

SURGICAL RESEARCH

REPORT

2015/16



Members of the Academic and Research Board

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CHAIRMAN'S INTRODUCTION



Derek Alderson
Chairman, Academic
and Research Board

Interest in research seems to be at an all-time high. Applications for RCS fellowships are increasing and the clinical trials initiative continues to develop. The National Institute for Health Research (NIHR) call for surgical trials resulted in nearly £28 million being awarded. Much of this expansion in research activity reflects the growing enthusiasm among the trainee collaboratives that exist now on either a regional or national basis in virtually every surgical specialty. The 5 surgical trials centres have all made significant progress and along with the 15 surgical specialty leads (almost every specialty has one), there is every sign that more new surgical trials are likely to be initiated in 2015 and beyond.

This expansion inevitably makes demands of the Research Committee and the Development Office to find the necessary funds to support this increased activity. Martyn Coomer and Johnny Fountain continue to promote all aspects of research, encouraging financial contributions through research evenings with potential donors across the UK. The College is grateful to them for the many evenings given up for fundraising, and to our research fellows who make presentations at these events. New funds this year include specific donations for research in obesity (The David Johnston Research Award) and surgical simulation (The Dinwoodie Charitable Company) along with partnership funding involving the British Association of Paediatric Surgeons, the National Joint Registry, the

Circulation Foundation and the British Association of Plastic, Reconstructive and Aesthetic Surgeons. Once again there have been increased donations from Freemasonry and the Dunhill Medical Trust, two of our longest-standing and most generous benefactors.

To date we have concentrated on our research fellowships as a means of helping trainees achieve more substantial sources of funding towards an appropriate higher degree, and the clinical research initiative has focused on the development of clinical trials mainly to encourage surgical leadership for randomised controlled studies. Regarding research fellowships, the scheme is clearly successful. Two Fulbright fellowships to undertake research at the MD Anderson Cancer Center in Houston and Harvard University, Boston were awarded this year. Virtually every trainee who has received an RCS fellowship has gone on to achieve further funding. Some 40% of awards have resulted in a PhD. The clinical trials initiative has resulted in 15 new trials in surgery being added to the NIHR portfolio in the last year. These success stories do, however, have inevitable consequences that need to be addressed.

The increasing interest in undertaking research as part of surgical training creates a number of practical difficulties. While some trainees may choose to undertake research during core training, most request 'out-of-programme' time during specialist training. Increasingly, trainees are encouraged to undertake PhD as the higher degree. This may be problematic if large numbers of trainees within a discipline opt for this, within the current training system. While all surgeons benefit from exposure to research, some will enjoy the rigour of a PhD while others are more likely to be suited by a more clearly defined programme of shorter duration. There are practical solutions, but these require liaison between training committees, trusts and universities to accommodate trainees undertaking research to do on-call rotas. This would help those still in clinical training to gain greater experience of elective surgery as they could be freed from excessive on-call commitments and eliminate contrived rotas that limit day-time continuity of care. Some on-call work, shared by trainees doing research, would allow them to maintain their clinical skills.

The success of the clinical trials initiative has accelerated the next stage of our research development programme. The introduction of new technologies, translational studies that bring laboratory based work to the bedside and bringing novel devices through to clinical application are all research areas that

precede the randomised trial. In addition, studies that explore the utility of diagnostic tests or evaluate prognostic factors are not tested in randomised trials. Surgeons are involved in all of these studies. The introduction of new technologies and novel devices are particularly problematic and many good ideas founder in a plethora of regulatory processes and difficulties accessing the correct funding stream. To address this, the College has proposed a technology evaluation programme that will work in a similar way to the clinical research initiative. Collaborations with existing and new partner organisations (NCRI, NICE, MHRA, ABHI, CRUK, MRC, IDEAL) will result in a common portal of entry for the introduction of new devices and technologies. By using the expertise of the existing trials centres and specialty leads, it is hoped that this route can provide a rapid and informed opinion regarding the need for a new device or technology, the degree of interest in its development and future use, and how it can be evaluated. Ideas that seem worthwhile can then be taken forward with more detailed proposals. Some may be industry funded, others will require grant support, but the system should be more efficient than the current situation.

It seems that we are entering a period where a culture of research as part of the surgeon's role is becoming more widely accepted. The College recognises the need to provide education for young researchers so that an understanding of clinical research methodology and participation in clinical trials, are seen as essential elements of training rather than optional extras. The training programme in trauma and orthopaedics now includes these elements within the curriculum and it is likely that other specialties will follow. A number of training days devoted to these areas have been organised by the trials units, for trainees at core and specialist levels this year. It is planned to make this training available nationally over the next 18 months.

An important, yet often poorly appreciated element in the

development of a clinical research proposal is formulating the right question and how best to answer it. This is heavily dependent on careful evaluation of existing evidence in a systematic fashion. In conjunction with the Clinical Effectiveness Unit, an Evidence Synthesis programme has been initiated to teach new investigators how to undertake this process correctly. Currently five systematic reviews are under way, covering topics in maxillofacial, ENT, hand, upper GI and neurosurgical disciplines.

What next? The momentum achieved by the clinical trials initiative must be maintained. Not all specialties began from the same point in terms of an existing or previous research culture, but there is an expectation that no specialty will fail to have a reasonable portfolio of trials in the future. We aspire to a situation where any patient attending a surgical clinic should have access to a study if they wish to participate in research. The success of the trials initiative, and the proposals to create a research pipeline from the laboratory through novel devices and technologies to randomised trials, has created interest across Europe. We believe that there are great advantages in an international approach to research, particularly for clinical trials. Hopefully, there will be news from our efforts in that area in 12 months. In the meantime, research will remain at the forefront of College strategy. The College acknowledges that these developments owe much to the drive and enthusiasm of our Director of Research, Professor Dion Morton, as well as the individuals from our partner organisations who provide oversight through the Clinical Research Initiative Steering Committee. Last, but by no means least, Sarah King and her team, who under the direction of Martyn Coomer, provide all of the administrative support to turn these plans into reality.

I'm sure all members of the surgical research community would join me in congratulating Norman Williams on being awarded a Knighthood in the recent New Years Honours.

AN IMPORTANT, YET OFTEN POORLY APPRECIATED ELEMENT IN THE DEVELOPMENT OF A CLINICAL RESEARCH PROPOSAL IS FORMULATING THE RIGHT QUESTION AND HOW BEST TO ANSWER IT.



Fellowships are awarded to subscribing fellows or 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.



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EXPANDING THE ORGAN DONOR POOL: PREVENTING BRAIN DEATH INDUCED KIDNEY INJURY



**MOHAMMED
ZEESHAN AKHTAR**

FELLOWSHIP/SPONSOR

Philip King Research Fellowship

SUPERVISORS

Professor Rutger Ploeg, Professor Christopher Pugh and Professor Susan Fuggle

SITE OF WORK

Old Road Campus, University of Oxford

PUBLICATIONS

1. Akhtar MZ, Sutherland AI, Huang H, Ploeg RJ, Pugh CW. The role of hypoxia-inducible factors in organ donation and transplantation: the current perspective and future opportunities. *American Journal of Transplantation*. 2014.

2. Rebolledo R, Liu B, Akhtar MZ, Ottens PJ, Zhang J, Ploeg RJ, Leuvenink HG. Prednisolone has distinct effects on the kidney and liver of brain dead rats. *Journal of Translational Medicine*. 2014.

PRESENTATIONS:

1. World Transplant Congress, San Francisco, USA, 2014.
2. International Meeting on Ischemia Reperfusion Injury, Poitiers, France, 2014.

FURTHER FUNDRAISING

Medical Research Council for two years.

1 out of 3 patients will either die or become too unwell to receive a life-saving organ transplant while on the waiting list.

Kidney transplantation has been one of the medical success stories of the last half-century. It is the treatment of choice for patients with end-stage renal failure, offering both an improvement in their quality of life and also extending life expectancy. For example, a patient on dialysis will visit hospitals 3 to 4 times a week for several hours. A transplant offers freedom from visiting hospital and allows patients to return to work and to lead a normal life.

However, the major challenge in transplantation is the expanding waiting list, which now means that 1 in 3 patients will either become too unwell or die while awaiting a life-saving transplant. To address this transplant, centres are turning to donors who previously would not have been considered suitable for transplant, including older donors with more medical problems. In addition, despite improvements in immunosuppression (drugs used to prevent rejection of organs), the length of time a kidney works for after transplantation has not improved in the past decade.

The aim of my research is to improve the quality and protect kidneys from braindead organ donors (our major source of kidneys for transplantation), thereby making previously *untransplantable kidneys transplantable and to allow the kidneys to work for longer after transplant*. Using a rat model of brain death, I have been characterising what molecules change in the kidney as a consequence of brain death process. The results have indicated that the way that energy production and metabolism occurs in kidney cells is drastically altered, leading to them being more prone to damage, even before the organs are removed for transplantation.

This has led to further work to determine if we can protect

the kidneys by using novel drugs. This is a very new area of research that has real potential to result in expanding the number of kidneys available for transplantation. There is also a possibility that by protecting the kidneys at an early stage, we can make kidneys work for longer.



Operating with a cardiothoracic surgeon and a urological surgeon to remove a renal tumour extending into the inferior vena cava and right atrium.



The Consortium on Organ Preservation includes Professor Sir Peter Morris, Professor Rutger Ploeg, Professor Jacques Pirenne, Professor Tom Minor and Professor Andrea Paul.

INCIDENCE AND MECHANISMS OF CEREBRAL ISCHAEMIA FOLLOWING TRANSCATHETER AORTIC VALVE IMPLANTATION COMPARED WITH SURGICAL AORTIC VALVE REPLACEMENT



**AIMAN
ALASSAR**

FELLOWSHIP/SPONSOR

Hong Kong Freemasons' Fund for Surgical Research

SUPERVISOR

Professor Marjan Jahangiri and Professor Hugh Markus

SITE OF WORK

St George's University of London

PUBLICATIONS

1. European Association of Cardiothoracic Surgery Annual Meeting 2013, Vienna, Austria
2. Society of Cardiothoracic Surgery in Great Britain & Ireland Annual Meeting 2014, Edinburgh,

PRIZES

Ronald Edwards Prize, Best Oral Scientific Presentation, Society of Cardiothoracic Surgery in Great Britain and Ireland Annual Meeting 2014, Edinburgh.

PRESENTATIONS:

1. European Association of Cardiothoracic Surgery Annual Meeting 2013, Vienna, Austria
2. Society of Cardiothoracic Surgery in Great Britain & Ireland Annual Meeting 2014, Edinburgh,

FURTHER FUNDRAISING

Medtronic for 2 years.

Aortic valve narrowing is a common form of heart valve disease affecting up to 10% of people over age 75.

Transcatheter Aortic Valve Implantation (TAVI) is now considered standard of care in inoperable patients with severe aortic stenosis and as an alternative to aortic valve replacement (AVR) in those deemed high risk for surgery. However, neurological injury is significantly higher in patients undergoing TAVI compared with AVR. Different mechanisms have been proposed to account for this injury, mainly cerebral embolisation (particles that get dislodged to the brain) and hypoperfusion. The primary aim of this study was to compare the potential mechanisms of neurological injury following TAVI and AVR.

127 high-risk patients with severe aortic stenosis were recruited into the study, 85 of whom underwent TAVI and 42 underwent AVR. A range of outcomes were measured to assess cerebral embolism, cerebral oxygen saturation, cerebral lesions and cognitive function using transcranial Doppler, cerebral oximeter, MRI and neurocognitive assessment to give comprehensive profile of cerebral health.

We have shown that the number of cerebral emboli did not differ significantly between TAVI and AVR. There was no difference between the two groups in the incidence of cerebral desaturation. The cerebral desaturation during TAVI is mild and lasts for a short period of time with no effect on neurological outcomes. There was also no significant difference in the acute cerebral ischaemic lesions detected on MRI between TAVI and AVR. Interestingly, the majority of the lesions detected in our study resolved at three months follow-up scan. We have also shown that both groups showed better neurocognitive function at three months.

Our findings indicate that the incidence and mechanisms of



Aiman in theatre getting ready to perform neurological monitoring

neurological injury in patients undergoing TAVI are similar to those undergoing AVR. We suggest that less emphasis should be placed on the increased neurological injury associated with TAVI compared with AVR and, therefore, TAVI may be offered to moderate risk patients with severe aortic stenosis.

STRUCTURE-FUNCTION INSIGHTS INTO THE ANGIOPOIETIN-TIE2 SYSTEM



**DJAILIL
BAIOU**

FELLOWSHIP/SPONSOR

Joint RCS/Dunhill Medical Trust Fellowship

SUPERVISOR

Professor Nicholas Brindle

SITE OF WORK

University of Leicester

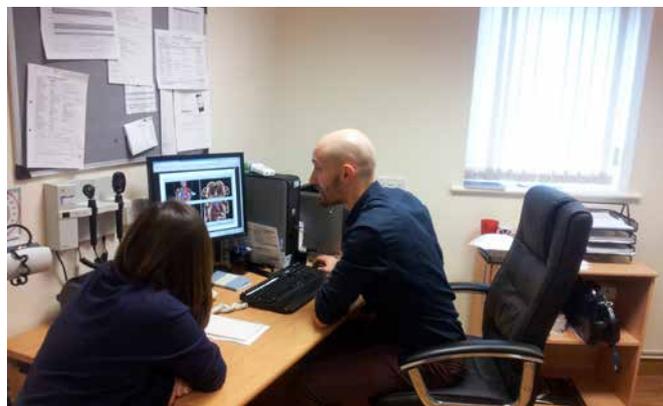
PRESENTATIONS

1. The European Society of Translational Medicine 2013
2. The European Society of Plastic and Aesthetic Surgeons 2014

Deaths from cancer rise with increasing age and the majority of cancer deaths occur in those aged over 65 (77%).



The research lab team at University of Leicester



Djailil in Clinic

Cancer causes more than one in four of all deaths in the UK. Often surgery offers the only cure; however, surgery may not be possible if the cancer has spread to other organs. This applies to many solid tumours, including breast, lung and prostate cancer.

Angiopoietin-2 (Ang2) is emerging as a key molecule in the growth and spread of cancer. Studies have found that blocking Ang2 can decrease the size and spread of cancer, as well as improve other conditions such as chronic inflammation and sepsis. A specific Ang2 blocker that could be administered to patients with minimal potentially harmful side effects does not exist yet.

Our study used computer modelling and a novel technique that accelerates the process of evolution to develop a drug that blocks Ang2. Using these methods a new drug was created called R3 which blocks Ang2 specifically.

Further attempts were made to improve R3 by making subtle alterations to it to better understand how it works. R3 was also combined with a potent detector of inflammation called Vascular Endothelial Growth Factor Receptor 1 (VEGFR1), which increases R3's efficacy and ability to target areas of inflammation and new blood vessel formation such as in cancer.

Test tube experiments have shown R3 to be effective and work has now begun on animal models of disease. Future work will concentrate on testing this new drug's ability to reduce inflammation and disruption of blood vessels as well as understanding how it works. Improvements in our understanding will help improve the health outcomes of future patients. We now have the first Ang2 specific trap, which could benefit the elderly suffering from advanced inoperable cancer, chronic wounds and sepsis.

SINONASAL EPITHELIAL INNATE IMMUNE SIGNALLING IN CHRONIC RHINOSINUSITIS



STEPHEN BALL

FELLOWSHIP/SPONSOR

Shears Foundation Northern Fellowship

SUPERVISORS

Professors Janet Wilson, Andrew Fisher and Derek Mann

SITE OF WORK

Institute of Cellular Medicine, Newcastle University Medical School

PUBLICATIONS

1. Stephen Ball, Anthony De Soya, Andrew Fisher, Derek Mann, Janet Wilson. Airway remodelling in chronic rhinosinusitis; is epithelial – fibroblast signalling to blame? *The Journal of Laryngology and Otology*, 2013.
2. Stephen Ball, Anthony De Soya, Andrew Fisher, Derek Mann, Janet Wilson. Are pro-inflammatory fibroblasts the driving force in chronic rhinosinusitis? *Clinical Otolaryngology* 2012; 37: 1–2.

PRESENTATIONS

1. Airway remodelling in chronic rhinosinusitis; is epithelial – fibroblast signalling to blame? Royal Society of Medicine, Section of Laryngology and Rhinology, London, February 2013.
2. Are pro-inflammatory fibroblasts the driving force in chronic rhinosinusitis? British Academic Conference in Otolaryngology, Glasgow, 2012.

PRIZES

1. Royal Society of Medicine, Section of Laryngology and Rhinology. Annual short paper prize. February 2013.

FURTHER FUNDING

Wellcome Trust Clinical Research Training Fellowship for three years

Chronic rhinosinusitis is one of our commonest conditions, affecting up to 12.5% of adults. Its disease mechanism is not understood and current medicines often fail, requiring surgical treatment.

The aim of our work is to advance the understanding of the mechanism of chronic sinusitis and ultimately drive the development of new sinusitis therapies in place of surgical procedures.

Nasal and sinus cells were harvested from participants undergoing operations for chronic sinusitis. Comparator healthy control cells were also isolated from participants undergoing keyhole pituitary gland surgery (a gland on the base of the brain) via the nose. Epithelial (nasal lining) cells

and fibroblast (supporting framework) cells were collected and grown in laboratory tissue culture conditions. Their identity was carefully characterised and verified using molecular biological techniques. Cells were stimulated with known environmental causes of sinusitis



Stephen with his supervisor Professor Janet Wilson in theatre recruiting research participants

including viruses, bacteria and oxidative stress particles. The inflammation response was studied in detail.

We have established and validated a cellular model to study the inflammatory relationship between two key cell types in the nose and sinuses. We have shown in sinusitis patients' cells for the first time that nasal surface (epithelial) cells can activate supporting fibroblasts. We think that these fibroblasts then promote further inflammation. These activated fibroblasts may be the key step when a patient starts to develop chronic sinusitis. Our model of the epithelial and fibroblast cell interactions allows me to go on to investigate how environmental insults may lead to the development of chronic sinusitis within my PhD fellowship.

The disease mechanisms of chronic rhinosinusitis have not been widely studied. This is probably reflected in the lack of new medical treatments for chronic rhinosinusitis during the past few decades. This RCS project will continue to develop following the award of a Wellcome Trust Research Training Fellowship for the next three years.

Our longer-term plan is to continue the project thereafter, with the ultimate aim of delivering clinical trials of novel therapies as an alternative to surgery for patients. The position of the nose and sinuses places them as ideal candidates for the development of locally applied medicines, and thus also avoid the problems of oral steroids or antibiotics, which are the current best available treatments.

THE ROLE OF THE AURORA FAMILY KINASES IN THE REGULATION OF THE CELL-CYCLE AND TUMOURIGENESIS



**RYAN
DAVID BARON**

FELLOWSHIP/SPONSOR

Freemasons' Fund for Surgical Research

SUPERVISOR

Professor Francis Barr

SITE OF WORK

Cancer Research Centre University of Liverpool and
Department of Biochemistry University of Oxford

PUBLICATIONS

1. Nunes Bastos R, Ghandi SP, Baron RD, Gruneburg U, Nigg EA, Barr FA. Aurora B suppresses microtubule dynamics and limits central spindle size by locally activating KIF4A. *J. Cell Biol.* 2013;202(4):605-21.
2. Hammond D, Zeng K, Espert A, Bastos RN, Baron RD, Gruneberg U, Barr FA. Melanoma-associated mutations in protein phosphatase 6 cause chromosome instability

and DNA damage owing to dysregulated Aurora-A. *J Cell Sci.* 2013;126(Pt 15):3429-40.

PRESENTATIONS

1. Baron RD, Nunes-Bastos R, Neoptolemos JP, Barr FA. United we stand, divided we fall – targeting mitosis to promote apoptosis. Invited Oral Presentation. CRUK Fellows Meeting. London. November 2012.
2. Baron RD, Nunes-Bastos R, Neoptolemos JP, Barr FA. Dissecting the role of Aurora B in the regulation of cell cycle progression. Invited Oral Presentation. CRUK Centre Meeting, Liverpool. May 2012.

FURTHER FUNDRAISING

Cancer Research UK Fellowship for three years

One in three people will die from cancer with one new person diagnosed every two minutes.

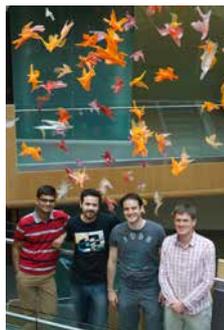


Starting the race for life at Aintree Racecourse

Understanding how cancer arises and continues to grow ignoring normal cellular control signals is therefore fundamentally important to our understanding of this disease process and will lead to novel future treatments. When cells divide they copy and separate their genetic material, DNA, exactly between the two daughter cells. This process of cell division is precisely controlled by protein kinases, which act as molecular switches ensuring the proper order of cell division. When this process goes wrong, cells can end up with the wrong number of chromosomes (aneuploidy), which is one of the hallmarks of cancer.



Laboratory tour with Amanda Harrington, a local model, columnist and star of *Desperate Housewives*



Research team featured in the *Journal of Cell Biology* editorial review of our recent paper, taken in the state of the art New Biochemistry Department, University of Oxford. Left to right: Sapan Ghandi, Ricardo Nunes-Bastos, Ryan Baron and Professor Francis Barr.

The Aurora Family of kinases is one of the major kinase families controlling this process. My project has characterised how Aurora kinase B is regulated in time and place during the various stages of the cell cycle using state-of-the-art biochemistry and molecular biology techniques including advanced microscopy, mass spectroscopy, and protein biochemistry. This has identified other proteins that interact with and are crucial for regulating the temporo-spatial activity of Aurora kinase B. These new interacting proteins are themselves potential drug targets that may be important in killing cancer. I have demonstrated that inhibiting Aurora kinase B, either directly or indirectly by targeting the proteins involved in its regulation, results in the controlled cell death (apoptosis) of cancer cells. This demonstrates that targeting this pathway may become a new approach to killing cancer.

Future work building on my project is ongoing. This will further characterise the molecular pathway and validate the interacting proteins involved as potential new drug targets to treat cancer.

IRON CHELATORS: THE NEXT GENERATION OF ANTI-NEOPLASTIC AGENTS IN COLORECTAL CANCER?



**MATTHEW
ROBERT
BEDFORD**

FELLOWSHIP/SPONSOR

H&S Charitable Trust

SUPERVISORS

Chris Tselepis and Professor Derek Alderson

SITE OF WORK

School of Cancer Sciences, University of Birmingham

PUBLICATIONS

Bedford MR, Ford SJ, Horniblow RD et al. Iron chelators in the treatment of cancer: A new role for Deferasirox? *Journal of Clinical Pharmacology* 2013; 53: 885–891.

PRESENTATIONS

1. Bedford MR, Evans S, Radulescu S et al. Iron chelation as a novel strategy for the treatment

of colorectal adenocarcinoma. Accepted for oral presentation at the Society of Academic and Research Surgery (SARS) annual meeting (Durham), January 2015.

2. Evans S, Bedford MR, Lal N et al. Iron metabolism in colorectal adenocarcinoma: A novel therapeutic target? Accepted for oral presentation at the Society of Academic and Research Surgery (SARS) annual meeting (Durham), January 2015.

More than 40,000 new people are diagnosed with colorectal cancer in the UK each year and the disease is responsible for almost 16,000 deaths annually. This research demonstrates that iron metabolism represents a promising therapeutic target in the treatment of this common cancer.

Bowel cancer is the fourth most common cancer in the United Kingdom. Surgical removal of the tumour is the primary treatment; chemotherapy, however, is also used in more advanced disease, albeit with variable success and significant side effects. The discovery of new agents effective against bowel cancer is therefore highly desirable.

Iron is crucial for the normal growth and function of cells. Insufficient iron results in anaemia; too much, however, can lead to ill health. Of note, there is now increasing evidence linking excess iron to cancer. This is not entirely surprising, given the plethora of processes iron is essential for, including DNA synthesis and ATP (energy) generation – both activities that are increased in cancer. A strategy to starve tumours of iron could thus serve as a novel therapy for the treatment of bowel cancer.

Iron chelators (drugs that remove iron from the body) are already used for the treatment of conditions such as β -thalassaemia. Our group has previously demonstrated that these agents are effective in laboratory models of oesophageal cancer. Their usefulness in treating bowel cancer, however, has never been assessed and thus the aim of this research has been to investigate whether iron chelators may offer an effective treatment.

My research has demonstrated that iron chelators display significant anti-cancer properties in laboratory models of bowel cancer. The drugs inhibit iron uptake and storage within colorectal cancer cells, which significantly reduces their viability and growth. Of note, iron chelators inhibit cells that are resistant to conventional chemotherapy.



Matthew at work in the laboratory

Their efficacy may also be increased by the presence of certain genetic mutations common in colorectal tumours (eg APC). Iron chelation may therefore serve as a ‘targeted therapy,’ reducing side effects in normal cells.



Matthew outside the Queen Elizabeth Hospital Birmingham

It is now hoped a clinical trial of iron chelation therapy may take place within 1 to 2 years.

ENHANCING HOST CELL RESPONSES VIA BIOFUNCTIONALISATION OF ORTHOPAEDIC TITANIUM



**JULIA
BLACKBURN**

FELLOWSHIP/SPONSOR

RCS Research Fellowship supported by the Cutner Legacy

SUPERVISORS

Jason Mansell and Professor Ashley Blom

SITE OF WORK

Avon Orthopaedic Centre

PUBLICATIONS

1. Blackburn J, Mansell JP. The Emerging Role of Lysophosphatidic acid (LPA) in skeletal biology. *Bone* 2012; 50: 756–762.
2. Mansell JP, Blackburn J. Lysophosphatidic acid, human osteoblast formation, maturation and the role of $1\alpha,25$ -dihydroxyvitamin D3 (calcitriol). *Biochim Biophys Acta* 2013; 1831: 105–108.

PRESENTATIONS

1. Lysophosphatidic acid (LPA)-functionalised titanium: a superior implant material for supporting human osteoblast differentiation, European Orthopaedic Research Society (EORS) Meeting, Amsterdam, 27–28 Sept 2012
2. Effect of local and systemic growth factors on the human osteoblast response to Lysophosphatidic acid and vitamin D3. Society of Academic & Research Surgery (SARS) Annual Meeting, Royal Society of Medicine, London. 9–10 Jan 2013.

PRIZES

1. Stefan and Anna Galeski Fellowship 2013
2. European Orthopaedic Research Society (EORS) Exchange Travel Grant, December 2012.

More than 160,000 total hip and knee replacements are performed each year in the UK, but 10% of these implants will fail owing to loosening at the interface of metal and bone.

Many orthopaedic implants are made from titanium (Ti) as the patient's own bone joins onto Ti via the body's natural healing processes. In some cases the patient's bone fails to join strongly to the Ti, so the implant works loose. This requires revision surgery that has worse results for patients than initial surgery.

Research in our laboratory has found a naturally occurring fatty molecule called lysophosphatidic acid (LPA) that enhances maturation of human bone-forming cells (osteoblasts). Therefore we bonded LPA to Ti to see if this was better than 'naked' Ti in supporting osteoblast growth.

The aim of this research is to develop 'next-generation' implants via the direct bonding of LPA to Ti with a view to improving overall implant longevity.

Work with human bone marrow stem cells (hBMSCs) sourced from patients undergoing total hip replacement, showed LPA-modified Ti did promote the development of osteoblasts from stem cells, which should improve the bond between bone and metal. We also found that LPA co-operates with and does not antagonise local growth factors, which is encouraging for how LPA-modified Ti may work in humans.

Infection can affect one in every hundred joint replacements and complicate one in ten revision operations. These infections are difficult to treat and often lead to removal of the implant and many weeks of antibiotics. LPA has been shown to slow the growth of some bacteria, and we found LPA-modified Ti also has antibacterial effects.

Worldwide, many research groups are bio-functionalising implants with other growth factors. However, LPA is much smaller than these other growth factors so we can achieve a greater surface coverage, and it is also significantly cheaper.



Julia teaching at a basic surgical skills workshop in Rio de Janeiro

Our research continues to further develop LPA-modified Ti as a surface that may increase implant survival and prevent the need for revision surgery for many patients.



Julia teaching at a basic surgical skills workshop in Rio de Janeiro

INVESTIGATION OF THE PATHOPHYSIOLOGY AND IN-UTERO TREATMENT OF GASTROSCHISIS-RELATED GUT DYSFUNCTION



HELEN CARNAGHAN

FELLOWSHIP/SPONSOR

Joint RCS/British Association of Paediatric Surgeons Research Fellowship

SUPERVISOR

Dr Simon Eaton

SITE OF WORK

Paediatric Surgery Unit, Institute of Child Health, UCL

PUBLICATIONS

1. Carnaghan H, Pereira S, James CP, Charlesworth PB, Ghionzoli M, Mohamed E, Cross KMK, Kiely E, Patel S, Desai A, Nicolaidis K, Curry JI, Ade-Ajayi N, De Coppi P, Davenport M, David AL, Pierro A, Eaton S. Is early delivery beneficial in gastroschisis? *Journal of*

Pediatric Surgery. in press.

2. Carnaghan H, Roberts T, Savery D et al. Novel exomphalos genetic mouse model: The importance of accurate phenotypic classification. *Journal of Pediatric Surgery* 2013; 48: 2,036–2,042.

PRESENTATIONS

1. Carnaghan H, Pereira S, James CP, Charlesworth PB, Ghionzoli M, Mohamed E, Cross KMK, Kiely E, Patel S, Desai A, Nicolaidis K, Curry JI, Ade-Ajayi N, De Coppi P, Davenport M, David AL, Pierro A, Eaton S. Is early delivery beneficial in gastroschisis? American Academy of Pediatrics National Conference and Exhibition,

Orlando, USA, Oct 2013.

2. Carnaghan H, Roberts T, Savery D et al. Novel exomphalos genetic mouse model: The importance of accurate phenotypic classification. Joint European Paediatric Surgeons' Association/British Association of Paediatric Surgeons Annual Paediatric Surgery Congress, June 2012.

FURTHER FUNDRAISING

Welcome Trust Research Training Fellowship for 2 years

PRIZES

First Prize in the Year 2 Category, UCL Institute of Child Health Poster Competition 2013.

43% of gastroschisis babies fall into the category of type two intestinal failure (> 28 days of drip feeds).

Gastroschisis is a belly wall defect arising during pregnancy resulting in bowel lying outside the abdomen in contact with irritant amniotic fluid. At birth the bowel is inflamed and sluggish resulting in poor oral feeding requiring drip feeds. However, the cause of sluggish bowels is poorly understood.

Previous research has shown that the amniotic fluid of fetal gastroschisis is inflamed and the pacemaker of the bowel – the interstitial cells of Cajal (ICC) – are underdeveloped in the bowel wall of gastroschisis babies. It is thought reduction of bowel wall inflammation will enable normal ICC development.

My objectives are to better understand the development of ICC in gastroschisis and develop a fetal therapy to improve gut function before birth.

Within the laboratory, I have developed techniques to accurately quantify ICC and other specialised nerve cells/



Helen outside the world-renowned UCL, Institute of Child Health

inflammatory cells in mouse and human bowel wall. This is being applied to my ongoing investigations (continuing for a further two years) in a gastroschisis genetic mouse model. Using this model I am performing a variety of fetal in-utero interventions to alter the levels of bowel inflammation to determine the effect of inflammation on ICC development and gut physiology. Additionally, I am analysing bowel wall ICC/neuronal development in human gastroschisis involving the largest series of archived gut specimens to date.

Finally, I have performed a retrospective review of 246 patients to determine whether sluggish bowels are simply linked to the duration of amniotic fluid exposure. However, my findings showed that the greater the gestational age at birth the less time the baby needed to reach full oral feeding. Suggesting the cause of sluggish bowels is more multifactorial than just amniotic fluid exposure.

