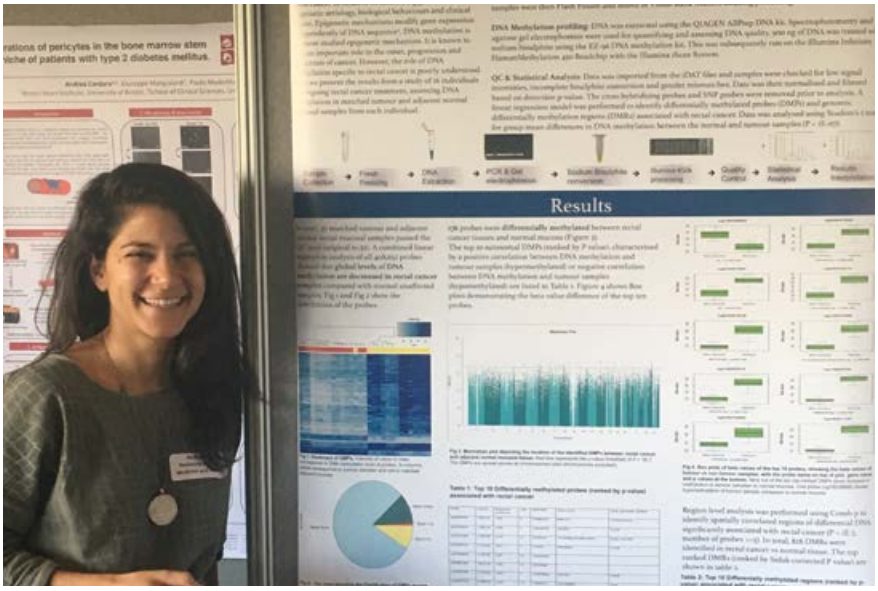
MEDICAL SCHOOL:
Peninsula College of Medicine and Dentistry, The University of Exeter Medical School

SITE OF WORK:
Royal Devon & Exeter Hospital and The University of Exeter Medical School, Exeter

Rectal cancer is a form of bowel cancer that needs surgery to try to cure it, with or without chemotherapy and radiotherapy. We don't yet have a way to identify people who will not respond to the combination of treatment and ultimately spare them unnecessary side effects.

There are chemical switches that control the activity of how our genes work, identified in other cancers, like lung cancer. They can tell us how people may respond to treatment.

My project looked at chemical switches in rectal cancer patients. We used new technologies to extract the genes, look at the chemical switches and analyse them. It is one of the first studies to identify relevant genes and regulators in rectal cancer specifically. Future studies can use this information to identify patients who would respond better or worse than others, to specific treatments, leading to the development of more personalised and successful treatments.



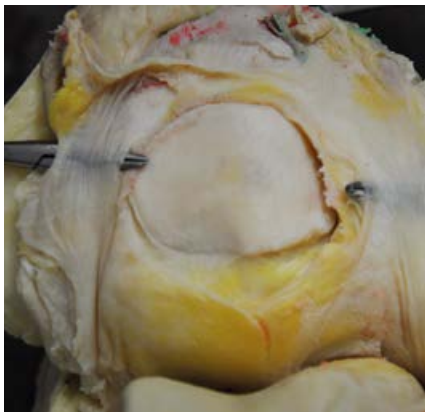
At the INSPIRE National Intercalators' Conference with best poster prize award

Are synovial plicae of the knee normal anatomical features or a consistent pathology?

ROBERT MICHAEL GERAGHTY

MEDICAL SCHOOL:
University of Southampton

SITE OF WORK:
Bristol University Centre for Comparative and Clinical Anatomy

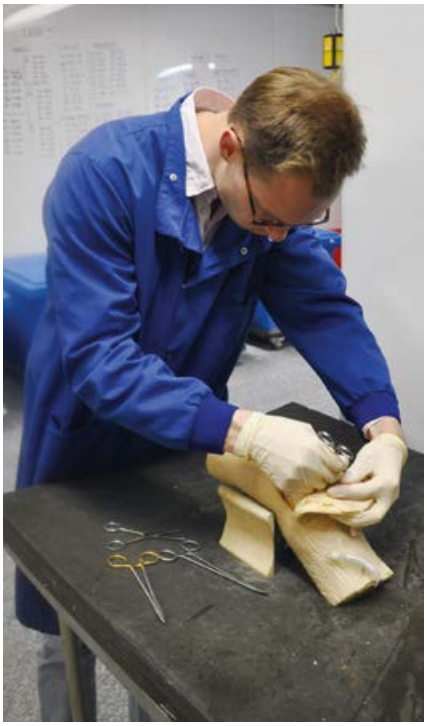


A knee with plicae, which may act in lieu of an anterior joint capsule

Synovial plicae around the knee are poorly investigated and are therefore poorly understood. My project aimed to identify plicae in cadaveric knees using a novel technique of latex injection and proximodistal dissection rather than the traditional distoproximal approach. After identification, plicae were then sampled for histological analysis.

This study has yielded some interesting results. Firstly, plicae are more common than the literature suggests. Secondly, plicae may act in lieu of an anterior joint capsule and thirdly, they may have a role in patellofemoral osteoarthritis. These topics will be covered in forthcoming abstracts and publications.

I would like to thank the College for their generous help this the year, without which I would not have been able to do. The skills I have gained this year in the dissection room and laboratory will help towards a future career in both surgery and academia.



Robert dissecting a knee

Exploiting the MT1-MMP/NG2 axis for surgical applications in human and canine sarcoma: a comparative oncology approach

LYSANDER JAMES GOURBAULT

MEDICAL SCHOOL:
Newcastle University

SITE OF WORK:
Northern Institute of Cancer Research, Newcastle and The Queen's Veterinary School Hospital, Cambridge

During my intercalated year I investigated sarcomas which are a rare form of cancer with high mortality. MT1-MMP and NG2 are biomarkers known to promote sarcoma metastases. Thanks to the generous support from The Royal College of Surgeons, I was able to investigate whether these biomarkers were linked to patients' survival. By staining patient tissues we showed that MT1-MMP, but not NG2, is expressed in most human and dog patient biopsies and is linked to how long patients survive.

We also wanted to use these biomarkers to detect human and dog sarcoma cells in the blood as they metastasize. By using flow cytometry we detected potential cancer cells in two human sarcoma patients' blood.

In conclusion our research has shown that MT1-MMP may prove invaluable in future sarcoma treatments and help guide diagnosis.

