

# 2013 SURGICAL RESEARCH REPORT 20<sup>TH</sup> ANNIVERSARY SURGICAL RESEARCH FELLOWSHIPS



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# CHAIRMAN'S INTRODUCTION



Derek Alderson  
Chairman, Academic  
and Research Board

This year sees the completion of 20 years of RCS surgical research fellowships. From a relatively humble start in 1993, when a total of £70,000 was awarded to 2 fellows, the scheme now provides about £1.5 million in funding each year. In the most recent round of awards 121 applicants from a broad range of surgical disciplines had their applications assessed, resulting in 48 individuals being called to undergo 'poster vivas'. We were able to make 21 awards. When added to named awards offered in partnership with other funders, more than 30 young surgeons will be the recipients of RCS badged research fellowships this year.

In many respects the scheme has changed little during the 20 years since its inception. The original idea was developed during the presidency of Professor Sir Norman Browse, with Professor Sir Peter Morris becoming the first Chairman of the Research Board. The idea at the outset to support mainly young researchers to help them get preliminary data that might form the basis of a substantive grant from a major funding body still holds good. The many joint awards that we now have reflect the expansion of the scheme under the leadership of Professor Sir Peter Bell, who also oversaw the relocation of an administrative base for our activities to the seventh floor of the Nuffield building and led the negotiations resulting in the establishment of the Clinical Effectiveness Unit within the College. Many of the partnerships developed with benefactors are now long-standing relationships,

reflecting commitment by both parties and satisfaction from all those who donate money for research, having confidence that it is spent wisely and distributed fairly. The poster viva was introduced by Professor Tony Mundy to add a further dimension to the overall assessment process and ensures the applicants are fully conversant with their project.

The board is particularly proud that virtually all of the money raised from historic legacies and endowments is spent on the research fellows and no deductions are made from the various bodies who currently contribute to the research fellowships. We spend less than 15% of our income on staff costs, administration of all of our research activities and the cost of maintaining a base within the College.

Some things have changed. The application process has become increasingly rigorous, considering not only the quality of the project, but also the potential of the individual and the environment in which the research will take place. The overall quality of the projects also seems to have improved with the passage of time. Although we have no objective evidence to support this assertion, clinical audits and reviews of NHS practice are rarely proposed, basic research in the laboratory nearly always has a translational link into clinical practice and early- and late-phase clinical studies can be devised and executed by surgical trainees. More than half of the applicants who presented at the poster viva stage in the past few years have already undertaken some work in relation to their project, such as learning a laboratory technique or gaining ethical approval for a clinical study. More often than not, this has been done in parallel with clinical training, indicating that the awards are valued and emphasising the need for a competitive edge in order to be successful. Like many awards, there are a few myths that seem to circulate among potential applicants. The notion that some specialties are favoured, that we don't give money for educational research and that you can't do research outside the UK are all untrue!

One often-overlooked aspect of the programme is the time and effort devoted to feedback on the strengths and weaknesses of the application. Whenever possible this is a personal call from our secretary. It is not surprising, therefore, that we receive few complaints about the process, the quality of the written assessment or conduct of the poster vivas. We certainly now have more 'worthy' applications that reach the standard justifying support than we are able to fund. Reapplication is encouraged as a result, but clearly the onus is on the board to make every effort to identify new sources of funding to increase the number of awards.

The progress made with our Surgical Trials Initiative

since it began last year has exceeded most expectations. The idea that the College should play a greater role in research owes much to my predecessor as chairman, Professor Norman Williams. In partnership with the National Institute for Health Research (NIHR), Cancer Research UK, the Medical Research Council and representatives from the surgical specialist associations, we were able to hold interviews for the Surgical Clinical Trials Units in July 2012. We now have five funded centres in Oxford, Bristol, Birmingham, Manchester/Liverpool and Queen Mary College, London. The response of specialist associations and, in many cases, their links to specific charities was overwhelmingly positive. By setting up the surgical specialist lead posts, 11 individuals are already in post with a further round of interviews scheduled for September. Workshops have already taken place to introduce the leads to the trials units, so that the generic and specialist skills of each centre can be fully exploited, along with meetings with existing and potential new industrial partners.

The units are currently responsible for 37 trials in progress with a further 15 that are funded in their set-up phases. The surgical community has clearly responded to the NIHR call. With this increased activity comes the need to ensure that all surgeons are provided with the skills necessary to recruit patients to surgical trials and to be able to participate in trials at a variety of levels. We see the development of new

to discuss its scientific merit or the philosophical and political arguments used to underpin the process, but as the results roll out, it is worth remembering that over 95% of those surgeons who contributed to the audits have consented to having their data published and that reanalysis of institutional data to make it surgeon specific has taken place rapidly with virtually no money. The College wishes to see openness, but if this is to evolve sensibly to create something that is meaningful to patients, the Clinical Effectiveness Unit will need much more support.

Success has a price. In addition to monies raised to support individual research fellowships, we have raised over £2.5 million to get the Surgical Trials Initiative this far. We must acknowledge the continued efforts of freemasonry in increasing their support for the former and the Rosetrees Trust that provided the substantial initial donation to start the Surgical Trials Initiative. The College is always grateful to fellows and members who assess grants, sit on interview committees and attend fundraising events on our behalf. All these activities that are voluntary. While not wishing to play down our gratitude to our many research partners, the surgical associations and all who make this successful, some special thanks must go to the teams led by David Cromwell in the CEU, Johnny Fountain in the Development Office, Professor Dion Morton, our Director of Research and last, but my

## THE COLLEGE WISHES TO SEE OPENNESS, BUT IF THIS IS TO EVOLVE SENSIBLY TO CREATE SOMETHING MEANINGFUL TO PATIENTS, THE CEU WILL NEED MUCH MORE SUPPORT.

researchers and principal investigators as an important aspect of the whole programme and plans to implement these next steps will be announced later this year.

A steering committee involving partner organisations, specialty, patient and medical charity representatives provides independent oversight under the chairmanship of Professor Sir Michael Rawlins.

In the past six months, the Clinical Effectiveness Unit has been incredibly busy preparing information from the audits chosen by the Medical Director of the NHS, Sir Bruce Keogh, to describe individual surgeons' results. This is not the place

no means least, Martyn Coomer, who has served as Secretary to the Board since its inception.

I feel sure that the 4 previous chairmen would echo my personal feeling that surgical research would not be in its current healthy position, had it not been for Martyn's efforts to promote research for much of the last 20 years in the face of little enthusiasm from funders, denigration of surgical research by medical journals and just a bit of apathy in the occasional disillusioned surgeon!

We continue to set ourselves challenging targets in terms of research activity and outputs. I am confident we will meet them.

# THE RCS SURGICAL TRIALS INITIATIVE

Currently, less than 5% of government funding for medical research is targeted at surgical conditions, despite surgical admissions accounting for over 40% of in-hospital care. The RCS believes this is a major limiting factor to improving surgical care. The RCS is therefore working with partners on a programme to substantially increase surgical research capacity for the benefit of patients across the UK and beyond.

The programme, the RCS Surgical Trials Initiative, is overseen by the independent Clinical Research Initiative Steering Committee<sup>1</sup> (CRISC), chaired by Sir Michael Rawlins. CRISC meets three times a year and its membership encompasses research funders, patient liaison representatives, specialist surgical association representatives and clinical trials experts.

CRISC has appointed five Surgical Trials Units (STUs) across England, providing each with core funding to support the development of surgical trials. It has also appointed 11 Surgical Specialty Leads (SSLs) to develop new trials across the different surgical disciplines. The STUs are supporting and developing new researchers, ensuring that surgical innovations are introduced promptly and safely, benefitting patients through improved standards of care, better clinical outcomes and a reduction in regional variations in care.

## Surgical Trials Units

The STUs were established in early 2013 and are located in Bristol, Oxford, London, Birmingham and Liverpool/Manchester. The key deliverables for each STU are:

- » to instigate two new national surgical trials per annum;
- » to develop three new Chief Investigators over the first three years; and
- » to work with 50 different hospitals and 50 new surgical investigators over the next 4 years.

This equates to recruiting 600 surgical patients through each STU over the first 4 years of the programme. In the first year, we are substantially ahead of target.

## Surgical Specialty Leads

These newly created posts have been appointed with the remit to establish clinical networks and, working in partnership with patients groups/charities, to develop and deliver new and innovative trials within their surgical discipline. In the first year, 11 national SSLs have been appointed. The SSLs are the key not only to recruiting patients into trials, but to developing new researchers within their field by engaging consultants and surgical trainees into their trials networks.

The first-year goals for the Surgical Specialty Leads are

to establish a working group, set up an open day for surgeons in their specialty, take forward a new study in their discipline and to establish a working platform with their specialist association. This activity will be supported by the STUs.

## Delivering

Unit	STU Director	Location	STU Manager
Surgical Intervention Trials Unit	Professor David Beard Professor Freddie Hamdy	Oxford	Victoria Rush
Bristol Surgical Trials Unit	Professor Jane Blazeby	Bristol	Amy Collings
North West Surgical Trials Centre	Professor Nigel Bundred Professor Paula Ghaneh	Liverpool/ Manchester	Jenna Pagila
Birmingham Surgical Trials Consortium	Professor Jon Deeks	Birmingham	Dr Laura Magill
National Facial Oral and Oculoplastic Research Study Centre	Professor Peter Sasieni Professor Iain Hutchison	London	Fran Ridout

Specialty	Name	Association/Funder	Hospital
Orthopaedics	Professor Amar Rangan	Orthopaedic Research UK	Middlesbrough
Orthopaedics	Professor Matt Costa	Orthopaedic Research UK	Coventry
Otolaryngology	Professor Anne Schilder	Get A-Head	London
Transplantation	Professor Peter Friend	Rosetrees Charitable Trust	Oxford
Neurosurgery	Mr Peter Hutchinson	Henry Lumley Charitable Trust	Cambridge
Cardiothoracics	Professor David Taggart	George Drexler Foundation	Oxford
Head and Neck	Mr James McCaul	The Facial Surgery Research Foundation - Saving Faces	London
Coloproctology	Mr Simon Bach	Bowel Disease Research Foundation	Birmingham
Endocrine	Mr Radu Mihai	British Association of Endocrine and Thyroid Surgeons	Oxford
Endocrine	Mr Dae Kim	British Association of Endocrine and Thyroid Surgeons	Portsmouth
Plastics and Hand	Mr Abhilash Jain	The British Society for Surgery of the Hand/ The British Association of Plastic, Reconstructive and Aesthetic Surgeons.	London

### *Meetings*

An industry day event on March 2013, and a *Research in the 21st Century* event on April 2013, brought in around 200 people to encourage trials, boost collaborations and promote the initiative. Out of the *Research in the 21st Century* event, the NIHR are proposing a themed funding call named *Surgical Research in 21st Century*, to support new trials in surgery.

The Surgical Specialty Leads have established a clinical study group, which acts as a forum to share expertise and optimise the use of the infrastructure support, such as the Surgical Trials Units.

A two day methodology workshop was run by Professor Jane Blazeby (Bristol Surgical Trials Unit Director) on 27 and 28 June 2013 and brought together some of the national experts in surgical trial design. This workshop is developing new guidance for trialists and surgeons in designing, delivering and monitoring surgical interventions within randomised clinical trials.

The CRISC members, STU directors and SSLs meet tri-annually to implement future strategies for the initiative and share ideas between one another.

### *Trials Portfolio*

A national portfolio of all the trials being undertaken by the Surgical Trials Units has been established. This interactive portfolio includes: open trials, trials in set-up and trials submitted for funding. This document is a unique resource for investigators to access information and contact details of trials being undertaken by the RCS's STUs and to plan for new trials.