If I show an in-utero intervention to be successful at improving ICC development and bowel physiology then I could soon be translating this research into a clinical trial.



Helen next to her winning poster



Helen working in the laboratory

MINIMALLY INVASIVE SPINE AND SPINAL CORD INJURY SURGERY – IMPROVING INDICATIONS AND OUTCOMES



**BEDANSH
ROY
CHAUDHARY**

FELLOWSHIP/SPONSOR

Harry Morton Fellowship

SUPERVISORS

Professor M Fehlings, R Rampersaud and S Lewis

SITE OF WORK

Krembil Neurosciences Centre, Toronto Western Hospital, Canada

PUBLICATIONS

Chaudhary BR, Fehlings MG. Adult-Onset Syringomyelia – From theory to practice and beyond. *World Neurosurg* 2014; S1878-8750(14)00754-2.

PRESENTATIONS

1. Minimally invasive decompression in focal lumbar spinal stenosis with or without stable spondylolisthesis. Comparative outcomes and re-operation rates at two years and beyond. Society for Minimally Invasive Spine Surgery Global Forum, Miami, USA. September 2014.
2. Two-year comparative outcomes of minimally invasive decompression in focal lumbar spinal stenosis – AO Spine North America Fellows Forum, Banff, Canada. March 2014

The need for spine surgery is exponentially increasing and assessing treatments is vital to deliver optimal patient and healthcare resource benefits

Implant spine surgery for optimising management following spinal cord injury and spinal degenerative change is on the increase. Spinal cord injury is estimated to occur in 2,500 people (mostly under 30 years of age) in the UK every year, with an approximated lifetime healthcare cost of up to £1 million per patient. Such complex cases will increasingly need urgent surgery with the recent publication of research showing significant gains from early operative intervention.

Support from the College has allowed me to undertake my AO North America-approved clinical spinal training fellowship programme at the centre that led the above trial. The placement also provides a unique opportunity to further my experience of some of the latest minimally invasive spinal surgery techniques and spinal deformity, as well as treatment of spinal cord injury patients and its complications including syringomyelia. Surgical techniques learnt included using new technology like CT guided (O-Arm) intraoperative spinal navigation, which allows surgeons to take real-time CT scans during the operation and accurately guide spinal surgery and implant positioning. This significantly increases patient safety and allows more complex procedures to be undertaken, like en bloc resection of tumours, which has been shown to lead to longer survival in tumour patients.



O-Arm and navigation equipment used in the OR to provide surgical guidance

Further clinical research during my fellowship is aimed at determining the best surgical management of degenerative spinal disease from mal-alignment of the lower spine called Spondylolisthesis. Tradition fusion spine surgery for this condition carries greater risks and is more expensive. It also predisposes patients to developing later complications called Adjacent Segment Disease. My work builds on the continuing work of the spine research programme and scientifically details the benefit of minimally invasive spine surgery in these patients. Such surgery not only allows patients to go home on the same day of the operation, but altogether avoids fusion operations (in certain types of spondylolisthesis) thus minimising risks, optimising costs and improving outcomes.

Reference

1. Fehlings MG, Vaccaro A, Wilson JR, Singh A, W Cadotte D, Harrop JS *et al*. Early versus delayed decompression for traumatic cervical spinal cord injury: results of the surgical timing in acute spinal cord injury study (STASCIS). *PLoS ONE*. 2012; 7:e32037.



Roy with one of his mentors, Dr Stephen Lewis, outside the SickKids Hospital in Toronto



Reviewing a patient who had surgery around the base of the brain four days earlier

MRNA EXPORT AND CANCER



**MARCUS
GEORGE KWESI
CUMBERBATCH**

FELLOWSHIP/SPONSOR

Joint Wellcome Trust/RCS Research Fellowship

SUPERVISOR

Professor Stuart Wilson and Professor James Catto

SITE OF WORK

University of Sheffield

PUBLICATIONS

1. Viphakone N, Hautbergue GM, Walsh M, Chang CT, Holland A, Folco EG, Reed R, Wilson SA. TREX exposes the RNA-binding domain of Nxf1 to enable mRNA export. *Nat Commun* 2012; 3: 1,006.

2. Hautbergue GM, Hung ML, Walsh MJ, Snijders AP, Chang CT, Jones R, Ponting CP, Dickman MJ, Wilson SA. UIF, a New mRNA export adaptor that works together with REF/ALY, requires FACT for recruitment to mRNA. *Curr Biol* 2009; 19: 1,918–1,924.

PRESENTATIONS

RNA Society Conference, June 2014, Quebec, Canada.

FURTHER FUNDRAISING

The Wellcome Trust for three years

Bladder cancer is the most expensive to treat and undertake surveillance on. In the USA it costs between \$90,000 and \$200,000 per patient from diagnosis to death.

Cancer is one of Britain's biggest killers. Bladder cancer in particular is debilitating, expensive to treat and associated with a high morbidity and mortality.

The normal human cell provides an environment for genes to be made into proteins used to promote and maintain our survival. A key step is to take the mRNA (a complimentary product of DNA) out of the nucleus and into the cytoplasm to be made into a protein. To facilitate this process there are exporter proteins that provide taxi-rides for mRNA to optimise this transport.

There is a number of key exporter proteins already identified and at baseline we knew that the most canonical exporter was at low levels in some cancer cells. Hence, our project aims were to identify alternative means of mRNA transport used by these cancer cells, which we demonstrated using techniques such as western blotting and polymerase chain reactions.



Marcus sat at Davinci Robot with supervisor Professor Jim Catto

We sought to evaluate the range of cancers that use these alternative transport mechanisms and to interrogate the biological mechanisms that trigger the switch from normal to alternative RNA transport and to test whether these alternative pathways could be exploited to kill cancer cells selectively.

We performed a screen to

see if we could artificially knock these alternative pathways out of cancer cells and thus induce cell death, and this proved successful. This provides hope that these pathways could be used as drug targets.

We also performed studies such as immunohistochemistry and polymerase chain reactions to see if the levels of these exported proteins could be detected in tissues and/or urine and serum samples of patients to provide a platform for a diagnostic tool. This work remains in progress. This would be invaluable to help clinicians decide on the best course of action for patients diagnosed with cancer and may lead to more 'tailored' bladder cancer (and wider) investigations and treatments.



Marcus in Wilson laboratory with colleagues

So far this work has led to the discovery of a new exporter protein and we have found that a wide range of cancers are using alternative RNA export mechanisms, which we have gone on to characterise.

We may also have identified one of the ways in which a cell with damaged DNA 'switches off' the usual RNA exporter.

This research builds upon work established in the Wilson laboratory and other laboratories worldwide that specialise in these processes. Our work furthers knowledge of the cellular process involved in mRNA export in cancer and is being put forward as a PhD thesis.

INVESTIGATING THE ROLE OF THE IGF AXIS IN HEAD AND NECK CANCER



**OLIVER
THOMAS DALE**

FELLOWSHIP/SPONSOR

The Dr Shapurji H Modi Memorial Research Fellowship

SUPERVISOR

Valentine Macaulay

SITE OF WORK

John Radcliffe Hospital, Oxford

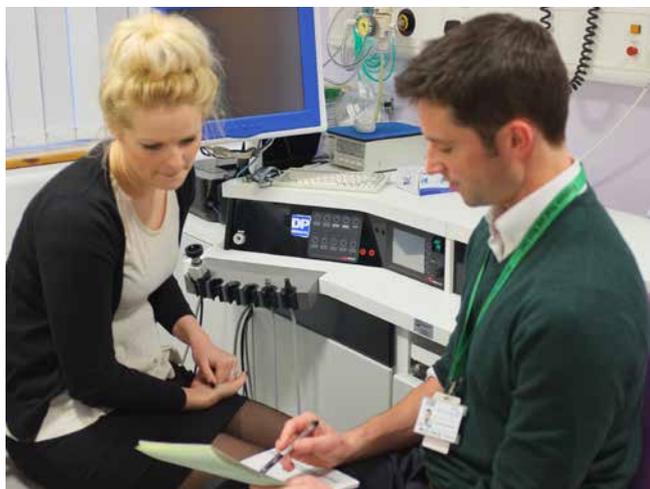
PRESENTATIONS

1. Investigating the role of the IGF axis in Head and Neck cancer. British Association of Head and Neck Oncologists (BAHNO). April 2013.
2. Investigating the role of the IGF axis in Head and Neck cancer. Oxford Cancer Research Centre Symposium. April 2013.

FURTHER FUNDRAISING

Heads Up and the Oracle Cancer Trust for one year

Head and neck cancer is the sixth most common cancer in the UK and two thirds of patients present with advanced disease.



Oliver gaining consent to use patient tissue for research purposes

Current treatment regimens for head and neck cancer (HNC) involve surgery and radiotherapy \pm chemotherapy. However, despite recent advances five-year survival rates have remained static over the past 20 years – particularly in Human Papilloma Virus (HPV)-negative disease.

Insulin-like Growth Factor (IGF) is a protein, which stimulates the growth and development of cells, and is thought to be important in the development of several common cancers including HNC. This project aims to investigate whether blocking the action of IGF could reduce the survival of cancer cells and provide new treatment options in head and neck cancer.

Using tissue from 190 HNC samples I have demonstrated that the IGF receptor is over-expressed in HNC, compared to normal tissue, and that this is particularly true in HPV-negative tumours.

In addition, I have demonstrated that blocking the IGF receptor in HNC cells that are growing in the laboratory significantly reduces the survival of cancer cells. When IGF blocking drugs are used in combination with radiotherapy this enhances the ‘cell killing’ effect of radiotherapy.

Future research will focus on identifying ‘biomarkers’ which predict the response of tumours to IGF blocking drugs.

My research findings to date suggest that IGF plays an important role in the biology of HNC, particularly in HPV-negative disease, and that using IGF blocking drugs in this context may provide an attractive new therapeutic target. Ultimately I hope this research will form the basis for a clinical trial investigating the combination of IGF receptor-blocking drugs with current treatment regimens in head and neck cancer patients.



Laboratory-based research into the IGF receptor in Head and Neck cancer

THERAPEUTIC FLAPS FOR RECONSTRUCTIVE SURGERY AFTER CANCER



CHRISTOPHER DAVIS

FELLOWSHIP/SPONSOR

RCS Fulbright Scholar Award

SUPERVISOR

Professor A O Grobbelaar

SITE OF WORK

Stanford University, USA

PUBLICATIONS

Davis CR, Rappleye CT, Than P, Whitmore AJ, Maan ZN, Rodrigues M, Bishop SN, Ghali S, Grobbelaar AO, Gurtner GC. Sutureless microvascular anastomosis for clinical application using Poloxamer 188 as an optimal transient

thermoreversible stent. *Journal of the American College of Surgeons* 219:S89.

PRESENTATIONS

1. Davis CR, Rappleye CT, Than P, Whitmore AJ, Maan ZN, Rodrigues M, Bishop SN, Ghali S, Grobbelaar AO, Gurtner GC. Sutureless microvascular anastomosis for clinical application using poloxamer 188 as an optimal transient thermoreversible stent. American College of Surgeons – 100th

Annual Clinical Congress. October 2014, San Francisco, CA, USA.

2. Davis CR. Can plastic surgery cure cancer? Fulbright Visiting Scholars Research Presentations. March 2014, University of California, San Francisco, USA.

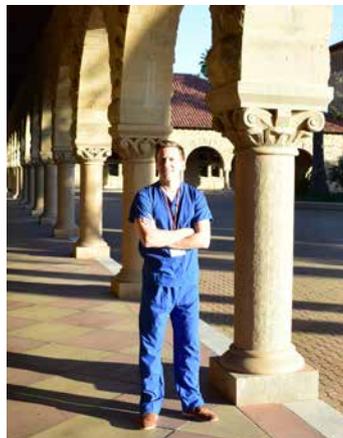
PRIZE

Stanford University School of Medicine 7th Annual Plastic Surgery Research Symposium (Stanford University, USA) Co-author of Best Basic Science Paper.

Cancer recurs in up to one in three unfortunate patients, despite optimal combinations of surgery, chemotherapy and radiotherapy. Can therapeutic reconstructive surgery prevent cancer returning?

Cancer kills 150,000 people in the UK each year. After surgical removal of cancerous tumors, plastic surgical reconstruction may involve moving tissue from a different anatomical location to reconstruct the defect. For example, after mastectomy for breast cancer, tissue is frequently moved from the abdomen to reconstruct a breast. This tissue is termed a ‘free flap’. Currently, a free flap has no oncological benefit to protect against cancer recurrence, and provides reconstruction only. Scientific evidence suggests free flap tissue may be primed to release proteins to the local environment with anti-cancer properties.

This international research collaboration between Stanford University and University College London aims to genetically alter reconstructive tissue to release proteins with anti-cancer properties and prevent cancer recurrence at the exact anatomical location of the initial tumour. To achieve this goal, our initial experiments have confirmed:



Stanford University Campus

1. Cancer eradication via a therapeutic protein
2. Successful delivery of the gene encoding the therapeutic protein to the cells of the free flap and subsequent release of the therapeutic protein
3. A contemporary means of joining blood vessels during reconstructive surgery.

Future translational benefits from this research includes developing a free flap for patients with cancer that reduces the risk of recurrent disease, thus increasing quality and duration of life by offering a potential cure to a patient’s initial cancer in a single oncological and reconstructive operation immediately after diagnosis.



Research dissemination at Downing Street



Rodin Sculpture Garden, Stanford University



Google Inc, Mountain View, California

POST-CCT COLORECTAL FELLOWSHIP IN TORONTO



**NICOLA
JAYNE EARDLEY**

FELLOWSHIP/SPONSOR

Harry Morton Fellowship supported by H&S Charitable Trust

SUPERVISORS

Robin Mcleod and Helen Macrae

SITE OF WORK

Mount Sinai and St Michael's Hospitals, Canada

To learn about pouch surgery, in particular laparoscopic pouch formation and various aspects of surgery related to Crohn's disease



Nicola being presented with a piece of artwork by a patient in appreciation of the hard work of the team during his cancer treatment

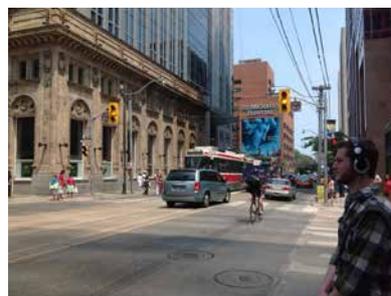
I trained in general and colorectal surgery in the UK but was keen to undertake a post-CCT fellowship in colorectal surgery so that I had a greater level of experience and expertise with which to treat my patients on commencing as a Consultant Surgeon. The American Society of Colon and Rectal Surgeons recognises a number of colorectal surgery residency programs, including at the University of Toronto. Having visited the surgeons

at the University of Toronto I was offered a place on their residency program for 1 year.

I spent the year working at Mount Sinai and St Michael's Hospitals, both located in downtown Toronto. I had the opportunity to be involved in the management of a high volume of patients with colorectal malignancy and inflammatory bowel disease. Working at specialist centres gave me a chance to greatly increase my colorectal experience, particularly of patients with complex inflammatory bowel disease and those requiring pelvic pouch surgery. I had the opportunity to



Mount Sinai hospital



St Michael's hospital

perform both open and laparoscopic surgery, complex reoperative surgery and observe less common procedures such as the Koch pouch formation and rectourethral fistula repair.

As well as increasing my operative experience, I attended clinics and multidisciplinary team meetings, performed endoscopy, joined ward rounds and had on call commitments.

My time working in Toronto gave me more than just the operative experience that I was expecting. It gave me an insight into complex decision-making and teamworking and also the opportunity to work in a different healthcare system. It also gave me the chance to witness a different surgical training program and to see how the surgeons in Toronto are training surgeons over a shorter timeframe than in the UK.

Since returning to the UK I have started work as a consultant general and colorectal surgeon and I am certain that I am a better surgeon as a result of this post-CCT fellowship.

CHARACTERISATION OF THE OESOPHAGEAL MICROBIOME AND ITS FUNCTIONAL RELEVANCE IN OESOPHAGEAL CANCER



**DAFFOLYN
RACHAEL
FELS ELLIOTT**

FELLOWSHIP/SPONSOR

Harry Morton Fellowship

SUPERVISOR

Rebecca C Fitzgerald

SITE OF WORK

Hutchison/MRC Cancer Unit, University of Cambridge

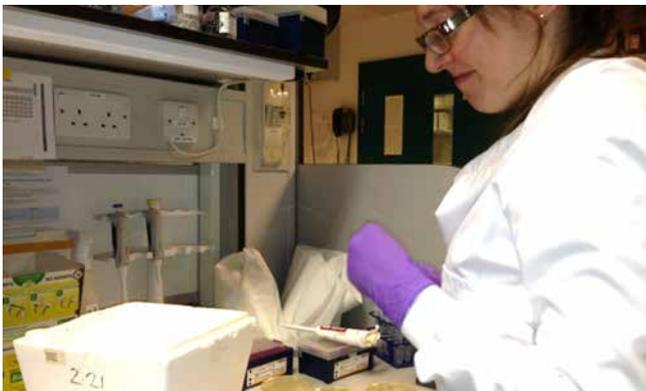
PUBLICATIONS

D Fels Elliott, Fitzgerald RC. Molecular markers for Barrett's oesophagus and its progression to cancer. *Current Opinion Gastroenterology* 2013; 29: 437-445.

FURTHER FUNDING

Cambridge Cancer Centre Clinical Research Fellowship (Cancer Research UK) for three years

There has been a six-fold increase in oesophageal cancer in the United Kingdom during the past three decades, and the reason behind this increase has not yet been discovered.



Daffolyn examining bacteria colonies grown in Petri dishes, trying to isolate colonies that contain her gene of interest

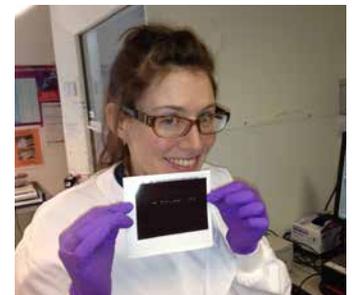
I am enrolled in the General Surgery training programme at the University of Toronto, Canada, and have completed the third postgraduate training year (PGY3). I came to study at the University of Cambridge to do oesophageal cancer research in Professor Rebecca Fitzgerald's lab with a CRUK Cambridge Cancer Centre Clinical Fellowship.

Oesophageal adenocarcinoma is a cancer of the oesophagus that is becoming increasingly common in the Western world, with a six-fold increase over the past three decades. This disease has a poor overall survival rate (<20%) unless detected and treated at an early stage. Oesophageal adenocarcinoma has a known precursor lesion called Barrett's oesophagus, which is associated with chronic acid reflux and inflammation. However, little is known about the relationship between inflammation in Barrett's oesophagus and the oesophageal microbiome (ie all bacterial species in the oesophagus).

My PhD research aims to characterise the composition of the oesophageal microbiome at different stages of progression from Barrett's oesophagus to cancer. To do this we are using different methods of sampling the microbiome, including the novel Cytosponge™

(Barrett's oesophagus Screening Trial, Fitzgerald lab). The Cytosponge™ consists of a spherical mesh compressed within a gelatine capsule and attached to a string. Once swallowed, the capsule dissolves and the Cytosponge™ expands in the patient's stomach. After five minutes, the Cytosponge™ can be withdrawn on a string through the patient's mouth, collecting cells and bacteria along the entire oesophagus.

A pilot study has already been performed to confirm whether it is possible to analyse tiny amounts of DNA from bacteria in the oesophagus using a technique called 16S rRNA gene sequencing. The purpose of this technique is to identify and classify the different species of bacteria. The next step is to complete a larger study (>300 samples) to investigate whether there is any difference in bacterial species along the progression sequence from Barrett's oesophagus to cancer. Discovering whether alterations in the microbiome have any functional role in the development of oesophageal cancer is clinically important, because it may improve detection of early cancers and guide possible therapies (such as antibiotics or probiotics) for these patients.



Daffolyn visualising her gene of interest, which has been successfully cloned in seven bacteria colonies

THE ENDOCRINE RESPONSE TO SEVERE TRAUMA: THE STEROIDS AND IMMUNITY FROM INJURY TO REHABILITATION (SIR) STUDY



MARK ANTHONY FOSTER

FELLOWSHIP/SPONSOR

Joint RCS/Military Research Fellowship

SUPERVISORS

Professors Janet Lord, Wiebka Artl, Julian Bion and Mark Midwinter

SITE OF WORK

NIHR Surgical Reconstruction and Microbiology Research Centre, Birmingham

PUBLICATIONS

Two papers are currently in draft around the neutrophil function after major trauma and the endocrine response to severe trauma.

PRESENTATIONS

1. Mark Foster, Taylor A, Hill N, Staruch R, O'Neil D, Bion J. The endocrine response to severe trauma: the steroids and

immunity from injury to rehabilitation (SIR) study. 2013. Endocrine Society 2013 – San Francisco.

2. Mark Foster, Angela Taylor, Neil Hill, Rob Staruch, Donna M. O'Neil, Julian F Bion, Stephen Young, Mark Midwinter, Joanne Fallowfield, Janet Lord, Wiebke Artl. The endocrine response to severe trauma. British Endocrine Society 2014.

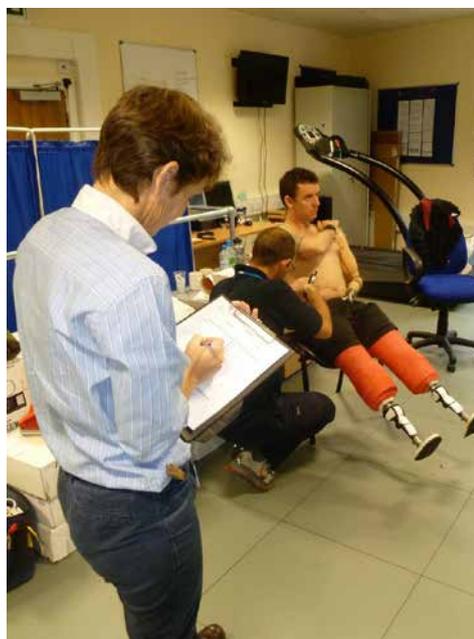
PRIZES

Best Registrar Presentation, Travelling Surgical Society, Birmingham 2013.

FURTHER FUNDING

The National Institute for Health Research Surgical Reconstruction and Microbiology Research Centre (NIHR SRMRC), Royal Centre for Defence Medicine, Drummond Foundation, Wellcome Trust Birmingham CRF for consumables, research staff and laboratory support.

Severely traumatised patients lose more than 20% of their muscle thickness by 6 weeks after injury



Mark measuring recovery

There are 1.2 million deaths from Road Traffic Accidents worldwide and 5,400 deaths each year from trauma in England. This dwarfs the 40,000 severely injured people surviving trauma in England. With the recent advances

in military trauma care and the setting up of civilian trauma centres improving survival, it was time to investigate how to improve the survivors' recovery.

We set up a study that would examine how the body responds to and recovers from trauma.

In 100 severely traumatised patients, half military and half civilian, we collected blood and urine from injury and at periodic intervals for 6 months. We also measured muscle loss

using ultrasound. In blood, we measured hormones (substances which control organ systems) that are released under stress and also those that build muscle (steroids).

The military injuries were inflicted by bullet or bomb whereas the civilian injuries were mainly road-traffic accidents. Stress hormone levels were high during the first 6 weeks and the anabolic steroid hormones were very low and took several weeks to recover. Muscle loss was 22% on average and reached its lowest point by 6 weeks. We measured the body's ability to fight infection and this was lowest at two weeks following injury.

We found a clear imbalance between the stress hormones and steroids that is associated with severe muscle loss and the ability to fight infection. DHEA is one of these hormones that may reverse this imbalance. Our next steps are to set up a trial to supplement this naturally occurring hormone in the severely injured that may improve survival but, almost more importantly, improve recovery and return more injured to independent living will reduce the costly burden of care to families and the country alike.



Mark in trauma surgery

TARGETED GRAFT SPECIFIC THERAPY DELAYS ACUTE REJECTION IN VASCULARISED COMPOSITE ALLOTRANSPLANTATION



CHARLES ANTON FRIES

FELLOWSHIP/SPONSOR

Joint RCS/Military Research Fellowship

SUPERVISOR

Lt Col M R Davis MD USAF MC

SITE OF WORK

United States Army Institute of Surgical Research, San Antonio, Texas

PUBLICATIONS

1. C Villamaria, C A Fries, J R Spencer, M Roth, M Davis. Hydrogen sulphide mitigates ischemia reperfusion injury in a porcine model of vascularised composite allotransplantation. *Ann Plas Surg* 2014; 72: 594–598.

2. Villamaria CY, Rasmussen TE, Spencer JR, Patel S, Davis MR. Microvascular porcine model for the optimisation of vascularised composite tissue transplantation. *J Surg Res* 2012; 178: 452–459.

PRESENTATIONS

1. Military Health Systems Research Symposium, Fort Lauderdale, Florida, August 2014.
2. Association of Trauma and Military Surgery (ATMS), Harrogate, April 2014.

PRIZES

The Richard Wiseman Medal, for best podium presentation of original research at ATMS 2014.

Half of upper limb amputees do not use their prosthetic limb as it does not provide adequate function



Charles presenting at the MHSRS meeting

Vascularized composite allotransplantation (VCA), most commonly hand or face transplantation, can replace any tissue deficit with ‘like for like’ tissue achieving optimal functional and aesthetic results. Patients who have suffered hand amputation can become independently self-caring, patients living in social isolation owing to facial disfigurement can return to normal function.



Charles operating in the tented field hospital Afghanistan

Injuries that are unreconstructible using current gold-standard techniques can be treated by this method; however, life-long immunosuppression that confers morbidity and mortality to VCA recipients is required to support a graft that improves quality of life but is not lifesaving.



Charles on patrol in Afghanistan

The aim of this research is to investigate strategies that can reduce the systemic toxicity associated with immunosuppression by

pre-treating the graft *ex vivo* prior to transplantation.

To date I have developed the world’s first orthotopic model of hand transplantation in swine to enable gold-standard evaluation VCA immunology in a translatable model. Unlike all other models of VCA it comprises all relevant tissue types and enables the evaluation of nerve regeneration, tendon and bone healing and functional recovery.

Experiments using this model and our previously described model of gracilis musculocutaneous flap transplantation have demonstrated the ability of hydrogen sulphide, an *ex vivo* hyperbaric warm perfusion device and topically delivered immunosuppressive agents (using drug eluting microparticles) to delay the onset of acute rejection. The homology between humans and swine enables these results to be translated into clinical trials.

Projects are ongoing, with current protocols evaluating enzyme-activated drug eluting hydrogels, delivering immunosuppressive agents.

The RESTOR project is a long-term endeavour with particular focus on the reconstructive benefits to service personnel injured in recent conflicts. This has yielded a cadre of patients with devastating extremity and maxillofacial injuries, who have very high reconstructive demands and expectations based on their high levels of pre-morbid function and young age.



Charles at an outreach clinic in Afghanistan

OPTIMAL USE OF TRANSFUSION RESOURCES IN TRAUMA SURGERY AND MASS CASUALTY EVENTS



**SIMON
GLASGOW**

FELLOWSHIP/SPONSOR

RCS Research Fellowship with the support of the Rosetrees Trust

SUPERVISORS

Professor Karim Brohi and Lieutenant Colonel Nigel Tai

SITE OF WORK

The Blizzard Institute, Queen Mary University of London

PUBLICATIONS

1. Glasgow S, Davenport R, Perkins Z, Tai N, Brohi K. A comprehensive review of blood product use in civilian mass casualty events, *Journal of Trauma-Injury, Infection and Critical Care* 2013; 75: 468–474.

2. Glasgow SM, Allard S, Doughty H, Spreadborough P, Watkins E. Blood and bombs: the demand and use of blood following the London Bombings of 7 July 2005.

Transfus Med 2012; 22: 244–250.

PRESENTATIONS

1. World Trauma Congress – The impact of damage control resuscitation on blood provision for mass casualties. Rio de Janeiro, Brazil, August 2012.
2. Annual Meeting of The Society of Academic and Research Surgery – A 100-year review of blood use in civilian mass casualty events. London, UK. January 2013.

PRIZES

President's Poster Prize Winner, Annual Meeting of SARS, Royal Society of Medicine, London January 2013.

FURTHER FUNDING

The National Institute of Health Research for one year.

Disaster-related deaths have risen 23% in the past decade, with more than one million lives lost. Bleeding is the leading preventable cause of death in these mass casualty events.

In the past decade more than 2.6 billion people have become casualties of disasters. Mass casualties following disasters are characterised by a quantity of severely injured patients that can rapidly overwhelm available medical resources. Bleeding due to trauma causes almost 50% of deaths in the first 24 hours following injury and is the leading preventable cause of death in this population. These casualties require urgent operations and large volumes of blood to survive, which can lead to rapid exhaustion of hospital blood supplies.



The trauma science exhibit Simon helped develop alongside his research to teach children

The objective of this research project is to increase our understanding of how blood is consumed in mass casualty events and investigate a method for improving blood planning for events, which could reduce future disaster-associated mortality.

Following an extensive 100-year worldwide review of blood



Simon in action, teaching children how bleeding is controlled in theatre

use in mass casualty events, I have developed the first computer-based simulation model of a hospital blood system during a disaster. The computer

model has been designed with software commonly used in industry to optimise system outputs and improve efficiency.

Application of this technology in medical disaster planning allows the investigation and experimentation of blood provision under the surge conditions of a mass casualty event, across a range of scenarios and hospital constraints. The results will identify system bottlenecks, and help develop best-practice guidelines for managing bleeding casualties using a more time, resource and financially efficient method, than could be achieved through real-life simulation experiments.

Results from the development stage of the model have already been used in the public service; assisting emergency planners in ensuring adequate blood supplies were available to meet the expected demands of a disaster during the 2012 Olympic Games. The results from the current experimentation phase will hopefully further add to our understanding and improve policymaking for optimal blood provision in future events.

MOLECULAR AND CLINICAL DETERMINANTS OF MALIGNANT PROGRESSION IN ORAL DYSPLASIA



**MICHAEL
WING
SUNG HO**

FELLOWSHIP/SPONSOR

RCS Research Fellowship

SUPERVISORS

JB Wilson, Professor RJ Shaw and JM Risk

SITE OF WORK

University of Liverpool

PUBLICATIONS

1. Ho MW, Field EA, Field JK, Risk JM, Rajlawat BP, Rogers SN, Steele JC, Triantafyllou A, Woolgar JA, Lowe D, Shaw RJ. Outcomes of oral squamous cell carcinoma arising from oral epithelial dysplasia: rationale for monitoring premalignant oral lesions in a multidisciplinary clinic. *Br J Oral Maxillofac Surg* 2013; 51: 594–599.

2. Ho MW, Risk JM, Woolgar JA, Field EA, Field JK, Steele JC, Rajlawat BP, Triantafyllou A, Rogers SN, Lowe D, Shaw RJ. The clinical determinants of malignant transformation in oral epithelial dysplasia. *Oral Oncol* 2012; 48: 969–976.

PRESENTATIONS

1. American Head and Neck Society; 8th International Conference for Head and Neck Cancer, Toronto – July 2012.
2. British Association of Oral and Maxillofacial Surgeons Annual Scientific Meeting, London – June 2012.

PRIZES

British Society of Oral Medicine Annual Meeting 2012 – Poster Prize

FURTHER FUNDING

BAOMS/FSRF Fellowship 2013 and FDS Small Grant Award 2013 for 3 years

Oral dysplasia in non-smokers is seven times more likely to progress to oral cancer compared with smokers.