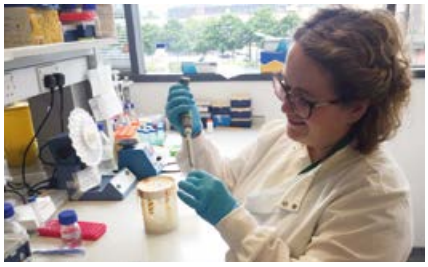
Lysander (far right) with the Cambridge Surgical Discovery Centre Team

Renal ischaemia reperfusion injury; the mitochondrial perspective

ALEXANDRA CAROLINE GRIFFITHS

MEDICAL SCHOOL:
Newcastle University

SITE OF WORK:
Institute of Genetic Medicine, Newcastle Upon Tyne



Alex performing in gel activity assays at the Centre for Life

The RCS award helped finance my MRes in Transplantation Sciences investigating the response to ischaemia (inadequate blood flow) and reperfusion (restoration of blood flow) in kidney transplants, with a focus on mitochondria (small energy producing organelles).

Mitochondria induce damage during ischaemia and reperfusion, termed ischaemia-reperfusion injury (IRI), through harmful free radical production. Understanding this process could enable the development of targeted treatments to prevent IRI to increase the function and survival of transplanted kidneys.

My project analysed changes in mitochondrial proteins during ischaemia and reperfusion using an animal model. We also investigated the use of isofluorane, a commonly used anaesthetic agent. We found that this could prevent the changes that occurred in mitochondria exposed to ischaemia.

I am grateful for the support from the RCS and my supervisors which made this study possible, enabling me to gain valuable research experience and skills that will be useful throughout my career.

To identify the differences in gaze behaviours of junior and expert bariatric surgeons

SIMON ERRIDGE

MEDICAL SCHOOL:
Imperial College School of Medicine

SITE OF WORK:
Department of Surgery and Cancer at St Mary's Hospital London

We used a set of eye tracking glasses to distinguish between the dwell times of surgeons gaze on different areas of interest. The results from the project have been submitted for presentation at a national surgical conference and aim to be published in a peer-reviewed publication.

This experience was invaluable to my on-going education as it allowed me to gain a new range of skills in research and academia and has reaffirmed my desire to pursue a career in academic surgery. I would like to thank the Royal College of Surgeons for making my project possible and my supervisors Mr Mikael Sodergren and Mr Sanjay Purkayastha.

Mr Sanjay Purkayastha, Simon's co-supervisor, wearing the eye tracking glasses

Using MR optic radiation tractography to predict visual field deficits after epilepsy surgery

KIT WING LAM

MEDICAL SCHOOL:
Cardiff University

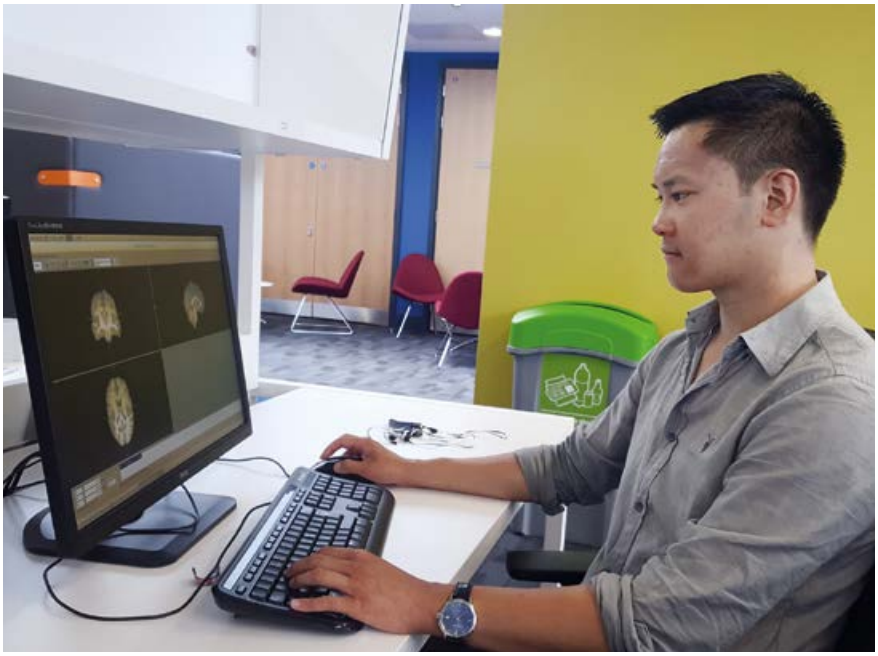
SITE OF WORK:
Cardiff University Brain Imaging Centre (CUBRIC)

For some patients with medial temporal lobe epilepsy surgery is a viable option. However, a major complication is visual field defects. This arises due to damage to nerves carrying visual information, known as the optic radiation, in particular, the region called Meyer's loop.

The grant funded Magnetic Resonance Imaging (MRI) of the patients pre and post-operatively. The MRI technique (tractography) enabled mapping of the nerve bundles in the brain. In doing so, we were able to overlay the pre-operative nerve pathways onto a template resection. The template resection consisted of MRI scans of previous patients; all of whom were operated on by Professor William Gray (Project Supervisor).

The average resection plot can be used to predict visual outcomes after surgery. The hope is that this model can provide further support for informed consent.

This model correctly predicted the visual outcomes of two patients. Further work is being undertaken to validate the model.



Kit Lam interpreting an MRI scan in CUBRIC

Prosthetic deep venous valves for deep venous reflux

CHOONG NGAN LOU

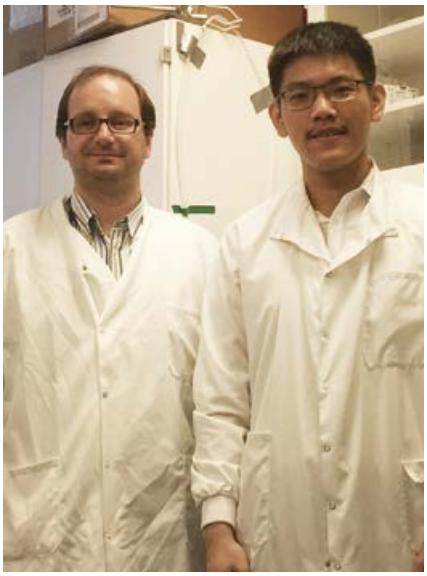
MEDICAL SCHOOL:
Imperial College London

SITE OF WORK:
Imperial College London, Bessemer Building, South Kensington Campus

No good treatment currently exists for chronic venous insufficiency caused by dysfunctional valves in the deep veins. Despite efforts to restore structure and function to the deep venous system, a suitable valve prosthesis has not been developed.

With the funding provided by the Royal College of Surgeons, we developed two bench-testing setups using additive manufacturing for testing valve prostheses and conducted a systematic review on the developmental considerations of prosthetic deep venous valves. We identified gaps in our understanding of the deep venous system and in the design and testing of valve prostheses for further focused research.

I am grateful to the College for the award that has made this possible and would like to thank my supervisors Professor Alun H Davies and Mr Andrew Busuttil for their guidance and support.