### *CI and PI document*

This interactive document allows investigators to access information about current trials being undertaken by the STUs and the trials chief investigator. This document also includes the contact details of over 600 principle investigators who are actively recruiting to trials within England and Wales.

## **The future**

### *Funding*

The overall cost of the programme is £3 million and to date £2.5 million has been raised. Active fundraising continues with help from the Association of Medical Research Charities (AoMRC). The RCS is also seeking additional funding for further specialty leads in the priority areas of breast, urol-

ogy and vascular surgery and for evidence synthesis, which will provide the evidence base to support the next round of national clinical trials. The RCS has held preliminary discussions to consider expanding our trials into Europe and accessing EU funding streams.

### *Involving the trials community*

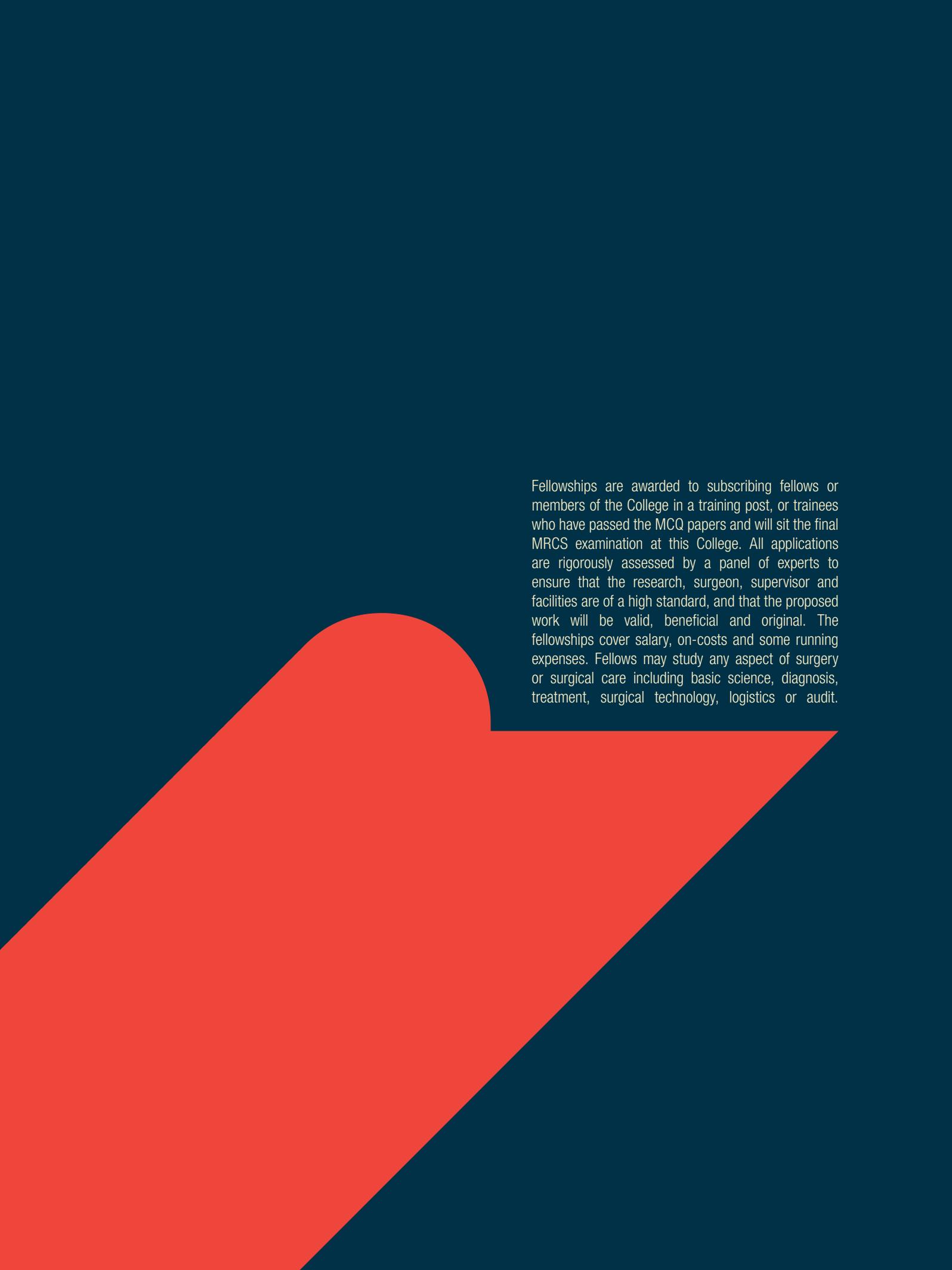
A strong focus in the early stages will be to grow the surgical trials community. This will be done through the SSLs engaging with trainees and the specialist surgical associations. In addition, the STUs will develop their accessibility strategy and the RCS will help this by promoting the STUs and their methods of entry into them.

### *Future meetings*

- » The STUs are due to hold launch days for their centres and the Northwest Surgical Trials Centre (NWSTC) is the first to do so, in September 2013.
- » A new surgical trials day has been established at the NCRI cancer conference in Liverpool in November 2013.
- » We are also hosting the national collaborative meeting for surgical trainees which will be held at the RCS on 6 December 2013.
- » A communications course run with the MRC will be held at the RCS in mid-January 2014.
- » Oxford will hold a national surgical trials day on 7 February 2014, with keynote speakers.

## **CRISC Members include**

- » Chair – Sir Professor Michael Rawlins (NICE)
- » Professor Derek Alderson (Chair of RCS Academic & Research Board)
- » Dr Jonathan Sheffield (CEO of NIHR Clinical Research Network)
- » Dr Kate Law (Clinical Research Director, Cancer Research UK)
- » Dr David Cromwell (Clinical Effectiveness Unit – RCS)
- » Professor Max Parmar (Director of MRC Clinical Trials Unit)
- » Dr Jenni Macdougall (NCRI Senior Programme Manager)
- » Mr Ian Martin (President of FSSA)
- » Ms Sharmila Nebhrajani (Chief Executive of the Association of Medical Research Charities, AoMRC)
- » Ms Kate Williams (Patient Liaison Group)



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.

# RESEARCH FELLOWS' REPORTS

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# THE DEVELOPMENT AND EVALUATION OF A NOVEL GENERATION OF ONCOLYTIC VACCINIA VIRUSES DESIGNED TO STIMULATE ANTITUMOUR IMMUNITY

Up to 50% of mortality in patients with certain head and neck cancers is accounted for by recurrent disease

## FELLOWSHIP/SPONSOR

College Research Fellowship with the support of the Rosetrees Trust

## SUPERVISOR

Dr Y Wang, Mr G Alusi, Prof N Lemoine

## SITE OF WORK

Barts Cancer Institute, London

## PUBLICATIONS

1. J Ahmed, M Yuan, G Alusi, N Lemoine, Y Wang. *The Lister strain of Vaccinia Virus as an anticancer therapeutic agent*. Book chapter in upcoming 3rd Edition of Gene Therapy of Cancer: Eds EC Lattime and SL Gerson.

## FURTHER FUNDING

Barts and London Charity and The Wellcome Trust Clinical Research Fellowships for 3 years



**JAHANGIR  
AHMED**

Despite recent advances in traditional treatment modalities, the outlook for many solid malignancies remains poor. There are of course many reasons for this, but an important cause of mortality is tumour recurrence following primary eradication. For instance, recurrence accounts for up to 50% of mortality in laryngeal carcinoma. Novel therapies are thus required, and oncolytic virotherapy holds particular promise.

Oncolytic viruses (OVs) are live biological agents that have been engineered to selectively replicate in and destroy tumour cells, sparing normal cells. In theory, if a sufficient viral load is delivered into the tumour microenvironment, such viruses will self-propagate and spread throughout the tumour, effectively 'melting' it away. Unfortunately clinical trials with early generation OVs have generally been disappointing.

A major problem with OV-therapy is its clearance by the host's immune response before it has a chance to completely eradicate the tumour. However, it may be possible to harness this strong antiviral immune response and subvert it against the culprit tumour. Any residual disease would thus be cleared by the host's immune system instead. Furthermore, this boosted antitumour 'immune surveillance' could prevent recurrence.

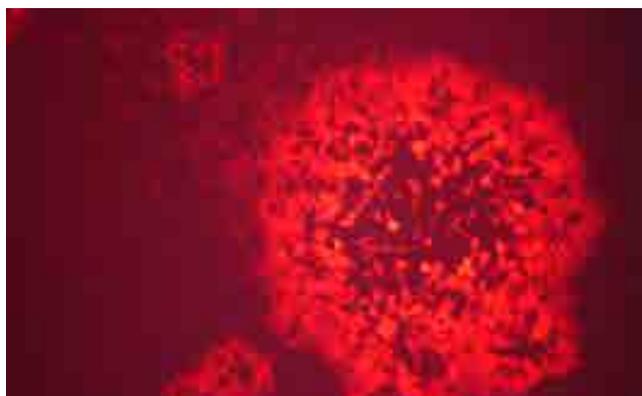
With this goal in mind, our group has been focusing on vaccinia virus (VV), famous for its role in eradicating smallpox. I deleted a particular gene in VV, thought to inhibit key immune cells. This mutant virus was delivered into immune-competent animal models of various solid tumours. I was able to demonstrate a heightened infiltration of immune cells into the tumour microenvironment, which reflected an enhancement of a 'specific' host antitumour immune response. For one model, designed to look at recurrence following primary surgical clearance, data suggested that ad-

juvant use of this novel virus could indeed reduce recurrence. The virus was further optimised as an immunotherapeutic by arming it with potent immune-stimulatory genes.

We hope this work is a prelude to clinical translation with the ultimate aim of minimising solid tumour recurrence following primary surgical clearance.



Jay at work



A colony of his genetically engineered Vaccinia virus

# TOWARDS OBJECTIVE ENDOSCOPIC DIAGNOSIS OF OESOPHAGEAL DYSPLASIA USING FIBREOPTIC RAMAN SPECTROSCOPY

Up to 57% of pre-cancerous lesions in the oesophagus may be missed using routine white light endoscopy



**MAX  
ALMOND**

## FELLOWSHIP/SPONSOR

Freemasons Research Fellowship

## SUPERVISOR

Professor Hugh Barr

## SITE OF WORK

Biophotonics Research Unit, Gloucestershire Royal Hospital

## PUBLICATIONS

1. Almond LM, *et al.* Raman spectroscopy: a potential tool for early objective diagnosis of neoplasia in the oesophagus. *J Biophoton* 2011; **4**: 685–95.
2. Almond LM, *et al.* Assessment of a custom-built Raman spectroscopic probe for diagnosis of early oesophageal neoplasia. *J Biomed Opt* 2012; **17**: 814–21.

## PRESENTATIONS

1. Almond LM, *et al.* Mapping of the distal oesophagus using fibre-optic Raman Spectroscopy. Presented at ASGBI International Surgical Congress, '21st Century Surgery', UK, 2011.
2. Almond LM, *et al.* Towards Endoscopic Detection and Targeting of Oesophageal Neoplasia using near-infrared spectroscopy. European Society of Esophagology. UK, 2011.

## PRIZES

1. First prize for best presentation of original research at the International 'Laser Europe' Conference, London, 2012.
2. Winner of the RSM Prize (Surgery Section) for best presentation of laboratory research. London, 2011.