Michael working in an operating theatre with colleagues

The challenge in the management of oral epithelial dysplasia (OED) lies in identification of patients in whom the risk of progression to oral cancer is high. OED often presents as white or red patches in the mouth.



Michael performing microvascular anastomosis for free tissue transfer reconstructive head and neck surgery

Diagnosis and grading of severity (mild, moderate or severe) requires a biopsy. Known risk factors for transformation to oral cancer include the size and appearance, but the importance of site of lesion in the mouth,

grade of dysplasia and exposure to environmental carcinogens remains controversial.

Patients with a diagnosis of OED were recruited to an observational study in a specialist oral dysplasia clinic. Clinical, histopathological and risk factor data were recorded at baseline and one of three clinical endpoints were determined for each patient: transformation to oral cancer and non-transforming/stable OED.

An estimated 22% of patients underwent malignant transformation within 5 years, with significant predictors being: non-smoking status (seven-fold risk compared to non-smokers), site (lesions on the sides of tongue are four times more likely to become cancerous), non-homogeneous appearance (red or red-white lesions), high histological grade and size of lesion >200mm². Gender, age, number of lesions and alcohol history did not predict for malignant transformation.

Although a number of these clinical determinants have previously been associated with higher malignant transformation in OED, the high-risk nature of lesions in non-smokers is of particular note and requires a greater emphasis and recognition among clinicians dealing with OED. It suggests that patients, with non-smoking OED should be treated more aggressively.

One possible hypothesis is that patients with non-smoking OED might have defective repair mechanism for endogenous DNA damage, leading to cancerous progression. Archival tissue from a selection of this group of patients was analysed for expression of the FANC-D2 protein, which is crucial in DNA damage repair. Preliminary findings have indicated that the FANC-D2 is under-expressed in OED that transformed to oral cancer and thus could help identify higher-risk OED in the future.

SPINAL FELLOWSHIP AT UNIVERSITY OF TORONTO



**AHMED
IBRAHIM**

FELLOWSHIP/SPONSOR

Harry Morton Fellowship

SUPERVISOR

Professor M G Fehlings

SITE OF WORK

Toronto Western Hospital, Canada

PRESENTATIONS

1. Surgical outcome of CSM management – Canadian Spine Society meeting, Lake Louise, Canada.
2. Management of CSM outcome of 479 patients, Society of British Neurosurgeons, Autumn meeting, Coventry, England.

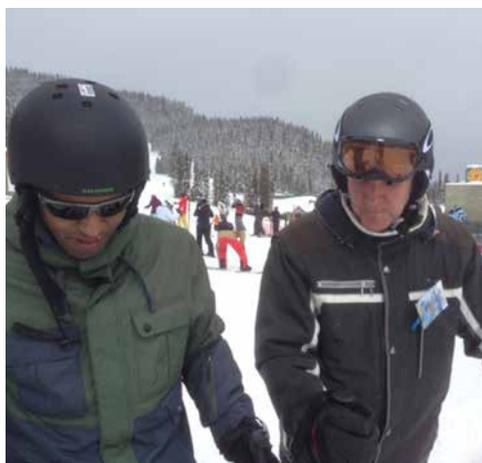
PRIZES

1. Best presentation – AONA 12th Annual Forum, Banff, Canada.
2. Winner of Best International Fellow – AANS/CNS Crockard International Fellowship Award.
3. Fellows/resident prize for the 2014 Cervical Spine Research Society (CSRS) in Orlando.

FURTHER FUNDING

HCA (Hospital Corporation of America) Scholarship, as a single payment.

I was provided with an unparalleled research opportunity under the supervision of the inspiring Professor Fehlings.



Ahmed with Professor Fehlings in Banff



Ahmed with other fellows



Ahmed with Professor Fehlings

I was based at the tertiary centre of Toronto Western Hospital where I rotated through placements including complex spinal tumours, advanced minimal access spine surgery, complex paediatric and adult deformity and intradural spinal surgery. I gained excellent surgical techniques through clinical practice and by attending numerous internal and external advanced cutting-edge AOSpine North America cadaver-based courses with world-leading faculty to acquire new and consolidate surgical techniques used.

I took part in one of the largest prospective multi-centre global studies ever to be undertaken on the management of cervical spondylotic myelopathy. I presented findings of the study at five international conferences, I won best abstract, best presentation and top research abstract, and three of my

manuscripts are under preparation, with one submitted for publication.

After completing this fellowship I have learned essential skills and strategies to avoid complications and I am better equipped to practise evidence-based advance spinal surgery. I have been inspired to develop a fellowship incorporating the best elements of my Canadian fellowship within the NHS for future trainees from the UK and abroad.

I believe that the knowledge I gained and the skills that I developed, in addition to the networks I established, will positively influence the management of my future patients and my career for a long time to come.

ENHANCED SURVEILLANCE FOR ULCERATIVE COLITIS-ASSOCIATED BOWEL CANCER



**FAREED
IQBAL**

FELLOWSHIP/SPONSOR

RCS Research Fellowship with the support of the Rosetrees Trust

SUPERVISORS

Glenn Matthew and Professor Dion Morton

SITE OF WORK

School of Cancer Sciences, University of Birmingham

PUBLICATIONS

Iqbal F, Tannahill L, Leong K, Caldwell GC, Wei W, Roelund K, Matthews G, Keolvraa S, Morton DG. Identification of novel candidate tumours suppressor genes in early colorectal tumourigenesis. *Journal of Colorectal Disease* 2012; 14: 14.

PRESENTATIONS

Association of Coloproctology of Great Britain and Ireland Conference, Dublin, July 2012.

PRIZES

First Place, University of Birmingham Research Poster Conference, July 2012.

There is a ten-fold increased lifetime risk of bowel cancer in patients with ulcerative colitis.



Fareed performing an endoscopy of a patient with ulcerative colitis

Ulcerative colitis (UC) is a common inflammatory disease of the large bowel, affecting young males and females equally. Bowel cancer risk in patients with chronic UC is heightened compared with the general population. Death from UC-cancer is disproportionately high, despite intensive endoscopic surveillance programmes.

This project aimed to examine DNA changes from bowel tissue taken from patients with UC and UC-cancers. It aimed to identify early DNA changes that corresponded to an individual's risk of bowel cancer.

UC bowel tissue taken during surgery or endoscopy was processed and DNA was extracted. Using a series of laboratory techniques, DNA changes called 'methylation' were measured in a panel of genes responsible for cancer and cell growth. This is particularly useful as DNA methylation changes occur early before a cancer has developed.

The results showed that two genes in particular, called sFRP2 and sFRP4, were more methylated in UC-cancer compared with someone who had UC but no cancer. Furthermore, sFRP2 was more methylated in early cancer compared with advanced UC-cancer. This would suggest that the methylation status of

sFRP2 could help identify UC patients at high risk of developing bowel cancer. A DNA-based test could be useful in the future as an adjunct to surveillance endoscopy.

This research will be followed up in a large-scale trial (funded by the NIHR), which will aim to identify further genes that can be used as markers of cancer risk in patients with chronic UC.



Fareed removing a colon cancer in theatre from a patient with ulcerative colitis

Patients with UC have an extremely poor quality of life. Some of the associated symptoms include bloody diarrhoea, abdominal pain, weight loss and faecal urgency. These can have negative influences on relationships,

job prospects and general well-being. Heightened bowel cancer risk adds to the burden of misery, which involves yearly endoscopies. Despite these, up to half of cancers develop in UC patients on surveillance. This suggests that the need to develop more accurate methods of predicting and detecting bowel cancer in UC are pressing.

This would serve as a huge benefit as patients would know their individual cancer risk. This would lower the number and frequency of endoscopies in patients deemed low risk and would promote early surgery or therapy in those patients at high risk for bowel cancer.

TARGETING INFLAMMATORY PATHWAYS IN DUPUYTREN'S DISEASE



**DAVID
IZADI**

FELLOWSHIP/SPONSOR

Blond McIndoe Research Fellowship

SUPERVISORS

Professor Jagdeep Nanachahal and Kim Midwood

SITE OF WORK

Kennedy Institute of Rheumatology, Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, University of Oxford

PUBLICATIONS

1. Verhoekx JS, Verjee LS, Izadi D, Chan JK, Nicolaidou V, Davidson D, Midwood KS, Nanchahal J. Isometric contraction of Dupuytren's myofibroblasts is inhibited by blocking intercellular junctions. *J Invest Dermatol*. May 7 2013.
2. Verjee LS, Verhoekx JS, Chan JK, Krausgruber T, Nicolaidou

V, Izadi D, Davidson D, Feldmann M, Midwood KS, Nanchahal J. Unraveling the signaling pathways promoting fibrosis in Dupuytren's disease reveals TNF as a therapeutic target. *Proc Natl Acad Sci USA*. 2013; 110: E928-937.

PRESENTATIONS

1. The British Association of Plastic Reconstructive and Aesthetic Surgeons and Irish Association of Plastic Surgeons Winter Scientific Meeting, Dublin, Ireland, November 2013.
2. British Society for Surgery of the Hand/British Association of Hand Therapists Combined Autumn Scientific Meeting, London, UK, October 2013.

FURTHER FUNDING

1. Kennedy Trust Funded Fellowship for 18 months.
2. RCSEd Small Project Grant for 1 year.

Dupuytren's disease is a common disorder affecting 4% of the general UK population, and up to 20% of patients over 60 years in Scotland. 20% develop complications and 10% of patients develop recurrence at 3 years. The direct cost of surgery to the NHS is £60m per annum.

Dupuytren's disease causes the fingers to curl into the palm, leading to severe impairment of hand function. Patients with advanced disease are most commonly treated by surgical excision of the diseased tissues. This requires extensive postoperative rehabilitation for three months.

The cell that produces the matrix, and is responsible for contraction in Dupuytren's disease, is the myofibroblast. Our group recently reported that the locally secreted pro-inflammatory cytokine, TNF, specifically controls the development of myofibroblasts in Dupuytren's disease. During the past year I have been investigating the TNF signalling pathways in Dupuytren's disease and the mechanisms underlying persistence of the localised inflammation.

My studies have been based on human tissues using techniques including cell culture, flow cytometry, RT-PCR, Western blotting, ELISA, Mesoscale Discovery, MTT assays, transfection, culture forced monitor, immunofluorescence and various histological techniques, as well as an *ex vivo* assay.

There is currently no approved treatment to prevent the progression of early disease or recurrence following surgery. Achieving my research objectives will aid the development of new drug-based therapies to treat



David disaggregating Dupuytren's tissue for cell culture

this disabling and chronic condition of the hand.

Musculoskeletal fibrotic disorders related to Dupuytren's disease include frozen shoulder and periarticular fibrosis, which together affect approximately five per cent of the general UK population. Their common pathological link is the persistence of myofibroblasts. The findings from my study may therefore translate to other localised musculoskeletal fibrotic conditions.

There is an urgent unmet need to develop targeted therapies to prevent progression of the early stages of Dupuytren's disease and prevent recurrence following surgery of this extremely common and disabling disorder.

Academic surgery is waning and few practising surgeons have the skills in the fields of molecular and cell biology. The RCS research fellowship has helped to fund a year of my DPhil research project and allowed me to gain the skills required to effectively join the next generation of surgeon scientists.



David examining a patient with Dupuytren's disease

EVALUATING TR040303 AS A POTENTIAL TREATMENT OF NECROTIZING PANCREATITIS



**MUHAMMAD
AHSAN JAVED**

FELLOWSHIP/SPONSOR

RCS Research Fellowship with support from the Surgical Research Fund

SUPERVISOR

Professor Robert Sutton

SITE OF WORK

NHHR Liverpool Pancreas Biomedical Research Unit

PRESENTATIONS

1. TR040303 reduces mitochondrial injury and ameliorates experimental AP. American Pancreatic Association meeting, November 2013, Miami, USA, and 39th annual meeting of Pancreatic Society of Great Britain and Ireland, December 2013, Liverpool, UK.

2. TR040303 reduces mitochondrial injury in response to fatty acid ethyl esters and ameliorates alcoholic pancreatitis. Japanese & American Pancreatic Association Meeting, November 2014, Hawaii, USA

PRIZES

1. Winner of the Lord Smith prize for best oral presentation, 39th annual meeting of Pancreatic Society of Great Britain and Ireland, December 2013
2. Young investigator award & travel fellowship, presentation at the annual American Pancreatic Association meeting, November 2013

FURTHER FUNDING

CORE for three years

One in five people with pancreatitis develop a severe form of the disease but there is still no targeted therapy for acute pancreatitis.



Fresh normal human pancreas tissue being retrieved in theatre

Acute pancreatitis is a common, serious illness where the pancreas becomes inflamed in a short period of time. One in five people with pancreatitis develop a severe form of the disease that may need intensive care and treatment in hospital for several months – chronic ill health or even death can result. Unfortunately there is no specific treatment for this disease thus far. This research project tested a new drug that can be used to treat acute pancreatitis.

Our team has discovered that there is a special channel (mitochondrial permeability transition pore – MPTP) in cells, which if kept open is harmful to the pancreas. Opening of the MPTP damages cells by injuring the parts of cells called mitochondria, which use the fuel from food to make energy. Blocking this bad channel protects the mitochondria and prevents cellular damage. We tested a new drug

(TR040303), which is known to block the MPTP in other cell types, on pancreatic cells.

Experiments were conducted using the most modern equipment with high-powered microscopes that show changes in living cells, including human cells – given freely and willingly by pancreas patients – to evaluate effect of TR040303 on mitochondrial function and cell death in response to pancreatic toxins. Once the protective effects of the drug were established on cells, TR040303 was tested in three different models of experimental acute pancreatitis and it reduced the severity of disease.



Macroscopic appearance of normal human pancreas tissue

people with other diseases and facilitate research in other areas of science as well. Further research can be undertaken to dissect the exact mechanism of action of TR040303 and how it modulates the opening of MPTP.

These findings can be translated into a clinical trial and hence provide an opportunity to treat patients with acute pancreatitis. As MPTP opening is implicated in other diseases like cardiovascular and neurological disorders, our research can potentially help

THE ROLE OF ALCOHOL METABOLISM IN THE DEVELOPMENT OF CHRONIC PANCREATITIS



MARIANNE JOHNSTONE

FELLOWSHIP/SPONSOR

RCS Research Fellowship supported by the Harold Bridges Legacy

SUPERVISOR

Professor Robert Sutton

SITE OF WORK

NIHR Liverpool Pancreas Biomedical Research Unit

PUBLICATIONS

1. DC Whitcomb, J LaRusch, AM Krasinskas, L Klei, JP Smith, RE Brand, JP Neoptolemos, MM Lerch, M Tector, BS Sandhu, NM Guda, L Orlichenko, Alzheimer's Disease Genetics Consortium. S Alkaade, S T Amann, MA Anderson, J Baillie, PA Banks, D Conwell, GA Coté, PB Cotton, J DiSario, LA Farrer, CE Forsmark, M Johnstone, TB Gardner, A Gelrud *et al.* Common genetic variants in

the CLDN2 and PRSS1-PRSS2 loci alter risk for alcohol-related and sporadic pancreatitis. *Nature Genetics* 2012.

2. Nicholson JA, Johnstone M, Greenhalf W. Divisum may be preserving pancreatic function in CFTR patients – but at a cost. *Am J Gastroenterol* 2012; 107: 1,758–1,759.

PRESENTATIONS

1. Pancreatic Society GB&I, Liverpool 2013. Carboxyl-ester lipase variable tandem repeat and its relationship to alcohol induced pancreatitis.
2. Pancreatic Society GB&I, Liverpool 2013. The diagnosis of chronic pancreatitis: a systematic review.

PRIZES

Winning team – NIHR Experimental Medicine Doctoral Research Training Camp 2013.

Chronic pancreatitis has a prevalence of approximately 70 per 100,000 population in the UK. It is not clear why certain individuals develop the disease, while the majority of people with equivalent exposure to risk factors do not.

Chronic Pancreatitis (CP) is a debilitating disease caused by acinar cell damage and fibrosis of the pancreas, affecting nearly 1 in every 10,000 people. The disease leads to malabsorption, malnutrition, diabetes mellitus and increased risk of pancreatic cancer, but probably most significantly for the patients, severe chronic abdominal pain. There is little treatment.

Alcohol is a common cause but only the minority of those who drink to excess develop the disease, although the reason is unknown. Liverpool researchers have discovered that pancreatitis

can be caused by a product of non-oxidative metabolism of alcohol. The majority of people get rid of alcohol by oxidation. We propose that there are differences in the genes related to alcohol metabolism, which may increase non-oxidative products in some people, leading to CP.

To explore this, I set up a biobank to collect blood samples from patients with a history of alcohol excess, both with a good history of CP and those who are otherwise healthy.

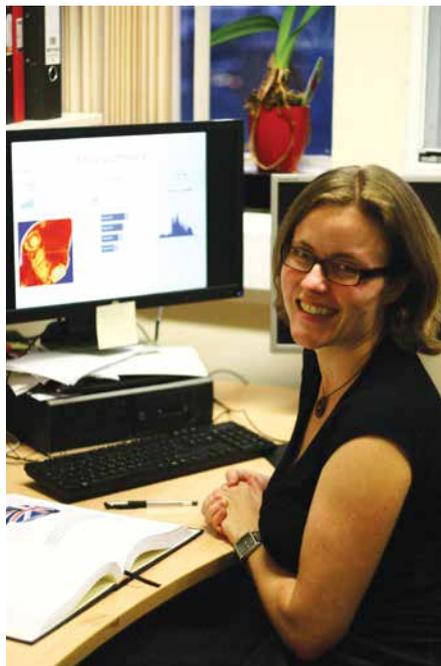
Using DNA extracted from the blood samples, I isolated the protein-coding region of 60 genes related to the metabolism of alcohol, using a technique called sequence capture.

I sequenced isolated DNA from 102 cases and matched controls, using techniques (Next Generation Sequencing) that have only recently become available on this scale.

This has highlighted 24 different variations that are statistically different in frequency between the two groups. Although I have finished my formal research time, work is ongoing with the NIHR Liverpool Pancreas Biomedical Research Unit to validate these differences in a second population of patients, and once this is complete we can examine the way in which these different genes contribute to CP.



Marianne preparing DNA in the lab ready for sequencing



Post-sequencing analysis of data

THE RADIOPROTECTION OF FREE FLAPS USING VIRALLY DELIVERED GENE THERAPIES



**AADIL
ALI KHAN**

FELLOWSHIP/SPONSOR

RCS Research Fellowship with the support of the Blond McIndoe Fund

SUPERVISORS

Professor Kevin J Harrington and Mr Paul A Harris

SITE OF WORK

Institute of Cancer Research, Fulham Road, London

PRESENTATIONS

1. British Association of Plastic, Reconstructive and Aesthetic Surgeons (BAPRAS) Winter Meeting, December 2013. Dublin, Republic of Ireland (invited lecture).
2. National Cancer Research Institute (NCRI) Annual Conference, January 2013. Liverpool, England.

PUBLICATIONS

Seth R, Khan AA et al. Targeted gene delivery by free tissue transfer in oncoplastic reconstruction. *Lancet Oncology* 2012; 13: 392–402.

PRIZES

Paton Massor Memorial Fund, BAPRAS, 2011.

FURTHER FUNDING

1. The Wellcome Trust
2. British Association of Plastic, Reconstructive and Aesthetic Surgeons (BAPRAS)
3. Masons Medical Research Foundation for 24 months.

Almost half of all women undergoing mastectomy and breast reconstruction will require radiotherapy after surgery.



Aadil planning laboratory experiments with a scientific colleague.



Discussing patient care with Mr Paul Harris (left) and Professor Kevin Harrington (right)



Presenting on free flap gene therapy techniques at the annual "Pint of Science" festival 2014 with Professor Kevin Harrington (right).

Women undergoing mastectomy commonly require postoperative radiotherapy, which is harmful to the reconstructive free flaps used for breast reconstruction. Irradiation of free flaps leads to contracture, volume loss and often requires further surgical procedures to correct. Therefore, when radiotherapy is anticipated breast reconstruction is delayed until after it has been delivered. Consequently, patients require multiple operations, a longer cumulative hospital stay and may have to live with a mastectomy deformity for a period before reconstruction can be performed. The over-arching goal of this work is to allow women undergoing mastectomy to have an immediate breast reconstruction at the time of their mastectomy, irrespective of their need for postoperative radiotherapy.

The aim of this project was to radioprotect reconstructive flaps using a virally delivered gene therapy strategy. Specifically, flaps were treated with viral particles carrying radioprotective genes by delivering them through the blood vessels of the flap in the interval in which it is detached from

the body's circulation. Once administered, the circulation is re-established by stitching the blood vessels of the flap to the systemic circulation.

So far, this project has developed and validated a novel model of flap irradiation and shown that radioprotective viral therapy reduces both contracture and volume loss after irradiation. Importantly, it achieves this without compromising the oncological efficacy of the radiotherapy itself against any residual cancerous disease.

This therapeutic modality (free-flap gene therapy) represents a highly novel opportunity for clinical translation and, indeed, the research programme at the Institute of Cancer Research and The Royal Marsden Hospital is currently the only one of its kind in the United Kingdom. The programme of work in this field is ongoing and aims, ultimately, to allow women undergoing mastectomy to have earlier, and more durable, breast reconstructions.

TRAUMATIC BRAIN INJURY: THE ROLE OF VEINS



**ANGELOS
G KOLIAS**

FELLOWSHIP/SPONSOR

Freemasons' Fund for Surgical Research with support from the Rosetrees Trust

SUPERVISOR

Professor Peter J Hutchinson

SITE OF WORK

Division of Neurosurgery, Addenbrooke's Hospital and University of Cambridge

PUBLICATIONS

1. Kolias AG, Kirkpatrick PJ, Hutchinson PJ. Decompressive craniectomy: past, present and future. *Nat Rev Neurol* 2013; 9: 405–415.

2. Kolias AG, Guilfoyle MR, Helmy A, Allanson J, Hutchinson PJ. Traumatic brain injury in adults. *Pract Neurol* 2013; 13: 228–235.

PRESENTATIONS

1. Post-traumatic Venous Outflow Obstruction: the Effects on Intracranial Pressure, Cerebrovascular Pressure Reactivity and Outcome. 15th International Conference on Intracranial Pressure and Brain Monitoring, Singapore, 2013.
2. The utility of CT Venography in patients with Traumatic Brain

Injury. International Brain Injury Association's 9th World Congress on Brain Injury, Edinburgh, 2012.

PRIZES

1. Best poster presentation at the 9th World Congress on Brain Injury 2012.
2. Junior doctor 'Teacher of the Year' award, East of England Deanery 2012.

FURTHER FUNDING

Raymond and Beverly Sackler Studentship (2011–2014) for 3 years

One in three patients who have a severe traumatic brain injury and a skull fracture develop blockage of the large veins inside the head.



Angelos (third from left) reviewing a patient with his colleagues in the Neurocritical Care Unit of Addenbrooke's Hospital.

Traumatic brain injuries (TBI) still claim the highest toll in terms of lost lives and disability for those under the age of 40. Treatment aims to control raised pressure within the head and maintain adequate blood flow to the brain. Despite optimal clinical management, about 10%–15% of patients require advanced therapies – such as a decompressive craniectomy or barbiturate coma – in order to control life-threatening rises in the pressure.

This project aimed to examine whether obstruction of the large veins inside the head – named intracranial venous sinuses – occurs following TBI. To do this, we screened TBI patients with a novel form of computed tomography (CT)

scanning named CT venography, which provides detailed three-dimensional images of the venous sinuses. The pressure, brain oxygenation and biochemistry were also continuously monitored in those patients who were treated in the Neurocritical Care Unit.

Our results have shown that about one-third of the patients who have a severe TBI and a skull fracture develop venous sinus obstruction. Importantly, we have found that patients with obstructed venous sinuses seem to develop more frequently life-threatening rises in the pressure within the head. In some cases, not even advanced therapies were able to avert a fatal outcome. We have also observed that obstructed venous sinuses can sometimes have long-

term effects such as severe headaches on patients who have otherwise gone on to make a good recovery after a severe TBI.

Previous work from our unit in patients suffering from another condition – named pseudotumour cerebri – that leads to high pressure within the head has shown that quite a few have obstructed venous sinuses. A novel treatment that was pioneered in Cambridge about ten years ago is the insertion of a stent to hold the vein open. As a result of this, the pressure is reduced and the patient's symptoms improve. The current project, which builds on past research, is paving the way for a prospective study that will evaluate whether stenting is effective and safe following severe TBI.

USHER SYNDROME 1B: A STEM CELL MODEL OF DEAFNESS



PETER KULLAR

FELLOWSHIP/SPONSOR

The Dr Shapurji H Modi Memorial Research Fellowship

SUPERVISOR

Lyle Armstrong

SITE OF WORK

Institute of Genetic Medicine, Newcastle University

PRESENTATIONS

Usher Syndrome 1B: A stem cell model of deafness. Deafblind Scotland Annual Conference, 5 March 2013.

PRIZES

Otology Section Matthew Yung Short Paper Prize 2013–14. Royal Society of Medicine, 7 February 2014. 'Generation of an in vitro disease model of Usher syndrome 1B (USH1B) using induced pluripotent stem cells (iPSC)'.

FURTHER FUNDING

Wellcome Trust for three years

Currently we have limited treatment options for the 1 in 6 people in the UK with hearing loss.



Presentation at Deafblind Scotland March 2013

There has been a growing interest in the use of stem cells to treat hearing loss. Recent work has shown it is possible to form early cochlear cells – the cells responsible for detecting sound in the ear – from stem cells. Our aim was to create a disease in a dish model of Usher syndrome, the most common deaf-blind syndrome.

Forming cochlear cells displaying the same disease as found in patients would enable us to try and manipulate and correct the cells using drugs or other compounds. Corrected cells could then be transplanted into patients potentially restoring hearing.

At the beginning of the fellowship we took skin biopsies from adult Usher patients and are the first group to derive stem cells from this disease. We have shown these stem cells are identical to patient cells and carry the same genetic change. It is as if we have taken adult cells and turned back the clock to the embryonic stage.



Institute of Genetic Medicine, Newcastle University

We then employed a protocol to form cochlear cells from these stem cells. This method was based on the chemical environment of the developing cochlea. We can now reliably create cells resembling those of the early cochlea.

The fellowship gave me a solid background for seeking further funding from the Wellcome Trust. This grant will fund an allied project and work within our group to further improve the protocol. During the next year we hope to be able to create more mature cochlear cells and our five-year plan would be then to correct the genetic defect in these cells. These could then be surgically implanted into the patient's ear and replace the damaged patient cells.

UNDERSTANDING FAILURE IN UNICOMPARTMENTAL KNEE REPLACEMENT



**ALEX
LIDDLE**

FELLOWSHIP/SPONSOR

RCS Research Fellowship with support from the Cutner Legacy and the Rosetrees Trust

SUPERVISOR

Professor David Murray

SITE OF WORK

University of Oxford

PUBLICATIONS

1. Liddle AD, Judge A, Pandit H, Murray DW. Adverse outcomes after Total and Unicompartmental Knee Replacement: a study of 101,330 matched patients from the National Joint Registry for

England and Wales. *Lancet* 2014 Oct 18

2. Liddle AD, Pandit H, Jenkins C, Lobenhoffer P, Jackson WFM, Dodd CAF, Murray DW. Valgus subsidence of the tibial component in cementless Oxford Unicompartmental Knee Replacement. *Bone Joint J* 2014; 96: 338–342.

PRESENTATIONS

1. European Federation of the National Associations of Orthopaedics and Traumatology (EFORT), London, June 2014:

Patient Reported Outcome Measures As Surrogate Endpoints For Randomized Trials In Total Knee Replacement.

2. American Academy of Orthopaedic Surgeons (AAOS), New Orleans, March 2014. Optimal usage of unicompartmental knee replacement: an analysis of 41,986 cases.

PRIZES

Rosetrees Trust Essay Prize 2013

FURTHER FUNDING

Arthritis Research UK for one year

90,000 knee replacements are performed each year in England and Wales and up to 20% of patients are dissatisfied.



Alex with his supervisor Professor Murray

Although total knee replacement (TKR) is an established and successful operation for end-stage osteoarthritis, a substantial proportion of patients (up to 20%) are dissatisfied following TKR.

found that the new implant demonstrates improved fixation and is as safe and reliable as the standard implant. The new implant is now being introduced worldwide.

We hope this research will improve patient care in four areas. By providing more evidence of the advantages and disadvantages of UKR, surgeons and patients will be better-informed when choosing between TKR and UKR. By providing a greater understanding of the patients likely to fare well after UKR, patient selection for UKR should improve. By determining surgical factors associated with success, UKR provision may be concentrated in units where success is more likely, leading to better outcomes overall. Finally, as the new implant provides improved fixation, patients receiving UKR in the future may have more reliable long-term outcomes.

Unicompartmental knee replacement (UKR) replaces only the diseased parts of the knee, preserving normal joint surfaces and ligaments, and restoring more normal knee function. It is a smaller operation than TKR, and has fewer complications, but it is more likely to need revision surgery, usually owing to loosening of the cement bond between the implant and the bone. This project involved a series of studies to understand why UKR has a high revision rate, and to identify factors that might improve this situation in terms of patient selection, surgical practice and implant design.

In the first part, we used data on 550,000 patients from a national cohort to examine outcomes in TKR and UKR. Using this cohort, we identified factors in terms of patient selection and surgical practice predisposing to poor outcomes after UKR. Finally, we performed studies of a new implant design, designed to improve bone-implant fixation. We have



Alex with one of his patients

THE PRODUCTION OF BIO-INSPIRED, 3D MINERALISED CELLULAR IMPLANTS USING INDUCED PLURIPOTENT STEM CELLS FOR BONE TISSUE ENGINEERING APPLICATIONS



**ROBERT JAMES
MACFARLANE**

FELLOWSHIP/SPONSOR

Arthritis Research Trust Fellowship

SUPERVISOR

Professor Athanasios Mantalaris

SITE OF WORK

Biosystems Engineering Laboratory, Department of Chemical Engineering, Imperial College London, South Kensington Campus

PUBLICATIONS

1. Gamie Z, MacFarlane RJ, Tomkinson A, Moniakis A, Tran GT, Gamie Y, Mantalaris A, Tsiroidis E. Skeletal tissue engineering using mesenchymal or embryonic stem cells: clinical and experimental data. *Expert Opin Biol Ther* 2014; 14: 1,611–1,139.

2. MacFarlane RJ, Graham SM, Davies PS, Korres N, Tsouchnica H, Heliotis M, Mantalaris A, Tsiroidis E. Anti-inflammatory role and immunomodulation of mesenchymal stem cells in systemic joint diseases: potential for treatment. *Expert Opin Ther Targets* 2013; 7: 243–254.

FURTHER FUNDING

Joint RCS–Dunhill Medical Trust research fellowship for two years

Up to 70% of bone grafting procedures fail within 10 years.



Robert at work in the Biosystems Engineering Laboratory, Imperial College London

With a growing and ageing population, the numbers of bone graft procedures in spinal, joint replacement and trauma surgery is growing exponentially. Current bone graft strategies, using cadaveric or synthetic bone are often unsuccessful and can transmit disease and be expensive. Using stem cells to create bone tissue from patients' own cells for use in bone graft procedures is an attractive solution. This work aims to investigate cost-effective methods of creating bone from stem cells, and produce spherical beads of bone tissue for use in bone graft surgery.

Stem cells were grown on two-dimensional plates within the Biosystems Engineering Laboratory at Imperial College London and were fed various combinations of proteins that are known to promote bone growth from stem cells. The oxygen content of the atmosphere was altered to investigate if this helped bone growth. The addition of two proteins (BMP4 and FGF2) to the growing cells was found to enhance the amount of new bone produced, and a lower amount of oxygen in the atmosphere compounded further improved production. These results have confirmed previous reports that adding proteins can improve bone tissue production from stem cells, and has shown for the first time that low concentrations of these proteins, at low oxygen levels, enhances bone tissue production.