Choong with his supervisor Mr Busuttil

The effects of sonic hedgehog on the proliferation of neural stem and progenitor cells

SIMON MCELLIGOTT

MEDICAL SCHOOL:
University of Southampton

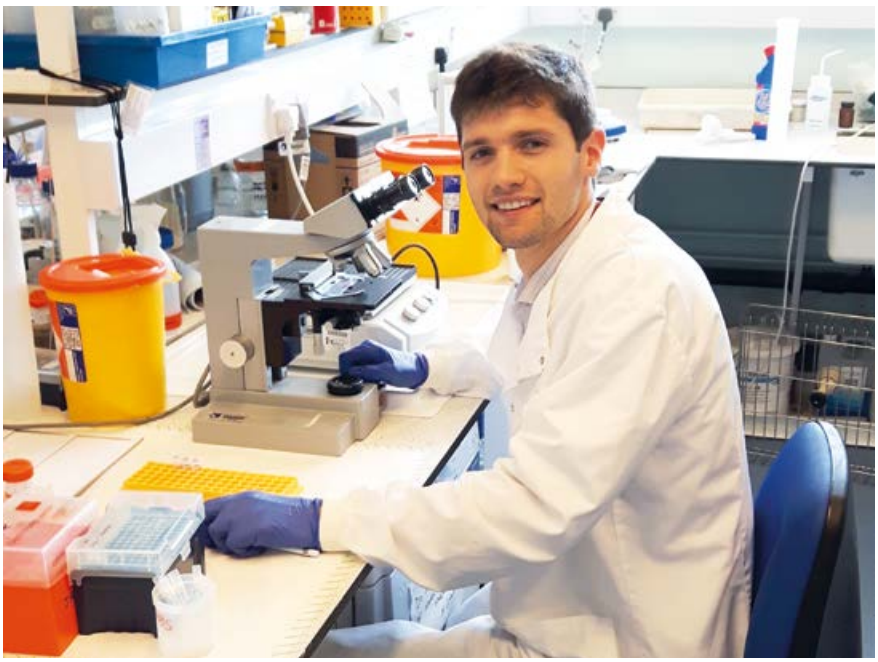
SITE OF WORK:
Southampton General Hospital, Southampton, Hampshire

During my intercalation year, the generous award from the Royal College of Surgeons of England enabled me to undertake a Master's degree in medical science in the Clinical Neurosciences Department at Southampton General Hospital.

The award allowed me to conduct a project that investigated the potential use of neural stem cells as a line of therapy in traumatic brain injury. More specifically, this involved using a range of laboratory techniques to mimic the processes that occur in traumatic brain injury and assess whether a specific molecule, called Sonic Hedgehog, was able to activate and stimulate the proliferation of endogenous neural stem cells.

I believe the skills that I have gained from this experience will provide me with a strong foundation to pursue a future career in academic surgery.

Therefore I would like to sincerely thank the College, and their funding partners, for their invaluable support.



Simon carrying out his research

The quantitative definition of the kynurenine pathway

TOBY BENJAMIN JAMES MURRAY

MEDICAL SCHOOL:
University of Edinburgh Medical School

SITE OF WORK:
Queens Medical Research Institute, Royal Infirmary of Edinburgh, Edinburgh. Scotland

The award provided fantastic support during my MScR in Surgery degree at the University of Edinburgh. I investigated the flux of tryptophan metabolism through the kynurenine pathway. This pathway is important in the pathogenesis of inflammation and multi-organ dysfunction syndrome following severe acute pancreatitis.

Our aim was to define the flux of the pathway pre-clinically, using stable isotope tracers and analysing plasma samples using liquid chromatography tandem mass spectrometry. The analytical method developed this year has proven to be extremely sensitive and precise. We have managed to detect, and quantify, each main compound involved in the kynurenine pathway at extremely low concentrations.

We have defined the rates of formation for the main compounds, along with identifying their metabolism, distribution and excretion parameters.

I am extremely grateful to the College for their support, this year has been an incredible experience and has cemented my desire to pursue a career in academic surgery.

Toby with the Deputy Lab Manager, Mr George Just who assisted with the development of the mass spectrometry assay. Behind is the liquid chromatography tandem mass spectrometry system we used

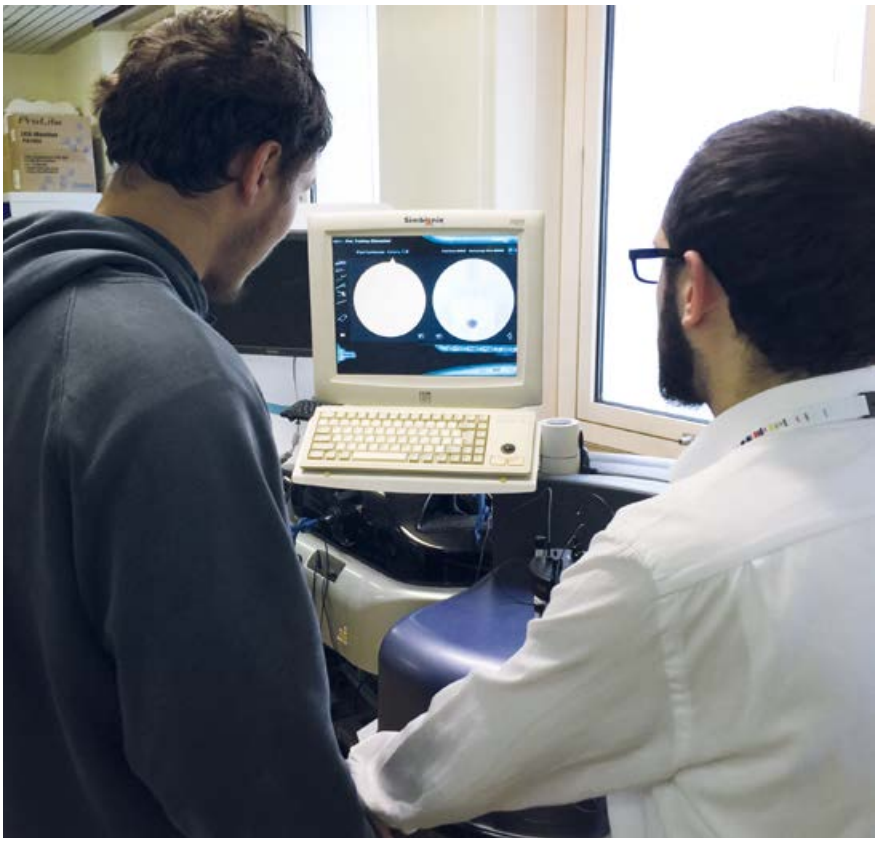
Multi-centre validation of simulation-based ureteroscopy curriculum – prospective study

AHMED MOHAMED ABDEL SHAFI

MEDICAL SCHOOL:
King's College London

SITE OF WORK:
MRC Centre for Transplantation, NIHR Biomedical Research Centre – King's College London, 5th Floor Tower Wing, Guy's Hospital, London

This was a year full of opportunity that I used to explore aspects of surgery and start to plan for the future aiming to pursue a career in surgery. I gained skills in basic surgical skills, laparoscopic skills, and virtual simulators. I was also able to spend time at the Royal Veterinary College, for part of my surgical anatomy project, which included comparing the difference between human and animal hearts and their possible use in heart transplant in the future. I had an article based on my BSc project accepted to The Surgeon Journal, 'The Role of Simulation in Urological Training – A Quantitative Study of Practice and Opinions', and I am preparing more articles to get published. I am truly grateful for the financial support that made it all possible.