Oesophageal adenocarcinoma is increasing more rapidly than any other tumour in the western world. It is usually not detected until late in its course, by which time it is often incurable – only 12% of patients survive for 5 years or more. Despite the recognition of Barrett's oesophagus (a common condition in patients with acid indigestion) as a precursor of cancer, no early diagnostic test has been developed. Patients with Barrett's may develop early precancerous changes in the cells lining their oesophagus which cannot be seen by doctors during endoscopy.

My research has translated a well-established laboratory technique called Raman spectroscopy into a specialised probe for use during endoscopy. The novel Raman probe, which is compatible with standard endoscopes, has optical components which focus onto the innermost lining of the oesophagus so that the earliest precancerous lesions can be detected.

Oesophageal tissue samples were collected from 62 patients with oesophageal cancer or 'pre-cancer' following

endoscopic biopsy, endoscopic mucosal resection or surgical removal of the oesophagus. A total of 798 Raman probe measurements were taken from different tissue sites.

One-second probe measurements have been shown to distinguish 'pre-cancer' and early cancer from normal oesophageal tissue with a sensitivity of 93% and a specificity of 92%.

Probe measurements were reproducible over the whole 20-month period of data collection. In addition, consistent measurements were recorded by two independent operators using two identically built probes.

This translational research has demonstrated potential for rapid, accurate diagnosis of 'pre-cancer' in the oesophagus using a novel endoscopic probe, without the need for stains or intravenous contrast agents. The diagnoses established are also objective, based on measured biochemical differences in tissue types. This new technology could enable early targeted therapy to prevent the development of invasive oesophageal cancer. A clinical trial is expected within the next one to two years.



Max performing an endoscopy in a patient with Barrett's oesophagus



Max with Professor Ken Wang and his team during a visit to the world famous Mayo Clinic in the US



Max consulting with a patient

# THE DEVELOPMENT AND VALIDATION OF A NOVEL EX VIVO POLYPECTOMY SIMULATOR

In 2012, 6,543 high-risk adenomatous polyps were detected following the first 1 million tests from the National Bowel Cancer Screening Programme

## FELLOWSHIP/SPONSOR

Joint WIMAT/RCS Brian Rees Research Fellowship

## SUPERVISOR

Mr Jared Torkington, Dr Neil Warren, Prof Keith Harding

## SITE OF WORK

Welsh Institute for Minimal Access Therapy

## PUBLICATIONS

1. Ansell J, Arnaoutakis K, Goddard S, *et al.* The WIMAT colonoscopy suitcase: a novel polypectomy trainer. *Colorec Dis* 2012; **15**: 217–23.
2. Ansell J, Mason J, Warren N, *et al.* A systematic review of validity testing in colonoscopy simulation. *Surg Endos* 2012; **26**: 3,040–52.

## PRESENTATIONS

1. Ansell J, Arnaoutakis K, Goddard S, *et al.* *The WIMAT colonoscopy suitcase: a novel polypectomy trainer.* European Association of Endoscopic Surgery (EAES): Brussels; 2012.
2. Ansell J, Hurley JJ, Horwood J, *et al.* *The WIMAT colonoscopy suitcase is a valid simulator for polypectomy training.* Society of American Gastrointestinal & Endoscopic Surgery (SAGES): Baltimore, USA; 2013.

## PRIZES

1. Steve Lovell Audio Visual Prize, ASGBI, 2013.
2. Stephan Galeski Travelling Fellowship, RCS, 2011.

## FURTHER FUNDING

1. EU Lifelong Learning Fund for one year.



**JAMES  
ANSELL**

The NHS National Bowel Cancer Screening Programme (BCSP) was introduced in 2006 as a means of identifying colorectal cancers at an early stage of development. This has led to a rise in the detection of adenomatous polyps, which are a precursor to bowel cancer. In most cases, these polyps can be treated by local excision in the form of colonoscopic polypectomy. This means that patients can avoid the need for major abdominal surgery.

The increase in polyp detection has resulted in a subsequent demand to train more endoscopists to manage this workload. One way of addressing this training issue is through the use of simulation. This allows the trainee to practise polypectomy in a controlled environment, reducing risk to the patient. Computer simulation training has been shown to be an effective teaching tool for endoscopy, with a resultant positive impact on patient comfort. This form of simula-

Performing simulated colonoscopic polypectomy. WIMAT technicians, Mr Stuart Goddard and Mr Konstantinos Arnaoutakis (Left), James with WIMAT Director, Dr Neil Warren (Right)



James with his supervisor, Mr Jared Torkington

tion is, however, not yet technically challenging enough for training experienced endoscopists. An alternative approach for therapeutic endoscopic interventions such as polypectomy is to use *ex vivo* animal tissue. This provides a realistic simulation with considerably less expense and greater flexibility. The aim of this project was, therefore, to develop and validate a novel *ex vivo* porcine polypectomy trainer.

The *WIMAT colonoscopy suitcase* uses porcine bowel to recreate a range of polypectomy procedures. Research has shown that this simulator has excellent mechanical, anatomical and visual realism. Participants perform simulated polypectomy using the *WIMAT colonoscopy suitcase* in accordance with their real-life level of expertise. Skills developed during simulator training are transferrable to the clinical setting, meaning that patients can benefit from better trained therapeutic endoscopists. Future work will be directed towards developing the range of procedures which can be practised on the simulator and attempting to develop an assessment process for trainee accreditation.

# THE ROLE OF FUNCTIONAL IMAGING IN AORTIC ANEURYSMS

Aortic aneurysms affect 5–8% of those over 65. Without surgery 5-year survival is only 16% for thoracic and 20% for abdominal aortic aneurysms

## FELLOWSHIP/SPONSOR

RCS Research Fellowship with the support of the Rosetrees Trust

## SUPERVISORS

Mr Matthew Waltham and Professor Alberto Smith

## SITE OF WORK

Kings College London BHF Centre of Excellence and NIHR, Biomedical Research Centre at King's Health Partners, Department of Academic Surgery, St Thomas' Hospital, London

## PRESENTATIONS

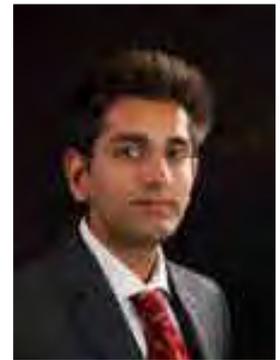
1. Society of Cardiothoracic Surgeons of Great Britain 2012 and 2013.
2. Vascular Society 2012.

## PRIZES

1. Rosetrees Trust Award 2012.
2. Royal Society of Medicine Cardiothoracic prize 2011 and 2013.
3. Society of Cardiothoracic Surgeons: Professor Bob Bonser prize in aortic surgery 2013.

## FURTHER FUNDING

1. National Institute of Health Research/ Biomedical Research Centre for one year.
2. British Heart Foundation Programme Grant for five years.



**RIZWAN  
ATTIA**

Aortic aneurysms are the 13th most common cause of death in the UK. The annual incidence of thoracic aortic aneurysms is 6/100,000 person years and abdominal aortic aneurysms affect 5.5% of men over the age of 65. It is estimated that around 12,000 people die of aortic aneurysm rupture or dissection annually.

This project aims to better understand how aneurysms develop. Functional imaging provides physiological and biochemical information on pathological processes that might be ongoing in the aortic wall. If we can predict aneurysm behaviour, we can monitor and perform timely surgery ensuring best outcomes. We can also aid in the development of new drugs that might treat aneurysms. Currently the most commonly used predictor for the risk of rupture is the aneurysm size. Some aneurysms, however, rupture or dissect at a small size while others grow to a considerable size without causing symptoms. We therefore need a better way of predicting risk than size alone. We know that in the wall of aneurysms there are cells that cause inflammation and breakdown of the extracellular matrix. As these cells are very active they take up glucose. We aimed to understand the biological correlates to increased aortic wall 18-fluorodeoxyglucose (18-FDG) uptake on positron emission tomography. We also aimed to develop and evaluate novel magnetic resonance imaging (MRI) tracers that are specific for biological processes ongoing in the aortic wall.

During this project, we have developed a novel method of performing highly accurate aortic wall biopsies at surgery to specifically analyse sites of varying 18-FDG uptake. We have also tested novel MRI tracers that bind to elastin to detect and predict aneurysm behaviour. Using a combination of flow cytometry, immunohistochemistry and molecular techniques, we have shown that B, T lymphocytes and NK cells are re-



Above: Flow cytometric analysis to phenotype immune cells extracted from the aortic aneurysm

Left: 3D reconstructed aortic phantom generated using laser scintigraphy being used to perform aortic aneurysm biopsy. (Picture courtesy of Mr Young Consultant Cardiac Surgeon)

sponsible for the radiotracer signal in the aortic wall. It is the likely effect of these cells on vascular smooth muscle cells that leads to altered elastin homeostasis with increased degradation and aneurysm progression.

This research is ongoing in order to gain further insight into the cellular mechanisms of aortic aneurysm development. If detected earlier there is opportunity to predict aneurysm behaviour or alter the course of the disease with drug therapies.

# CONVECTION-ENHANCED DELIVERY OF THERAPEUTICS FOR THE TREATMENT OF ALZHEIMER'S DISEASE

Over 27 million people worldwide are affected by Alzheimer's disease. With an aging population this number is set to rise over the coming years

## FELLOWSHIP/SPONSOR

Joint RCS/Dunhill Medical Trust Fellowship

## SUPERVISORS

Professor S Gill and Professor S Love

## SITE OF WORK

Functional Neurosurgery Research Group,  
University of Bristol

## PUBLICATIONS

1. Barua NU, Miners SJ, Bienemann AS, *et al.* Convection-enhanced delivery of neprilysin – a novel  $\beta$ -degrading therapeutic strategy. *J Alzheimers Dis* 2012; **32**: 43–56.
2. Barua NU, Bienemann A, Hesketh S, *et al.* Convection-enhanced delivery results in widespread perivascular distribution in a pre-clinical model. *Fluids Barriers CNS* 2012; **9**: 2.

## PRIZES

1. EPSRC Pathways to Impact Award, September 2011.

## FURTHER FUNDING

The Engineering and Physical Sciences Research Council for six months



**NEIL  
BARUA**



A neurosurgical robot is used to increase the accuracy and safety of implanting catheters in the brain



This diagram shows how a very fine microcatheter could be implanted deep within the brain in a clinical trial of CED for Alzheimer's Disease (Courtesy of Neuro Applications Group, Renishaw Plc)

Accumulation of the toxic protein beta-amyloid ( $\beta$ ) in the brain is thought to play a key role in the development of Alzheimer's Disease (AD). A failure to clear  $A\beta$  from the brain is partly responsible for  $\beta$  accumulation in most patients. Maintaining clearance of  $\beta$  represents a novel approach to combat the onset of disease that remains relatively unexplored. The aim of this study was to determine whether a novel neurosurgical technique called convection-enhanced delivery could be used to deliver an enzyme to the brain which promotes the breakdown and clearance of  $\beta$ .

Convection-enhanced delivery (CED) describes a direct method of drug delivery to the brain through very fine microcatheters. This technique has the advantages of delivering drugs to specific structures within the brain with high safety and accuracy, and allowing drugs to be delivered at effective doses while reducing the risk of side effects. We have previously used this technique to successfully treat patients with Parkinson's disease.

In this study we performed CED of the  $\beta$ -degrading enzyme Neprilysin into the brains of elderly rats, which develop deposits of  $A\beta$  as part of the normal aging process. We found that Neprilysin could be effectively distributed throughout large regions of the brain, without evidence of toxicity or damage to normal brain tissue. We also found that this technique resulted in a significant reduction in the levels of  $A\beta$  in the brain, indicating that this novel neurosurgical technique has potential for promoting the clearance of  $\beta$  in Alzheimer's disease.