As this work progresses, bone production will be continued in three-dimensional beads made from hydrogels. Other cost-effective ways of enhancing bone production from stem cells within the 3D bead environment will be investigated. This work is expected to generate personalised, biologically active bone graft implants, which could be used to improve the success rate for patients undergoing spinal, joint or trauma surgery requiring bone grafts, improve the pain levels experienced by many patients, and reduce the need for further surgery.

REGULATORY B CELL THERAPY IN TRANSPLANTATION



**MEKHOLA
MALLIK**

FELLOWSHIP/SPONSOR

Freemasons' Fund for Surgical Research

SUPERVISOR

Gavin J Pettigrew

SITE OF WORK

Department of Surgery, University of Cambridge

PUBLICATIONS

Intended submission to *American Journal of Transplantation*.

PRESENTATIONS

1. World Transplant Congress, Berlin 2013.
2. European Society of Organ Transplantation, Vienna 2013.

PRIZES

1. Patey Prize, Society of Academic and Research Surgery 2012.
2. Medawar Medal, British Transplantation Society 2014.

Half of all solid organ transplants fail within just ten years.

Using regulatory B cell therapy, we sought to address the problem of chronic allograft rejection and thereby improve the long-term outcomes of transplanted organs. Using a mouse heart transplant model of chronic allograft rejection, we were able to demonstrate that regulatory B cell therapy could prolong allograft survival and ameliorate the development of deleterious autoantibody and cardiac allograft vasculopathy.

These findings corroborate the demonstration of increased regulatory B cell frequency in kidney transplant patients that show stable graft function in the absence of immunosuppression, when compared to patients requiring ongoing immunosuppression or undergoing chronic rejection.

Further work is required to understand the mechanism of action of regulatory B cells in transplantation before their introduction into human clinical trials, although the production of the cytokine interleukin-10 is thought to be critical.

These findings highlight the potential for regulatory B cells to be used as cellular immunotherapy in clinical transplantation, and could avoid the need for re-transplantation in a significant proportion of patients and further burden on an already scarce supply of organs.



This patient lost his kidney transplant after three years and had to return to dialysis. My research seeks to prevent the late loss of transplanted organs.



Teaching Brazilian students Basic Surgical Skills as a Stefan and Anna Galeski Travelling Fellow



Winner of the first Scientific Meeting of the Brazilian College of Surgeons and Royal College of Surgeons of England Research Trainee Prize

INVESTIGATION INTO THE ASSOCIATION OF HELICOBACTER PYLORI AND LARYNGOPHARYNGEAL REFLUX



**NISHCHAY
MEHTA**

FELLOWSHIP/SPONSOR

H&S Charitable Trust Fund

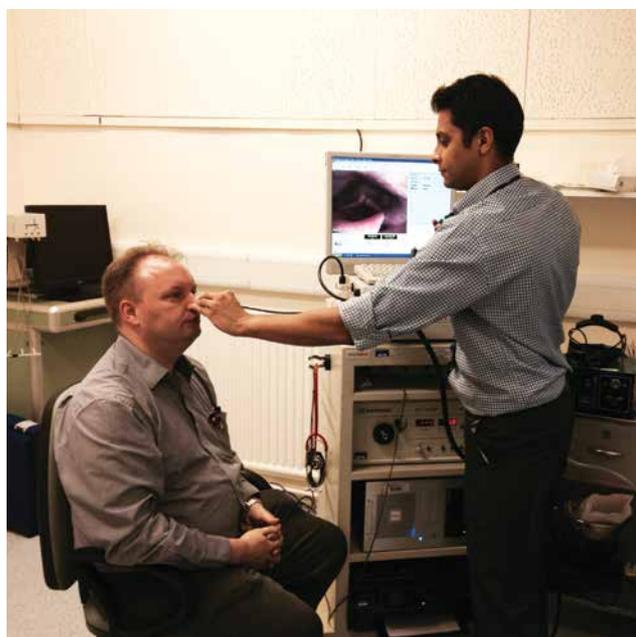
SUPERVISOR

Professor Martin Birchall

SITE OF WORK

Ear Institute, UCL, London

One in every three patients with laryngopharyngeal reflux was found to be colonised by a bacteria known to cause cancer when present in the stomach.



Nish taking a biopsy of the pharynx with a transnasal oesophagoscope

The aim of this project was to investigate the role of bacteria in causing symptoms of throat inflammation.

Twenty-two patients were recruited who had severe throat symptoms. All patients had failed to improve despite strong medical therapy. Patients were investigated through a symptom questionnaire, standardised examination findings score, robust physiological tests and finally biopsies performed of their throat under local anaesthetic using a

novel endoscopic technique. Biopsies were investigated by molecular techniques for the presence of *Helicobacter Pylori*.

All patients had rated their symptom burden as severe on a validated questionnaire and were found to have signs of throat inflammation on standardised endoscopic examination. However, no patient had acid reflux into their throat during physiological investigations. Thirty per cent of participants were found to be colonised with *Helicobacter Pylori*.

This work was undertaken to improve the treatment of symptoms related to throat inflammation. This condition causes great distress to patients, resulting in difficulty swallowing, breathing and speaking. Quality-of-life studies have shown that this condition has a large disease burden. In addition it is one of the commonest reasons for referral into the ENT team and treatment does not consistently work. This has led many groups to suggest the underlying mechanism of symptoms may not be related to reflux of acid into the throat, as has been traditionally held.

My preliminary findings suggest an interesting role of a bacteria causing throat irritation. This bacteria is already well known to cause inflammation in the stomach. My findings have prompted a collaboration with an American group and together we will continue to characterise the role of this bacterium in the throat, with the aim of finding novel ways to treat patients with this condition.

DEVELOPING A MOUSE MODEL OF COCHLEAR IMPLANTATION



**NINA
MISTRY**

FELLOWSHIP/SPONSOR

Enid Linder Foundation Research Fellowship

SUPERVISOR

Professor Shakeel Saeed and Professor Andrew Forge

SITE OF WORK

UCL Ear Institute, UCL, London

PUBLICATIONS

1. Mistry N, Nolan LS, Saeed SR, Forge A, Taylor RR. Cochlear implantation in the mouse via the round window: Effects of array insertion. *Hear Res* 2014. [Epub ahead of print]
2. Mistry N, Saeed SR, Forge A, Taylor RR. Cochlear implantation in the mouse: a

novel animal model. *ORS Spring Meeting Royal College of Surgeons of England. Clin Otol* 2013; 38: 361.

PRESENTATIONS

1. Cochlear implantation in the mouse: a novel animal model. Otorhinolaryngological Research Society (ORS) Spring Meeting, Royal College of Surgeons of England, London, UK. March 2013.
2. Developing a mouse model for cochlear implantation. Mistry N, Forge A, Saeed S, Taylor R. Association for Research in Otolaryngology 36th MidWinter Meeting, Baltimore, USA. February 2013.

PRIZES

1. The Philip Stell Prize (ORS Spring Meeting, Royal College of Surgeons of England, London, 2013).
2. Association for Research in Otolaryngology Travel Award (ARO Midwinter Meeting, Baltimore, 2013).

FURTHER FUNDING:

1. Research and MD Grant, Midland Institute of Otology (November 2011) for 2 years
2. Norman Gamble Research Fund, Royal Society of Medicine (February 2012)
3. Research Support Grant, Otorhinolaryngological Research Society (February 2012)

Hearing impairment currently affects more than 280 million people worldwide and by 2030 the World Health Organization predicts there will be an estimated 14.5 million, making it one of the Top 10 disease burdens, ahead of conditions such as diabetes.



Nina with a patient

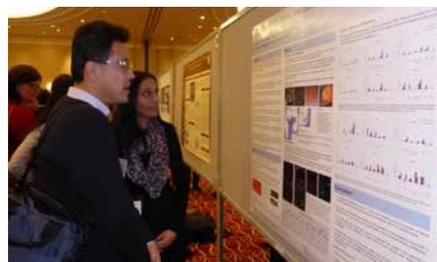
Hearing impairment is the most common sensory disability in humans. In terms of treating profound sensorineural hearing loss, cochlear implants play a key role and are the most successful sensory prosthetic device developed in the past 40 years. One area of growing research is cochlear implantation (CI) in patients with residual hearing such as those with age-related hearing loss. To date, the benefits of CI in these patients have been overshadowed by the fact that some can lose a substantial part of their residual hearing in the implanted ear. This is concerning, especially as the underlying cause of this loss remains unclear and prompts questions regarding the effects of CI on inner ear structure and function.

Investigation of CI and the inner ear in humans is mainly restricted to post-mortem studies. This relative inaccessibility has therefore led to the development of various animal models, which play a key role in research. The use of mice

has a huge advantage as there is a range of naturally occurring and genetically modified mouse strains that mimic human deafness. To date, there are very few studies of CI in mice. The primary aim of the project was to develop a reproducible and viable technique to enable long-term CI in the mouse and to assess the cochlea response to implantation.

Despite the technical challenges, we have developed a successful method for mouse CI with excellent survival rates to date. Analysis post-implantation showed evidence of greater threshold shifts in the implanted ear, but substantial preservation of residual hearing. There were no cases of profound hearing loss. Histological analysis revealed inflammation within the cochleae and encapsulation of the implant in tissue with characteristics suggestive of fibrosis. Research continues to more clearly define these effects on residual inner ear structure and function. It is hoped the research will help optimise surgical techniques and design more appropriate electrodes with regards to preserving hearing and therefore maximise benefits to patients. There is also huge interest in delivering therapeutics to the inner ear via CI to both preserve and enhance function. Our mouse

model will help pave the way for this research as, without a suitable animal model, this will not become a reality.



Nina presenting at the Association for Research in Otolaryngology

DEEP VENOUS HAEMODYNAMICS AND DEVELOPMENT OF A DEEP VEIN VALVE IMPLANT



**HAYLEY
MARIE MOORE**

FELLOWSHIP/SPONSOR

Freemasons' Fund for Surgical Research with the support of the Rosetrees Trust

SUPERVISOR

Professor Alun H Davies

SITE OF WORK

Imperial College London

PUBLICATIONS

1. Baldwin M, Moore HM, Rudarakanchana N, Gohel M, Davies AH. Post-thrombotic Syndrome: a Clinical Review. *Journal of Thrombosis and Haemostasis* 2013, 11:795–805.
2. Moore HM, Lane TRA, Thapar A, Franklin IJ, Davies AH. The European Burden of Primary Varicose Veins. *Phlebology* 2013, 1: 141–147.

PRESENTATIONS

1. Deep Venous Valve Management in the Future. Moore HM, Davies AH. Charing Cross International Symposium. invited oral presentation.
2. Haemodynamic measurements around a femoral vein valve by duplex ultrasound. Moore HM, Dharmarajah B, Gohel MS, Davies A H. XVII International Union of Phlebology World Meeting, Boston, USA. Oral presentation.

PRIZES

1. American College of Phlebology's 2013 International Travel Scholarship
2. Graham-Dixon Award for Excellent Contribution to Cardiovascular Research

Chronic venous disease affects a third of the adult population of Western Europe and the USA and costs approximately 1%–2% of the annual healthcare budget of these countries.



A patient having an MRI scan of the veins and valves in the leg



Professor Davies and the Academic Section of Vascular Surgery



Hayley presenting at the Charing Cross Symposium

Chronic venous disease is common, distressing and a significant cause of healthcare expense. The cause is failure of the valves in the superficial or deep veins of the legs. Patients with deep venous disease have limited options for treatment. A safe method of treating patients with this complex disease is needed.

The aims of this project were to make measurements around normal deep vein valves using ultrasound and magnetic resonance imaging, to develop computational and laboratory flow models for deep vein valves, to develop and investigate a new material to engineer a prototype deep vein valve replacement and to develop a valve for implantation into the deep venous system.

An observational study has been carried out evaluating subjects with normal deep veins with ultrasound, contrast enhanced ultrasound and dynamic magnetic resonance imaging of normal subjects. This has given the flow, velocity data and anatomical images required for the project.

A preliminary computational flow model has been developed using the data obtained from the imaging stage of the project.

This is a two-dimensional model incorporating flexible valve leaflets. A laboratory model of venous function, in the form of a flow rig has been created.

Presently, materials and coated metal stents used in the vascular system have several problems. They cause clotting of blood and are often not compatible with blood or body systems. In addition, they lack the required mechanical properties. I have synthesised a novel material that is very compatible with blood, based on the material Methacryloyloxyethyl phosphorylcholine (MPC). Its properties have been modified to change its solubility and mechanical properties.

This project aimed to guide the development of a treatment for patients, for whom few options are available. Chronic venous disease and venous ulceration are painful and debilitating, potentially requiring years of treatment. An effective treatment option that could be carried out without major surgery could result in ulcers healing quicker and improvements in patients' symptoms and quality of life, as well as reduced costs for the NHS as a whole.

ESTROGEN RECEPTOR BETA IS AN IMPORTANT MODULATOR OF PROSTATE CARCINOGENESIS



**ADAM W
NELSON**

FELLOWSHIP/SPONSOR

RCS Research Fellowship

SUPERVISORS

Jason S Carroll and Professor David E Neal

SITE OF WORK

Cancer Research UK Cambridge Institute,
University of Cambridge

PUBLICATIONS

Nelson AW, Tilley WD, Neal DE, Carroll JS.
Estrogen receptor beta in prostate cancer:
friend or foe? *Endocr Relat Cancer* 2014
Aug; 21: T219–34.

PRIZES

Health Education East of England
Celebration of Success Annual Awards
2013, Research Proposal of the Year.

FURTHER FUNDING

Medical Research Council Clinical
Research Training Fellowship for three
years and The Urology Foundation
Research Scholarship for one year.

Prostate cancer is the commonest cancer in men. Despite many years of research, the role of estrogen in the prostate is incompletely understood.

The steroid hormone estrogen has been shown to be important in the development and progression of prostate cancer (PC). To date, the mechanisms by which estrogen exerts its effects in the prostate are incompletely understood. There are two receptors in prostate tissue that mediate the effects of estrogen; estrogen receptor alpha (ER α) and estrogen receptor beta (ER β). ER α is thought to mediate the ‘bad’, tumour-promoting effects of estrogen, whereas ER β is thought to be mostly protective and tumour-suppressive. However, recent evidence would suggest that ER β may also have a harmful, tumour-promoting effect within the prostate. The aim of my research, therefore, is to improve understanding of the role of ER β and to establish whether it represents a target for future treatment of PC.

The broader study of ER β has thus far been hampered by problems with specificity of antibodies for detecting ER β in tissue samples or cultured human cell lines. This has led to conflicting and confusing results in the published literature. My research so far has been focused on testing a large number of ER β antibodies to ensure that I have a useful, accurate antibody that will specifically target ER β in the samples I will be working with. To do this, I have been working in a cell line with ER β expression that can be switched on or off with doxycycline. The result of this

work has been that I now have three validated ER β antibodies that I can confidently take forward to use for the rest of my research. These antibodies will be used for a wide range of studies on PC cell lines and human prostate tissue to assess if ER β expression correlates with patient prognosis, and to assess the function of ER β at a genetic level to see how it influences cancer development and progression.



Adam with one of his patients

AN INTEGRATED APPROACH FOR INDIVIDUAL TREATMENT PLANNING IN AORTIC DISSECTION



**ALIA
NOORANI**

FELLOWSHIP/SPONSOR

RCS Research Fellowship supported by Pearce Legacy and the H&S Charitable Trust

SUPERVISOR

C Alberto Figueroa

SITE OF WORK

St Thomas' Hospital, London

PRESENTATIONS

Image based modelling in aortic dissection, 10th International Symposium on Endovascular Therapeutics, Barcelona, Spain 2013

PRIZES

Winner of Best Poster Presentation, 10th International Symposium on Endovascular Therapeutics, Barcelona, Spain 2013.

FURTHER FUNDING

Heart Research UK for one year

Half of all patients with aortic dissection are dead within five years, regardless of the treatment they receive.



Alia and Dr Figueroa analysing simulation results

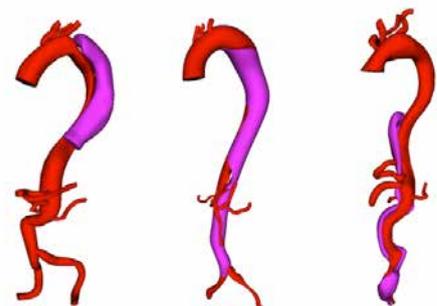
Aortic dissection is a life-threatening condition where a tear develops in the inner lining (intima) of the aorta, forming an additional false channel (lumen). As a result, blood flow in the true lumen may be compromised, affecting the viability of organs. Tear location and the presence of complicating factors (persistent chest pain due to ongoing aortic growth, compromised blood supply to organs and aortic rupture) largely dictate patient management.

Stable patients undergo regular imaging, monitoring changes in aortic size. Aortic growth of 0.5 cm from previous scans or a total aortic size of 5.5 cm, are deemed significant, requiring stent-graft insertion. Despite best medical and surgical care, patients continue to have variable outcomes and those with apparently similar types of dissection anatomy have different long-term outcomes. Unsurprisingly, managing these patients is difficult.

Although false lumen haemodynamics (blood pressure, velocity and wall shear stress) are thought to be responsible for complications, no study has proven this. The aim of this project is to develop an entirely non-invasive, tailor-made method to study haemodynamics in aortic dissection using a combination of computed tomography (CT) and magnetic resonance (MR) imaging and computer simulation techniques. This will allow development of a patient-specific method for treatment planning, providing a superior modality of care.

There are two parts to this study. In the first instance, patients due for stent-graft insertion (due to the presence of symptoms or adverse features on their clinical imaging) have an aortic MRI prior to surgery and invasive pressure wire measurements taken from within the aortic true and false lumen during their surgery.

Anatomical data from the CT and physiological haemodynamic data (velocity) from the MRI scan is used to develop a non-invasive simulation of aortic conditions. A comparison of invasive and non-invasive methods will determine validity. As a second stage, a follow-up study of patients using this non-invasive method will determine the effect of aortic haemodynamics on patient outcomes.



Aortic dissection models developed by Alia

VIBRATIONAL SPECTROSCOPY FOR EARLY DIAGNOSIS OF BARRETT'S NEOPLASIA



**OLIVER
OLD**

FELLOWSHIP/SPONSOR

Harry Morton Fellowship

SUPERVISORS

Professor Hugh Barr and Professor Paul Moayyedi

SITE OF WORK

McMaster University Medical Centre, Hamilton,
Ontario, Canada

The head of division is a Clinical Lead on the Barrett's Oesophagus Surveillance Study (BOSS), the largest randomised controlled trial of Barrett's surveillance worldwide, instigated and led by my MD research supervisor, and our team in Gloucester.

The Harry Morton Fellowship gave me the opportunity to visit McMaster University Medical Centre and the Farncombe Family Digestive Health Research Institute in Hamilton, Ontario. Farncombe has a reputation as one of the leading research groups in the world in gastrointestinal conditions. The research towards my MD has been focused on Barrett's oesophagus and early oesophageal cancer: this is one of many areas of expertise at the Farncombe Institute.

The Farncombe Institute is composed of both clinicians and full-time scientists, with daily presentations of current research and lively discussion. It was fantastic to experience this integrated research environment in a centre for academic medicine. Members of the group have a long history of Barrett's research, with particular interests in advanced endoscopic imaging techniques closely related to my research in optical diagnostics. Discussing my work with this group allowed me to benefit from their experience in this field.



Hamilton borders the Niagara Peninsula and is a short drive from Niagara Falls

The head of division is Professor Paul Moayyedi, an academic gastroenterologist and a clinical lead on the Barrett's Oesophagus Surveillance Study (BOSS), the largest randomised controlled trial of Barrett's

surveillance worldwide, instigated and led by Professor Hugh Barr, my MD research supervisor, and our team in Gloucester. The visit provided an opportunity to discuss the BOSS trial



Oliver with Professor Paul Moayyedi

in depth, and plan the initial output from the trial. This was a great learning experience for me to discuss aspects of clinical trials methodology and statistical analysis with a group of experts. We were then able to set up an international teleconference with key collaborators and share our thoughts on the analysis plan for the BOSS trial. As a result, we have recently submitted the first paper from this study.

I was also able to spend time observing endoscopy sessions and shadowing a senior resident during general surgical on calls at the nearby Juravinski Hospital (both McMaster and Juravinski hospitals form part of Hamilton Health Sciences). This gave me an insight into the Canadian healthcare system and some of the similarities and differences between our health services. Overall, this was a rich experience that provided many valuable lessons for my future clinical and research career.



The Toronto skyline from Lake Ontario

VIBRATIONAL SPECTROSCOPY FOR EARLY DIAGNOSIS OF BARRETT'S NEOPLASIA



**OLIVER
OLD**

FELLOWSHIP/SPONSOR

Enid Linder Research Fellowship

SUPERVISORS

Professor Hugh Barr (Upper GI Surgery, Gloucestershire Royal Hospital), Dr Catherine Kendall (Biophotonics Research Unit, Gloucestershire Royal Hospital), Professor Nick Stone (Professor of Biomedical Imaging and Biosensing, University of Exeter)

SITE OF WORK

Gloucestershire Royal Hospital

PUBLICATIONS

1. Old, OJ et al. Vibrational Spectroscopy for cancer diagnostics *Anal. Methods*, 2014;6:3901-17.
2. Almond LM, Old O, Barr H. Strategies for the Prevention of Oesophageal Adenocarcinoma. *Int J Surg*. 2014;12(9):931-5.

PRESENTATIONS:

1. Old O et al. Infrared spectral cytopathology as a diagnostic tool in screening for Barrett's esophagus. International Society for Diseases of the Esophagus (ISDE), Vancouver, September 2014. Oral.
2. Old OJ et al. Novel fibre-optic Raman probe for real-time diagnosis of early oesophageal cancer. SPEC, Krakow, Poland, August 2014.

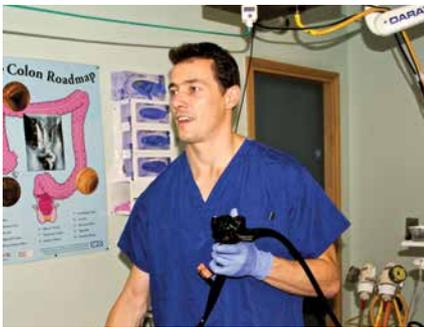
PRIZES

1. British Society of Gastroenterology, Poster Prize, June 2014.
2. The Doyle Award, Travelling Fellowship, Heartburn Cancer UK, 2014.

FURTHER FUNDING

Biophotonics Research Grant for 1 year

Under 10% of cases of oesophageal adenocarcinoma are detected as part of current Barrett's screening programmes.



Oliver performing an endoscopy

Cancer of the oesophagus (gullet) affects over 8,000 patients in the UK each year. Unfortunately, most patients are diagnosed at a late stage and curative treatment is not possible (only 13%

survive 5 years from diagnosis). Early diagnosis is the key to enabling timely intervention and improving survival.

Barrett's oesophagus is a pre-malignant condition which can sometimes progress to cancer, but most patients with the condition have mild symptoms of acid reflux, or no symptoms at all. There are an estimated one million people in the UK with Barrett's oesophagus, but only a small minority of these will have their condition diagnosed.

Current screening programmes use endoscopy to monitor patients with known Barrett's oesophagus for cancerous changes. Undertaking endoscopy as a screening tool in the general population would be expensive, invasive and impractical, and a number of groups have investigated non-endoscopic tests. One possibility is collecting cells



Oliver presenting work at a conference



Oliver discussing the project with a nurse in endoscopy

from the oesophagus using a miniature brush, which is swallowed and then withdrawn. Microscopic analysis of oesophageal

cells is rarely performed, lacks standardisation, and screening would be labour intensive and costly.

Infrared spectroscopy is an optical diagnostic technique that provides detailed biochemical measurements of cellular content. We investigated infrared spectroscopy as a method for accurate and automated detection of early oesophageal cancer in these cells.

We collected cells from the oesophagus in patients undergoing endoscopy. We then used infrared spectroscopy to measure each sample, and build classification models based on the known pathology of each patient. Testing our model has shown highly accurate identification of Barrett's and early cancerous changes, suggesting great promise for this technique in screening for early oesophageal cancer.

Next steps will include refining the collection and measurement techniques for widespread use in Barrett's screening, and a clinical trial testing infrared cytology screening against current gold-standard (endoscopy and biopsy).

ANALYSIS OF NATIONAL JOINT REGISTRY DATA ON HIP AND UNICOMPARTMENTAL KNEE REPLACEMENTS



**JEYA
PALAN**

FELLOWSHIP/SPONSOR

National Joint Registry/RCS Fellowship

SUPERVISORS

Professors Paul Gregg (NJR), David Murray (Oxford) and Ashley Blom (Bristol)

SITE OF WORK

Multiple sites including Leicester, Oxford and Bristol

PRIZES

1. First Prize ISAR 2014 Conference, Boston: Temporal trends in Revision Total Hip Replacements.
2. Third Prize Poster presentation: ISAR 2014, Boston: The influence of femoral stem design on the incidence of periprosthetic fracture after hip replacement.

FURTHER FUNDING

Gwen Fish Charitable Research Trust for up to two years

The National Joint Registry (NJR) for England, Wales and Northern Ireland is the largest arthroplasty registry in the world with over than 1.6 million records for total hip, knee, shoulder and ankle replacements.

My fellowship year was spent on a number of research projects.

1. *Service evaluation and validation of the NJR data on Oxford Medial Unicompartmental Knee Replacements.* This retrospective radiographic study using NJR data will identify the reasons for higher and lower than expected revision rates following Oxford unicompartmental knee replacements (UKR). This study will identify if inappropriate surgical indication or poor surgical technique can explain the reasons for higher than expected revision rates.



Jeya doing a total hip replacement

2. *Temporal trends in Revision Total Hip Replacements: an analysis of National Joint Registry data from 2003 to 2012.* The number of revision total hip arthroplasties (THA) being performed is increasing, but little is known about any changing pattern in patient demographics or reasons for revision over the past decade. This study has shown that patient characteristics have generally remained constant over the past decade. There has been an increase in the number of cases being revised for adverse tissue reaction and unexplained pain.
3. *The influence of femoral stem design on the incidence of periprosthetic fracture after hip replacement.* A periprosthetic fracture (PPF) following a total hip replacement (THR) is a devastating complication associated with increased morbidity and mortality for the patient. Different femoral stem designs and type of fixation (cemented or cementless) can influence the risk of having a revision for a PPF.
4. *Data validation in arthroplasty registries.* This review highlights some of the key issues on data validation in arthroplasty registries and describes the data validation process being developed in the NJR to improve data capture and accuracy. This project will work together with the British Orthopaedic Network Environment (BONE) in delivering a high-quality internal audit mechanism for data validation in units performing hip or knee replacements.

In summary, this fellowship has enabled me to undertake further analysis of the NJR data that will help clinicians and patients make informed choices about their hip or knee replacements, identify trends in revision hip or knee replacement surgery and to improve the data validation process in the NJR.

FEMOROACETABULAR IMPINGEMENT TRIAL (FAIT): A MULTI-CENTRE RANDOMISED CONTROLLED TRIAL COMPARING SURGICAL AND NON-SURGICAL MANAGEMENT OF FEMOROACETABULAR IMPINGEMENT



ANTONY PALMER

FELLOWSHIP/SPONSOR

Joint RCS/Dunhill Medical Trust Fellowship

SUPERVISORS

Professor Sion Glyn-Jones and Professor Andrew Carr

SITE OF WORK

Botnar Research Centre, Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, University of Oxford

PUBLICATIONS

1. Glyn-Jones S, Palmer AJR, Agricola R, Price AJ, Vincent TL, Weinans H, Carr AJ. A seminar in osteoarthritis: is

it possible to diagnose and treat early disease? *Lancet* 2014

2. Palmer AJR, Thomas G, Pollard T, Rombach I, Taylor A, Arden N, Beard D, Andrade T, Carr A, Glyn-Jones S. The feasibility of performing a randomised controlled trial for femoroacetabular impingement surgery. *Bone Joint Res* 2013; 2: 33-40.

PRESENTATIONS

1. Three-Dimensional Mapping of Cartilage and Labral Pathology in Femoroacetabular Impingement. American Academy of Orthopaedic Surgeons, Chicago, 2013.

2. A Feasibility Study for a Randomised Controlled Trial of Femoroacetabular Impingement Surgery. International Society for Hip Arthroscopy, Boston, 2012.

PRIZES

1. Senior Hulme Scholarship, Brasenose College, Oxford, 2014.
2. Annual Scientific Meeting Award Finalist, International Society of Hip Arthroscopy, 2013.

FURTHER FUNDING

Orthopaedic Research UK for 24 months. ear

The goals of treating femoroacetabular impingement are to improve patient symptoms and prevent the development of osteoarthritis.



The study allows high-resolution assessment of joint morphology that enables diagnosis and monitoring of early osteoarthritis

Osteoarthritis is the most common joint disease worldwide, affecting an estimated 10% males and 18% females over 60 years of age. It results from the action of hostile biomechanics upon a susceptible joint and correction of these biomechanics may offer a means of disease prevention. This would represent a paradigm shift in osteoarthritis treatment where currently the only effective treatment is joint replacement for advanced disease.

Femoroacetabular impingement (FAI) is a hip condition that gives rise to hostile biomechanics through abnormalities in the shape of the femoral head-neck junction (cam impingement) or orientation of the acetabulum (pincer impingement). The consequence is pathological abutment of the femoral head-neck junction against the acetabular rim. In the short term, FAI can cause pain and disability, and in the long term it significantly increases the risk of developing osteoarthritis. Studies suggest FAI may be responsible for

more than half of all cases of hip osteoarthritis.

There is considerable uncertainty surrounding how best to treat FAI. The principal two therapies adopted are physiotherapy and surgery. These aim to correct adverse joint biomechanics, either by improving core stability and movement control, or reshaping the hip joint. There is no long-term outcome data for either treatment and no study has compared their efficacy. This is an important area for research, given that the number of operations performed worldwide for this condition continues to rise exponentially.

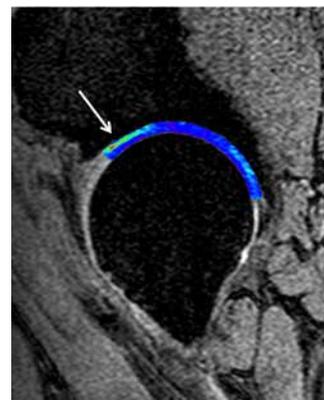


Image of the hip revealing early osteoarthritis

In a feasibility study, we demonstrated equipoise amongst patients and surgeons with respect to FAI treatment, and used our findings to design a multi-centre randomised controlled trial. This ongoing trial compares the efficacy of physiotherapy with arthroscopic surgery for both improving symptoms and preventing osteoarthritis. In addition to conventional radiographic measures

of osteoarthritis that only detect advanced disease, we are using novel markers of early degenerative change including physiological MRI and urinary and serum biomarkers of joint metabolism. These offer the potential to determine treatment efficacy within a short timeframe. (NCT01893034)

CHARACTERISATION OF MICRORNAS IN ULCERATIVE COLITIS AND COLITIS ASSOCIATED CANCER FOR USE AS POTENTIAL BIOMARKERS



**MALEENE
PATEL**

FELLOWSHIP / SPONSOR

The Professor Norman Williams and Ileostomy Association Fellowship

SUPERVISOR

Baljit Singh and Howard Pringle

SITE OF WORK

University of Leicester, Department of Cancer Studies and Molecular Medicine

PUBLICATIONS

Aslam MI, Patel M, Singh B, Jameson J, Pringle JH. MicroRNA manipulation in colorectal cancer cells: from laboratory to clinical application. *J Transl Med* 2012; 20:10.