Ahmed with his supervisor Dr Abdullatif Aydin after being taught different urological procedures/skills using The URO Mentor virtual reality simulator

Development of novel small-molecule inhibitors of Orai1

TITTU THOMAS

MEDICAL SCHOOL:
University of Leeds

SITE OF WORK:
Leeds Institute of Cardiovascular and Metabolic Medicine, Leeds

Vascular smooth muscle cell remodelling can lead to cardiovascular diseases including atherosclerosis and vascular aneurysms and the pathological process underpinning remodelling has been previously established; however there is no medication currently targeting remodelling. During my intercalated year I undertook a project aimed at developing novel inhibitors targeting this process.

With the generous support from the Royal College of Surgeons, the award was utilised to purchase consumables for tissue culture and Flexstation experiments, necessary to investigate and develop the multitude of compounds available. My project concluded with identifying three compounds with the potential for clinical use in the future.

Tittu using the FlexStation to analyse results with Dr Marc Bailey

I would like to thank the College for the grant which made it possible for me to conduct this project and introduce me to the world of novel research.

Development and validation of a cognitive training tool for laparoscopic surgery

LAUREN WALLACE

MEDICAL SCHOOL:
King's College London

SITE OF WORK:
Guy's Hospital, London

During my intercalated year I undertook a project focused on an exciting new approach to surgical training. Cognitive training, or the use of psychological processes to enhance performance of skilled behaviour, has proven valuable in the disciplines of sports and aviation, and has great potential as a method for training surgical skills.

My dissertation project, supported by the Royal College of Surgeons, sought to design and test a cognitive training tool to teach laparoscopic suturing. Following literature review and expert consultation, we produced a unique new tool that utilised different types of cognitive training. Results comparing the developed tool to traditional teaching methods were extremely positive, with technical skills being considerably improved in those participants using the tool.

Lauren supervising one of the study participants as they carry out a laparoscopic suturing task

Our research demonstrated that cognitive training can be an effective method for surgical skills training and paves the way for it to play a greater role in the future of surgical education.

Elective Prize Reports

The Elective Prize in surgery is awarded to clinical students at a UK medical school wishing to pursue a career in surgery and planning to undertake their elective attachment in surgery in the developing world. Each award is worth up to £500.

Ernest Chew
Keiran David Clement
Anna Craig-McQuaide
Graeme Downes
Francesco Fiorini
Zahra Jaffry
Caitlin MacLeod
Kyung-Hoon Moon
Seneka Nakagawa
Daniel Nash
Denise Osei-Kuffour
Vincent Quan
Alistair Reed
Rosa Sun
Patrick Hickland
Ankur Khajuria

Paediatric trauma and orthopaedics – a Cape Town experience

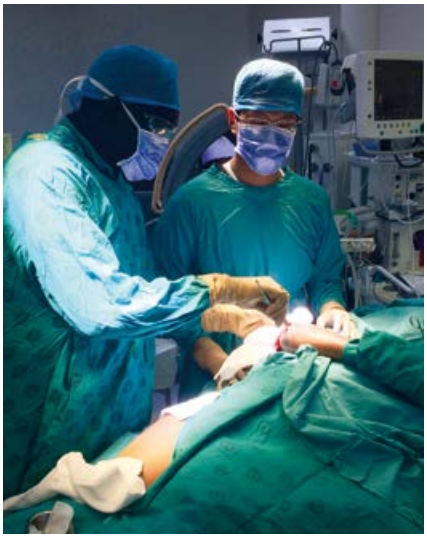
ERNEST CHEW
PREISKEL ELECTIVE

MEDICAL SCHOOL:
University College London

SITE OF WORK:
Red Cross Children's Hospital & Maitland Cottage Orthopaedic Hospital, Cape Town, South Africa

My elective was an awe-inspiring experience. It strengthened my surgical knowledge pertaining to childhood orthopaedic conditions and gave me a better understanding of how these diseases can drastically affect a child's quality of life. I was an active team member assisting in many operations, managing patients in the trauma unit and being involved in fracture and post operation clinics. The most inspirational moment for me was following up a previously disabled child learning to walk again after surgery. This has further re-enforced my enthusiasm for the speciality and the lessons learnt will stay with me throughout my career.

A ward round at Maitland Cottage Hospital



Ernest (on the right) assisting in an operation at Red Cross Hospital

The spectrum of paediatric urology presenting to a tertiary centre in a low-income country

KEIRAN DAVID CLEMENT
PREISKEL ELECTIVE

MEDICAL SCHOOL:
University of Aberdeen Medical School

SITE OF WORK:
Queen Elizabeth Central Hospital, Blantyre, Malawi

I spent my elective within the paediatric surgical department of the Queen Elizabeth Central Hospital (QECH), Blantyre. I scrubbed in on numerous interesting cases including large intra-abdominal tumours and spina bifida repairs. I also completed two departmental audits while there, one on the spectrum of paediatric urology presenting to QECH, and another on the outcomes of children with gastroschisis, a commonly fatal disease. The amount of work being carried out with the lack of resources was staggering, and re-kindled my desire to volunteer in a low-resource setting in the future. I thoroughly recommend Malawi to other students.

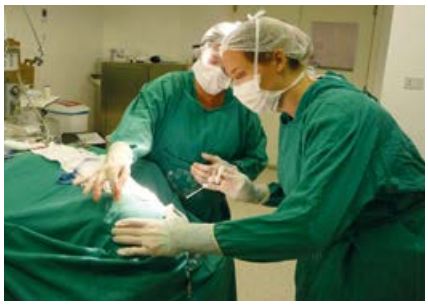
The outpatient department waiting area in QECH

Neurosurgery elective in Recife, Brazil

ANNA CRAIG-MCQUAIDE
PREISKEL ELECTIVE

MEDICAL SCHOOL:
Imperial College London

SITE OF WORK:
Hospital Pelópidas Silveira (HPS), Recife (Pernambuco), Brazil



Anna inserting a ventriculo-peritoneal shunt for the first time

My neurosurgery elective at Hospital Pelópidas Silveira, under the supervision of Dr Carolina Martins, was an invaluable experience. HPS is a new public tertiary hospital providing cardiology, neurology and neurosurgery services to a poor population and with limited resources. The staff were exemplary and I am indebted to them for all they taught me. This included invasive procedures (central lines, arterial lines, intubation and lumbar puncture). I assisted in theatre on a daily basis with a mixture of cases – elective and emergency, cranial and spinal, and I was given the opportunity to acquire many new surgical skills. It was a fantastic experience and one which confirmed my passion for neurosurgery.