Based on these promising results we plan to undertake further studies to identify the optimal dose of Neprilysin, which will allow us to progress to a trial of this novel therapy in patients with Alzheimer's disease.

# THE ROLE OF NAV1.9 IN VISCERAL AFFERENT SIGNALLING

Abdominal pain is the most common reason for surgical consultation

## FELLOWSHIP/SPONSOR

Frances and Augustus Newman Foundation Fellowship

## SUPERVISOR

Professor Charles H Knowles

## SITE OF WORK

Royal London Hospital/Queen Mary, University of London

## PRESENTATIONS

1. The role of Nav1.9 in the activation of visceral afferent fibres by human inflammatory supernatants. Joint International Neurogastroenterology and Motility Meeting, September 2012, Bologna, Italy.
2. The role of Nav1.9 in the activation of visceral afferent fibres by algogenic mediators. World Congress on Pain, August 2012. Milan, Italy.

## PRIZES

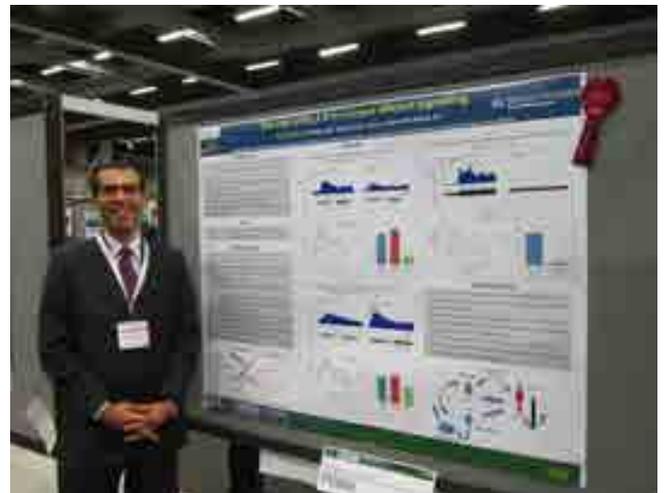
1. A top poster prize at the United European Gastroenterology Week (UEGW) in Stockholm, 2011.



**GEORGE  
BOUNDOUKI**



An overview of the Blizard Institute at Queen Mary, University of London where George undertook his research



George standing by his poster at the United European Gastroenterology Week (UEGW) in Stockholm, October 2011, where he was awarded a top poster prize

Abdominal pain is the most common reason patients give for consulting their surgeon. While most causes of pain are treatable, more than one in three patients seen in hospital clinics have recurrent unexplained pain. This places a great burden on patients as well as the NHS. It is estimated that in 2000, this cost the UK more than £1bn.

Current pain killers do not only affect nerves in the abdomen but affect all nerves including those in the heart and brain which leads to side effects. Nerves have a number of channels which allow them to function. One of those channels, Nav1.9, is only present on nerves in the abdomen and on the skin.

My research investigated the role of Nav1.9 in pain sensation by making recordings of the nerves in the mouse colon.

I added pain-causing chemicals to the colon specimens and showed that removing Nav1.9 meant the nerves were less activated by these chemicals. I then repeated the experiment with molecules taken from patients who came to hospital with pain and confirmed that the nerves lacking Nav1.9 were less activated.

This work highlighted that Nav1.9 is important in sensing pain from the colon. The fact that Nav1.9 is not present in the heart or brain means that if a medicine that blocks Nav1.9 is developed then patients will be able to take a pill which will relieve their pain but without some of the side effects of current medication.

# ACCELERATING FRACTURE REPAIR IN OSTEOPOROTIC BONE

Inflammation driven by TNF and the CCL2/CCR2 axis is a critical process that drives fracture repair

## FELLOWSHIP/SPONSOR

College Research Fellowship

## SUPERVISOR

Professor Jagdeep Nanchahal

## SITE OF WORK

Kennedy Institute of Rheumatology

## PUBLICATIONS

1. Chan JK, Roth J, Oppenheim J, *et al.* Alarmins: Awaiting a Clinical Response. *J Clin Invest* 2012; **122**: 2711–19.
2. Glass GE, Chan JK, Freidin A, *et al.* TNF- promotes fracture repair by augmenting the recruitment and differentiation of muscle-derived stromal cells. *PNAS* 2011; **108**: 1585–90.

## PRESENTATIONS

1. Chan JK, Glass GE, Ersek A, *et al.* Strategies to accelerate fracture repair. Portugese Congress of Internal Medicine, Portugal (Invited speaker). 2013.
2. Chan JK, Horwood N, Nanchahal J. *Regenerative role of inflammation and alarmins.* 4th International Münster Meeting on Danger Signaling in Autoinflammation, Münster, Germany. 2012.

## PRIZES

1. Bone Research Society (BRS) Best Oral Presentation Prize, 2012 July 2012, Manchester.
2. Barron Prize, Paton-Masser Memorial Fund, March 2013, awarded by BAPRAS.



**JAMES  
KWOK-KWAN CHAN**



James in the lab

Fractures in osteoporotic bone, or ‘fragility fractures’, represent an enormous unmet medical need. They are associated with permanent disability and premature death. There is currently no approved therapy for accelerating healing of fractures in osteoporotic bone.

Inflammation represents the earliest response following trauma and initiates a cascade of events that are crucial for wound healing (Chan *et al* JCI 2012). Our aim was to characterise these early inflammatory pathways in order to identify novel therapeutic strategies to accelerate fracture repair.

Prof Nanchahal’s group has previously reported that addition of low-dose recombinant human protein, rhTNF, at the fracture site accelerated fracture repair in a murine tibial fracture model (Glass *et al* PNAS 2011). We have now found that local rhTNF treatment is only effective when administered within 24 hours of injury, during which neutrophils (a type of white blood cell) represent the major component of

the inflammatory cell infiltrate. Mechanistically, the addition of rhTNF to the fracture environment enhanced the recruitment of neutrophils, which in turn promoted the recruitment of other cells that are crucial in the fracture healing process including monocytes and osteoclasts through the release of a protein named CCL2. Conversely, inhibition of neutrophil activity or CCR2, the main receptor for CCL2, resulted in significantly impaired fracture healing. Using a murine model of fragility fractures in which mice are rendered osteoporotic by removal of their ovaries, we found that rhTNF treatment improved fracture healing during the early phase of repair. Translated clinically, this accelerated healing would permit earlier load bearing and reduce the morbidity and mortality associated with delayed patient mobilisation.

# INFECTION AND IMMUNITY IN HEALTH AND SURGICAL DISEASE

For those who develop severe sepsis or septic shock the risk of death approaches 30%, which is equivalent to the risk of death associated with a heart attack

## FELLOWSHIP/SPONSOR

Frances and Augustus Newman Foundation Fellowship

## SUPERVISOR

Professor Dileep Lobo

## SITE OF WORK

NIHR Nottingham Digestive Diseases Centre Biomedical Research Unit, Queen's Medical Centre, Nottingham

## PUBLICATIONS

1. Chowdhury A, *et al.* Perioperative probiotics, probiotics or synbiotics for elective abdominal surgery in adults. *Cochrane Data Systematic Reviews* 2011. Issue 7. CD009246.

## PRESENTATIONS

1. *Effect of Bifidus BB536 and active hexose correlated compound on immune function in healthy volunteers.* International Congress of Nutrition and Integrative Medicine, Sapporo, Japan 2013.
2. *Perioperative probiotics, probiotics or synbiotics for elective abdominal surgery in adults – a systematic review and meta-analysis of randomised controlled trials.* International Surgical Week, Helsinki, Finland 2013.

## PRIZES

1. 2011 Annual Congress European Society of Parental and Enteral Nutrition Travel Award for best abstract from the UK.

## FURTHER FUNDING

National Institute of Health Research, Nottingham Digestive Diseases Centre, Biomedical Research Unit for three years



**ABEER  
CHOWDHURY**

Advances in surgical technology, critical care and antibiotics have improved outcomes for patients undergoing major abdominal surgery. However, for some patients, the risk of complications remains high. Following severe infections, the risk of death approaches 30%, which is comparable to the risk of death following a heart attack. Current therapies to combat infection rely very much on antibiotics, which has contributed to growing levels of resistance. This has led to the demand for novel or alternative strategies

The aim of this series of studies was to demonstrate the influence of bacteria and their products on human immune responses in both health and surgical disease. Previous studies indicate a potential role for probiotic bacteria in the treatment of infective disorders of the gastrointestinal tract. In this research, I have been able to show that probiotic bacteria administered in the perioperative period reduces the risk of infective complications following major abdominal surgery.

It is proposed that some of the beneficial effects of probiotics involve an effect on human immune responses. It is thought that some harmful bacteria are also able to alter the responses of some immune cells to favour their own survival leading to persistent infection. In this research, using blood donated by healthy volunteers and from patients with obstructive jaundice, I was able to demonstrate that bacteria can change the characteristics of human immune cells. In particular, potentially new mechanisms were uncovered for this phenomenon with bacterial molecules thought previously to be involved only in communication between bacterial cells.

Future research will aim to uncover in greater detail the mechanisms of bacterial interaction with human immune cells. It is possible that this knowledge could lead to therapeutic targets and provide an alternative strategy to antibiotics in the fight against postoperative infection.



Operating on patients with obstructive jaundice



Consultation with potential volunteers involved in study

# THE PEDAGOGY OF THE OPERATING THEATRE

Adequately preparing trainee surgeons to deal with complications and adverse events in the operating theatre is essential to ensure high-quality patient care

## FELLOWSHIP/SPONSOR

Harry Morton Travelling Fellowship

## SUPERVISOR

Professor Roger Kneebone

## SITE OF WORK

St Mary's Hospital, Paddington (Imperial College, London)

## PUBLICATIONS

Bezemer J, Cope A, Faiz O, Kneebone R. Participation of surgical residents in operations: challenging a common classification. *World J Surg* 2012; **36**: 2011–14.

## PRESENTATIONS

1. Cope AC, Bezemer J, Kneebone R, Lingard L. "You see?" *Learning through Co-construction of visual cues during operative surgery*. Association for Medical Education Europe, Lyon, France 2012.
2. Cope AC, Miskovic D, Mavroveli S, Kneebone R, Hanna G. *Why is learning in simulation effective?* Simulation Summit, Ottawa, Canada 2012.

## PRIZES

1. Cope AC Bezemer J, Mavroveli S, Hanna G, Kneebone R. *A steady hand or a sharp eye? What do surgical trainees learn in the operating theatre?* ASGBI 2012 Poster prize Education/ Training.



**ALEXANDRA  
COPE**

Surgical training has been put under pressure by the European Working Time Regulations – yet it has never been more important to prepare surgeons for the vast array of new technologies and professional challenges that await them.

Simulation holds much promise for learning operative techniques safely, away from direct contact with patients. Simulation allows trainees to engage in sustained deliberate practice, facilitating automation through repetition of motor skills. In addition, simulation may be used to develop more generic professional competencies such as team working, situational awareness and leadership qualities.

There are many questions around how best to use simulation for learning, and what attributes can be learned in simulation. This research investigated the content and process of learning in the operating theatre and then went on to systematically investigate different simulation strategies. Extensive experience was gained in surgical education research centres in Canada analysing data from the UK using qualitative methodologies. In addition, three months were spent in simulation centres in Canada studying the residency model and how simulation may be integrated into the curriculum.

Much of what is learned in the operating theatre may be termed sensory semiotics – the trainee understanding 'what they are seeing or feeling'. In laparoscopic surgery we showed that teaching occurred through a process of co-construction between trainer and trainee, gradually building a shared understanding of the visual image.