PRESENTATIONS

1. Screening of novel plasma MicroRNAs associated with

disease progression in Ulcerative Colitis, European Union of Gastroenterology Week, Vienna, Austria, October, 2014. Oral Presentation.

2. Colitis Associated Cancer: a UK institutions 12-year experience. Royal Society of Medicine, Coloproctology section, Geneva/Switzerland, May 2012. Oral Presentation.

PRIZES

1. European Union of Gastroenterology Week 2014: Travelling Grant Award.

2. Midlands Gastroenterology Society Research Award 2012.

Ulcerative colitis affects 1 in every 420 people in the UK and is an established risk factor for colorectal cancer.

Ulcerative Colitis (UC) is a life-long, inflammatory condition of the large bowel. Patients with UC require regular colonoscopies to detect pre-cancerous changes known as dysplasia. The colonoscopic surveillance method is user dependent and can miss dysplastic lesions. Furthermore it is resource intensive, invasive and has poor patient compliance. These pitfalls fuel the ongoing search for alternative-screening methods that can accurately diagnose dysplasia or colitis-associated-cancer (CAC) at an early stage.

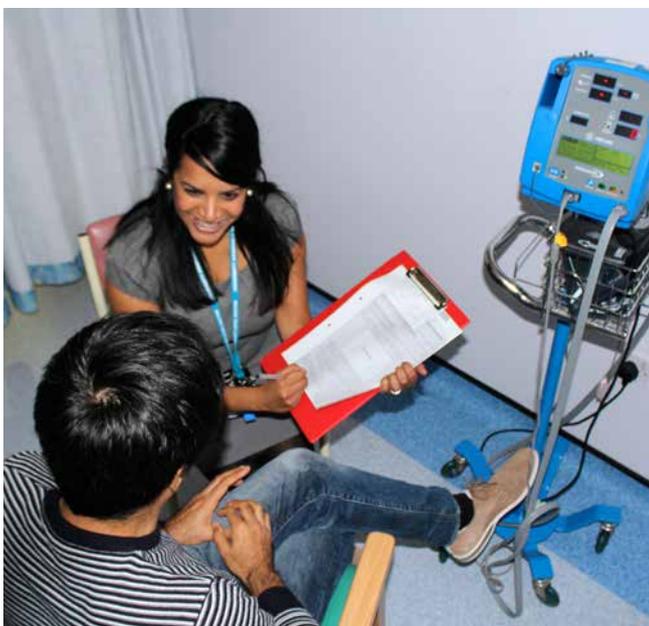
MicroRNA (miRNAs) are regulatory molecules that have been

implicated in many pathological processes, including cancer development. My research aimed to establish the miRNAs associated with UC and assess their potential as biomarkers for the detection of dysplasia and CAC.

The first part of the study utilised high-throughput discovery technology to profile the expression of 381 miRNAs in archived, UC-affected colonic mucosa. Real-time quantitative PCR was subsequently used to validate the results in an independent cohort. Combining different miRNAs together in a panel increased the capacity of the miRNAs to differentiate between disease states.

In the second part of the study, blood samples were collected from 120 patients undergoing colonoscopic surveillance for UC. Blood samples were allocated into groups based on biopsy results (Quiescent UC, Active UC, Dysplasia and CAC). Microarray technology was utilised to screen for more than 750 miRNAs within the groups, followed by PCR validation of 27 high-priority miRNAs of interest. Mir-375 was one of the miRNAs found to distinguish CAC cases from UC cases.

This feasibility study provides proof of concept of miRNAs as biomarkers. Future research will extrapolate these findings to a larger UC population to further evaluate the selected panel of miRNAs. This could lead to a blood test to monitor and identify patients that are at risk of developing CAC. Such a test would reduce unnecessary colonoscopies, and improve outcomes for patients through prompt surgical intervention.



Maleene consenting a research patient

REAL-TIME IMAGING OF THE HUMAN MIDDLE EAR USING HIGH FREQUENCY ULTRASOUND



**JAMES
RAINSBURY**

FELLOWSHIP/SPONSOR

Harry Morton Fellowship

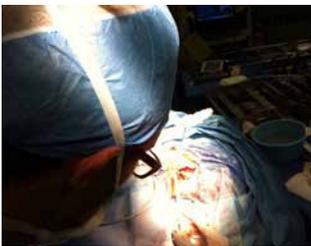
SUPERVISOR

Professor Manohar Bance

SITE OF WORK

Dalhousie University, Halifax, NS, Canada

High-frequency ultrasound (HFUS) allows excellent visualisation of much middle ear anatomy and pathology through an intact ear drum, or Tympanic Membrane (TM).



Implanting the Bonebridge, a novel bone conducting hearing implant



Halifax

I chose Halifax for my fellowship because of the excellent international reputation of the unit for high-quality research in middle ear mechanics. Professor Bance has built up a lab that is supported not only by a team of biomedical engineers but also a 'Fab Lab', or fabrication lab, which is purpose built for precision engineering anything from piezo-electric transducers for experimental bone conducting hearing aids to the cutting-edge handheld endoscopic ultrasound scanner used for my experiments in middle ear imaging.

Chronic middle ear disease and conductive hearing loss are two common problems managed by otologists. In the middle ear, direct visualisation of tissue or fluid, and the ability to evaluate the ossicles (the malleus, incus and stapes) would enhance the diagnosis of conductive hearing disorders and provide a non-surgical means of assessing the performance of implants used to reconstruct the ossicular chain. For imaging past the TM, modalities such as computed tomography are typically used, but these often do not provide sufficient resolution of structures of interest.

HFUS (>20MHz) is a relatively new area of ultrasonic imaging that provides an order of magnitude better resolution than

conventional low-frequency systems. Although HFUS has previously been implemented in some clinical applications, such as intravascular and ophthalmic imaging, it has not been widely accepted as a diagnostic tool because commercially available systems have a limited depth-of-field. In low-frequency ultrasound systems, improvement in depth-of-field is achieved by replacing the single element transducer with a transducer array and an electronic beamformer, and there has recently been some success in developing high-frequency 30-50MHz array transducers and beamformers. This may increase the clinical utility of HFUS and introduce new applications such as imaging the auditory system.



James presenting at the RCS, 12 Sept 2014

This study investigated the capability of HFUS using a transducer array to image the middle ear in real

time to demonstrate simulated clinical scenarios involving the ossicular chain, as well as measuring vibrations of TM and middle ear structures in response to sound stimuli.

In unfixed cadaver ears, the TM, ossicles and middle ear were all easily identifiable, with capabilities demonstrated for real-time imaging and video capture, three-dimensional reconstruction and vibrometry of middle ear structures. Based on these results, we conclude that HFUS is a relatively simple and minimally invasive technology with great potential to provide clinicians with new tools for diagnosing and monitoring middle ear pathologies.

STUDY OF SPERMATOGONIA STEM CELL PROPAGATION PRIOR TO CANCER TREATMENT IN A MOUSE MODEL



**RAVEEN
KAUR SANDHER**

FELLOWSHIP/SPONSOR

The Shears Northern Research Fellowship

SUPERVISORS

Professor Robert Pickard, Professor Mary Herbert and Kevin McEleny

SITE OF WORK

Newcastle University, Institute of Genetic Medicine, Bioscience Centre, Centre for Life

PUBLICATIONS

Sandher RK, Pickard R, Herbert M. Spermatogonial stem cells: a route to preserving fertility. *BJS* 2014; 101: 56–68.

PRESENTATIONS

1. International Society For Stem Cell Research, Stem

Cells in Translation, Palazzo dei Congressi, Florence, Italy, September 2013.

2. BAUS Academic Section at SARS meeting, Robinson College, Cambridge, UK. January 2014.

PRIZES

1. North East Surgical Society – Feggetter Prize for Best Presentation. May 2013.

2. BAUS Academic Section at SARS meeting, Cambridge – Prize for presentation. January 2014.

FURTHER FUNDING

The Urology Foundation for two years

In the UK, more than 850 boys are diagnosed with cancer every year, the treatment of which can often lead to irreversible infertility.



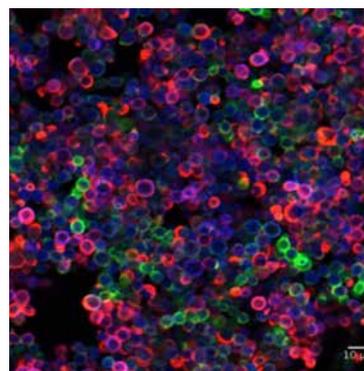
Raveen discussing her research project with a patient with male infertility

In the UK more than 850 boys are diagnosed with cancer annually. With improving cancer survival there has been a greater focus on life after cancer. Cancer treatment can have an irreversible effect on boys' fertility. Treatment depletes the precursors to sperm, the Spermatogonial Stem Cells (SSCs). SSCs only develop into sperm at puberty; so freezing of sperm is not an option as it might be in adults. Currently we are not able to preserve fertility in these patients.

Exciting research has shown that by taking a testicular biopsy before cancer treatment, growing (culturing) the SSCs in a laboratory and then transplanting them back into the testicle can restore fertility in a mouse model. The

published methodology for culturing SSCs was slow and produced a low cell number. In addition, freezing SSCs was extremely difficult, with many cells being non-viable upon warming. Therefore the aim of my research was to develop a rapid, reliable and reproducible method to culture and freeze mouse and eventually human SSCs.

In order to optimise the culture method, I decided to grow SSCs alongside the other supporting cells in the testicle. These cells are important because they release growth factors. By mimicking the *in vivo* environment I saw a dramatic increase in SSC number at several time-points. Very few groups across the world have been able to grow human SSCs in the laboratory; however, using this technique I have been successful. In addition, using a rapid freezing method that prevents ice crystal formation within the cell, and therefore less cell wall disruption upon thawing, I have been able to demonstrate excellent viability rates after freezing.



Spermatogonial stem cells on a confocal microscope

In conclusion, I have been successful in maintaining long-term cultures of human SSCs. My findings are an important advancement for the future clinical application of SSCs restoring fertility to male childhood cancer survivors.

IMPROVED DIAGNOSTIC OUTCOMES IN CRANIOFACIAL SURGERY BY USE OF NEXT GENERATION DNA SEQUENCING



**VIKRAM
PRAMOD
SHARMA**

FELLOWSHIP/SPONSOR

Blond McIndoe Research Fellowship supported by the Rosetrees Trust

SUPERVISOR

Professor Andrew Wilkie and Steven Wall

SITE OF WORK

Weatherall Institute of Molecular Medicine, University of Oxford

PUBLICATIONS

1. Diagnostic outcomes in craniofacial surgery are improved by use of next-generation DNA sequencing. *J Plas Recon Surg* 2014; 67: 1,462.
2. De novo and rare inherited mutations implicate the transcriptional coregulator TCF20/SPBP in autism spectrum disorder. *J Med Genet* 2014; 51: 737–747.

PRESENTATIONS

1. Twelfth Congress of the European Society of Plastic, Reconstructive and Aesthetic Surgery, Edinburgh International Conference Centre, Edinburgh. 6–11 July 2014.
2. Fifth European Plastic Surgery Research Council meeting, MS Cap San Diego. Hamburg, Germany, 22–25 August 2013.

PRIZES

Douglas Murray Prize (first place), Tenth West Midlands Plastic Surgery Meeting, Birmingham, 19 September 2013.

Despite major craniofacial surgery to remodel the skull in patients with craniosynostosis to relieve raised intracranial pressure or deteriorating head shape, an underlying causative gene defect can only be identified in 21%–24% of cases.

Craniosynostosis is the premature fusion of growth points or sutures in the skull. It is relatively common, affecting approximately 1 in 2,200 people. This early fusion can have adverse effects on airway, breathing and brain development. At least one major surgical procedure is required to correct skull deformity, allow normal brain growth and prevent complications. Coronal synostosis is the second commonest pattern of premature fusion. Scientific evidence suggests it is enriched for single gene mutations and associated with secondary complications requiring further surgery.



Vikram and Douglas Murray (former BAPRAS President) following the former's prize-winning national presentation at the Tenth West Midlands Plastic Surgery Meeting (September 2013)

This project used new DNA technology and advanced computational methods to analyse the fraction of the human genetic code that makes proteins. The aim was to search for novel disease genes in patients with bilateral coronal synostosis where all gene tests were negative. Damaging genetic variants shared between two or more patients were prioritised as this strategy previously identified a new disease gene and condition, known as TCF12-related craniosynostosis. During this project, a further novel

disease gene (TCF20) was identified in a single patient with coronal synostosis and autistic spectrum disorder. As further patients later identified with this gene mutation had autism only, it is not thought to cause coronal synostosis.

Further investigation into the genetic background of TCF12-mutation-positive individuals with or without craniofacial problems suggests it is important in disease development. Analysing parental origins in cases where TCF12 mutations arose as a new condition ('de novo') revealed a paternal origin in some cases and two instances of maternal origin. Sequencing DNA of parents of selected patients looking for de novo mutations revealed in one family a novel variant in MYH4, providing a new candidate for future studies.

Finally, lists of genes with damaging variants have been compiled so future researchers can continue this work to improve diagnostic outcomes, surgical risk stratification and genetic counselling for patients.



Members of the Wilkie Lab, where molecular research was conducted

THE DIFFERENTIAL EXPRESSION OF MICRORNA IN ABDOMINAL AORTIC ANEURYSMS



**PHILIP
STATHER**

FELLOWSHIP/SPONSOR

Joint RCS/Dunhill Medical Trust Fellowship

SUPERVISORS

Professor Robert Sayers and Matthew Bown

SITE OF WORK

University of Leicester

PUBLICATIONS

1. Stather PW, Sidloff DA, Dattani N, Gokani VJ, Choke E, Sayers RD, Bown MJ. Meta-analysis and meta-regression analysis of biomarkers for abdominal aortic aneurysm. *Br J Surg*. 2014; 101: 1,358–1,372.

2. Stather PW, Sylvius N, Wild JB, Choke E, Sayers RD, Bown MJ. Differential microRNA expression profiles in peripheral arterial disease. *Circ Cardiovasc Genet* 2013; 6: 490–497.

PRESENTATIONS

1. Stather PW, Sylvius N, Sidloff D, Wild JB, Butt HZ, Choke E, Sayers RD, Bown MJ. MicroRNAs let-7e, -15a, -196b and -411 circulating regulators of atherosclerotic abdominal aortic aneurysms. American Heart Association, Denver, USA. 17–20 November 2013.

2. Stather PW, Sylvius N, Sidloff D, Wild JB, Butt HZ, Choke E, Sayers RD, Bown MJ. Post-transcriptional dysregulation of extracellular matrix modifying genes in patients with abdominal aortic aneurysms. The Vascular Society of Great Britain and Ireland, Manchester, UK. 27–29 November 2013.

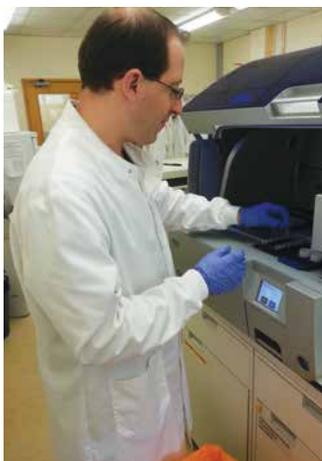
PRIZE

British Journal of Surgery Prize, Vascular Society of Great Britain and Ireland 2013.

FURTHER FUNDING

Leicester Biomedical Research Unit

Abdominal aortic aneurysms are the tenth leading cause of death in men over 65 years.



Preparing samples for microRNA analysis

An abdominal aortic aneurysm (AAA) is an enlargement of the biggest blood vessel in the body. It typically causes no symptoms prior to rupturing, which commonly results in death. AAA account for 5,251 deaths per year in the UK. Currently 1.8% of men aged 65 have an aneurysm, however the vast majority are small. These patients therefore undergo surveillance prior to the need for surgical intervention to decrease the chance of rupture.

Several studies have attempted to find a protein that can be used to detect people with AAA. This research combined data from all previous protein studies identifying 16 proteins that were increased and 2 that were decreased in patients with AAA. However, none of these proteins demonstrated sufficient sensitivity and specificity to be used as a screening tool for AAA.

Therefore this study aimed to



Being awarded the *British Journal of Surgery* Prize

look at the expression of a new marker, namely microRNAs. MicroRNAs are small RNAs which are not converted into protein. They exert their effect by attaching to messenger RNA and causing it to be degraded, thereby decreasing protein expression. MicroRNAs are crucial in the regulation of cardiovascular disease, and represent novel therapeutic strategies to decrease AAA expansion.

This study identified a significant difference in expression of 29 microRNAs in blood, 4 of which were validated in a second larger study in blood. One of these microRNAs was also found to be significantly increased in plasma, but none were found to be differently expressed in aortic tissue.

The four microRNAs identified within this study were found to interact with several of the proteins associated with aneurysms, making them plausible markers of abdominal aortic aneurysms. However, these four miRNAs were also found to be differently expressed in patients with peripheral arterial disease; therefore they may be due to generalised atherosclerosis rather than specific to aneurysms.

The results of this research will help us to understand why both aneurysms and peripheral arterial disease occur, taking a step towards treating these conditions, which are a considerable burden in those with advanced age.



Presentation at the Vascular Society of Great Britain and Ireland

PAEDIATRIC NEUROSURGERY WITH SPECIAL INTEREST IN PAEDIATRIC EPILEPSY SURGERY



**MARTIN
TISDALL**

FELLOWSHIP/SPONSOR

Harry Morton Fellowship

SUPERVISORS

James Drake and James Rutka

SITE OF WORK

Hospital for Sick Children, Toronto, Canada

FURTHER FUNDING

HCA foundation for one year

400 children per year in the UK could benefit from neurosurgery to treat epileptic seizures.



Martin in the OR at Sick Kids

In September 2012 I left London to take up a fellowship in paediatric neurosurgery at the Hospital for Sick Children in Toronto, Canada.

Sick Kids is one of the

premier paediatric neurosurgery departments worldwide and a significant proportion of international paediatric neurosurgeons have passed through their training programme.

I arrived to find Toronto bathed in glorious sunshine: a surprise given the stories I had heard of arctic winters and deep snow. I spent a year at Sick Kids developing my knowledge and skills. The fellowship covered all aspects of paediatric neurosurgery including elective and emergency



Martin trialling the 3D operating microscope camera

cases, and inpatient and outpatient care. I have a particular interest in the surgical management of paediatric epilepsy and the exceptional strength of Sick Kids' epilepsy surgery program was one of the attractions of the fellowship.

I gained experience in all aspects of the management of epilepsy surgery patients, including the use of magnetoencephalography (MEG) as a technique to non-invasively identify seizure foci. A MEG scanner is essentially an extremely powerful detector of magnetic fields, able to detect synchronised neuronal currents and thus identify epileptic foci. A significant number of the surgical candidates also underwent placement of invasive grid and depth electrodes, in order to more fully characterise the seizure onset zone prior to resective surgery. This allowed me to learn new techniques in the analysis of invasive EEG.

I am returning to the UK to take up a consultant post at Great Ormond Street Hospital, with a subspecialty interest in paediatric epilepsy surgery. The techniques I have learnt at Sick Kids will be immensely useful in my new job. The award



Martin with James Rutka in front of the cornerstone donated to Sick Kids by Great Ormond Street Hospital

I received has been incredibly helpful in coping with the financial burden of my fellowship and I am extremely indebted for the assistance it has provided.

EXPLORING THE IMMUNOLOGICAL RESPONSE TO SEVERE TRAUMA AND IDENTIFYING POTENTIAL TREATMENT OPTIONS



**HEW
DAVID
THOMAS
TORRANCE**

FELLOWSHIP/SPONSOR

RCS Research Fellowship supported by the Sorab (Soli) Jamshed Lam Legacy

SUPERVISORS

Michael J O'Dwyer, Professor Charles J Hinds and Professor Karim Brohi

SITE OF WORK

Royal London Hospital, Barts Health NHS Trust/Barts and the London School of Medicine and Dentistry, Queen Mary University of London

PUBLICATIONS

1. Torrance HD, Brohi K, Pearse RM, Mein CA, Wozniak E, Prowle, JR, Hinds CJ, O'Dwyer MJ. Association between gene expression biomarkers

of immunosuppression and blood transfusion in severely injured polytrauma patients. *Annals of Surgery* 2014.

2. Fragkou PC, Torrance HD, Pearse RM, Ackland GL, Prowle JR, Owen HC, Hinds CJ, O'Dwyer MJ. Perioperative blood transfusion is associated with a gene transcription profile characteristic of immunosuppression: a prospective cohort study. *Critical Care*. 2014; 18: 541.

PRESENTATIONS

1. Blood transfusion following severe trauma is associated with the

development of an early anti-inflammatory response. European Society of Intensive Care Medicine. Paris, October 2013.

2. Patterns of cytokine gene expression are related to nosocomial infectious complications following severe trauma. Intensive Care Society: State of the Art Meeting, London, December 2013.

PRIZES

1. RCS – Galeski and Lawrie Fellowship, 2014.
2. Best Research Poster Presentation Award – The Intensive Care Society (ICS): The State of the Art Meeting, London, 2013.

Trauma remains one of the most frequent causes of death in those aged under 45 worldwide. It results in six million deaths annually worldwide. Up to a staggering 60% of patients admitted to the ICU following severe traumatic injury develop infectious complications. The development of sepsis in these patients is associated with a three-fold increase in mortality.

As the immediate treatment given to severely injured trauma patients continues to improve, more and more patients who previously would have died either at the scene of injury or shortly afterwards are now surviving. These patients require ongoing care in an intensive care unit (ICU) and now are much more likely to die from infections contracted there or from multi-organ failure than to die directly from their injuries. Frequently these are young, previously healthy people and it is unclear why they are so susceptible to normally innocuous infections.

At the Royal London Hospital our research has already changed the way we identify and treat the bleeding trauma patient. However, I am concentrating on those severely injured patients admitted to the ICU. Blood samples are taken immediately following arrival to the emergency department and at two later time-points. Along with other clinical information, we are able to explore the effects that injury and blood loss, as well as commonly administered treatments (such as blood transfusions), have on their immune systems.



Hew on the Royal London Helipad overlooking the City of London

As a well-functioning immune system is crucial to fight infection, we therefore focused on changes to this induced by severe trauma. Our experimental data demonstrates that within two hours of injury, the immune system is severely affected and is, in essence, shutting down. In our patients a staggering 60% of them developed infections during their ICU stay.

Our experiments, which measure the activity of the immune response, are beginning to show us a link between severe traumatic injury, a defective immune system and previously healthy patients now at risk of developing serious infections. Ultimately the goal will be to develop a bedside test of the trauma patients' immune system, which will identify those at greatest risk of infection. Then we may be in a position to treat these patients with novel immune therapies.



Hew in Algiers, Algeria, teaching a basic surgical skills workshop as a Galeski and Lawrie fellow



Hew in Algiers, Algeria, with some of the surgical trainees from the workshop

MICROSURGERY FELLOWSHIP



**WILLIAM
ARTHUR
TOWNLEY**

FELLOWSHIP/SPONSOR

Harry Morton Fellowship

SUPERVISOR

Professor Stefan Hofer

SITE OF WORK

Toronto General Hospital

PUBLICATIONS

Townley WA, Mah E, O'Neill AC, Wunder JS, Ferguson PC, Zhong T, Hofer SO. Reconstruction of sarcoma defects following pre-operative radiation: Free tissue transfer is safe and reliable. *J Plast Reconstr Aesthet Surg* 2013;66.

PRESENTATIONS

1. Townley WA, Mah E, Wunder JS, Ferguson PC, Zhong T, Hofer SO. Soft tissue reconstruction of sarcoma defects following pre-operative radiation – free tissue transfer is safe and reliable. Canadian Society of Plastic Surgery, Calgary 2013.
2. Townley WA, Baluges N, Zhong T, Hofer SO. Antibiotic prophylaxis in implant-based breast reconstruction. Canadian Society of Plastic Surgery, Calgary 2013.

Developing subspecialist skills in microsurgery, head and neck reconstruction, facial paralysis surgery and breast reconstruction

I spent a year working with Professor Stefan Hofer at the University Health Network in Toronto. My fellowship was mostly clinical, allowing me to develop subspecialist skills in microsurgery, head and neck reconstruction, facial paralysis surgery and breast reconstruction. The volume and complexity of work was fantastic and therefore my fellowship was very productive. My own interest is facial paralysis surgery, an area that I will be pursuing as a consultant at Guy's and St. Thomas' Hospital.

During my time in Toronto, I was able to learn much to facilitate running a successful facial palsy practice –

multidisciplinary team organisation, specialist skill acquisition, research and patient communication.

In addition, I was able to participate in clinical research completing two projects, which were both presented at national meetings and published. The focus on clinical research at UHN was phenomenal and I was able to learn much in terms of the key factors that lead to successful research projects – leadership, database organisation, funding and collaboration. My supervisor, Stefan Hofer, was an excellent mentor, helping me develop clinically as a surgeon and being very supportive of my academic interests.



Braving a Toronto snowstorm while running between hospitals



Collecting a fellowship award from Toni Zhong



Team building camping trip in Killarney National Park with Stefan Hofer

INJURED SPINAL CORD PRESSURE EVALUATION



**MELISSA
CHENG-HWA
WERNDLE**

FELLOWSHIP/SPONSOR

RCS Research Fellowship supported by the Fletcher Legacy

SUPERVISORS

Professor MC Papadopoulos and Professor BA Bell

SITE OF WORK

St George's University of London

PUBLICATIONS

1. Werndle MC, Saadoun S, Phang I, Czosnyka M, Varsos GV, Czosnyka ZH, Smilewski P, Jamous A, Bell BA, Zoumprouli A, Papadopoulos MC. Monitoring of spinal cord perfusion pressure in acute spinal cord injury: Initial findings of the Injured Spinal Cord Pressure Evaluation Study. *Crit Care Med* 2014; 42: 646–655.
2. Werndle MC, Zoumprouli A, Sedgwick P, Papadopoulos MC. Variability in the treatment of acute spinal cord

injury in the United Kingdom: results of a national survey. *J Neurotrauma* 2012; 29: 880–888.

PRESENTATIONS

1. Thirtieth Annual Meeting of American Association of Neurological Surgeons (AANS) and Congress of Neurological Surgeons (CNS) on Spine, Orlando, USA, 2014.
2. International Neurotrauma Society meeting, Budapest, Hungary, 2014.

PRIZES

Society of British Neurological Surgeons, British Journal of Neurosurgery Prize, September 2013.

FURTHER FUNDING

Neurosciences Research Foundation for three years.

One thousand people each year, predominantly young men, survive a traumatic spinal cord injury and are left paralysed or wheelchair bound.



Melissa with her supervisor, Professor Marios Papadopoulos, operating on a spinal cord-injured patient

Traumatic spinal cord injuries are sudden and catastrophic events, with a cost to the NHS of approximately £1 billion per year. The management of these injuries remains highly variable and the current focus of treatment is on fixing and stabilising the bone, while largely ignoring the spinal cord. Developments lag decades behind brain injury research.

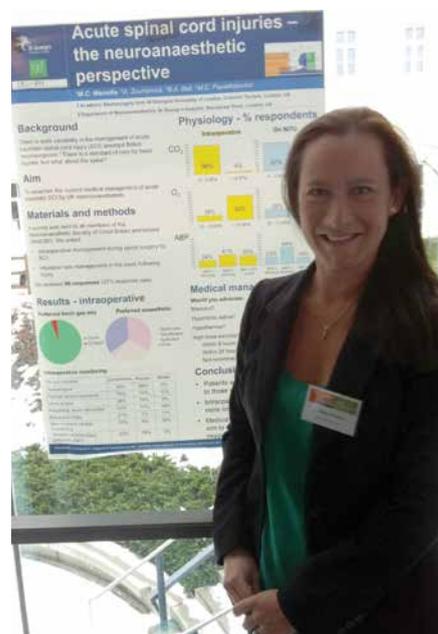
The aim of this study was to take well-known principles of brain injury management and for the first time apply them to the spinal cord.

We have developed a novel technique to measure spinal pressures in patients who had a severe traumatic spinal cord

injury at the site of injury, which is not currently in clinical use. We have defined new variables called intraspinal pressure (ISP), and spinal cord perfusion pressure (SCPP = arterial blood pressure – intraspinal pressure).

We have discovered that spinal pressure is high and spinal cord perfusion pressure is low after traumatic injury. Changing blood carbon dioxide levels, administration of mannitol and altered doses of the anaesthetic agent sevoflurane had no effect on ISP or SCPP. Inotropes increased SCPP. By improving spinal cord perfusion pressure, we could improve motor-evoked potentials (linked to improved leg strength recovery), cord blood flow and restore autoregulation to the spinal cord.

The findings provide proof-of-principle that intraspinal pressure at the injury site can be safely measured after traumatic spinal cord injury.



Presenting the study findings at the EuroNeuro International Conference in Orlando, Florida

POLYMER-GUIDED CHONDROGENESIS OF HUMAN ADIPOSE-DERIVED PERIVASCULAR STEM CELLS



**CHRISTOPHER
CHARLES
WEST**

FELLOWSHIP/SPONSOR

RCS Research Fellowship

SUPERVISOR

Professor Bruno Péault

SITE OF WORK

University of Edinburgh MRC Centre for Regenerative Medicine

PUBLICATIONS

1. West CC, Murray IR, González Z, Hindle P, Hay DC, Stewart KJ, Péault B. Ethical, legal and practical issues of establishing an adipose stem cell bank for research. *J Plast Reconstr Aesthet Surg* 2014; 67: 745–751.
2. Murray IR, West CC, Hardy WR,

James AW, Park TS, Nguyen A, Tawonsawatruk T, Lazzari L, Soo C, Peault B. Natural history of mesenchymal stem cells, from vessel walls to culture vessels. *Cellular and Molecular Life Sciences* 2014; 71: 1,353–1,374.

PRESENTATIONS

1. Adipose derived perivascular stem cells are a source of purified autologous mesenchymal stem cells for regenerative medicine – is the need for ex vivo culture over? European Association of Plastic Surgeons. Ischia, Italy. June 2014.

2. The effects of synthetic polymer based biomaterials on the behaviour of adipose derived peri-vascular stem cells (PSC) in vitro. International Federation for Adipose Therapeutics and Science. New York, USA. November, 2013.

PRIZE

Three-minute thesis competition – University of Edinburgh winner, 2013.

FURTHER FUNDING

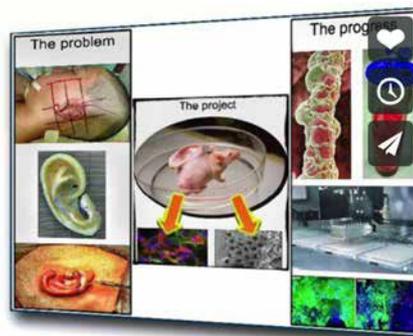
Chief Scientist Office Clinical Academic Training Fellowship (three years) and William Rooney Plastic Surgery and Burns Research Trust (three years).

One in every 4,000 children are born missing one or both of their ears

One in 4,000 children are born missing one or both of their ears, and the surgical technique used to reconstruct ears requires surgeons to remove ribs from the patient, and the cartilage from the ribs is used to carve a new ear. Removing ribs has many risks including pain, punctured lung and chest deformity. Patients undergoing this surgery spend 8 hours in the operating theatre and a week recovering in hospital, costing the NHS £25000. Therefore, the ability to 'grow' an ear would be a major advancement both in patients and the NHS. The focus of my project is to identify the two vital ingredients required when engineering any solid tissue. First the correct cell type, as these are the

building blocks, and, second, a scaffold on which they can grow, as this is the cement that binds the tissue together.