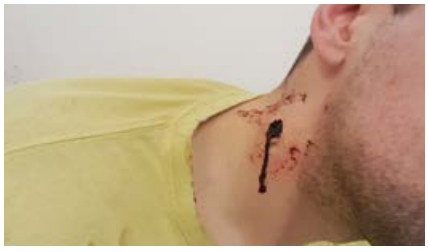
Anna with a post-operative patient and his family whom she assisted with his ten-hour tumour resection

Trauma care in Johannesburg

GRAEME DOWNES
RCS ELECTIVE

MEDICAL SCHOOL:
Imperial College London

SITE OF WORK:
Charlotte Maxeke Hospital/Baragwanath Hospital, Johannesburg, South Africa



Simulated gunshot patient

The elective student team

It was my aim that during my trip that I would get the chance to experience how healthcare is different in Johannesburg to the UK, due in part to the different financial constraints and greater numbers of seriously injured patients.

I also wished to gain first-hand experience of treating patients who had suffered traumatic injuries and to get a chance to become more familiar with the gold standard ATLS (advanced trauma life support) methodology.

I certainly learnt a great deal about the treatment of trauma patients and would recommend such an elective to any student interested in this area.

Trauma clerkship and outreach township clinics

FRANCESCO FIORINI
PREISKEL ELECTIVE

MEDICAL SCHOOL:
GKT School of Medicine at
King's College London

SITE OF WORK:
Groote Schuur Hospital,
Cape Town, South Africa

Medical electives are our best chance to immerse ourselves in a specialty that we intend to pursue and everything that comes with it: the people, values, and challenges. I spent mine in the busy trauma room of Groote Schuur hospital in Cape Town. In addition to scrubbing in on various emergency surgeries, it was an excellent opportunity to start developing some independence in clinical management and refine practical skills – from suturing complicated wounds to the occasional chest drain. Moreover, volunteering at student-led township clinics offered great insight into the local public health and social needs. This was a truly phenomenal experience, which I definitely recommend to fellow students and thank the RCS for its generous award.

Francesco (far right) in the trauma room at Groote Schuur hospital, with some great local and elective medical students

Trauma and general surgery in Empangeni, South Africa

KYUNG-HOON MOON
PREISKEL ELECTIVE

MEDICAL SCHOOL:
Imperial College School of Medicine

SITE OF WORK:
Ngwelezana Hospital, Empangeni,
South Africa

For my elective, I travelled to the land of African warriors, Kwa-Zulu Natal in South Africa. I spent six weeks in general surgery at Ngwelezana Hospital. It was an incredible experience with great teachings. I had a lot of theatre time as the second surgeon and learnt that patience at times of stress is an important surgical skill. I also conducted a retrospective study looking at recovery of trauma patients and organised teaching for nurses on resuscitation equipment.

This placement gave me the confidence that I needed before starting my first job and I strongly recommend Ngwelezana for other future trauma surgeons.

Hoon teaching nurses on resuscitation equipment during lunchtime

Hoon (middle) with the general surgery theatre nurses

Perspectives of global surgery: Malawi and the World Health Organisation

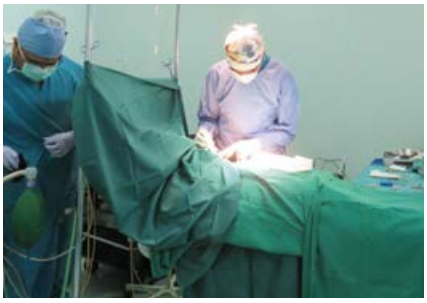
ZAHRA JAFFRY
PREISKEL ELECTIVE

MEDICAL SCHOOL:
King's College London

SITE OF WORK:
Beit Cure International Hospital, Blantyre, Malawi and The World Health Organisation, Geneva, Switzerland

My elective has been an incredible experience. In Malawi, I had the opportunity to see, first-hand, the problems with access to safe and good quality surgical care and how successful projects such as the Beit Cure International Hospital can be. Efforts in addressing the problem were happening on an even larger scale during my time as an intern at the World Health Organisation. Throughout, I was able to develop both clinical and academic skills, assisting in theatre and learning about a range of orthopaedic conditions as well as working on projects in global surgery. It was life-changing.

Interns at the World Health Organisation, Geneva, Switzerland



Theatres at the Beit Cure International Hospital, Blantyre, Malawi

Surgery for children with cardiac disease at the Aswan Heart Centre, Egypt: a medical student's perspective

CAITLIN SARA MACLEOD
PREISKEL ELECTIVE

MEDICAL SCHOOL:
University of Aberdeen

SITE OF WORK:
Aswan Heart Centre (also known as the Magdi Yacoub Heart Foundation), Aswan, Egypt

My elective at the Aswan Heart Centre (AHC) was one of the best experiences of my life. Further to the fantastic abundance of learning opportunities in adult and paediatric cardiology clinics, catheterisation lab, on the wards and in theatre, what struck me most was the human experience. The AHC is the tertiary referral centre for cardiac conditions, serving all of Egypt and the surrounding area, providing world-class care free of charge to those in need. Parents travel hours or even days, commonly in a cramped, sweltering mini-bus, to reach the AHC, which often is the only hope to the save the life of their child. I cannot fully express how tremendously privileged and humbled I am to have met those that I did at the AHC, witnessing the journeys of patients and their families from diagnosis to treatment and recovery, not to mention the remarkable industry and teamwork of the staff. I was also fortunate enough to meet the extraordinary man who has deeply inspired and motivated me: Professor Sir Magdi Yacoub. This opportunity has only affirmed my desire to become a surgeon, and my determination to add what I can to life, in any small way – so I offer my unreserved gratitude to those who helped to make this exceptional experience a reality.

The truly phenomenal staff of the Aswan Heart Centre

Caitlin with staff nurse Amany and a 21-day-old boy following an arterial switch operation

General surgery in Kingston, Jamaica

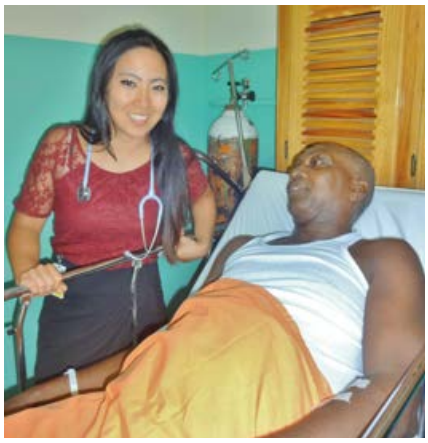
SENEKA CHOI NAKAGAWA
RCS ELECTIVE

MEDICAL SCHOOL:
University of Nottingham

SITE OF WORK:
University of the West Indies (UWI) Hospital, Kingston, Jamaica

I carried out my medical elective at the UWI hospital in Jamaica, where I clerked patients, attended ward rounds, surgeries and clinics. The majority of surgical patients were admitted due to road traffic accidents and abdominal emergencies, however a large number were also admitted due to stabbings and shootings.