This in-depth understanding of how teaching and learning are undertaken in the operating theatre has led to the development of specific simulation-based interventions which are currently under trial within the core training program. It is hoped that these carefully designed interventions will better prepare surgeons for safe independent practice.



Alex teaches how to perform a lap chole in a simulated theatre environment

# HISTONE DEACETYLASE INHIBITORS TO MODULATE PANCREATIC CANCER STROMA

Pancreatic cancer is the fourth most common cause of cancer-related death in the UK, with surprisingly few therapeutic options

## FELLOWSHIP/SPONSOR

Enid Linder Foundation Fellowship

## SUPERVISOR

Mr Hemant M Kocher

## SITE OF WORK

Barts Cancer Institute

## PUBLICATIONS

1. Kadaba R, Birke H, Wang J, *et al.* Imbalance of desmoplastic stromal cell numbers drives aggressive cancer processes. *J Pathol* 2013; **230**: 107–17.

## PRESENTATIONS

1. *Targeting pancreatic cancer stroma by HDACi*. Poster. DDW Florida, May 2013.
2. *Targeting pancreatic cancer stroma by HDACi*. Oral presentation. SARS, January 2013.

## PRIZES

1. Lord Smith Medal. Pancreatic Society of Great Britain and Ireland annual meeting 2012. Best Oral presentation at the annual National meeting.



**MOHAMMED  
A GHALLAB**

Pancreatic cancer is characterised by surrounding non-cancerous tissue called ‘stroma’, which is increasingly recognised to play a vital role in cancer progression.

My research aimed to isolate pancreatic stellate cells or PSC (the main cell in the stroma) from surgical pancreatic cancer samples and secondly to study the cancer stroma cross talk and effect of a drug, histone deacetylase inhibitors, on both cancer and stroma using the established 3D organotypic tissue (OT) model.

Isolation of PSC has been done before, however only from chronic pancreatitis samples rather than pancreatic cancer. PSC normally store vitamin A, but lose it when activated in cancer and inflammation. Previous authors either used methods where cells grow out of pieces of pancreas, or when using the whole tissue, only isolated the cells storing vitamin A.

I managed to develop a protocol isolating the PSC from both cancer and non-cancer samples of surgically resected pancreatic tissue using whole tissue digest. This novel protocol enables isolation of primary PSC from cancer patients

without excluding the activated cells. This is an important tool in the field of tumour stromal biology, a topic that is at the forefront of cancer therapeutic research.

Furthermore I established 3D organotypic tissue model (OT) where collagen and matrigel (proteins similar to stromal matrix) form a gel and both cancer cells and PSC are cultured on top, thus mimicking the 3D structure of normal tissue. HDACi an FDA approved class of drug for blood malignancies, was used to treat the OT gel for seven days. While having minimal effect when cancer cells are cultured alone, HDACi showed a dose-dependent effect in reducing proliferation, invasion, cell number and epithelial-mesenchymal transition (a key step in cancer progression) when both PSC and cancer cells were cultured together.

The work is still going on after the fellowship, and I am working towards finishing a PhD degree. The work on primary PSC is continuing and they will be used in the OT model to further dissect the stromal cancer cross talk.



A fresh donated specimen from a surgically resected pancreas. The direct access to the bed side allows to be one step closer to translational research



The specimen is handled in an aseptic work area and processed to extract a single cell suspension from a piece of tissue

# THE ROLE OF INFLAMMATORY CELLS IN THE DEVELOPMENT OF COLORECTAL HEPATIC METASTASIS

One in six patients with colon cancer has disease that has already spread to the liver at the time of diagnosis

## FELLOWSHIP/SPONSOR

College Research Fellowship

## SUPERVISOR

Professor Ruth Muschel

## SITE OF WORK

Gray Institute for Radiation Oncology and Biology, University of Oxford

## PUBLICATIONS

1. Zhao L, Lim SY, Gordon-Weeks AN, *et al.* Recruitment of a myeloid cell subset (CD11b/Gr1 (mid)) via CCL2/CCR2 promotes the development of colorectal cancer liver metastasis. *Hepatology* 2012; **57**: 829–39.

## PRESENTATIONS

1. *Myeloid Cells are Recruited by Liver Metastases and Aid their Development.* Society of Academic and Research Surgery Meeting, RSM prize presentation category. 9–10 January 2013, UK.

## FURTHER FUNDING

Cancer Research UK for two years



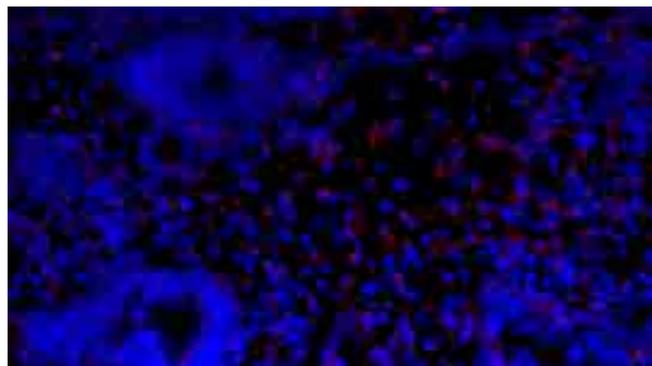
**ALEX NICOLAS  
GORDON-WEEKS**

Bowel cancer is the third most common cancer in the world, with disease that has spread (metastasised) to the liver being a common cause of death. Surgery is the only treatment capable of providing long-term survival for patients with liver metastases and is frequently not possible owing to the extent of disease at the time of presentation. As a result, patients with hepatic metastases from colon cancer have a particularly grave prognosis. Development of new treatment modalities for hepatic metastasis is urgently required in order to increase operability and improve patient survival.



Left: The Gray Institute for Radiation Oncology and Biology

Below: Immune cells (red) infiltrate the liver metastases of a patient with metastatic colon cancer



The aim of this research project is to identify factors of the immune system that aid the spread of bowel cancer from the colon to the liver. While various arms of our immune system initially help to limit the development of metastases, as the cancer evolves it is able to alter this immune response to its own benefit. Previous research by other groups<sup>1</sup> has shown that specific immune cells are recruited to metastatic sites by tumour cells. At various metastatic sites, the functions of such immune cells include stimulation of blood vessel growth and breakdown of structural proteins; both mechanisms that help the growth of metastatic tumour deposits.<sup>2</sup>

In mouse models that recapitulate human colon cancer we have identified a population of immune cells recruited to help colon cancer cells colonise the liver.<sup>3</sup> Using laboratory techniques and magnetic resonance imaging we have identified the molecular signalling pathways used by cancer cells to recruit this immune population and have shown that inhibition of such pathways delays the development of hepatic colon cancer metastasis. The research highlights the importance of immune cells for the development of metastatic colon cancer and in doing so identifies novel therapeutic targets.

There are currently no targeted treatments for patients with hepatic colon cancer metastases, however our research gives hope to the notion that metastases could be down-staged in a targeted fashion to improve operability and ultimately patient survival.

## References

1. Kitamura T, Fujishita T, Loetscher P, *et al.* Inactivation of chemokine (C-C motif) receptor 1 (CCR1) suppresses colon cancer liver metastasis by blocking accumulation of immature myeloid cells in a mouse model. *Proc Natl Acad Sci USA* 2010; **107**: 13,063–68.
2. Hanahan D, Coussens LM. Accessories to the crime: functions of cells recruited to the tumor microenvironment. *Cancer Cell* 2012; **21**: 309–22.
3. Zhao L, Lim SY, Gordon-Weeks AN, *et al.* Recruitment of a myeloid cell subset (CD11b/Gr1 (mid)) via CCL2/CCR2 promotes the development of colorectal cancer liver metastasis. *Hepatology* 2012; **57**: 829–39.

# CONTUSION PROGRESSION AND BLOOD BRAIN BARRIER PERMEABILITY FOLLOWING TRAUMATIC BRAIN INJURY

Traumatic brain injury is the leading cause of death and disability amongst young people in the UK

## FELLOWSHIP/SPONSOR

Philip King Research Fellowship

## SUPERVISOR

Mr Peter J Hutchinson

## SITE OF WORK

Addenbrooke's Hospital/University of Cambridge

## PUBLICATIONS

1. Guilfoyle MR, Seeley HM, Corteen E, *et al*. Assessing quality of life after traumatic brain injury: examination of the short form 36 health survey. *J Neurotrauma* 2010; 27: 2173–81.
2. Helmy A, Antoniadou CA, Guilfoyle MR, Carpenter KL, Hutchinson PJ. Principal component analysis of the cytokine and chemokine response to human traumatic brain injury. *PLoS One* 2012; 7: e39677.

## PRESENTATIONS

1. *Assessing Outcome following Traumatic Brain Injury: Combining the Glasgow Outcome Scale and SF-36 Quality of Life Survey*. Society of British Neurological Surgeons, London, Sept 2010.
2. *Incidence and Aetiology of Low Brain Extracellular Glucose Following Traumatic Brain Injury*. Society of British Neurological Surgeons, Brighton, Sept 2011.

## PRIZES

1. Beverley and Raymond Sackler Studentship.



**MATHEW  
R GUILFOYLE**



Analysing samples in the laboratory

Traumatic brain injury (TBI) is a devastating condition that remains the most common cause of death and disability in people under the age of 40 in western countries. Following the initial trauma a number of secondary events can compound the severity of injury; the main target of current intensive care and surgical treatment is to limit raised pressure within the head, which can compromise blood flow to the brain. One of the main causes of raised pressure is brain swelling around regions of brain contusion (bruising) but it remains unclear which biological signalling pathways are most important in causing this.

This project sought to characterise how brain swelling progresses over time, and identify signalling molecules that play key roles in mediating this process. To do this we used intracerebral microdialysis probes, which allow measurement of proteins and other substances within the human brain,

that were placed close to regions of contusion in patients with TBI. This technique was combined with a novel form of computed tomography (CT) scanning that provides detailed images of blood flow in the brain and also highlights fluid leakage from blood vessels that could contribute to brain swelling.

Our results have revealed profound reductions in blood flow within areas of contusion and also in the surrounding swollen brain. In addition, we have shown there is increased expression of inflammatory proteins, and of enzymes that break down normal tissue structure, close to contusions, both of which are likely to exacerbate the development of brain swelling.

These findings build on previous work in our group examining the inflammatory response in the brain following TBI. Together, these studies are informing the design of clinical trials of drugs that block specific inflammatory pathways and which will hopefully reduce the degree of brain swelling following TBI and, in turn, improve patient outcomes.

# INVESTIGATION OF NOVEL ADJUVANT THERAPIES IN THE ERADICATION OF BACTERIAL BIOFILMS IN CHRONIC RHINOSINUSITIS

Chronic rhinosinusitis (chronic infection of the sinuses) affects up to 15% of the UK population and is more common than high blood pressure and arthritis

## FELLOWSHIP/SPONSOR

RCS Research Fellowship with support from the Rosetrees Trust

## SUPERVISOR

Mr Rami Salib, Dr Luanne Hall-Stoodley, Dr Saul Faust

## SITE OF WORK

University Hospital Southampton NHS Foundation Trust

## PRESENTATIONS

1. *Characterisation of bacterial biofilms in nasal polyps*. Biofilms 5 International Conference, Paris, Dec 2012.
2. *Characterisation of bacterial biofilms in nasal polyps*. British Academic Conference for Otolaryngology & Expo, Glasgow, 2012.