Mesenchymal stem cells are the cells that can generate cartilage and my research has shown that these cells live in direct relationship with the smallest of blood vessels in the human body. As there are blood vessels in every tissue, these cells can be purified from an easily accessible source – adipose tissue (fat). Adipose tissue is a superb source of stem cells as it contains significantly more cells and is much less painful to harvest, compared to traditional sources such as bone marrow.



To identify scaffolds, I used a special printer that prints tiny spots of thousands of individual polymers onto the surface of a microscope slide, allowing them to be rapidly screened. I have identified five polymers to support the attachment, proliferation and subsequent differentiation of the cells into cartilage-like cells. The next phase of this project is to combine the cells and polymers to produce three-dimensional pieces of cartilage for ear reconstruction surgery.



Chris delivering an award-winning presentation in the international final of the Three-Minute Thesis Competition

UNDERSTANDING AXONAL REINNERVATION OF MOTOR UNITS



**ALEXANDER
CS WOOLLARD**

FELLOWSHIP / SPONSOR

Enid Linder Foundation Research Fellowship

SUPERVISORS

AO Grobbelaar, K Rolfe and Professor JW Lichtman

SITE OF WORK

Harvard University, USA, and UCL, UK

PRESENTATIONS

1. The Society of Neuroscience, New Orleans, USA.
2. The American Association of Plastic Surgeons, New Orleans, USA.

PRIZES

1. Grant from the Roan Trust
2. Rosetrees Essay Prize, The Royal College of Surgeons of England

FURTHER FUNDING

The Roan Trust for two years and The Anton Jurgens Trust for one year

20% of patients undergoing gold-standard facial reanimation surgery do not achieve a satisfactory, symmetrical smile.



Alex Woollard presenting his research results at EURAPS, Italy 2014

Facial palsy is caused by numerous factors and can affect all age groups. Most patients recover without the treatment, but those that don't spontaneously recover are left with a permanent disability. Speech, eating and eye-closure can all be affected, which may result in permanent damage to the eyes and teeth,

and can result in awkward social interaction and can affect development in children.

Surgical reconstruction is an option. This involves nerve and muscle transfers to restore function back to normal. However, surgical outcomes remain variable and the cause of this variability is unclear. Previously, our group has proposed that changes in the proportion of nerves to muscle fibres after surgery may hold the key to how the muscle will function. Our current research aims to understand how nerves reform their connections to muscles.

This study models facial reanimation. A special coloured protein expressed in the nerves makes it possible to watch the recovering nerve as it re-grows and makes new connections with the muscle. The model provides information about the characteristics of the regenerating nerve and the patterns of the new connections in the muscle.

Results suggest that only about half of the nerves repopulate the muscle; however, all of the muscle fibres make a new connection. This means each nerve powers twice as many muscle fibres than before. Previous research in this area has suggested that as this proportion increases the nerves can become over-worked and therefore ineffective. This results in poor functioning of the muscle.

We believe this may explain what is occurring in the facial palsy patients where the surgery is unsatisfactory. This will enable us to try and tailor reconstructions to the capacity of the re-growing nerve.



Performing microsurgery as part of the team at The Royal Free Hospital NHS Foundation Trust



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Legacies do not need to be huge sums of money to make a difference. A gift, whatever the amount, will help us continue to advance surgical standards by developing and delivering world-leading training and research programmes.

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The Pump Priming award is given to a limited number of newly appointed Consultants and Senior Lecturers (appointed since 2006) in surgery, who are working at hospitals and universities within the UK, to assist 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

CLAIRE HOPKINS
CARL PHILPOTT
JONATHAN SUTCLIFFE

58
59
60

IMPROVING OUTCOMES FROM ENDOSCOPIC SINUS SURGERY



CLAIRE HOPKINS

CURRENT POSITION

Consultant in Otolaryngology in Guys Hospital

TITLE OF FELLOWSHIP

PUMP PRIMING AWARD

SITE OF WORK

Guys & St Thomas NHS Foundation Trust

SPECIALTY

Otolaryngology

PUBLICATIONS

1. Hopkins C, Gillett S, Slack R, Lund VJ, Browne JP. Psychometric validity of the 22-item Sinonasal Outcome Test. *Clin Otolaryngol* 2009; 34(5): 447-54.
2. Nanayakkara J, Roberts D, Hopkins C. The impact of mental health on chronic rhinosinusitis symptom scores. *Eur Arch ORL-NHS* 2013; 270; 1361 – 4

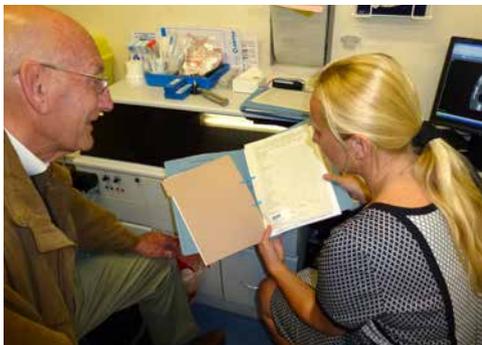
3. Hopkins C, Rimmer J, Lund V. Does timing of surgical intervention in CRS impact outcomes? - Data from the UK Audit of Surgery for Chronic Rhinosinusitis. Accepted for publication to *Rhinology*
4. Hopkins C, Andres P, Holy C. Does timing of surgical intervention in CRS impact outcomes? - Analysis of CPRD data. Accepted for publication to *Rhinology*

PRIZES

Carter A, Timms S, Hopkins C. Is man-flu really the worst? Women in Surgery Meeting May 2013, Awarded best poster prize

Chronic rhinosinusitis affects 11% of UK adults with 1 in 3 patients requiring surgery.

The aims of ongoing research are to further develop and refine a validated Patient Rated Outcome Measure (PROM) for chronic rhinosinusitis (CRS), and to use this to collect data in patients undergoing surgery for CRS in order to improve outcomes.



Claire in a busy clinic

CRS patients suffer with nasal blockage, facial pain, loss of smell, chronic catarrh and sleep disturbance resulting in days off work, reduced productivity whilst at work and a negative impact on quality of life that has been shown to be greater than angina. Currently patients are treated medically, but roughly 1 in 3 patients require surgery to relieve their symptoms.

Measuring the impact on quality of life requires PROMs. During a Research Fellowship in the Clinical Effectiveness Unit at the RCS as a surgical trainee, I developed and validated the 22-item sinonasal outcome test (SNOT-22); this is now the most widely used CRS PROM internationally, and is recommended for future research by the European Position Paper on Rhinosinusitis and Nasal Polyps. My current work builds on this preliminary research.

I have shown that the impact of symptoms and benefits from surgery can be modified by patient related factors. For example, women (surprisingly!) report higher levels of symptoms for the same radiological stage of CRS than men. Previously undiagnosed co-existing anxiety and depression are common amongst sufferers with CRS, and again report greater symptom severity for the same extent of disease. While gender is obviously fixed, treatment of co-existing depression may reduce the impact of CRS on quality of life. Identifying disease modifiers is essential to optimizing outcomes.

Perhaps more importantly as surgeons, we need to identify which aspects of our own practice determine outcome. I have found that timing of surgical intervention is important; patients undergoing surgery who have had CRS symptoms for more than 5 years get significantly less improvement than patients undergoing surgery within a year of symptom onset. Furthermore, improvements in symptoms are better maintained over 5 years in the 'early' group. Utilising data from CPRD, an administrative database in primary care, I was able to support these findings by showing that patients having 'late' surgery have higher on-going utilization of health care services, with more frequent GP visits and a greater number of prescription. These findings have been incorporated into the RCS/NICE Commissioning Guidance for Rhinosinusitis.

I am now developing this project into a large Programme Grant with NIHR, where we will incorporate routine eHealth data into a national database for sinonasal surgery, and use this to develop pragmatic study designs to determine the best treatment for this common condition.

A FEASIBILITY STUDY FOR A RANDOMISED CONTROLLED TRIAL OF CLARITHROMYCIN FOR CHRONIC RHINOSINUSITIS



**CARL
PHILPOTT**

CURRENT POSITION

Honorary Consultant ENT Surgeon, James Paget University Hospital Senior Lecturer in Otorhinolaryngology at University of East Anglia

TITLE OF FELLOWSHIP

PUMP PRIMING AWARD

SITE OF WORK

James Paget University Hospital (Great Yarmouth), Guys & St Thomas Hospital (London), Royal Surrey County Hospital (Guildford), Queens Medical Centre (Nottingham), Freeman Hospital (Newcastle) and Queen Elizabeth Hospital (Birmingham).

SPECIALTY

ENT

PUBLICATIONS

1. Under submission – OTOHNS journal
2. Under submission – Int Forum Rhinol All

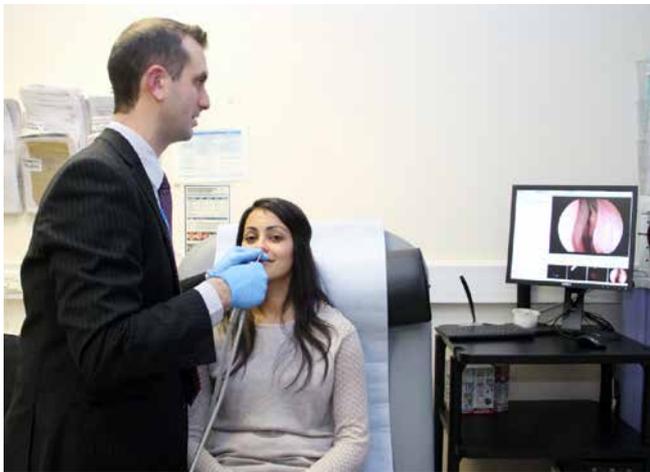
PRESENTATIONS

1. Clarithromycin for Chronic Rhinosinusitis. *European Rhinologic Society Congress* (Amsterdam) June 2014
2. Clarithromycin for Chronic Rhinosinusitis. American Association of Otolaryngologists and Head and Neck Surgeons Annual Conference (Orlando) September 2014

FURTHER FUNDING

RN was funded by the Bernice Bibby Trust and some of the equipment was paid for by the Anthony Long Trust.

This preliminary study for antibiotics over 12 weeks in chronic sinusitis showed a recruitment rate of 83% with 76% of patients retained in the study and an average recruitment rate of 4.23 per month across all sites. 1 in 2 patients appeared to benefit with an improvement in symptoms.



Patient undergoing nasal endoscopy with image captured using the D-scope system

The aim of this study was to assess the recruitment and retention of patients into a trial using long-term (12-week course) antibiotics to treat their chronic rhinosinusitis (long-term swelling of the nose and sinuses). Patients were recruited from 6 different hospitals and underwent a range of clinical (e.g. tests such as examination, scans and smell testing) and questionnaire (to assess both symptoms and quality of life) evaluations prior to commencing the antibiotic and nasal treatment.

Patients were re-assessed at the end of the 12-week medication period and sent repeat questionnaires at 6 months also. Feedback regarding the patients' involvement in the study was also sought.

Fifty-five patients were recruited to the study, 45 patients attended the 3 month visit and 41 the 6 month follow-up questionnaires. One patient was unable to take the medication, 4 patients suffered

side effects (3 unable to complete the full course). Unfortunately there were some failings in data collection at some study sites and this study has highlighted some important areas for improvement if the study is to be repeated in the future. Fifty percent of the patients completing the study showed an improvement in their symptomatic scores at the end of the antibiotic course which was sustained at 6 months also.

This study has provided valuable information for an application to the National Institute of Health Research for a full scale trial where some patients will also take a placebo (medication without the active antibiotic) which should give definitive answers as to the correct course of treatment for patients with this disease. Although a small number of patients were included here, the results may suggest that half of the patients stand to benefit from this treatment and potentially avoid sinus surgery.



Patient with RN going through questionnaires

OPTIMAL IDENTIFICATION OF INTERSTITIAL CELLS OF CAJAL IN HUMAN TISSUE



**JONATHAN
SUTCLIFFE**

CURRENT POSITION

Consultant Paediatric Surgeon

TITLE OF FELLOWSHIP

PUMP PRIMING AWARD

SITE OF WORK

Faculty of Biological Sciences,
University of Leeds and
Department of Paediatric Surgery,
Leeds General Infirmary

SPECIALTY

Paediatric Surgery

New cell markers may advance the understanding of muscle abnormalities both within the bowel and more widely.

Smooth muscle is important for function in a range of organs including the bowel, bladder and within blood vessels. When co-ordination of muscles fails, patients can experience serious symptoms. In the intestine, patients can reach a point where they are unable eat and require long-term intravenous nutrition. If the bladder fails to empty effectively, there is an increased chance of infection and ultimately renal failure. Patients with spinal cord injury experience particularly troublesome symptoms due to bladder and bowel dysfunction.



Jonathan demonstrating the close working relationship that is essential with the family of a patient with Hirschsprung Disease



Jonathan with his team

Smooth muscle tone in blood vessels can cause problems in the neonatal period when vessels narrow inappropriately (Coarctation) or, alternatively, fail to close following birth (Patent Ductus Arteriosus). These conditions are common indications for surgery. Our understanding of the control of smooth muscle is limited and a clearer understanding could allow more accurate diagnoses and allow new treatments to be considered.

Our aim was to identify how one particular cell type, the Interstitial Cell of Cajal (ICC), could best be demonstrated in tissues. We performed a structured review of the literature to see how ICC had been demonstrated in the past, and tested some of these techniques in our laboratory to be ready to study human tissues reliably. We identified all 392 papers examining the role of ICC in human motility in a range of tissues. Although the type of antibody used can be seen to produce different levels of staining, at least 30 antibodies had been used. Because many conditions (57) had been studied, often with low numbers of patients and controls in each (on average 16 and 7 respectively), it was rare to find conclusive proof for any one condition.

Based on our review, we have set out to identify the best way to study ICC. We are now using a new antibody (PDGFA) and are testing it against the traditional antibody (cKit). We have used the antibody in the bladder in animals who had undergone spinal cord injury and found for the first time that the number of ICC stained with this antibody increases significantly. This finding gives new insights into how the bladder functions in these patients.

Using the same antibody, another area we have been able to investigate for the first time has been the distribution of ICC in the vagina. This might be important in the development of treatment of children born with cloaca, a complex malformation.

We have successfully applied for ethical approval to begin to study ICC in human tissue, including blood vessels. Using our experience, we are now well placed to develop a long-term study of these cells.

THE RCS SURGICAL TRIALS INITIATIVE

THE SURGICAL TRIALS INITIATIVE

The interest generated in the first two years of this novel programme has exceeded expectations. The creation of five surgical trials centres and appointments of surgical specialty leads (SSLs) was completed by the end of 2014. This was generously supported by the Rosetrees Trust, several charities and many surgical specialist associations.

While the emphasis remains on the development and delivery of high quality randomised trials, the centres are involved with feasibility, pilot and safety studies as well as evidence synthesis. These are important preliminaries to full trials. The remit of the surgical trials centres therefore has been to support all aspects of work that might inform a clinical trial.

This article focuses on the views of one of our SSLs, Mr Abi Jain, and a trials unit co-lead, Professor Jane Blazeby.



Oxford Surgical Trials launch day



Professor Freddie Hamdy and David Beard (SITU Co-Director) at SITU launch day

ACHIEVEMENTS

- An NIHR call for surgical studies resulted in the award of some £28m of funding in 2014
- The number of patients entering surgical trials in the portfolio has doubled in the last year
- The Surgical Trials centres currently have 53 open trials, 26 trials in set up and 42 funding applications under review
- 156 new principal investigators are recruiting to surgical trials
- 53 new NHS trusts are now recruiting to trials.

PLANS

Meetings

Centres continue to run regional meetings to engage existing and new investigators. Innovations for the coming year will include a greater emphasis on education and training of new researchers in trials methodologies, as well as the broader aspects of research including research ethics.

Evidence synthesis

The RCS is running seven systematic reviews for competitively selected projects. These are based in the Clinical Effectiveness Unit and they will inform the design of future funding applications for new trials.

Trials portfolio

A national portfolio of all trials being undertaken by the Surgical Trials Centres has been established and includes: trials closed to recruitment, open trials, trials in set up and trials submitted for funding. This document is a unique resource for investigators to access information and obtain contact details for surgical trials.

The portfolio will also help investigators identify where there is a need for studies within their discipline.

Technology Access Pathway

The NIHR and the RCS, together with partners (including NICE, MHRA, ABHI, CRUK, MRC, IDEAL) are developing a technology evaluation programme to facilitate easier



Professors Dion Morton and Frank Smith at the Bristol launch



Professor Iain Hutchison, Kate Law CRUK and Professor Hisham Mehanna at the launch of the Birmingham Surgical Trials Consortium

access for industry, innovators and researchers to develop and evaluate new surgical medical devices and technologies. A combined RCS/NIHR infrastructure will provide a route to access specialist advice and build multidisciplinary partnerships to take new ideas and technologies forward, into early phase clinical studies as appropriate. It is hoped that a number of benefits will be realised:

- A common and easily accessible pathway for innovators and companies should eliminate unnecessary barriers and speed up the adoption of new technologies
- Early engagement of specialist clinical teams with researchers and specialist trials methodologists should lead to rapid feedback to the innovator or company
- Efficient development of the device or technology with safe, high quality evaluation for NHS and patient benefit.

International trials and a global surgical initiative

An International Trials Symposium will take place in November 2015 with a view to launching a trials programme across many countries. This will initially focus on Europe as a way of achieving faster recruitment to trials. This is only one strand in a wider RCS strategy to make a greater contribution to progress in global surgery.

But what do the people on the ground make of it?

THE VIEWS OF A SPECIALTY LEAD



(Mr Abilash Jain, SSL appointed in conjunction with The British Society for Surgery of the Hand and The British Association of Plastic, Reconstructive and Aesthetic Surgeons)

Plastic surgery is a small surgical specialty covering hand surgery, trauma, congenital defects, burns and cancer. Plastic surgeons work with all other surgical specialties to undertake complex reconstructions. Much evidence is based on poorly conducted clinical research with only 3% of published work classified as randomized controlled trials (RCTs). While it is recognised that large scale research, undertaken as multicentre randomised controlled trials, generate the highest level of evidence on which to base best practice, in plastic surgery only 2–3 multi-centre RCTs are published *globally* each year.

Plastic and hand surgery were poorly represented on the clinical research landscape, with virtually no clinical trials or patients recruited to the NIHR portfolio. The reason for such poor clinical evidence was multifactorial but probably stemmed from the lack of a defined pathway that practising plastic surgeons could access to rigorously test the interventions they perform.

The RCS clinical trials initiative has changed this and has been embraced by the plastic and hand surgery community.



Professor Jane Blazeby presenting at the Reconstructive Surgery trials Network (RSTN) meeting at the RCS

It provides a mechanism to allow plastic and hand surgeons to directly access the expertise needed to undertake high quality clinical research with direct benefit to patient care. It has allowed us to develop a culture of clinical trials within plastic surgery and its sub-specialty, hand surgery, within the space of just 2 years.

I took up the role of RCS SSL in 2013 representing both the BSSH and BAPRAS and we have had a tremendous response from both associations, with over 260 members of the Reconstructive Surgery Trials Network (RSTN) set up to deliver clinical research. We have over 60 units involved providing us with representation across England, Wales, Scotland and Northern Ireland; we even have members in Italy, Australia and the USA.

We have run two very successful trials days at the RCS in which 160 surgeons have been taught on trials-related topics, trained in good clinical practice (GCP) and where they have had the opportunity to present their trial ideas. At the last winter BAPRAS meeting we had a hugely popular trials session and the next RSTN trials day is already booked for 6 June 2015 at the RCS.

Our first trial (NINJA – nail bed injuries) has ethical approval, will be adopted onto the NIHR Children’s portfolio and the pilot will start recruiting from four centres in the spring of 2015. A collaborative trial with the Association of Breast Surgeons has been awarded RfPB (Research for Patient Benefit) funding from the NIHR and plastic surgeons have recruited a third of the patients in total so far. There are five other trials at various stages of development and at least two will start to recruit this year. There are also two large multicentre audit projects that will

be run nationally and, to inform future trials, plastic surgeons are also collaborating with the dermatologists and general surgeons on other projects. Further information is available on our website: <http://reconstructivesurgerytrials.net>

From a personal point of view this initiative has been very rewarding. As a relatively young academic surgeon I have learned from more experienced colleagues and have been able to approach them for advice and share the difficulties that inevitably occur. The process has taught me about a new area, research, as my background was in basic science. I have gained a lot of self-confidence and have a real pride in what has been achieved. The initiative has raised my profile not only nationally, but also internationally. I have learnt skills that have enhanced my clinical practice. Overall the future is looking very bright for clinical trial research in my specialty. While I have made rapid progress, it is clear that a national trials framework cannot be developed in just three years, which is the term of the current SSL position. I have enjoyed the process so much that I am keen to see through the initiatives that I have begun and continue as an SSL. I have no doubt that this initiative will act as a focus for a global shift towards high quality, evidence based plastic surgery clinical research, with its focus in the UK.

THE VIEWS OF A TRIALS CENTRE LEAD



(Professor Jane Blazeby, co-lead for the Bristol Surgical Trials Centre)

The Royal College of Surgeons clinical trials initiative is changing the face of surgical research in the UK. Investment directly facilitates the centres to work with NHS, academic surgeons and registered clinical trials units to design high quality studies. The hall mark of approval from RCS attracts new and experienced investigators to work with the surgical trials centres. It creates a centre of attention for NHS trusts, deaneries and the CLRNs to be involved in RCTs in surgery. It provides a badge of authority for new and ongoing training courses in RCT methodology for trainees and NHS consultants. The initiative sets standards for a culture of collaboration between the five trials centres which underpins important discussions about working together on new and ongoing studies, rather than competing.

The initiative is useful to write about in grant applications to demonstrate that the College is supporting surgeons to deliver high quality research and to show that there are administrative



Triallists presenting their trials idea to the 'dragons' at the 'dragon's den' style session at the Bristol Launch

staff in place to facilitate the proposed research and training. It has allowed us to consolidate our strategy to create an evidence base for surgery in the UK, invest in a new generation of surgeons to design, participate and lead new trials and gain further funding to sustain the work.

The increasing number of funded trials that are recruiting on time and target because of this support has benefit for patients. These benefits apply both to those patients currently participating in trials as well as future patients. The close monitoring and follow up of trial patients along with access to trial staff are all additions to standard care. The research effort also facilitates partnership working, to identify future research topics of importance to patients and surgeons.

In Bristol, we are pleased and proud to be part of the initiative and look forward to continuing this endeavour on behalf of the College and those who supported the initiative.

With grateful thanks for the support of:

- Association of Upper Gastrointestinal Surgeons of Great Britain and Ireland (AUGIS)
- Association of Breast Surgeons (ABS)
- British Association of Endocrine and Thyroid Surgeons (BAETS)
- British Association of Plastic, Reconstructive and Aesthetic Surgeons (BAPRAS)
- British Society for Surgery of the Hand (BSSH)

- Bowel Disease Research Foundation (BDRF)
- Breakthrough Breast Cancer
- Breast Cancer Campaign
- Cancer Research UK
- Get A-Head Charitable Trust
- George Drexler Foundation
- Mary Kinross Charitable Trust
- Henry Lumley Charitable Trust
- The National Institute for Health Research (NIHR)
- Orthopaedic Research UK
- The Rosetrees Trust
- The Enid Linder Foundation
- The Facial Surgery Research Foundation – Saving Faces



Mr Jon Snow, Prof Jenny Donovan, Dr Jonathan Gower, Dr Andrew Cook and Prof Amar Rangan at the Orthopaedic Trials meeting at the RCS.

FACULTY OF DENTAL SURGERY – RESEARCH COMMITTEE

THE FACULTY OF DENTAL SURGERY REPRESENTS AND SUPPORTS DENTAL SPECIALISTS TO ACHIEVE THE **HIGHEST POSSIBLE STANDARDS** OF ORAL HEALTH CARE FOR PATIENTS AND THE PUBLIC.



Professor Paul Speight,
Chair of the FDS
Research Committee

To this end the Faculty provides training and examinations for dental specialties, advises the profession and the NHS on clinical guidelines and also produces a range of specialist publications. The Faculty also promotes and supports oral and dental surgery research in its broadest sense to a national and international audience.

Through our Research Committee, the Faculty offers two full-time fellowships for up to three years, to allow early career researchers to take time out of clinical training to undertake a PhD or to consolidate their research training. One of these fellowships is funded by the Wellcome Trust and is awarded jointly on an annual basis. The Faculty also offers up to five smaller research grants per year, which provide ‘consumables’ costs for clinical trainees beginning to establish a career in research. Since 2008, the Faculty has awarded 10 Fellowships and almost 30 small grants. Many of our successful awardees have now established themselves in successful clinical academic careers and in some cases are already professors in their chosen specialties.

The Faculty also organises national research symposia, which have been sponsored and are therefore provided free to over 120 delegates on each occasion. These are held jointly with the Faculty of General Dental Practice and promote research opportunities for early career researchers and clinical academic trainees. We have particularly targeted the whole dental team, from both general practice and hospital settings, and promoted

collaborative research and research in primary care. Speakers at the symposia are leaders in the field from NIHR (National Institute for Health Research) and the British Society for Oral and Dental research, as well as national figures covering topics including clinical trials, international collaborations, working with industry and research governance. As well as talks, the experts have run a number of hands-on workshops at each symposium.

Areas of oral and dental research which have been supported by the Faculty:

Oral cancer

Oral cancer affects over 6,000 people per year in the UK, of whom over 50% will die within 5 years of diagnosis. Against this background, our research priorities include early diagnosis and prevention and understanding mechanisms of disease progression, with the aim of developing new treatments. In line with this, the Faculty has funded several cancer research projects. These have included studies into the role the widespread human wart virus (papillomaviruses) in oropharyngeal cancer, as well as studies of the molecular mechanisms of cancer spread (metastasis) and public health approaches to reducing alcohol consumption.

Periodontal disease

Periodontal diseases are inflammatory diseases of the gums and supporting tissues of the teeth, which often lead to loss of bone and eventually the tooth or teeth. Over 90% of the population is affected by some form of gum disease, with 10% of the population affected by chronic periodontal disease. As well as the direct oral affects, these chronic inflammatory disorders can affect the whole body and are associated with diabetes and an increased risk of heart disease. Faculty funded projects in this area have included studies to investigate the relationships between periodontal disease and diabetes, inflammatory bowel disease and cardiovascular disease.

Craniofacial abnormalities

There are many inherited and acquired craniofacial anomalies that often have severe consequences for patients. The loss of function and poor facial appearance associated with many of these conditions often affects the sufferers self esteem and hence their ability to socialise and achieve their full potential. Research in this area has focussed on understanding the cause of facial anomalies and investigating approaches to management. The Faculty have funded a number of specific



FDS Research Faculty and Speakers at the Symposium

projects ranging from studies of the genetic mechanisms of cleft lip and palate, developing tissue engineering approaches to managing facial deformities, and exploring methods to engage patients in decisions about their management.



Poster competition Runner-Up Miriam Khan. Are water pipe smokers aware that there are associated health risks with water pipe smoking?

In June 2014, the Faculty of Dental Surgery held its second national research symposium in collaboration with the Faculty of General Dental Practice. This year the theme of the symposium was Collaborative Research and Opportunities for

the Dental Team. The Faculty are keen to promote research for the whole dental team and the purpose of the symposium was to provide advice and encouragement, particularly to those who are just starting their research careers.

The invited speakers covered topics in three main areas: international collaborations, opportunities for Dental Care

Professionals (DCPs) and working with industry. In all, 120 delegates attended the day, including 42 general dental practitioners, 43 specialty registrars and academic trainees and 35 DCPs. The DCPs included hygienists and therapists, dental technicians, clinical dental technicians and dental nurses.

The morning session started with a talk from Drs James Fenton and Kieron Lee from the NIHR Trainees Coordinating Centre, who described all the various schemes available for funding research. They outlined the Integrated Academic training programme for academic fellows and lecturers, as well as opportunities for grant funding for PhD fellowships and career awards.

Following this, a series of renowned speakers covered the main themes. Professor Mike Curtis, Dean of the Institute of Dentistry, Barts and the London School of Medicine and Dentistry, described his own journey in developing international collaborations and highlighted the key attributes needed for successful partnerships – enthusiasm, trust and in depth knowledge of your subject area. Professor Paul Hatton, Professor of Biomaterials and Tissue Engineering, School of Clinical Dentistry, University of Sheffield, presented an overview of the European Union funding processes and outlined particular areas under FP7 that would be of interest and relevance to dental research.



Poster competition winner Jennifer Hawarth. Platelet interactive domains of *Streptococcus gordonii* surface protein PadA

willing to collaborate and share ideas. She summarised how industrial research was managed and suggested ways in which researchers with good ideas can approach potential industrial partners.

Fiona Sandom, a Tutor Hygienist and Therapist from Cardiff and Postgraduate Tutor in North Wales, outlined opportunities for DCPs. Fiona had started from nothing

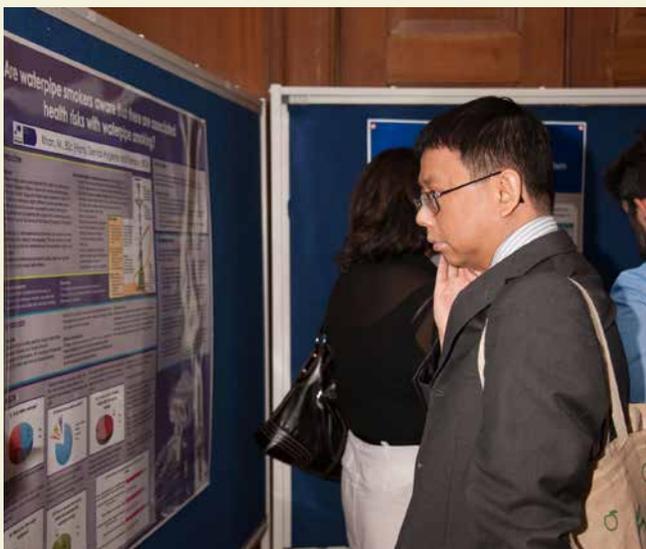
He gave a number of valuable tips on how to write proposals and win funding. Dr Anousheh Alavi, Scientific Affairs Manager at Colgate Palmolive, talked about working with industry and explained how our industrial colleagues are very keen and

except a good idea and had won a number of small grants to kick start her research. She inspired the audience with her tales of determination and enthusiasm to get grants and to undertake research in a difficult environment. During the meeting Professor Mike Lewis, President of the British Society for Oral and Dental Research (BSODR), gave a brief presentation outlining the benefits of membership and how the society can benefit and support early career researchers.

In the afternoon there were four research skills workshops, and each delegate had the opportunity to attend two. The choices were: How to write a grant and obtain funding (Professor Paul Hatton and Dr Kathryn Hurrell-Gillingham), 101 Common mistakes which prevent your paper's acceptance (Professor Ario Santini), Design of clinical trials (Professor Ivor Chestnutt) and Working with Industry (Dr Anousheh Alavai and Dr Mark Ide).

The day was free to all delegates and the Faculty are grateful to National Institute for Health Research (NIHR), Colgate Palmolive and the BSODR for funding the day.

In all, 120 delegates attended the day, including 42 general dental practitioners, 43 specialty registrars and academic trainees and 35 DCPs. The DCPs included hygienists and therapists, dental technicians, clinical dental technicians and dental nurses.