My elective allowed me to see a range of interesting cases, and gave me a lot of hands-on experience, while making me appreciate the difficulties faced when practicing medicine in a developing country. I thoroughly enjoyed my time in Jamaica and would highly recommend it to anyone as an elective destination.



Seneka clerking patients prior to elective surgery

Doctors and medical students Seneka worked with

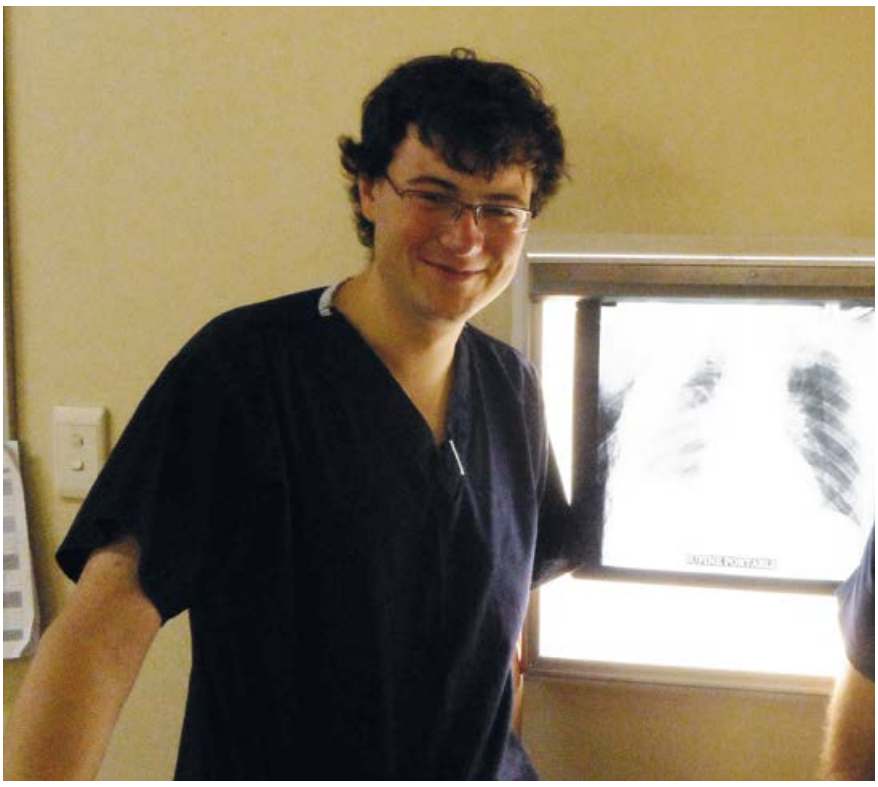
Trauma and orthopaedics at Baragwanath Hospital in Johannesburg

DANIEL NASH
RCS ELECTIVE

MEDICAL SCHOOL:
Peninsula College of Medicine and Dentistry

SITE OF WORK:
Chris Hani Baragwanath Academic Hospital in Johannesburg, South Africa

I undertook my elective in Trauma and Orthopaedics at Chris Hani Baragwanath Academic Hospital in Johannesburg, South Africa. I spent four weeks in trauma and four in the orthopaedic department observing operations, attending ward rounds and clerking patients. In the trauma department there were opportunities to extensively practise clinical skills such as arterial blood taking, cannulation, suturing and more, as well as to become involved with resuscitations. In orthopaedics I saw many conditions that are uncommon in the UK, for example spinal tuberculosis and untreated clubfoot, and was also able to examine a large number of X-rays.



Daniel at Baragwanath Hospital

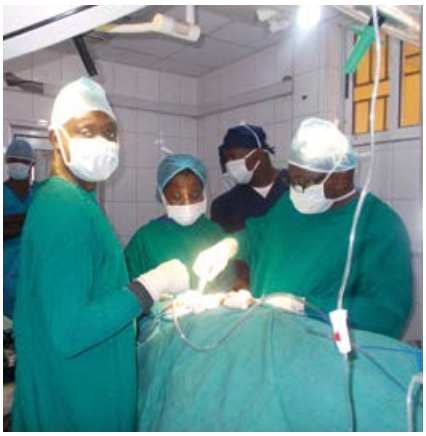
Surgical elective in plastic surgery and cleft lip and palate surgery

DENISE OSEI-KUFFOUR
PKK ELECTIVE

MEDICAL SCHOOL:
Imperial College London

SITE OF WORK:
Komfo Anokye Teaching Hospital (KATH), Kumasi, Ghana

My elective took place in Kumasi, Ghana in the joint specialities of Plastics and Maxillofacial surgery. There was ample opportunity to observe both specialities whilst attending weekly clinics, ward rounds and theatre. I learnt about the multidisciplinary management of cleft lip and palate in clinic and observed the complex surgery involved. I gained further experience of the breadth of reconstructive work undertaken by plastic surgeons from burns to neoplasms to congenital anomalies and the humanitarian role of the speciality. It was enlightening to observe and discuss the similarities and differences in healthcare provision, and I would thoroughly recommend this elective.



Denise (centre) assisting in maxillofacial theatre with Dr Michael Yelibora (right) and Dr Kofi Bedu-Addo (left)

Plastic surgery ward round at Emergency Centre. Denise (centre) with Dr Emmanuel Adu (far left), Dr Yaw Asiedu Anokye (left) and Dr Robert Sagoe (right)

General surgery in Johannesburg

VINCENT QUAN
RCS ELECTIVE

MEDICAL SCHOOL:
Barts and The London School of Medicine and Dentistry

SITE OF WORK:
Chris Hani Baragwanath Academic Hospital, Johannesburg, South Africa

The CHBAH Surgical Pit where we saw acutely unwell surgical patients

Middle of the night vascular surgical emergency

I travelled to Johannesburg to complete my medical elective in general surgery, a city famous for its surgical and trauma training. During my time there I spent time on ward rounds, assisting in theatres and often did 27-hour shifts in the surgical pit where all surgical emergencies are handled. This elective has allowed me to gain a great deal of hands on experience and work in the pit allowed me to broaden my experience beyond that of general surgery. I aim to bring back the confidence that Baragwanath has instilled in me back to the NHS.

Plastic surgery and trauma in India and general surgery in Zambia

ALISTAIR REED
PKK ELECTIVE

MEDICAL SCHOOL:
The University of Oxford

SITE OF WORK:
Postgraduate Institute of Medical Education and Research (PGIMER), Chandigarh, India and Monze Mission Hospital, Monze, Zambia

Alistair with surgical colleagues in the theatre coffee room at PGIMER

Alistair teaching the basics of chest radiography to nursing students at Monze Missions Hospital

At PGIMER, I immersed myself in the busy plastic surgery department spending time on the wards, in clinics and theatres. In the trauma unit I saw many cases of severe trauma from road traffic and construction-related injuries, which highlighted the urgent assessment and initial care of critically ill patients.