**STEPHEN HAYES**

Chronic rhinosinusitis (CRS), with or without polyps, is an extremely common condition affecting up to 15% of the UK population. The impact of the disease is often under-appreciated with afflicted patients having a significant impaired quality of life. Despite the millions of pounds of antibiotic and surgical procedures prescribed for this condition, there appears to be a subset of patients who remain resistant to established treatments. To this day, we know little about the underlying causes of this disease.

Our research project has focused on the emerging field of bacterial biofilms (complex colonies of bacteria) as potential mediators of the ongoing inflammation in CRS. The aim of our project was to identify first and characterise these bacterial biofilms in the tissue lining the sinuses of patients suffering with CRS, and second to develop and test new therapies to help eradicate them.

Using imaging techniques, we successfully identified and characterised bacterial biofilms on the tissue lining the sinuses in patients suffering with CRS, compared to tissue from patients not affected by the condition. In patients with nasal polyps (boggy swellings of the nose and sinus lining), we made the novel finding that these bacterial biofilms appear to migrate beneath the tissue lining and conceal themselves within the patient's own cells in a bid for survival, creating an environment where chronic inflammation can ensue. Work on eradicating these bacterial biofilms using novel therapies is ongoing and preliminary results are promising.

We hope that, if successful, these therapies could help to prevent infective exacerbations, reduce the overall antibiotic burden and the requirement for multiple operations in these patients, thus making significant financial savings for the NHS and improving patients' quality of life.



Stephen presenting his project at the Biofilms 5 International Conference, in Paris



Stephen (left) with his main supervisor Mr Rami Salib (right) in the operating department at the University Hospital Southampton

# TISSUE ENGINEERING OF THE KIDNEY USING A WHOLE ORGAN DECELLULARISATION APPROACH

Number of UK patients with end stage renal failure in 2010: 50,000.

Number of kidney transplants performed: 2,500

## FELLOWSHIP/SPONSOR

Grand Lodge Freemasons 250th Anniversary Fund

## SUPERVISOR

Professor Molly M Stevens

## SITE OF WORK

Department of Bioengineering & Materials, Imperial College, London

## PUBLICATIONS

1. He M, Callanan A. Comparison of methods for whole organ decellularisation in tissue engineering of bio-artificial organs. *Tissue Eng Part B* 2013; **19**: 194–208.
2. He M, Callanan A, Lagaras K, Stevens MM. Optimisation of perfusion decellularisation in whole kidney bioscaffolds for whole kidney bioengineering. [manuscript in preparation]

## PRESENTATIONS

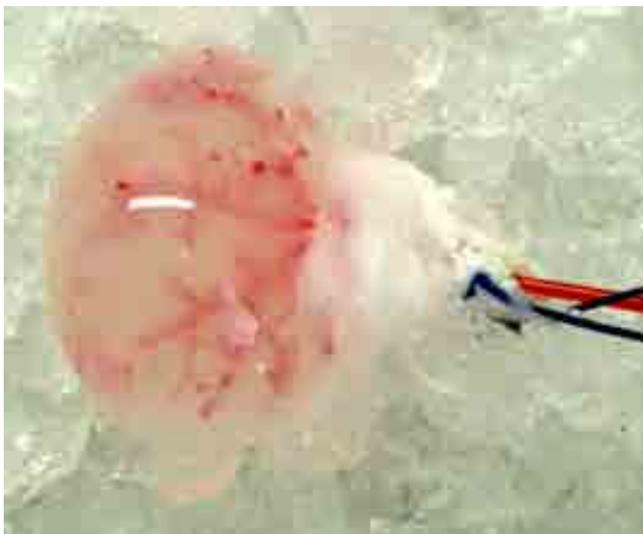
1. TERMIS (Tissue Engineering and Regenerative Medicine International Society) World Congress 2012, Vienna/Austria, September 5–8 2012. Poster presentation.
2. SARS (Society of Academic and Research Surgery) Annual Meeting 2013, London/UK, January 9–10 2013. Oral presentation.



**MING  
HE**



A whole kidney scaffold



The preservation of the blood vessel network within the scaffold as shown by resin injection

Renal transplantation is the optimal treatment for end stage renal failure (ESRF) and can restore function, quality of life and life expectancy to virtually normal. However, this option is severely restricted by the limited pool of organs available from cadaveric donors and there is a huge disparity in numbers of patients with ESRF (~50,000 in UK) and kidney transplants performed (~2,500 in 2010). Tissue engineering – an interdisciplinary field that aims to generate biological tissues for replacement – may offer a potential solution.

This project involves an exciting new technique called ‘whole organ decellularisation’. This creates naturally derived biological scaffolds with all the structural and biological molecules of native kidney as well as its complete 3D organ and blood vessel architecture. This ‘whole kidney scaffold’ can then be re-populated with various cell types to support cell growth and specialisation into potentially functional kidney tissue or even a whole kidney. We have successfully produced whole kidney scaffolds using rat kidneys and extensive cell studies on the scaffolds are ongoing with renal cells cultured on the kidney scaffolds. These constructs have been shown to form ‘kidney-like’ structures under microscopy. Studies are also being done with a potential source of ‘adult stem cells’ called mesenchymal stem cells as these have been shown to have a role in regeneration of the kidney. The next stage is to implant these kidney constructs in animals, as has been carried out in other promising studies with different organs (eg lungs).

There is huge therapeutic potential in this technique whereby organs from any source (eg pigs) could be used to create a whole organ scaffold and then repopulated with stem cells from the patient for functional tissue/organ regeneration. Not only would this be ‘on-demand’ but it could even potentially overcome the risk of rejection and the need for immunosuppressive therapy.

# DELINEATING THE ROLE OF INTEGRINS IN THE REPAIR AND REGENERATION OF THE HUMAN VESTIBULAR SYSTEM

Dizziness is the major reason for visits to the GP by those over 75. Balance dysfunction contributes to falls in the elderly costing the UK government £1 billion annually

## FELLOWSHIP/SPONSOR

One year College Research Fellowship with the support of the Rosetrees Trust followed by Two year Joint RCS/Dunhill Medical Trust Fellowship

## SUPERVISOR

Shakeel Saeed, Andrew Forge and Ruth Taylor

## SITE OF WORK

UCL Ear Institute, London

## PUBLICATIONS

1. Hussain K, Saeed SR, Dawson S, Forge A, Taylor, R. Defining the role of integrins in the repair and regeneration of hair cells in the human vestibular system. *BJS* Abstract. [in press]

## PRESENTATIONS

1. 49th Inner Ear Biology Meeting. Tubingen, Germany. 29th September. 2 October 2012.
2. Association for Research in Otolaryngology – Mid Winter meeting. Baltimore, USA. 16–20 February 2013.



**KIRAN  
HUSSAIN**



Presenting my work at a fundraising event at a Freemasons meeting and receiving a cheque on behalf of the College

Loss of the sensory ‘hair’ cells from the vestibular (balance) system of the inner ear is the major cause of dizziness. Balance problems can be debilitating for people preventing them functioning as ‘normal.’

The vestibular system has capacity for hair cell regeneration. Enhancement would provide a therapy to alleviate the condition. Integrins are proteins involved in regulating repair and recovery responses in tissues. Evidence implicates them in repairing the damaged vestibular organ of mice. We will examine their role in human vestibular tissue.

Integrins are made up of one alpha and one beta subunit. Patients undergoing a specific procedure for an unrelated condition have their vestibular system removed as routine providing us with the tissue to study.

During the first stage of the project we have been identifying which integrins are present. The results to date implicate the following integrins: Alphas 5, 6, 8 & V, and Betas 1 and 5. We have also been locating where in human vestibular tissue these integrins are found. Locating them can potentially

identify their interactions and roles in the repair and regeneration of hair cells.

These are novel findings as there is no published literature on integrins in human vestibular tissue. This project will be continued as we further delineate the role of integrins by studying their expression during different stages of the repair and recovery and also by ‘knocking out’ their activity and assessing the effect.

The consequence of imbalance and its potential sequelae can have catastrophic consequences in the elderly population. Vestibular dysfunction has been shown to be a significant contributor to falls in the elderly. Furthermore, there is a loss of both confidence and independence that has huge psycho-social implications. Balance disorders are estimated to cost the NHS and social services approximately £1bn per annum in direct and indirect costs. Understanding how this complex system works would direct future therapies, be cost-effective and, most importantly, give the elderly their independence back.

# IN VIVO AND IN VITRO RESPONSE TO EGF-SUBA (NOVEL CYTOTOXIN) IN LARYNGEAL SCC CELLS

Epidermal Growth Factor Receptor, Squamous Cell Carcinoma, Laryngeal Carcinoma

## FELLOWSHIP/SPONSOR

Philip King Research Fellowship

## SUPERVISOR

Prof Mark Boyd and Prof Terrence Jones

## SITE OF WORK

University of Liverpool

## PUBLICATION

1. Thornton M, Aslam MA, Tweedle EM, *et al*. The unfolded protein response regulator GRP78 is a novel predictive biomarker in colorectal cancer. *Int J Cancer* 2013; **133**: 1408–18.

## PRESENTATIONS

1. Jaiswal V, Aslam M, Backer J, Behrendt A, Jones TM. *EGF-SubA is Cytotoxic to Laryngeal SCC Cells*. American Academy of Otolaryngology and Head and Neck Surgery (AAO-HNS) San Francisco 11–14 September 2011.
2. Jaiswal V, Aslam M, Backer J, Boyd M, Jones T. *In vitro effects of EGFSubA: a potential new treatment for Squamous Cell Carcinoma of the Head and Neck (SCCHN)*. ENT Wales, 19 October 2012.



**VIBHA  
JAISWAL**

There has been no real improvement in the outcome of patients diagnosed with squamous cell carcinoma of the head and neck (SCCHN). It is the 6th most common cancer worldwide, with overall survival of 50% and no real improvement in outcomes for 30 years. SCCHN affects a person's ability to swallow, speak, taste, and communicate. The ultimate aim of head and neck cancer surgeons is improve a patient's outcome while maximising their quality of life.

In order to improve outcomes we are testing a new drug called EGF-SubA which may be applied topically to the voice box, or other sites of the head and neck, after less invasive surgery, such as transoral laser resection (removing the cancer via an operation through the mouth). EGF-SubA is made by fusing human epidermal growth factor to subtilase A, a

toxin derived from the bacteria E coli. This novel drug is being tested in a number of cancers that respond to epidermal growth factor itself – the idea being that the toxin is more selective for cancer cells than normal cells.

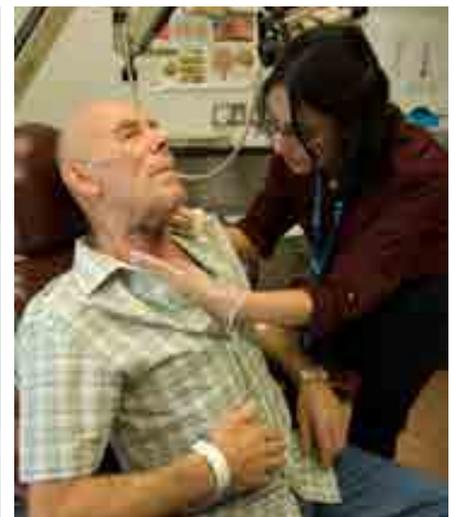
As part of the preclinical testing of EGF-SubA we have shown that it kills up to 11 different laryngeal cancer cells taken from patients but grown under laboratory conditions. This drug also radiosensitises laryngeal cancer cell lines. Autophagy (a form of cellular remodelling) does not appear to play a role in the first 24 hours after exposure to EGF-SubA. The exact mode of cell death from EGF-SubA is unclear. Parallel to this we have shown that mouse models of laryngeal cancer cells can be made which is a prerequisite for animal testing of this drug.