Poster Competition Display



Professor Paul Speight, Chair of FDS Research Committee

INVESTIGATION OF POTENTIAL PLATELET INTERACTIVE PROTEINS EXPRESSED BY INFECTIVE ENDOCARDITIS (IE) PATHOGEN *STREPTOCOCCUS GORDONII*, AND THEIR POSSIBLE ROLE IN THE PATHOGENESIS OF IE



**HELEN
PETERSEN**

FELLOWSHIP/SPONSOR

FDS Research Fellowship

SITE OF WORK

UCL Eastman Dental Institute

PUBLICATIONS:

Ciara Keane*; Helen J. Petersen*; Dorothea O. Tilley; Jennifer Haworth; Dermot Cox; Howard F. Jenkinson; Steve W. Kerrigan (2013) Multiple sites on *Streptococcus gordonii* surface protein PadA bind to platelet GPIIb/IIIa. *Journal of Thrombosis and Haemostasis* doi:10.1160/TH13-07-0580 (*These authors contributed equally). Impact factor 6.081
Petersen HJ. *Oral Bacteria: Masters of disguise and distant site invaders*. *Faculty of Dentistry Journal*, Oct 2012

PRESENTATIONS:

SGM annual meeting, York 2011, UCL Infection, Immunology and Inflammation Domain – London 2011

PRIZES:

1st Place, Research Presentation Prize,
1st Place, Poster Competition,

Oral bacteria produce cell surface proteins that trick human platelets in to thinking they are areas of vascular damage in order to hide from the immune system. This may be a way that they can travel from the oral cavity to cause distant site infections.



A patient undergoing dental treatment

Infective endocarditis is a severe life-threatening disease caused by bacterial infection of damaged heart valves. A well recognised cause is deposition of oral bacteria, which may get into the blood stream as a result of periodontal disease. The purpose of this study was to identify proteins on the surface of oral bacteria, which may interact with platelets and promote adhesion to the surface of the heart. Our results showed that oral bacterium (*Streptococcus gordonii*) a known endocarditis pathogen, expresses cell surface molecules that interact with adhesion molecules (integrins) on the surface of platelets. In vitro experiments showed that this interaction could facilitate platelet adhesion and spreading (activation).

These results suggest that cell surface proteins on *Streptococcus gordonii* interact with platelets and likely contribute to the production of infected adhesions, which causes infective endocarditis. This raises the possibility of developing drugs to target these interactions for combating this disease.

Reference; Keane C, Petersen HJ, Tilley DO, Haworth J, Cox D, Jenkinson HF, Kerrigan SW. Multiple sites on *Streptococcus gordonii* surface protein PadA bind to platelet GPIIb/IIIa. *Thromb Haemost*. 2013 Dec;110(6):1278-87

FEASIBILITY OF ALCOHOL SCREENING AND TREATMENT INTERVENTIONS IN DENTAL SETTINGS



**ZAIRAH
YUSUF
ROKED**

FELLOWSHIP/SPONSOR

FDS Research Fellowship

SUPERVISORS

Professor Simon Moore and Professor Jonathan Shepherd

SITE OF WORK

Cardiff University School of Dentistry and Glynneath Dental Practice

PUBLICATIONS

1. Faculty Dental Journal, Volume 5, Number 3, July 2014, pp. 134–137.
2. FDI World Dental Federation Oral Health Atlas, Second Edition due to be published September 2015.

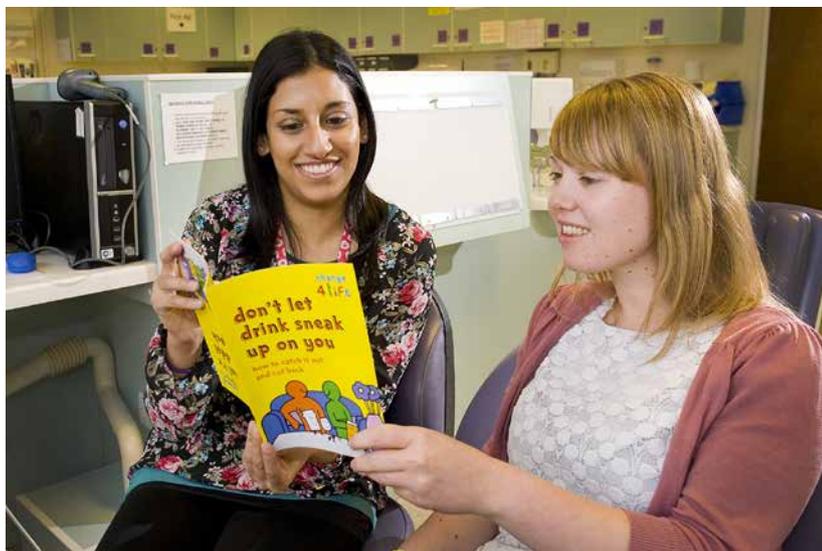
PRESENTATIONS

1. Oral presentation 2014 British Association of Oral Surgery conference, RCS Edinburgh
2. Poster presentation 2014 British Association of Oral Surgery conference, RCS Edinburgh

PRIZES

First Prize DF2/SHO/Career Development Post category at the 2014 British Association of Oral Surgery conference

Alcohol misuse is a major risk factor for periodontal disease, dental caries, tooth erosion, mouth cancer and maxillofacial injury.



Zairah with a patient

The aim of the study was to determine the feasibility of screening patients for alcohol misuse in a primary dental care setting and providing those identified as hazardous drinkers with a brief treatment intervention. This work was also designed to prepare the way for a large-scale clinical trial.

A randomised controlled trial was carried out in a general dental practice in South Wales. Patients aged 18–65 were approached and written consent received from those who agreed to participate. Patients were stratified according to appointment (with a dentist or hygienist) and screened using the Modified-Single Alcohol Screening Question, M-SASQ. Those scoring positively for alcohol misuse were randomly allocated to receive either a motivational interview from either the dentist or hygienist

or usual care. The outcome assessor and patients were blind to allocations. The outcome measure at three months was M-SASQ score.

In total, a single hygiene patient and 106 dental patients were recruited. The hygiene patient did not score positively on the M-SASQ for alcohol misuse. Of the 106 dental patients recruited, 46 patients (43%) scored positively, with 26 allocated into the intervention group and 20 to the control. Follow-up data were available for 22 (48%) out of the 46 patients (12 in the intervention and 10 in the control group). M-SASQ scores changed from positive to negative for two patients in the intervention and five in the control group.

Alcohol misuse screening and treatment was feasible in a primary dental care setting. This suggests a new approach involving the dental team, which could potentially reduce burdens on specialist dental and medical services alike. Overall, the dentist was best placed to deliver the intervention rather than the hygienist. Contamination may have been a problem as more patients in the control group changed M-SASQ score. Building on these findings, a multi-centre, cluster randomised controlled trial is planned.

A STUDY OF SHARED DECISION MAKING IN ORTHOGNATHIC TREATMENT



**FIONA
RYAN**

FELLOWSHIP/SPONSOR

FDS Research Fellowship

SUPERVISORS

Professors Susan J Cunningham, Nigel P Hunt & David R Moles

SITE OF WORK

Eastman Dental Hospital, University College London
Hospitals NHS Foundation Trust

The level of patient involvement in orthognathic consultations was relatively low at 22.55%.



Fiona and a patient engaged in shared decision-making

Recently there has been increasing emphasis on shared decision-making (SDM) as the pinnacle of patient-centred care. There is evidence that SDM leads to improved outcomes, however, it remains to be widely adopted in healthcare to date. The aim of this study was to measure the extent of SDM in orthognathic consultations using the OPTION scale.

This was a cross-sectional study involving pre-treatment orthognathic patients and the clinicians involved in their care. Multidisciplinary clinic consultations were audio recorded and rated by two independent raters using the OPTION scale.

Consultations with 61 orthognathic patients were rated: 36% were male and 64% female. The mean age was 26 years and the mean consultation length was 12 minutes and 44 seconds. Agreement between the raters was acceptable, with an intra-class correlation coefficient of 0.794 (95% confidence interval 0.678 to 0.871). The mean OPTION score was 22.55% (range 3–54%, SD 10.73%), indicating a low level of SDM.

The levels of SDM recorded in orthognathic consultations in this study were relatively low, although similar to other studies. It was felt that these results were largely due to patients attending a new 'group information clinic' one week prior to their MDT clinic appointment. This clinic is designed to provide detailed information of all general aspects of orthognathic treatment to patients and family members in a group. Thus, much of the information had already been provided and was not repeated at the second rated consultation.

The results of this study suggested that the extent of SDM in orthognathic consultations was relatively low but there are circumstances that are specific to this hospital that may account for this. This is the first study investigating SDM in the field of orthodontics. Improvements in SDM are necessary in order to ensure that patients are adequately involved in their treatment decisions.

THE CENTRE FOR EVIDENCE IN TRANSPLANTATION

The Centre for Evidence in Transplantation (CET) is situated in the College's Clinical Effectiveness Unit (CEU). The centre was established in 2005 to evaluate the quality of evidence available in solid organ transplantation (www.transplantevidence.com).



The CET team

The CET has been involved in a number of projects since its establishment, one of which has been to establish a registry of all randomised controlled trials in organ transplantation and to evaluate the methodological quality of those trials since January

2004. This registry was published as a regular feature in the journal *Transplantation*, but from January 2008 this has been replaced by the Transplant Library.

The Transplant Library is an electronic library of all RCTs in solid organ transplantation from 1970 to the present and more recently includes systematic reviews that are regarded as of reasonable quality. The development of an electronic library has been a major project and includes all randomised controlled trials in solid organ transplantation. Through Ovid (a global provider of information for the healthcare industry) it became available to all members of the British Transplantation Society (BTS), Scottish NHS libraries and various other medical school libraries.

Evidentia Publishing has also taken on the library and is currently in the process of marketing and providing free trials to expand awareness of the Transplant Library, their current subscribers include the Canadian Transplantation Society, Brazilian Transplantation Society and the European Society of Transplantation (ESOT).

It is often asked why we need an electronic library in transplantation but if we remember that RCTs and systematic reviews/meta-analyses of RCTs are level-one evidence in any medical discipline then the aim was to develop a very easily searched and comprehensive library that could produce the relevant references in minutes rather than hours. Indeed, the great Archie Cochrane, after whom the Cochrane library is

named, predicted the need for specialist/subspecialist libraries of RCTs some 30 years ago: this is the first!

In an analysis of the methodology of randomised controlled trials in organ transplantation between 2004 and 2006 it was found that only around one third of those trials were methodologically sound in their design. A smaller sample of 91 RCTs published in 2004 was evaluated for the quality of reporting of outcomes of RCTs and again we found significant defects in a majority of trials. As RCTs represent the highest level of available evidence this does detract from the value of the evidence available. On the basis of this information an agreement has been reached with ESOT that the CET would become the Knowledge Centre for ESOT and would offer advice in the design of RCTs, as well as provide assistance with the reporting of RCTs. Trials that were methodologically sound in design would be given ESOT/CET accreditation.

Some recent publications include, *Antifungal Prophylaxis In Liver Transplantation: A Systematic Review And Network Meta-Analysis* (Jonathan Evans), *Social media and online attention as an early measure of the impact of research in solid organ transplantation* (Simon Knight) and *A systematic review of the use of rituximab for desensitisation in renal transplantation*. (Philip Macklin)



Dr Liset Pengel teaching on the Evidence in Transplantation Course

Within the past year Dr Liset Pengel, the CEO of the CET and a member of the staff of the Nuffield Department of Surgery, has been granted a distinction award by the NDS for her work with the CET. Peter Morris was inducted into the Research Hall of Fame at The Royal Melbourne

Hospital. Neil Russell, who was the first Research Fellow at the CET, has finished his surgical training at Addenbrooke's Hospital in Cambridge and has been appointed as a consultant abdominal transplant surgeon there. Nishanthi Talawila was promoted to a Research Associate in November 2013 after gaining her MSc in Public Health, and Katriona O'Donoghue joined the Centre for Evidence in Transplantation in April 2014 as a Research Assistant. John O'Callaghan has been awarded his DPhil and has produced a number of critically important papers arising from the work of his thesis which is devoted to organ preservation.

The CET submitted four posters to the World transplant Congress in San Francisco in 2014 and all were given a distinction award.

CLINICAL EFFECTIVENESS UNIT

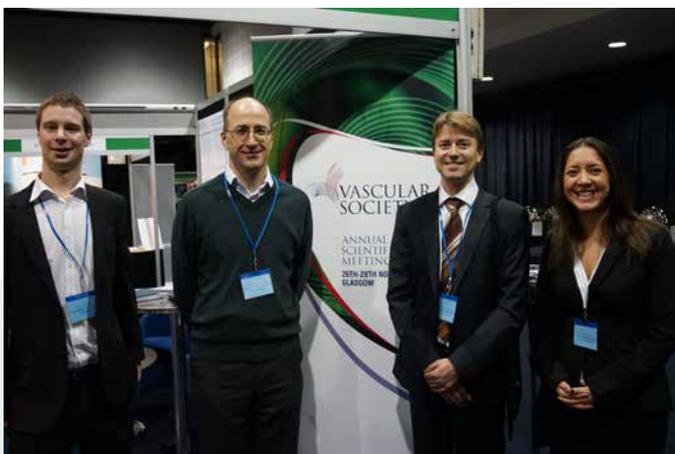


David Cromwell, Director of the CEU

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. In undertaking these studies, it aims to provide timely comparative information to surgeons and hospitals about the process of care and patients

outcomes. It is also involved in the RCS initiative to develop and implement a quality and outcomes strategy across the College and speciality associations.

The CEU is largely self-funded by obtaining external project grants and contracts, although it receives an annual contribution from the College's research funds and the College underwrites five senior academic posts within the LSHTM. Its 16 staff members have a variety of backgrounds (eg health services research, epidemiology, medical statistics, clinical medicine, public health and social science) which gives it a multi-disciplinary outlook and approach. Dr David Cromwell, Senior Lecturer at the LSHTM, has been the CEU Director since May 2011.



CEU team at Vascular Society Meeting in Manchester



Professor Ian Loftus, Professor Julian Scott and David Cromwell at the Vascular Society meeting in Manchester

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.

In April 2013, the CEU was commissioned to begin the National Prostate Cancer Audit (NPCA), which became the fifth national cancer audit within NCAPOP. The NPCA is designed to examine the treatment choices of men with newly diagnosed prostate cancer, and the outcomes of care including long term survival and quality of life. A challenge for the audit was to provide hospitals with information that would support continuous quality improvement for patients with early disease (who may simply require surveillance) as well as for patients with advanced disease (who are likely to require multi-modal therapy).

The NPCA represents the first of a new generation of national cancer audits. The core of its patient data will come from the English National Cancer Registration Service and the Welsh Cancer Information System, both of which will be linked to information on survival from the Office for National Statistics. This will keep the burden of data collection on staff to a minimum. This clinical data will be supplemented with data from patients, who will be asked to complete patient-reported outcomes (PROMS) and experience (PREM) questionnaires. The combination of clinical, PROMS and PREMS data is fundamental to understanding the many dimensions of quality health care for these patients, and it is a unique feature among current national cancer audits.



CEU team meeting with American guest speaker Professor Dennis Scanlon from the Pennsylvania State University

The CEU was also commissioned in 2013 to run the National Vascular Registry, in collaboration with the Vascular Society of Great Britain and Ireland. The registry is another NCAPOP audit and was formed by the amalgamation of the National Vascular Database and UK Carotid Interventions Audit projects. These projects had been used by vascular surgical services in the UK to monitor their practice and outcomes since 2005, and were part of a broad quality improvement programme undertaken by the Vascular Society in collaboration with other organisations. The registry will evaluate the quality and outcomes of care for patients who undergo vascular surgery in England and Wales, and covers five main procedures: repair of abdominal aortic aneurysm (AAA); carotid endarterectomy; and lower-limb angioplasty / stent, bypass and amputation among patients with peripheral arterial disease. While NCAPOP audits tend to cover just NHS hospitals in England and Wales, hospitals in Scotland and Northern Ireland are also encouraged to participate in the registry, so that work of the Vascular Society to improve the care provided by vascular services within the UK is still supported.

In its first year, the registry produced reports on the patterns of care for elective repair of infra-renal AAA and for carotid endarterectomy. The report on elective AAA repair continued the public reporting of outcomes on AAA begun by the Vascular Society, and updated the results from its 2012 report. This had examined the outcomes of 8,380 procedures between 1 October 2008

and 30 September 2010 and found that the overall in-hospital mortality after surgery for that period had been 2.4%. The registry AAA report, published in November 2013, found that outcomes had continued to improve, with in-hospital mortality after surgery dropping to 1.8% for AAA repairs performed between January 2010 and December 2012.

A brief description of other major CEU projects undertaken in 2013 is given in Box 1.



Professor Sir Norman Williams and Dr Torsten Olbers from Sahlgrenska University Hospital in Gothenburg, Sweden

Box 1: Other major CEU projects undertaken in 2013

- **National Bowel Cancer Audit**

The National Bowel Cancer Audit (NBCA) is funded by the Healthcare Quality Improvement Partnership (HQIP) and was developed by the Association of Coloproctology of Great Britain and Ireland (ACPGBI). The analyses for the 2013 Annual report were carried out by the CEU with support from the NHS Information Centre. It is managed by the Clinical Audit Support Unit within the NHS Information Centre.

- **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. CRANE is funded by the NHS – specialist commissioners involved in cleft care.

- **Breast Cancer Outcomes project.**

This project is using national routine data to examine the patterns of care and outcomes of breast surgery among women with breast cancer. It is being carried out with the Association of Breast Surgeons, British Association of Plastic, Reconstructive and Aesthetic Surgeons (BAPRAS) and is part funded by Johnson & Johnson.

- **National Oesophago-Gastric Cancer Audit**

This audit restarted in June 2011 and is being carried out in partnership with the Association of Upper Gastrointestinal Surgeons, the British Society of Gastroenterology, The Royal College of Radiology, and the National Clinical Audit Support Programme of the Health and Social Care Information Centre. The audit is funded by the Healthcare Quality Improvement Partnership.

The publication of consultant-level surgical outcomes

As part of the NHS Commissioning Board's publication *Everyone Counts: Planning for Patients 2013/14*, ten national clinical audits were asked to report on surgical outcomes by consultant in the summer of 2013. This initiative was part of NHS England's drive to produce information that supports local clinicians to improve the outcomes of care and that provides more transparency for patients, and is seen as a complement to the NHS Outcomes Framework.



CEU team with Dr Torsten Olbers from Sahlgrenska University Hospital in Gothenburg, Sweden

The CEU played an active role in producing the consultant-level information for three of the ten national audits that participated in the *Everyone Counts* initiative, namely: the National Vascular Registry, the National Bowel Cancer Audit and the National Oesophago-gastric Cancer Audit. A challenge for the project teams was that the audits were designed primarily to support quality improvement at an organisational level, and not all captured the name of the consultant undertaking the surgery. Consequently, the months between the announcement of the policy in February 2013 and the publication on the figures in the summer became an extremely busy time for the CEU. Communicating with consultants and NHS organisations was a fundamental component of the task preparing the reports, and took a lot of organising. Preliminary information was circulated to surgeons for checking, which was followed by periods to allow for additional or corrected data to be returned to the audits. We were grateful for the incredible support we received from surgeons in this process, though it is fair to say that there was a wide range of opinions about the value of the exercise.

Reporting the outcomes of specific procedures in a way that is accepted by the surgical profession and understood by the public is challenging. A particular issue concerns whether surgeons are performing sufficient procedures for poor performance to be detected reliably. We examined this issue for four procedures: adult cardiac surgery, curative resection for oesophago-gastric cancer; bowel cancer resection; and hip fracture surgery [Walker et al 2014]. We found that most cardiac surgeons do a sufficient number of operations for there to be a reasonable chance of detecting someone whose mortality rate is twice the national average. However, much fewer surgeons were performing the other procedures

in sufficient numbers to identify this lower level of performance. Consequently, a potential risk of this policy is that the reporting of surgeon-level outcomes could lead to a false sense of security and could lead to inaction rather than support quality improvement.

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.

Selected publications by CEU staff in 2013 and 2014

1. Callaghan CJ, Charman SC, Muiesan P, Powell JJ, Gimson AE, van der Meulen JH; UK Liver Transplant Audit. Outcomes of transplantation of livers from donation after circulatory death donors in the UK: a cohort study. *BMJ Open* 2013; 3: e003287.
2. Fitzsimons KJ, Copley LP, Deacon SA, van der Meulen JH. Hospital care of children with a cleft in England. *Arch Dis Child* 2013; 98: 970–74.
3. Neuburger J, MacNeill F, Jeevan R, van der Meulen JH, Cromwell DA. Trends in the use of bilateral mastectomy in England from 2002 to 2011: retrospective analysis of hospital episode statistics. *BMJ Open* 2013; 3: e003179.
4. Palser TR, Cromwell DA, Hardwick RH, Riley SA, Greenaway K, van der Meulen JH. National Oesophago-Gastric Cancer Audit. Impact of route to diagnosis on treatment intent and 1-year survival in patients diagnosed with oesophagogastric cancer in England: a prospective cohort study. *BMJ Open* 2013; 3: e002129.
5. Walker K, Neuburger J, Groene O, Cromwell DA, van der Meulen J. Public reporting of surgeon outcomes: low volumes lead to false complacency. *Lancet* 2013; 382: 1674–77.
6. Chadwick G, Groene O, Hoare J, Hardwick RH, Riley S, Crosby TD, Hanna GB, Cromwell DA. A population-based, retrospective, cohort study of esophageal cancer missed at endoscopy. *Endoscopy* 2014; 46: 553–60.



Research Fellows studying at a research methods course



David Cromwell teaching at a research methods course

7. Jeevan R, Cromwell DA, Browne JP, Caddy CM, Pereira J, Sheppard C, Greenaway K, van der Meulen JH. Findings of a national comparative audit of mastectomy and breast reconstruction surgery in England. *J Plast Reconstr Aesthet Surg* 2014; 67: 1333–44.
8. Wallace D, Walker K, Kuryba A, Finan P, Scott N, van der Meulen J. Identifying patients at risk of emergency admission for colorectal cancer. *Br J Cancer* 2014; 111: 577–80.
9. Tovikkai C, Charman SC, Praseedom RK, Gimson AE, Watson CJ, Copley LP, van der Meulen J. Linkage of a national clinical liver transplant database with administrative hospital data: methods and validation. *Transplantation* 2014; 98: 341–47.
10. Cathcart P, Nossiter J, Aggarwal A, Rashbass J, Lyratzopoulos Y, Payne H, Neal DE, van der Meulen J; National Prostate Cancer Audit group. The first national clinical audit of prostate cancer care. *BJU Int* 2013; 112: 883–84.

PRIZES & 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 & Jean Lawrie and Stefan & Anna Galeski Travelling Fellowships 2014

The College is most grateful to the Lawrie and Galeski families for supporting trainee surgeons to be part of the faculties which teach introduction to surgical skills workshops to trainees and medical students in Borneo, Sri Lanka, Algeria and Rwanda

Recipients 2014

Andrew Beamish
Aneel Bhangu
Andrew Cowie
Edward Fitzgerald
Kathryn Gash
Vimal Gokani
Rhiannon Harries
Sreelakshmi Mallappa
Jo Mennie
William Muirhead
Oliver Old
Georgios Orfanotis
Hew Torrance

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 October 2013

Mr Jonathan Hutt FRCS – 1 year
Montreal, Canada
Mr Harry Powell FRCS – 9 months
Sydney, Australia
Mr Paul Sutton MRCS – 5 weeks Mayo
Clinic and Cleveland Clinic, USA
Mr Saket Tibrewal FRCS – 4 weeks
Toronto, Canada
Mr Ewan Wilson FRCS – 1 month Texas,
USA

Recipients May 2014

Mr Mathew Sewell FRCS – 1 year
Brisbane, Australia
Mr Parag Jaiswal – 1 year Calgary, Canada
Mr Sammy Hanna FRCS – 1 year Ontario,
Canada
Mr Amit Shah FRCS – 1 year Sydney,
Australia
Mr Vincent Tang FRCS – 1 year
Melbourne, Australia
Mr Simon Thompson FRCS – 1 year
Sydney, Australia
Mr Tim Halsey FRCS – 1 week France

Recipients October 2014

Mr Daniel Rolton FRCS – 1 year City
Hospital, Auckland, New Zealand
Mr Hugh Sims-Williams MRCS – 5
months CURE Children's Hospital
Uganda
Mr Nirav Patel FRCS – 1 year Rubin
Institute for Advanced Orthopaedics,
Sinai Hospital of Baltimore
Mr Prabhakar Rajan FRCS – 4 months
Karolinska University Hospital, Solna,
Stockholm, Sweden
Mr Khaled Sarraf FRCS – 6 months St
Michael's Hospital, Toronto
Mr Iain McGraw FRCS – 1 month

Shriners Hospital for Children and the
Philadelphia Hand Center
Dr Alastair Hunter FRCS – 2 weeks
Institut Kaplan, Barcelona, Spain

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.

Recipients 2013:

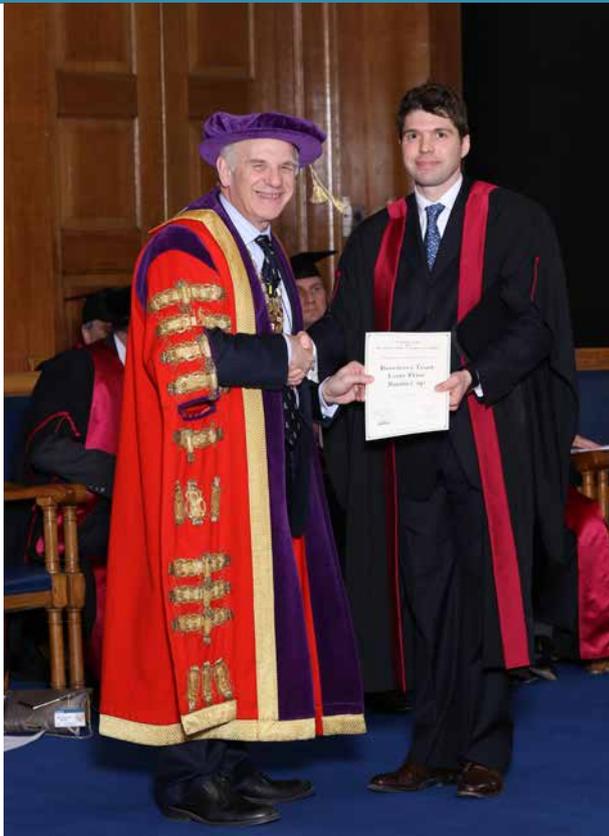
Mr Jonathan Michael Bernstein FRCS
Mr Philip John Clamp FRCS
Mr Enyinnaya Ofo FRCS
Mr Harry Richard Franklin Powell FRCS

Recipients 2014:

Mr Jonathan Hughes FRCS
Mr Rohit Kumar FRCS
Mr Sergios Georgiou Latis FRCS
Mr Joel Anthony Smith FRCS
Mr Joseph David Wasson FRCS

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



Mr Alexander
Woollard MRCS



Joint runners up receiving their prize from Professor Sir Norman Williams

overseas that is approved by The Royal College of Surgeons of England and the Royal College of Physicians of London.

Recipients 2013:

Mr Glenn Kunnath Bonney MRCS
Mr Henry Guy Francis Burnand MRCS

Recipient 2014:

Dr Rachel Wake

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'.

Recipient 2014

Miss Charlotte Lucy Bendon MRCS

The Rosetrees Trust Prize

The Rosetrees Trust Prize was established in 2009 and applicants are invited to submit an essay describing how their research project will contribute to improvements in patient care within the next five years.

2013 Winner

Mr Alexander Liddle MRCS, *Understanding failure in uni-compartmental knee replacement*

2013 Joint Runners Up

Mr Alexander Woollard MRCS, *Nerve regeneration in facial reconstruction*

Mr James Chan MRCS, *Accelerating fracture repair*

2014 Joint Winners

Miss Katherine Gash MRCS, *Hitting cancer where it hurts*

Miss Michelle Griffin MRCS, *3D-printing nanocomposite polymers for ear and nose reconstruction; the new generation of organ replacements*

Mr James
Chan MRCS



Medical Students Grants are awarded to medical students wishing to undertake an intercalated Bachelor of Science degree related to surgery. This has come about in particular from the onset of the Modernising Medical Careers reforms and the demands placed on medical students who wish to consider a career in 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.

HIGHER DEGREES FOR INTERCALATED

MEDICAL STUDENTS

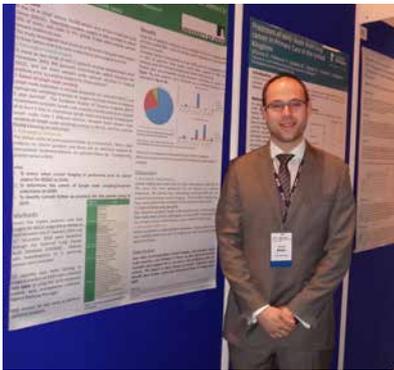
DANIEL BEDER	82
GEORGE BETHELL	82
OLIVER BRUNCKHORST	83
ALEXANDRA BURKE-SMITH	83
NICK CORK	84
NICOLAAS JANSEN VAN RENSBURG	84
CHIA YEW KONG	85
PEDRAM KORDROSTAMI	85
CATHERINE ELIZABETH LOVEGROVE	86
KYUNG-HOON MOON	86
CHANDNI NIGAM	87
JOON FAI ONG	87
MICHAEL JOHN RICE	88
SAYINTHEN VIVEKANANTHAM	88

MEDICAL STUDENTS

AN ANALYSIS OF THE CURRENT MANAGEMENT PRACTICES OF RADICALLY TREATABLE NON-SMALL CELL LUNG CANCER IN ST JAMES'S UNIVERSITY HOSPITAL

DANIEL BEDER

Medical School: University of Leeds
Location of research: St James's University Hospital (SJUH), Leeds



Daniel with his poster illustrating his audit findings at the annual British Thoracic Oncology Group conference in Dublin, March 2014

Non-small cell lung cancer (NSCLC) affects 42,000 people each year in the UK but only a small proportion can be cured with surgery. We audited three areas where changes may improve patient care in St James's University Hospital (SJUH), Leeds.

- 1) NSCLC commonly spreads to the brain and brain imaging may identify patients at risk of relapsing. We offered brain imaging to 5% of patients, and 2% actually developed brain metastases.
- 2) Complete lymph node removal during surgery greatly improves chances of achieving cure. We sample and remove important lymph nodes in every patient, and completely remove them in 42% of patients; this is higher compared with other institutions.
- 3) Follow-up aims to detect relapses early; we found that chest x-ray is performed routinely and that follow-up practices varied between specialties and needs streamlining.

In summary, we are doing well compared with other institutions but aim for continued improvement.

STEM-CELL THERAPY FOR HIRSCHSPRUNG'S DISEASE

GEORGE BETHELL

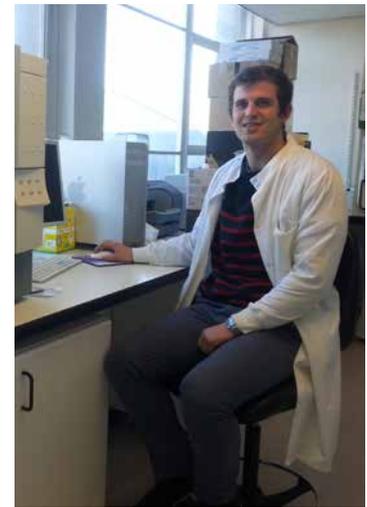
Medical School: University of Liverpool
Location of research: Institute of Child Health



George presenting at the British Association of Paediatric Surgery Conference 2014

The RCS award allowed me to undertake lab-based research working towards an MPhil in Children's Health. The research was based at the University of Liverpool in partnership with Alder Hey Children's hospital and supervised by Simon Kenny and Professor David Edgar.