At a small mission hospital in Zambia, I took an active role in surgical patient care. Resources were limited, but working without investigations provided a fantastic opportunity to develop my clinical skills.

Overall, my elective was an inspiring, humbling and memorable experience and I have made lasting links for the future.

An elective in trauma and neurosurgery, Johannesburg

ROSA SUN
RCS ELECTIVE

MEDICAL SCHOOL:
University of Cambridge

SITE OF WORK:
Chris Hani Baragwanah Hospital, Soweto, Johannesburg, South Africa

I completed an elective in trauma and neurosurgery in the biggest government hospital in Johannesburg. I set out to learn traumatology from the world leading experts, and also wished to witness the variety of exaggerated pathology Africa had to offer.

Johannesburg offered even more than I could wish for. With a massive caseload, I worked day and night shifts assisting in surgery and resuscitating major trauma

First patient on Sunday morning

patients. This was the best two months in my medical training thus far, and I would fully recommend to those who are not faint-hearted.

Paediatric orthopaedics

PATRICK HICKLAND

MEDICAL SCHOOL:
University of British Columbia

SITE OF WORK:
British Columbia Children's Hospital

My final year elective in British Columbia Children's Hospital was extremely rewarding. As an orthopaedic intern, I had newfound responsibilities; lengthy surgeries seemed shorter as I was involved throughout, and clinics more educational because I assessed patients independently. My time on call acutely managing fractures was exciting but also difficult, in discovering non-accidental injuries. Fortunately my supervisors were quick to help, and their tutorials and ad hoc discussions were enlightening. Having chosen this elective due to a similar healthcare system to the UK, I have no doubt that my experience will help me in my future practice as a surgeon.

Patrick still smiling at the end of a lengthy scoliosis surgery

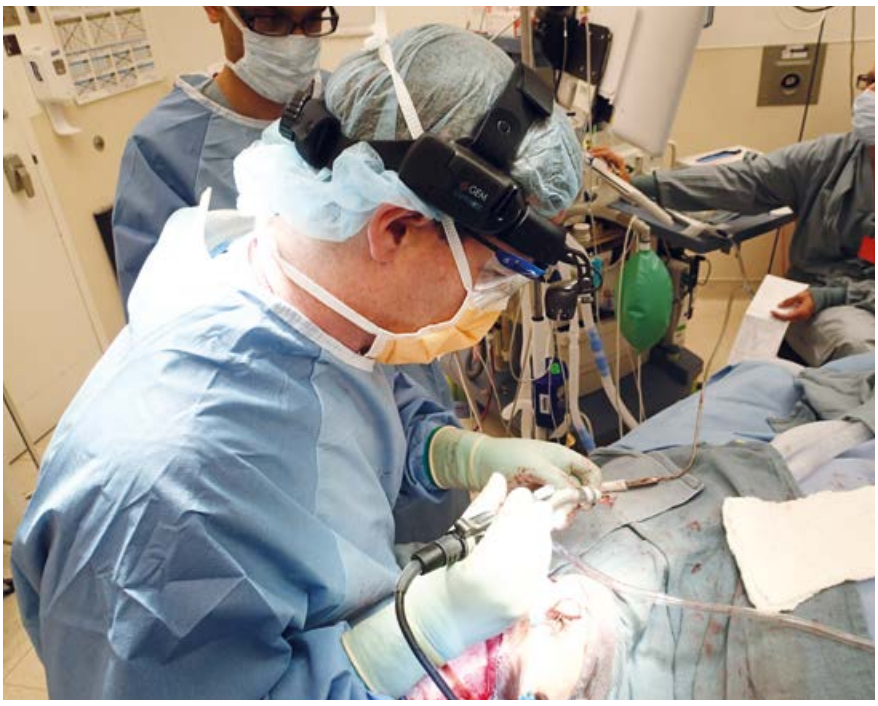
Plastic and reconstructive surgery sub-internship

ANKUR KHAJURIA

MEDICAL SCHOOL:
Harvard Medical School

SITE OF WORK:
Brigham and Women's Hospital,
Boston, USA

I undertook a Plastic and Reconstructive Surgery sub-internship at Harvard Medical School. Team rounds started at 5.30am every day, followed by assisting in cases in theatre with ample opportunities for wound closure using sutures, and teaching on anatomy/ operative techniques. I also taught anatomy to 3rd year Harvard students. I witnessed exemplary teamwork and operative skills in challenging eight to ten hour procedures and in turn enhanced my knowledge and technical skills. I was also able to establish research collaborations; I am currently leading a project on national guidelines implementation in the US. I would highly recommend this sub-internship to others interested in Plastic Surgery.



Ankur assisting in a craniofacial case in the Operating Room

Hunterian, Arris & Gale, Arnott, Zachary Cope, Joseph Toynbee & Lionel Colledge Memorial Lectures 2015/16

Hunterian	Mr KM John Chan, SCTS, Birmingham, 25th March 2015 Pathophysiology and surgical treatment of functional ischaemic mitral regurgitation
The Lionel Colledge Memorial Lecture	Mr Jonathan Bernstein – BACO Meeting, Liverpool, 8-10th July 2015
Hunterian	Mr Richard Shaw, BAOMS ASM, Liverpool, 23rd July 2015 Nature or Nurture? The Epigenetics of Head & Neck Cancer
Hunterian	Mr Michael Douek, BASO/RSM, London, 2nd November 2015 Magnetic technique for sentinel node biopsy in cancer surgery
Joseph Toynbee Memorial Lecture	Dr Lloyd Minor – RSM, London, 6th November 2015
Hunterian	Mr David Leonard, BAPRAS, Birmingham, 25th November 2015 Transplant Tolerance for Vascularized Composite Allotransplantation through Induction of Stable Hematopoietic Mixed Chimerism in a Clinically-relevant Large Animal Model
Hunterian	Dr Ernest Azzopardi BAPRAS, Birmingham, 27th November 2015 Multidrug resistant burn wound infection: establishing the causative profile and novel translatable theranostic strategies
Zachary Cope Memorial Lecture	Mr John Hunt – SARS, RCS London, 6th January 2016
Hunterian	Professor Dileep Lobo, SARS, RCS London, 7th January 2016 Experiments in fluid and electrolyte pathophysiology: Effecting change in clinical practice
Arnott	Mr Pankaj Chandak, BTS Meeting, Glasgow, 24th February 2016 Living Donor Transplantation - a journey from open to minimally invasive nephrectomy
Arris & Gale	Mr Jonathan Hyam, SBNS, Gordon Holmes Prize neuroscience meeting, RSM, London, 28th April 2016 Using Surgery to Identify the Neural Anatomy Governing Cardiovascular and Respiratory Physiology
Hunterian	Mr Christopher Gibbons, BOOS annual meeting, Dublin, 20th May 2016 Orthoplastic Reconstruction in Sarcoma Surgery
Hunterian	Mr Peter Thompson – BAUS Academic Urology annual meeting, Liverpool, 27th June 2016 The difficulty interpreting endotoxaemia post transrectal prostate biopsy
Hunterian	Mr Stephen Price, SBNS, Telford, 21st September 2016 Local Control of Glioblastomas: Lessons from John Hunter and Advanced MR Imaging of the Peritumoural Region
Hunterian	Mr John Greenwood, BAPRAS Winter Scientific Meeting, London, 24th November 2016 The Evolution of Acute Burn Management – Retiring The Split Skin Graft

Fundraising in focus

Make a donation or leave a legacy to Surgical Research

Research at the College relies exclusively on voluntary income that has been gifted through donations, legacies and grants. We need your help if this work is to continue and flourish. Future innovations in surgery will continue to be driven by research and surgical research continues to provide significant advances in a wide range of areas.