Vibha watching Professor Jones perform trans-oral laser resection of laryngeal squamous cell carcinoma



Vibha performing an examination under anaesthetic for a patient with suspected head and neck carcinoma



Vibha examining a laryngectomy patient (neck breather)

# A NOVEL MAGNETIC RESONANCE DIFFUSION TENSOR IMAGING SEGMENTATION AND VISUALISATION TECHNIQUE FOR BRAIN TUMOUR DIAGNOSIS

More people under the age of 40 die from a brain tumour in the UK than any other form of cancer. In terms of the average years of life lost per patient, brain tumours represent one of the most lethal cancers with over 20 years of life lost

## FELLOWSHIP/SPONSOR

Joint RCS/Freemasons Fellowship

## SUPERVISOR

Dr TR Barrick

## SITE OF WORK

St George's University of London

## PRESENTATIONS

1. International Society of Magnetic Resonance in Medicine ISMRM, Melbourne Australia, 2012.
2. Congress of Neurological Surgeons Meeting, San Francisco, USA, 2010.

## PRIZES

1. British Neurosurgical Research Group Annual Meeting, Best presentation prize 2010.
2. International Society of Magnetic Resonance in Medicine Travelling Fellowship 2012-2013.

## FURTHER FUNDING

Cancer Research UK for three years



**TIMOTHY JONES**

The term 'brain tumour' refers to a heterogeneous group of lesions with variable degrees of malignancy and associated morbidity and mortality. A total of 4,700 cases of primary brain tumour are diagnosed annually in the UK and are the fifth most common cause of death from cancer under the age of 65 with a 5-year survival of only 18%. Treatment decision making relies on preoperative magnetic resonance imaging (MRI) to identify likely tumour type and thus guide surgical resection. It has been proposed that conventional scans may underestimate the extent of tumour and their diagnostic accuracy is not yet good enough to preclude the requirement for lesion biopsy with its associated risks.

The research fellowship allowed me to acquire advanced MRI scans (diffusion tensor images, DTI) from patients with a range of brain tumour subtypes and develop a novel technique to display tumour specific characteristics and investigate its role in clinical practice.

DTI scans were obtained from 96 patients with newly diagnosed brain tumours prior to surgical treatment and definitive diagnosis from tissue biopsy. I devised a technique of defining a boundary on the DTI-MRI scan between tumour tissue and normal brain using an image segmentation method. This incorporated an automated method of labelling tumours according to their constituent patterns of water diffusion. These patterns were different between tumour regions and normal brain as well as between different tumour types. We tested the diagnostic role of the technique using a statistical model and have shown that it compares favourably with the diagnostic accuracy of conventional MRI in practice.

Our method has the advantage of being non-invasive, not requiring intravenous contrast injection, fully automated and may potentially be performed using scanners present within most hospitals. Ultimately, it may be employed to

reduce the requirement for tumour biopsy which is associated with morbidity and in some cases mortality. The ability of this technique to identify a boundary between tumour and normal appearing brain may have other uses such as guiding the margins of tumour resection, monitoring response to chemo/radiotherapy or evaluating subtle changes in lesion size over time in the case of inoperable or partially resected tumours.



Top: Acquisition of MRI scans using 3 Tesla system

Bottom left: Right frontal mini-craniotomy performed using guidance system to expose brain surface prior to tumour resection

Bottom right: The segmentation technique

# INVESTIGATING BIOMARKERS IN PREDICTING RELAPSE POST-RADICAL THERAPY IN PROSTATE CANCER

Despite major technological advances in prostate cancer treatment over the last 10 years, over 30% of patients with potentially curable disease still fail primary treatment, which can be fatal



**NAVEEN  
KACHROO**

## FELLOWSHIP/SPONSOR

College Research Fellowship

## SUPERVISOR

Mr Vincent Gnanapragasam and Professor David Neal

## SITE OF WORK

Hutchison/MRC Research Centre, University of Cambridge

## PUBLICATIONS

1. Kachroo N, Gnanapragasam VJ. The role of treatment modality on the utility of predictive tissue biomarkers in clinical prostate cancer: a systematic review. *J Cancer Res Clin Oncol* 2013; **139**: 1–24.
2. Kachroo N, Valencia T, Warren AY, Gnanapragasam VJ. Evidence for downregulation of the negative regulator SPRED2 in clinical prostate cancer. *Br J Cancer* 2013; **108**: 597–601.

## PRESENTATIONS

1. *MicroRNA expression profiling of different Gleason grades in prostate cancer.* American Urological Association Annual Meeting; May 2012; Atlanta, USA.
2. *The predictive value of the number of positive diagnostic biopsy cores in prostate cancer outcome.* BASO – The Association of Cancer Surgery Scientific Conference; November 2011; London, UK.

## PRIZES

1. BASO–ACS Prize, 2011.
2. Stefan and Anna Galeski Fellowship, October 2012.
3. BAUS Best Poster Prize, 2011.

One man is diagnosed with prostate cancer every 13 minutes and one man dies from it every 49 minutes. Despite advances in potentially curative therapies, over 30% of patients still fail treatment as current clinical models are not equipped to stratify patients correctly. My research project is addressing



Naveen training on the Da Vinci Robot operating console – used to perform robotic surgery to remove the prostate



Naveen teaching surgical skills as a Stefan and Anna Galeski Fellow in a workshop in Borneo

this crucial dilemma by identifying practical ways of enhancing treatment outcome prediction at the point of diagnosis to ensure each patient receives the optimal treatment for their individual cancer. The cancerous material obtained at diagnosis is a readily available, untapped resource containing the critical molecular signatures underpinning the aggressiveness of a tumour and my work has highlighted novel ways to directly exploit this material in our fight against prostate cancer.

My study began with the construction of an annotated clinical database of patients with five-year follow-up data. My analysis discovered a new clinical marker related to the tumour content within the biopsy tissue that can be used by clinicians at the time of treatment planning to facilitate a better informed decision. My data showed that those patients having greater than 50% positive biopsy cores containing tumour, are more likely to fail surgical treatment and could therefore benefit from non-surgical options such as radiotherapy.

This clinical database provided the pivotal foundation to obtain the archival diagnostic biopsy material from targeted groups of patients (good and poor treatment responders), which I have profiled in the laboratory using multiple scientific discovery platforms, to extract the critical molecular signatures lying within each patient's tumour that are responsible for the failure of particular treatments. My preliminary findings have identified a panel of molecular markers (biomarkers) whose presence in the tumour tissue, can accurately predict radical treatment failure. I am currently validating this in an extended cohort and if successful, I will be able to develop a robust test to accurately screen the diagnostic biopsies of all patients with prostate cancer to identify the best treatment to tackle their particular tumour.

# KYPHOPLASTY VERSUS VERTEBROPLASTY FOR SEVERE VERTEBRAL WEDGE FRACTURES

Comparing treatments for osteoporotic spinal fractures

## FELLOWSHIP/SPONSOR

Cutner Legacy Research Fellowship

## SUPERVISOR

Dr Patricia Dolan and Prof Michael Adams

## SITE OF WORK

Centre for Comparative and Clinical Anatomy, University of Bristol

## PUBLICATIONS

1. Dolan P, Luo J, Pollintine P, Landham PR. Intervertebral disc decompression following endplate damage: implications for disc degeneration depend on spinal level and age. *Spine (Phila Pa 1976)* 2013; **38**: 1,473–81.

## PRESENTATIONS

1. *Kyphoplasty restores vertebral height and shape better than vertebroplasty following severe wedge fractures.* Society for Back Pain Research 2012, Isle of Man.
2. *Anterior 'wedge' deformities of human thoracolumbar vertebrae develop in a two-step process.* British Orthopaedic Research Society 2012, London.

## PRIZES

1. Award for Best Oral Poster, Society for Back Pain Research 2012.
2. Best Presentation, Intervention Section, American Society of Spinal Radiology 2013.

## FURTHER FUNDING

The Gloucestershire Arthritis Trust for 18 months



**PRIYAN  
LANDHAM**



Priyan in the operating theatre with Mr Pradeep Madhavan

Osteoporosis weakens aging bones, and vertebrae are the bones most severely affected. Over 40,000 vertebral fractures occur each year in the UK, often involving anterior collapse, and these injuries lead to pain, disability and deformity ('senile kyphosis').

Vertebroplasty is a therapeutic intervention that involves injecting bone cement into a fractured vertebra to stabilise it and relieve pain. Kyphoplasty is a newer adaptation that involves inflating a small balloon within the vertebral body prior to cement injection. This may reduce the risk of cement

leakage and, by elevating the endplate, may help restore vertebral height. However, kyphoplasty is much more expensive than vertebroplasty, and the only clinical study to compare these procedures in patients found minimal differences between them. For the clinician, it is therefore unclear which procedure to offer patients.

Our study investigated, in human cadaver spines, whether kyphoplasty has any physical benefits over vertebroplasty when used to treat severe vertebral wedge fractures. Typical 'anterior wedge' fractures were created in cadaveric spines. Two vertebrae were fractured in each spine. One was treated with vertebroplasty, the other with kyphoplasty, enabling us to compare the two procedures in a matched study design. Outcomes were measured in terms of vertebral shape and stiffness, and the distribution of applied loading.

Both procedures were equally effective at restoring mechanical stiffness and load-bearing to fractured specimens. However, kyphoplasty was better than vertebroplasty at restoring vertebral height and reversing wedge deformity. The distribution of cement had some effect on outcomes following vertebroplasty, but not kyphoplasty, which may reflect a more consistent placement of cement.

A randomised clinical trial comparing these procedures could help to build on these results by demonstrating whether kyphoplasty has any longer-term benefits compared to vertebroplasty in terms of deformity correction, and whether the latter actually correlates with symptom relief.

# GENOTOXIC EFFECTS OF ORTHOPAEDIC WEAR DEBRIS ON THE BLADDER

One in five patients with a metal-on-metal hip resurfacing was found to have abnormal urinary cytology

## FELLOWSHIP/SPONSOR

College Research Fellowship

## SUPERVISOR

Dr Patrick Case, Professor Ashley Blom

## SITE OF WORK

Bristol Musculoskeletal Research Unit, Southmead Hospital, Bristol

## PUBLICATIONS

1. Maclean AD, Case CP, Figgitt M, Li W. Genotoxic effects of orthopaedic wear debris on the bladder. *J Clin Urol* 2010 **3**: 263-264. [abstract]
2. M Figgitt, M Parry, A Maclean, *et al.* Genotoxicity of orthopaedic wear debris: A patient study. *Toxicology* 2011; **290**: 115. [abstract]

## PRESENTATIONS

1. *Metal on metal hip resurfacing: Is there a risk of bladder cancer?* Podium presentation British Hip Society, Annual General Meeting, Manchester, UK. March 2012.
2. *Genotoxic effects of orthopaedic wear debris on the bladder.* Poster presentation British Association of Urological Surgeons, Annual Oncology Meeting, London, UK. October 2010.

## PRIZES

1. Best presentation: Bristol Urological Institute 17th Annual Scientific Meeting 2010

## FURTHER FUNDING

Bristol Urological Institute: four months and Edwin Luff Fund: three months.



**ANGUS DOUGLAS  
MACLEAN**

Around 60,000 people in the UK have been fitted with a metal-on-metal hip replacement. Previous studies have suggested that metals are released from metal-on-metal implants and are found at high levels in patients' urine. Furthermore, in patients with all forms of hip replacement, there is an increase in bladder cancer after ten years. This study has investigated whether there is evidence of genotoxic damage in patients' bladders.