Following surgery for Hirschsprung's disease 10%–30% of children suffer from long-term faecal incontinence or constipation, which can worsen as the patient grows older. It is thought that stem-cell therapy could resolve these issues. My work involved collection of human gut samples to determine the location and identity of enteric nervous system stem cells that are present in the gut. As well as achieving this, I have had the opportunity to present at two international conferences and am currently preparing two papers for publication.



George using the flow cytometer in the lab

I am grateful to the RCS for their support, which has made this degree and the attendance at conferences possible for me.

DEVELOPMENT AND VALIDATION OF A SIMULATION-BASED URETEROSCOPY CURRICULUM – A RANDOMISED CONTROLLED TRIAL

OLIVER BRUNCKHORST

Medical School: King's College London

Location of research: Guy's Hospital, London

Training the modern surgeon is increasingly difficult, with the evermore complicated procedures and the decreased training hours. Simulation-based training may offer a much-needed adjunct to regular training pathways. However, surgery is much more than just learning technical skills, as non-technical skills such as communication are also vital.



Oliver with supervisors Professor Prokar Dasgupta (Consultant Urological Surgeon) and Kamran Ahmed (Urology Registrar) at Guy's Hospital Theatres

We have therefore developed a curriculum for the common urological procedure of a ureteroscopy, using simulators and a simulated operating room environment to develop technical and non-technical skills together. Results have been positive, with

both skills considerably improved in those that underwent the curriculum. This is significant, as little research has been conducted to demonstrate that teaching both skill sets together is feasible and is useful for the development of future surgical curricula.

I am extremely grateful to the College for their support, which has allowed me to conduct this project, introducing me to the world of surgical education research.

A COMPARISON OF NON-INVASIVE PORTABLE IMAGING MODALITIES FOR THE ASSESSMENT OF BURN DEPTH IN ADULT BURN INJURIES

ALEXANDRA BURKE-SMITH

Medical School: Imperial College London

Location of research: Chelsea and Westminster Hospital, London

Thanks to the RCS grant during my Intercalated BSc in Surgery and Anaesthesia at Imperial College, I was able to purchase a thermal imaging camera for my clinical



Alexandra holding the infrared thermal imaging camera purchased with her RCS grant and standing next to the Chelsea and Westminster laser Doppler unit

study at Chelsea and Westminster Hospital. I compared the current gold-standard laser Doppler imaging (LDI) with the currently unproven Infrared Thermography (IRT) and the

Spectrophotometric Intracutaneous Analysis (SIA) for accurate early assessment of burn depth, recommended to support early appropriate surgery and timely healing.

Our initial results indicated SIA has the potential for becoming the new preferred scanning modality as it is of equal/greater accuracy, reduced cost, easier and quicker when compared with LDI. These results now need to be corroborated in a larger series, in parallel



Alexandra (right) with one of her clinical supervisors, Isabel Jones

to developing the software to modify the representation of the images to improve ease of interpretation. I plan to continue this project myself and have applied for an MSc in order to do so.

CONTEMPORARY ISSUES IN PAEDIATRIC NEUROSURGERY – IMPROVING OUTCOMES IN PAEDIATRIC CNS TUMOURS

NICK CORK

Medical School: University of Bristol Medical School
Location of research: Frenchay Hospital, Bristol

My year of research in the Department of Neurosurgery at Frenchay Hospital would not have been possible without this generous award from the College.



Nick examining a newly dissected brain in the Neuropathology laboratory at Frenchay Hospital

The grant supported me in conducting a retrospective study of children diagnosed with brain or spinal tumours in the South West region, with a view to streamline and quality improve the process. Our aim was to identify factors guiding successful surgery, improve safety and effectiveness through better presurgical screening, and enable earlier diagnosis.

I was also able to organise a personal education programme, observing post-mortems, learning the principles of neuropathological dissection and attending subspecialty teaching and multidisciplinary meetings. The opportunity to assist in theatre on elective and emergency neurosurgical cases was a particular highlight, confirming my interest in pursuing a career in academic neurosurgery.

My thanks again to The Royal College of Surgeons of England, and their funding partners, for facilitating this rare and invaluable opportunity.

DEVELOPING AN OPEN-SOURCE-BASED 3D PRINTER AND METHODS FOR FABRICATION OF POSS-PCU TISSUE ENGINEERING SCAFFOLDS

NICOLAAS JANSEN VAN RENSBURG

Medical School: University College London
Location of research: Royal Free Campus, London

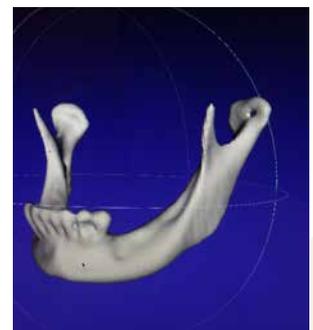


Professor Alexander Seifalian and myself in front of our first 3D Printer. We now have four!

During my IBSc year, the award allowed me to purchase the parts for the first 3D printer in our department. Using an open-source design, we built and modified a 3D printer and developed methods to produce patient-specific lab-grown tissues. Our research has enabled us to use standard patient imaging (eg CT, MRI scans), convert these into

three-dimensional models and, finally, print accurate replicas using a novel nano-composite biopolymer developed at the lab.

The technique developed isn't limited to the initial application of spinal fusion cages and has since been applied to maxillofacial reconstruction and refinement of a tissue-engineered trachea. For the research conducted, I was awarded the Best Research Presentation and *viva voce* 2013/14 Prize. I have also been offered the chance to continue the research, working towards a PhD. This year would not have been possible without the generous award from the RCS. Thank you.



3D model of mandible from CT scan

THE RELATIONSHIP BETWEEN THE TUMOUR MICROENVIRONMENT AND EPITHELIAL-MESENCHYMAL TRANSITION

CHIA YEW KONG

Medical School: University of Glasgow

Location of research: Wolfson Wohl Cancer Research Centre, Glasgow

I have had a fruitful and productive year gaining key skills in conducting medical research and successfully completed a research project at the Wolfson-Wohl Translational Cancer Research Centre.

My research project's aim looked at the process named epithelial mesenchymal transition, which allows cancer cells to break off from the tumour and spread to distant sites of the body. We examined its interplay with factors within the microenvironment of the tumour (the area surrounding the tumour) – an example of which are the cells of the immune system surrounding the tumour, which have been shown to have a protective effect against it. We plan to present these results at scientific conferences and write a manuscript for publications.



Chia Yew in the lab



Chia Yew (middle) with supervisors, James Park, Clinical Research Fellow in Surgery (left) and Campbell Roxburgh, Clinical Lecturer in General Surgery (right)

I would like to thank the College for this generous grant. The year has further inspired me to continue to pursue my aspirations of becoming a surgeon-scientist in the future.

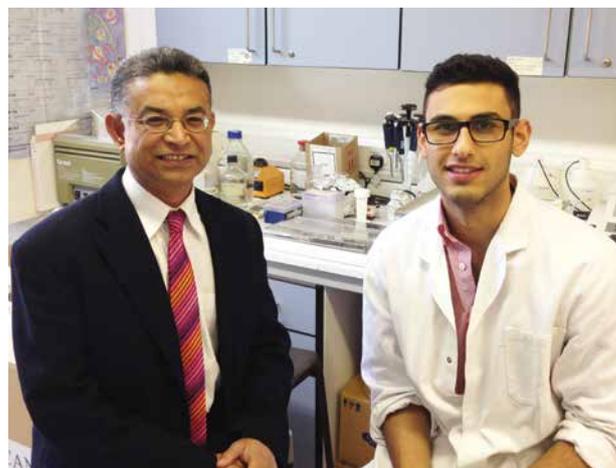
DOES TGF-BETA (TGF- β) SIGNALING INITIATE AND DRIVE THE PROGRESSION OF OSTEOARTHRITIS?

PEDRAM KORDROSTAMI

Medical School: University of Bristol

Location of research: Bristol University Centre for Comparative and Clinical Anatomy

Osteoarthritis is the most common cause of disability in the elderly, affecting hundreds of millions of people worldwide. Currently, there are no drugs that reverse or slow down the progression of disease and medical management is limited to pain relief, physiotherapy and surgery. My research investigated the role of TGF- β in the initiation and/or progression of osteoarthritis. This growth factor has an integral role in the maintenance of healthy cartilage and is a potential target for the development of new disease-modifying therapy. The research I carried out adds to the current knowledge and provides a platform for future research in the area.



Pedram (right) with supervisor Mo Sharif

I am very grateful to the College for its invaluable support towards my research project, which has given me the opportunity to experience laboratory techniques under expert supervision. I have developed a range of new skills that will undoubtedly benefit my future surgical training.

DEVELOPMENT AND VALIDATION OF THE RARP ASSESSMENT SCORE FOR TRAINING AND ASSESSMENT OF ROBOT-ASSISTED RADICAL PROSTATECTOMY (RARP)

CATHERINE ELIZABETH LOVEGROVE

Medical School: University of Edinburgh/King's College London

Location of research: King's College London

During my intercalated year I undertook a project focused on Robot-Assisted Radical Prostatectomy (RARP). The rise in robot-assisted surgery has changed the treatment offered for prostate cancer. It is imperative that surgeons be well trained in robot-assisted surgery, which requires unique technical and non-technical skills.

My dissertation project, supported by the Royal College of Surgeons, sought to identify the hazards within RARP to create a safety checklist for the protection of patient safety. The observational, longitudinal, multi-institutional study undertook qualitative and quantitative analysis for eight months.



Kamran Ahmed, Catherine Lovegrove and Professor Prokar Dasgupta beside the new DaVinciXi

a Robotic Surgery Fellowship with the European Association of Urology. Using an assessment score, their learning curve in a total of 145 RARP cases was considered. This is the first time that learning curves for procedural steps have been examined in the literature.

Information about identified hazards was applied to the training and assessment of 17 surgeons across Europe who were undertaking

ECHOCARDIOGRAPHY DURING THE ENDOTHERMAL ABLATION AND MECHANOCHEMICAL ABLATION OF VARICOSE VEINS: DO BUBBLES CAUSE NEUROLOGICAL SYMPTOMS?

KYUNG-HOON MOON

Medical School: Imperial College London

Location of research: Charing Cross Hospital, London



Local Anaesthetic Varicose Veins Unit, Charing Cross Hospital

With the generous financial support from The Royal College of Surgeons of England, I conducted a project within the academic section of vascular surgery at Charing Cross Hospital as a part of my intercalated BSc in Surgery and Anaesthesia at Imperial College.

The project investigated the safety of two types of varicose vein treatments: a radio-wave heat technique and a novel device that simultaneously uses chemical and mechanical irritation to close the diseased veins. The safety was assessed by monitoring patients' hearts with ultrasound for any errant bubbles produced that have been linked to stroke-like symptoms with other varicose vein treatments.

The RCS grant helped fund accurate ultrasounds of the heart and subsequent data analysis. The study was successfully completed and results have shown that the two techniques have an equally safe profile and do not produce heart ultrasound findings linked to stroke.

PERSONALISED PHENOTYPING OF AXILLARY TISSUE: IDENTIFYING BIOMARKERS FOR PRESENCE OF AXILLARY METASTASIS IN BREAST CANCER

CHANDNI NIGAM

Medical School: Imperial College London
Location of research: Charing Cross Hospital, London

Breast cancer frequently spreads to the axilla (armpit), requiring surgical clearance of the local nodes. However, at present it is not always possible to determine the extent of this spread prior to surgery. My project aimed to develop a rapid intra-operative test for biomarkers of axillary metastasis using liquid chromatography-mass spectrometry (LC-MS)-based analysis of axillary tissue, which could facilitate complete surgical resection of the primary tumour and its metastases in one operating session.



Chandni collecting intra-operative axillary samples at Charing Cross Hospital



Chandni conducting pre-analytical sample preparation of axillary tissue at Charing Cross Hospital

During the project, I worked with the research team at the world-class International Phenome Centre and became acquainted with state-of-the-art analytical techniques that are currently at the forefront of cancer research. I wish to thank the College for their generous funding of this project. Preliminary results of this study are promising and we are currently awaiting more data for analysis and eventual publication.

MESENCHYMAL STEM-CELL IMMUNOSUPPRESSANT POLYMER MICROCARRIERS FOR LOCAL IMMUNOSUPPRESSION IN VASCULAR COMPOSITE ALLOGRAFTS

JOON FAIL ONG

Medical School: Imperial College London
Location of research: Guy's Hospital, King's College London

I am deeply grateful to the RCS for supporting my surgical aspirations and one of the projects I had initiated at the Harvard-MIT Health Sciences and Technology Division. This project seeks to develop a novel immunosuppression platform for transplant recipients. Given that medicine-free acceptance of complex face and limb transplants is still significantly in the future, patients now need intermediate platforms to reduce the quantity of immunity medication and the accompanying toxic side effects as much as possible.



Joon Fai with Professor Lucy Di Silvio, teacher, mentor, friend and inspiration

With the award we have been able to complete a significant portion of the *in vitro* work and continue to work at King's College London. We are still pursuing development of the platform.

Without the RCS it would have been exceedingly difficult to tie my experiences with the face and limb transplant group at Harvard Medical School with clinical and research work in the UK.

It is in no small part because of the support of the College that



Joon Fai with colleagues from the Karp Laboratory

I have been fortunate to graduate with First Class Honours from King's College London. This backing from the College provides a critical link between my research experience, graduate school and future innovations.

THE ROLE OF HYPOXIA ON NEUROBLASTOMA CELL MIGRATION AND INVASION

MICHAEL JOHN RICE

Medical School: The University of Liverpool
Location of research: University of Liverpool Centre for Cell Imaging and Alder Hey Children's Hospital

During my intercalation year I used a bursary from the College to undertake a Master's degree at the University of Liverpool Centre for Cell Imaging in partnership with Alder Hey Children's Hospital. Working under the guidance of Professor Paul Losty, Violaine Sée and Diana Moss, I investigated the effects of oxygen starvation on the vicious children's cancer neuroblastoma (NBL).

NBL is a common, highly lethal tumour with poor survival. Current management includes tumour biopsy, chemotherapy, surgery, radiotherapy and bone marrow transplantation. Previous research has shown oxygen deprivation is linked to the formation of more aggressive tumours, which can evade treatments and result in

increased mortality.

Our research has confirmed: the chick embryo is a suitable model for the study of NBL, oxygen starvation results in increased tumour



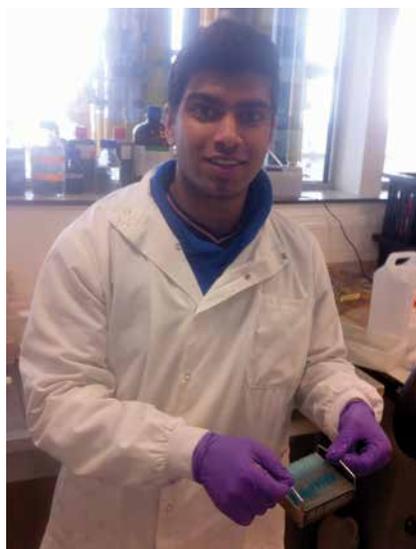
Lab team outside University of Liverpool (Back L-R Rosalie Richards, Michael Rice, Marco Marcello) (Front L-R Carol Fan, Violaine Sée, Anne Herrmann, Amelie Schober, Sarah Taylor)

proliferation and metastasis of NBL, and exposure to hypoxia results in long-term changes on the cellular level. Using this work we hope to identify therapeutic targets associated with oxygen starvation in order to develop novel treatments that improve prognosis.

FALLS IN PARKINSON'S DISEASE: WHERE IS THE PATHOLOGY?

SAYINTHEN VIVEKANANTHAM

Medical School: Imperial College London
Location of research: Charing Cross Hospital, London



Sayinthen staining sections of brain tissue at Charing Cross Hospital

The RCS award supported me through my Intercalated BSc in Neuroscience and Mental Health at Imperial College London, allowing me to pursue my research interest in functional neurosurgery.

My research aimed to

correlate the clinical presentation of falls with pathological changes in post-mortem tissue of Parkinson's disease patients. The structure we focused on is currently being considered as a target for functional neurosurgery.

We found the area of tissue that we had sampled based on neuroanatomical atlases was incongruent with the tissue structures we were expecting to see. Moving forward, we plan to sample the post-mortem tissue in a slightly different location, where we suspect our structure of interest will be present.

The skills I have gained include writing and presenting my research coherently, effectively critiquing data to be presented and, most importantly, understanding research methods. These enable me to potentially solve the clinical problems I come across. I believe this strong foundation will stand me well in future research and clinical roles.



CAN YOU MAKE A DIFFERENCE?

We need to develop our surgeons through training and research opportunities so that they excel and fulfill their potential and provide the highest standards of patient care.

To provide these opportunities the College relies almost exclusively on legacies, gifts and donations.

Legacies do not need to be huge sums of money to make a difference. A gift, whatever the amount, will help us continue to advance surgical standards by developing and delivering world-leading training and research programmes.

To ensure that our surgeons can meet the challenges of the future please consider supporting the College.

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.**



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.

ELECTIVE PRIZE REPORTS

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ELECTIVE PRIZE REPORTS

PAEDIATRIC ORTHOPAEDICS ELECTIVE IN CAPE TOWN PRIESKEL PRIZE WINNER

CLARE CONNELLY

Medical School: The University of Edinburgh
Site of work: Red Cross War Memorial Children's Hospital and Maitland Cottage Home Hospital, Cape Town, South Africa



Clare assisting in theatre

The exposure both to trauma and elective paediatric surgery that I gained during my time in Cape Town was incredible. I was able to play an active role both in clinic and in theatre and my knowledge and skills improved exponentially. The team were incredible and extremely welcoming. The



Clare with the team from the Red Cross

patients were so inspiring in the way they overcame their disabilities, and often numerous operations with lengthy hospital stays, with good humour and positive attitudes. From my time in Cape Town I have gained understanding of orthopaedics in a different culture and have renewed and increased my enthusiasm for the specialty.

A GENERAL SURGICAL ELECTIVE IN A HIGH-VOLUME, RESOURCE-LIMITED SETTING PRIESKEL PRIZE WINNER

JAMES GLASBEY

Medical School: Cardiff University School of Medicine
Site of work: Chris Hani Baragwanath Academic Hospital, Soweto, South Africa



James acting as primary operator for a lipoma excision as part of a weekly day-case list

I conducted my elective period working in the general surgery and trauma departments.

Working on a busy admissions unit I was able to develop confidence in the management of acutely unwell surgical patients and procedural skills under the tutelage of my surgical trainers. While in South Africa, I undertook feasibility testing of the GlobalSurg protocol (globalsurg.org) and developed regional networks to deliver data collection in Autumn 2014.

An elective at this centre, with its unique blend of world-leading clinical practice and resource-limited facilities, would come highly recommended to all general surgical enthusiasts with an interest in global health.



Morning song on the trauma ward after a busy night's intake

FACIAL RECONSTRUCTIVE SURGERY IN ETHIOPIA

PRIESKEL PRIZE WINNER

ANDREW JENKINSON

Medical School: Cardiff University
Site of work: Yekatit 12 hospital, Addis Ababa, Ethiopia

I spent my elective period with a charity called Project Harar, who provide facial surgery for some of the poorest people in Ethiopia.



Andrew with a patient who had his nose reconstructed following a hyena bite

One of my roles was to see new referrals and prepare them for assessment by the surgical team. With limited resources and a remarkable mix of pathology, making a diagnosis was a hugely rewarding challenge. The cases ranged from Hyena bites to Noma, a gangrene which eats the facial tissues of the malnourished.



A typical rural Ethiopian household living near my accommodation

Caring for such a wonderful group of people was an inspirational experience, which I hope will stay with me throughout my career.

PLASTIC AND RECONSTRUCTIVE SURGERY IN BORNEO

ROSALIND MARSHALL

Medical School: Imperial College London
Site of work: Kuching General Hospital, Sarawak, Malaysia



Rosalind (far left) assisting in theatre with John Ranjit (second from right)

My elective experience in the Plastic and Reconstructive Surgery Department at Kuching General Hospital was absolutely fantastic. Serving the whole of Sarawak, the department gets referrals from all over the state, and cases ranged from reconstruction after hunting accidents to burns. I had many opportunities to scrub in and assist in surgery, and learnt how to harvest, prepare and apply split-skin grafts. I was also able to go on an outreach clinic with a charity, giving GP services to villages and longhouses deep in the Borneo rainforest. I thoroughly recommend this elective for anyone considering a career in plastic surgery.



Rosalind (far right) with John Ranjit (second from right) and the rest of the team in the operating department

PAEDIATRIC ORTHOPAEDICS IN MALAWI

CLARE STEPHANIE HALCRO MORGAN

Medical School: University of Aberdeen
 Site of work: Beit-CURE international Hospital, Blantyre, Malawi



Clare scrubbed up to assist with an operation to correct a club foot, a common part of the hospital's workload

Clare with some of the surgical team

I was made to feel part of the team at Beit-CURE and thoroughly enjoyed my stay. The hospital's paediatric operations are funded using private patient income, so I saw an interesting cross-section of adult as well as paediatric cases. Assisting in theatre under careful supervision, allowed me to improve my basic surgical skills and my time in paediatric outpatient clinics was a great opportunity to experience working within a different culture. The challenges Malawian children with physical disabilities can face was highlighted to me during the study I was involved in. I am now keen to undertake further voluntary work.

PAEDIATRIC SURGERY AND ORTHOPAEDICS IN CAPE TOWN

NIOVI PAPALEXOPOULOU

Medical School: King's College London Medical School
 Site of work: Red Cross Children's Hospital/Maitland Cottage Home, Cape Town, South Africa



Helping fit a child with a spica cast following surgical correction of developmental dysplasia of the hip

My elective was in paediatric surgery and orthopaedics in Cape Town. I wished to compare the practice of surgery in the developing world and the UK. In general surgery I assisted in theatre and participated in patient management in the ward. In burns theatres I witnessed the massive impact on children's health from unsafe housing in townships. During orthopaedics I appreciated the skill of knowing when to and when not to operate in order to improve function. It was a fantastic learning opportunity that allowed me to experience the dichotomy of South African society and how it reflects in healthcare.



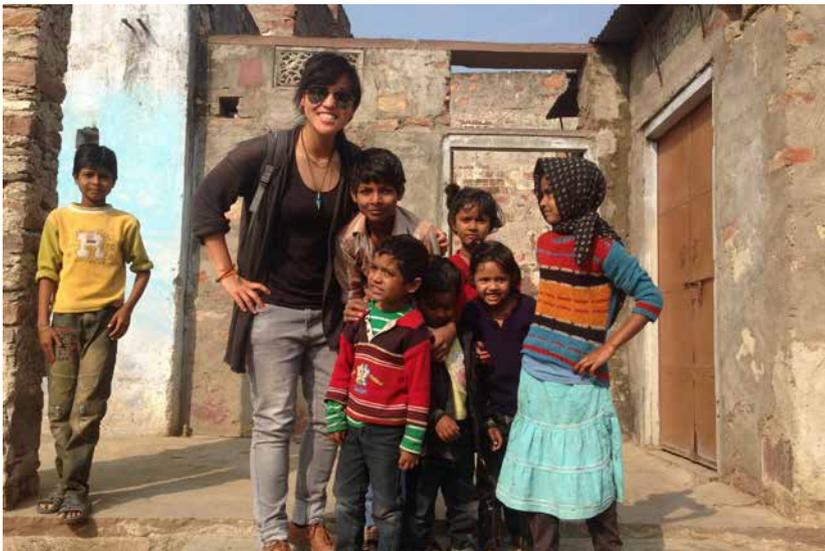
Hungry elective students waiting for a South African braai at Mzoli's in the township of Gugulethu after a spinal defects clinic at a local school

AN EVALUATION OF SECONDARY ALVEOLAR BONE GRAFTS IN PATIENTS WITH CLEFT LIP AND PALATE

PKK PRIZE WINNER

CISSY SZE SZE YONG

Medical School: UCL Medical School
Site of work: St John's Medical College, Bangalore, India



Cissy (second left) with some local village children

This elective has afforded me invaluable experience in academic surgery in a developing country. Participating in ward rounds, assisting in theatre and attending night shifts have enabled unparalleled hands-on experience that will greatly enhance my development as an aspiring future surgeon. My research with the plastic surgery department enabled a better understanding of the clinical condition, the current literature and development of research skills, such as using software tools to facilitate and expedite data collection. Participating in this project serves as a reminder of the crucial importance research has in ensuring that optimal patient care is delivered at all times.



Cissy (left) with some local student nurses at St John's hospital



Cissy (left) taking a history from a patient with a corrected cleft lip and palate

LECTURES DELIVERED IN 2013–2014

Hunterian, Arris & Gale, Arnott, Zachary Cope, Joseph Toynbee and Lionel Colledge Memorial Lectures

Hunterian	Mr Daniel Carradice, Venous Forum at RSM, 25 April 2013 <i>Lower limb venous insufficiency - assessing associated quality of life impairment and effectiveness of intervention</i>
The Lionel Colledge Memorial Lecture	Mr Dipan Mistry, ENT UK, 13 September 2013 <i>My Year in the Ear in Halifax, Nova Scotia</i>
Arnott	Vikas Khanduja, British Orthopaedic Association (BOA), Birmingham, 3 October 2013 <i>Arthroscopic Anatomy of the Hip Joint</i>
Joseph Toynbee Memorial Lecture	Professor Richard T Ramsden, The Royal Society of Medicine, 1 November 2013 <i>Consent – can it ever be truly informed?</i>
Hunterian	Mr Matthew Bown, Circulation Foundation, Manchester, 29 November 2013 <i>Genomic insights into abdominal aortic aneurysms</i>
Zachary Cope Memorial Lecture	Professor Derek Alderson, SARS Annual Meeting, Cambridge, 9th January 2014 <i>How to get your work published</i>
Arris & Gale	Professor Michael Nicholson, British Thoracic Society (BTS) Annual Congress, Glasgow, 26 February 2014 <i>Renal Transplantation after Ex-Vivo normothermic perfusion</i>
Hunterian	Mr Stuart Smith, The Society of British Neurological Surgeons (SBNS), London, 26 March 2014 <i>Into the third dimension: surgically targeting blood vessel development in aggressive brain tumours</i>
Hunterian	Mr David James Dunaway, European Society of Plastic, Reconstructive and Aesthetic Surgery (ESPRAS), Edinburgh, 8 July 2014 <i>3D modelling and the craniofacial surgeon; how geometric morphometrics in the assessment of deformity aids reconstruction for both congenital and acquired abnormalities</i>
Hunterian	Mr Erlick Abilio Coelho Pereira, Society of British Neurological Surgeons (SBNS), Warwickshire, 17 September 2014 <i>Mapping dorsal to ventral streams and somatotopy in midbrain periaqueductal grey</i>
Hunterian	Mr Imran Ahmad, Société Internationale d'Urologie (SIU), 4 October 2014 <i>The role of WNT signalling in urothelial cell carcinoma</i>
Hunterian	Professor Paul John Finan, Yorkshire Chapter meeting of the Association of Coloproctology and the Leeds Regional Surgical Club, St James Hospital Campus, 17 October 2014 <i>Transferring the lessons of personal audit in colorectal cancer to the national arena – an ongoing challenge!</i>

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 including:

- » cancer survival rates
- » less invasive surgery and quicker recovery
- » joint replacements
- » transplantation
- » prevention of strokes
- » surgery for trauma and war-wounded victims
- » operations to improve hearing and sight.

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:

- » Association of Coloproctology of Great Britain & Ireland
- » Association of Upper Gastrointestinal Surgeons of Great Britain & Ireland
- » Arthritis Research Trust
- » British Association of Plastic Reconstructive & Aesthetic Surgeons
- » British Association of Endocrine & Thyroid Surgeons
- » British Society of Surgery of the Hand
- » Ballinger Charitable Trust
- » Cancer Research UK
- » Cardy Beaver Foundation
- » Dunhill Medical Trust
- » Edwin George Robinson Charitable Trust
- » Enid Linder Foundation
- » Facial Surgery Research Foundation (Saving Faces)
- » Family of the late Mr Stefan Galeski
- » Frances & Augustus Newman Foundation
- » Fullbright Commission
- » George Drexler Foundation
- » Golden Bottle Trust
- » Freemasons' Fund for Surgical Research

- » Henry Lumley Charitable Trust
- » Lord Leonard and Lady Estelle Wolfson Foundation
- » Mary Kinross Charitable Trust
- » Oakdale Trust
- » Orthopaedic Research UK
- » Philip King Charitable Settlement
- » Rosetrees Charitable Trust
- » Royal Arch Masonry
- » Shears Foundation
- » Wyndham Charitable Trust
- » W D Macpherson Trust

ENDOWMENTS, RESTRICTED AND LEGACY FUNDS:

- » Anderson Reid Fund
- » Barlow Research Fellowship
- » Bernhard Baron Fund
- » 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
- » Shirley M Kanaar Legacy
- » Sir Arthur Sims Fund
- » Sorab (Soli) Jamshed Lam Legacy
- » Tudor Edwards Fellowship
- » Vandervell Research Fund

JOINT FELLOWSHIPS:

- » British Association of Endocrine and Thyroid Surgeons (BAETS)
- » British Association of Paediatric Surgeons (BAPS)
- » British Association of Plastic, Reconstructive and Aesthetic Surgeons (BAPRAS)
- » British Association of Surgical Oncology (BASO)
- » British Society for Surgery of the Hand (BSSH)
- » Get-A-Head Charitable Trust
- » Prostate Cancer UK





Teaching surgical skills in Algeria, Sri Lanka and Tooting!

1. Research fellows Hew Torrance and Kathryn Gash teaching suturing at the University of Algiers
2. Miss Sue Hill in Bechar with local medical students at the opening of the first medical school in south west Sahara
3. Andrew Cowie with trainee in Anuradhapura workshop in Sri Lanka
4. Oliver Old teaching vein patches in Anuradhapura, Sri Lanka
5. Andrew Beamish teaching surgical skills to 6th formers at Graveney School, Tooting
6. Miss Sue Hill & the British Ambassador talking to Algerian trainees in Algiers
7. Sreelakshmi Mallappa, Oliver Old & Andrew Cowie on a ward round in Kandy Hospital, Sri Lanka
8. The skills workshop in Oran, Algeria
9. Sreelakshmi Mallappa teaching surgical skills in Kandy, Sri Lanka

The research fellow selection process

10. Professor Rob Sayers questioning Bynvart Sandhu at poster vivas
11. The interview panel for military research fellows at the RCS
12. Dr John Williams of the Wellcome Trust in discussions with Professor Martin Birchall at the Academic & Research Committee meeting
13. Professor Jim McEwen, Professor Gus McGrowther & Professor Rob Sayers interviewing candidates for the five joint RCS/Dunhill Medical Trust research fellowships
14. Lord Cadogan talking to research fellows Michelle Griffin, Tim Jones and Liza Osagie at the Freemasons' HQ
15. Clare Marx with Professor Sir Norman Williams on the day of her election to President

SARS Cambridge 2014 and Durham 2015

16. Professor Alun Davies & Professor Dion Morton at SARS, Cambridge
17. Olga Tucker, Matthew Bedford & Professor Derek Alderson at SARS, Cambridge
18. Derek Alderson & Charlie Knowles at SARS in Durham
19. RCS/Fulbright scholar Marc Bullock & Derek Alderson at SARS, Durham
20. Professor Andrew Bradley at the Academy of Medical Sciences stand at SARS, Durham
21. Patricia Hagan, Anne Bishop & Professor Howard Kynaston of BAUS at SARS, Cambridge



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