Currently we are unable to support 80% of those applying for research grants due to lack of funds. **If you would like to make a donation or discuss a legacy, please contact the College's Development Office on 0207 869 6086, or by email at fundraising@rcseng.ac.uk**

Grants are not restricted to research fellowships and we are delighted to discuss opportunities to encourage and develop the potential of young surgeons through education, training and research by way of travel and educational grants or annual prizes and awards.

Funding Partnerships:

- Addenbrooke's Charitable Trust
- Association of Breast Surgery
- Association of Coloproctology of Great Britain & Ireland
- Association of Upper Gastrointestinal Surgeons of Great Britain & Ireland
- Ballinger Charitable Trust
- Bowel Disease Research Foundation
- Breast Cancer Now
- British Association of Endocrine & Thyroid Surgeons
- British Association of Paediatric Surgeons (BAPS)
- British Association of Plastic, Reconstructive & Aesthetic Surgeons (BAPRAS)
- British Association of Surgical Oncology (BASO)
- British Orthopaedic Association (BOA)
- British Society of Endovascular Therapy (BSET)
- British Society of Surgery of the Hand
- Cancer Research UK
- Colin and Anna Frizzel Charitable Trust
- Colledge Family Fund
- Dinwoodie Charitable Company
- Dunhill Medical Trust
- Edwin George Robinson Charitable Trust
- Eido Healthcare Limited
- Enid Linder Foundation
- ENT UK
- Facial Surgery Research Foundation (Saving Faces)
- Frances & Augustus Newman Foundation
- Freemasons Fund for Surgical Research
- Get A Head Charitable Trust
- George Drexler Foundation
- Golden Bottle Trust
- Henry Lumley Charitable Trust
- Mary Kinross Charitable Trust
- McKinsey
- Michael & Anna Wix Charitable Trust
- Miss N Shotts FDSRCS
- National Joint Registry
- Orthopaedic Research UK
- Philip King Charitable Settlement
- PKK
- Prostate Cancer UK
- Reuben Foundation
- Rosetrees Charitable Trust
- Sahlgrenska Hospital, Gothenburg
- Shears Foundation
- Vascular Surgical Society of Great Britain & Ireland
- Virginia Mason Hospital, Seattle
- Wellington Hospital
- Welton Foundation
- Wyndham Charitable Trust

Endowments, restricted and legacy funds:

- Anderson Reid Fund
- Annie Julia Speight Legacy
- Albert Pomfret Legacy
- Barlow Research Fellowship
- Bernhard Baron Fund
- Black Legacy
- Blond McIndoe Fund
- Buckston Browne Gift
- Burghard Bequest
- Carol Rummey Legacy
- Cicely Fay Simpson Legacy
- Dennis F Clark Legacy
- Doris K King Legacy
- Dr Shapurji H Modi Memorial ENT Research Fund
- Edward Lumley Fund
- Eleanor M Heslop Legacy
- Gwendoline Shrimpton Legacy
- Harold Bridges Bequest
- Harry S Morton Fund
- John L Williams Legacy
- Laming Evans Research Fund
- Lea Thomas Fund
- Lillian May Coleman Legacy
- Osman Hill Collection & Research
- Parks Visitorship
- Patricia Constance Curry Legacy
- Philip & Lydia Cutner Legacies
- Renee Recheal Liebesny Legacy
- Shirley M Kanaar Legacy
- Sir Arthur Sims Fund
- Sorab (Soli) Jamshed Lam Legacy
- Tudor Edwards Fellowship
- Vandervell Research Fund


1


2


3


4


5


6

7


8


9


10


11

Picture gallery

International surgical skills workshops

1 Bill Thomas teaching in Addis Ababa
2 Bynvant Sandhu demonstrating suturing in Addis Ababa
3 Derek Alderson teaching in Guatemala
4 Tom Pinkney teaching in Guatemala
5 Rhiannon Harries teaching knot tying in Veracruz
6 Derek Alderson teaching in Veracruz
7 The Faculty in Veracruz

Society of Academic and Research Surgery (SARS)
2017 meeting in Dublin

8 Professor Michael Kerin delivering the John Farndon Lecture
9 Professor Monty Mython & Professor Mike Grocott from the Royal College of Anaesthetists
10 Delegates from Belfast
11 Professors Dion Morton, Arnie Hill and Derek Alderson
12 Professor Sir John Temple delivering the BBA lecture

Miscellaneous

13 Professor Harold Ellis celebrating his 90th birthday at the College with former Westminster Hospital Nurses
14 Professor Malcolm Reed and Clare Marx at Brighton Medical School
15 Martyn Coomer with the Fulbright Scholars Harveer Dev and Katherine Gash before they went to the States, at a Fulbright Reception at Lancaster House
16 2015/16 Research Fellows Vanessa Brown, Mohammed Chowdhury, Tom Wiggins & Peter Szatmary with the Trustees of the Freemasons' Research Fund at their annual meeting at the College

You can make a difference.

We need to develop our surgeons through training and research opportunities so that they excel and fulfil their potential and provide the highest standards of patient care.

Future innovations in surgery will continue to be driven by research and surgical research continues to provide significant advances in a wide range of areas.

Research at the College relies almost exclusively on legacies, gifts and donations. We need your help if this work is to continue and flourish. Making a will is a significant personal responsibility and the people and causes you remember in your will are a positive recognition of all that is important to you.

We understand that the welfare and concern for your family and friends comes first. Just as a will brings security to those closest to you, a legacy to the Royal College of Surgeons plays a crucial role in maintaining and supporting the improvement of surgical care for patients.

For more information or an informal chat about a legacy to the College, please contact us at fundraising@rcseng.ac.uk or call 020 7869 6086.

Royal College of Surgeons
ADVANCING SURGICAL CARE

For information on donating
visit **www.rcseng.ac.uk/donate**
email **fundraising@rcseng.ac.uk**
or call **020 7869 6086**

To contact the research department
email **research@rcseng.ac.uk**
or call **020 7869 6614**

The Royal College of Surgeons
@RCSnews