A group of 71 patients with metal-on-metal hip resurfacing were compared with a group of 23 controls with no implant. Metal levels were tested in both groups' blood and urine. The number of chromosomes was evaluated in patients' urine and mouth cells using the UroVysion test. Genetic mutations in bladder cancer genes p53 and FGFR3 were screened for using DNA sequencing. Patients' urinary cells were assessed for alterations in morphology by a cytologist.

Levels of urinary cobalt and chromium were found to be about 25 times higher in the hip resurfacing patients, compared to controls. Levels of chromosomal abnormality were significantly raised in hip resurfacing patients' urine, and in their mouths. No mutations were found. In 15 patients' urinary samples, and in one control, there were occasional cells with cellular atypia. In two hip resurfacing patients there were cells suspicious of carcinoma and one had a low-grade early bladder cancer diagnosed on cystoscopy.

This work suggests that there are genotoxic effects within the bladder. It is not clear that this is due to metal exposure. Recent reports suggest that there is no short-term increase in bladder cancer in patients with metal-on-metal implants. Continuing surveillance would appear to be important.



Angus teaching a colleague how to extract DNA from urine



Metal-on-metal hip resurfacing

# OUTCOMES AFTER LOWER LIMB REVASCULARISATION AND AMPUTATION IN ENGLAND

Performing lower limb arterial bypass surgery in high volume centres is better for patient outcomes

## FELLOWSHIP/SPONSOR

Joint RCS/Dunhill Medical Trust Fellowship

## SUPERVISOR

Mr Peter Holt

## SITE OF WORK

St George's Vascular Institute, Tooting, London

## PUBLICATIONS

1. Moxey PW, *et al.* Volume-outcome relationships in lower extremity arterial bypass surgery. *Ann Surg* 2012; **256**: 1,102–27.
2. Moxey PW, *et al.* Delay influences outcome after lower limb major amputation. *Eur J Vasc Endovasc Surg* 2012; **44**: 485–90.

## PRESENTATIONS

1. *Establishing a volume-outcome relationship in lower limb bypass surgery using multi-level logistic regression modelling.* Vascular Society Great Britain Annual Conference. Brighton, England, November 2010.
2. *Delay influences outcome after major lower limb amputation.* European Society of Vascular and Endovascular Surgery Annual Meeting, Athens, 2011.

## PRIZES

1. *Trends and outcomes after surgical lower limb revascularisation in England 2002–2007.* Poster presentation – 2nd Prize, Diabetic Limb Salvage Conference, USA, 2010.
2. *Delay influences outcome after major lower limb amputation.* 3rd Prize poster presentation. Diabetic Limb Salvage Conference, USA, 2011.



**PAUL MOXEY**

Peripheral arterial occlusive disease is a burden of the elderly. Prevalence of peripheral vascular disease has been evaluated in range of 15% to 20% in persons over 70 years and up to 60% in those aged over 80 years. Half of all arterial bypass procedures performed in England between 2003 and 2008 and half of all major amputations were in patients over the age of 70. Death rates after major amputation and lower limb arterial surgery are high in the United Kingdom with 20% of patients not surviving to leave hospital. This project is concerned with identifying what features of a patient, their disease and their hospital predict what happens to them.

We started by 'benchmarking' current English practice as no such data had been previously published. We demonstrated that significant variation in outcome exists between English strategic health authorities. This data was used to brief a House of Commons select committee set up to specifically examine this 'postcode lottery' of outcome. The data has

also been used to help develop the Vascular Society 'quality improvement framework' that is designed to standardise the care of amputees and drive down mortality rates.

We analysed over 10 million records held in the English Hospital Episodes Statistics (HES) database. This is anonymised patient-level data on every admission in English hospitals stretching back ten years. By developing new ways of tracking patients through this database and combining the HES data with that collected on death certificates by the Office of National Statistics we have been able to determine individual characteristics that may predict a patient's outcome (ie death in hospital, loss of a leg within a year, etc).

We already know that increasing age, diabetes and kidney failure play a significant role in a patient's chance of surviving an amputation or bypass but we have been able to quantify the risk. Significantly, we have shown that the hospital in which a patient has his or her operation is important. Those units performing more amputations and bypass procedures per year have a better success rate and less mortality than those performing fewer operations.

Finally, we have shown that if there is no other option but to amputate a limb then the longer a patient waits for the operation, the worse the outcome. This hard data is vital to help guide and plan surgical services in the future and help drive down mortality and morbidity after major amputation.



Paul performing an amputation of a toe



Paul examining the peripheral pulses of a patient on the ward

# ANALYSIS OF ADULT HUMAN SPINAL CORD FOR STEM CELLS

The incidence of spinal cord injuries is estimated to be over 50 per million per annum

## FELLOWSHIP/SPONSOR

College Fellowship with support from the Fletcher Legacy and the Cardy Beaver Foundation

## SUPERVISOR

Professor Marysia Placzek

## SITE OF WORK

MRC Centre for Developmental Biology and Genetics

## FURTHER FUNDING

MRC Centre Grant, Sheffield



**LAURENCE  
O'CONNOR-READ**

The incidence of spinal cord injuries is estimated to be over 50 per million per annum (over 3,000 individuals per year in the UK), resulting in significantly morbidity. Recent studies have suggested that a layer of cells surrounding the central canal of adult mammalian, including human, spinal cord exist in a latent form and have stem cell characteristics. A critical question is whether these cells can be reactivated to proliferate, migrate, differentiate and integrate, generating functional adult neurons and/or support cells. Such knowledge is critical to future regenerative therapies, which rest on the hope that stem-like cells may be deployed in the repair of spinal cord trauma and pathology.

The characteristics of 'stem cells' around the adult mouse and human central canal were investigated by analysing various widely accepted stem cell markers. A tissue culture technique was optimised and utilised to evaluate behaviour of the cells surrounding the central canal.

Our work has shown that a group of cells in a region of the spinal cord show highly conserved features in both adult human and mouse. In normal conditions the cells express many neural stem/progenitor cell markers; however, they do not actively multiply. Interestingly after culture of both human and mouse tissue in a defined condition with growth factors, we observed a significant increase in the numbers of the cells.

Overall we have optimised a tissue culture technique to demonstrate for the first time that that a layer of cells in intact human spinal cord tissue have the potential to be activated and proliferate. This is promising evidence and a step forward in the eventual development of a regenerative therapy for patients with spinal cord injuries.



Top: Processing of spinal cord tissue before transportation back to laboratory.

Bottom: Adult human spinal cord retrieved from organ donor

# THROMBIN PATHWAY ACTIVATION IN BREAST CANCER

Over 40,000 women are diagnosed with breast cancer each year. One in seven women diagnosed with breast cancer will not survive more than five years

## FELLOWSHIP/SPONSOR

College Research Fellowship

## SUPERVISOR

Professor Nigel Bundred, Dr Cliona Kinwan and Professor Goran Landberg

## SITE OF WORK

University Hospital of South Manchester and Paterson Institute for Cancer Research, Manchester

## PRESENTATIONS

1. *The procoagulant response to cancer surgery is increased in early breast cancer with poor prognosis phenotypes.* International Conference on Thrombosis and Haemostasis Issues in Cancer, April 2012, Bergamo, Italy.
2. *Procoagulant Biomarkers May Direct Axillary Nodal Surgery.* San Antonio Breast Cancer Symposium, December 2012, San Antonio, USA.

## FURTHER FUNDING

University Hospital of South Manchester Endowment Fund Research Fellowship Mason Medical Foundation Research Fellowship for two years



**HUDHAIFAH  
SHAKER**



Top: Hud in the laboratory testing patient samples for clotting factor levels using the ELISA technique

Bottom: Hud talking to a breast cancer patient taking part in the clinical study

The clotting system in cancer is known to be hyperactive resulting in clots in the legs and lungs which are a frequent cause of death in cancer patients. Research has shown, however, that the clotting system may also directly promote the growth of cancer cells and assist them in spreading to and destroying other organs, such as the liver, in a process called metastasis.

The clotting system may also play a role in cancer stem cells, a sub-population of cancer cells that are able to initiate tumours and that are resistant to conventional anti-cancer treatments (eg chemotherapy). With the aid of the RCS fellowship, I have been able to continue my research into the role of the clotting system in breast cancer using techniques in the laboratory as well as patient samples.

My early laboratory work in breast cancer cells shows that inhibiting tissue factor, an important clotting protein, activity may block the growth and self-replication of cancer stem cells. Inhibiting tissue factor and the clotting system may be a means by which cancer stem cells can be targeted to reduce metastasis and improve survival in breast cancer.

In my patient study, I am researching cancer markers that can identify breast cancer patients in whom the clotting system plays an important role in the spread of their cancer. My results show that blood clotting markers can predict breast cancer patients in whom the cancer has spread to local lymph glands, a sign of aggressive disease. These clotting markers have the potential to be used by clinicians to identify patients who are at risk of metastasis and manage them appropriately. It may also lead help to identify cancer patients who will most benefit from targeted anti-cancer therapies that block clotting, reduce the spread of cancer and improve survival from breast cancer.

# TARGETING AND TREATMENT OF PANCREATIC CANCER USING MULTIFUNCTIONAL NANOPARTICLES

Pancreatic cancer carries a dismal prognosis, with only 3.7% of patients surviving more than 5 years. Advances in treatment of this disease are therefore desperately required



**PAUL SYKES**

## FELLOWSHIP/SPONSOR

College Research Fellowship with the support of the Rosetrees Trust

## SUPERVISOR

Mr Christopher Halloran

## SITE OF WORK

Liverpool Cancer Research UK Centre, Liverpool

## PUBLICATIONS

1. Sykes PD, Neoptolemos JP, Costello E, Halloran CM. Nanotechnology advances in upper gastrointestinal, liver and pancreatic cancer. *Expert Rev Gastroenterol Hepatol* 2012; **6**: 343–56.
2. Olariu CI, Yiu HHP, Bouffier L, *et al*. Multifunctional Fe3O4 nanoparticles for targeted bi-modal imaging of pancreatic cancer. *J Mater Chem* 2011; **21**: 12,650–59.

## PRESENTATIONS

1. American Pancreatic Association Annual Meeting, Miami 2012.
2. European Pancreatic Club Annual Meeting, Prague 2012.

## PRIZES

1. Liverpool North West Society of Surgeons, Higher Surgical Trainee Oral Presentation Prize 7. 2012.

## FURTHER FUNDING

Liverpool Cancer Research UK Centre for one year.

The aim of the project is to develop a nanoparticle-based drug delivery vehicle capable of targeting pancreatic cancer cells and intracellular delivery of a chemotherapy payload. A novel micellar iron oxide nanoparticle was developed with superparamagnetic properties and to facilitate the attachment of a targeting molecule, such as antibodies against antigens found on the surface of pancreatic cancer cells. A modified form of gemcitabine, a chemotherapy agent, designed to release in the acidic conditions found within tumour cells was loaded into the particles.

Using the immunofluorescent microscope to track nanoparticles

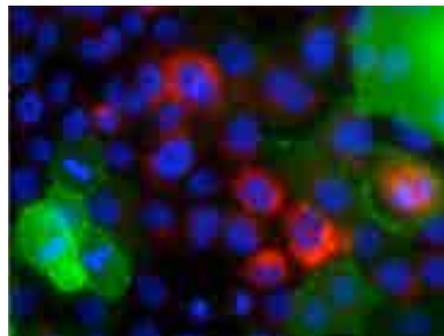


The ability of these particles to target pancreatic cancer cells *in vitro* was assessed using fluorescent microscopy to quantify the rate of uptake either in the presence of a focused magnetic field or following the attachment of a targeting antibody. Intracellular delivery of the chemotherapy payload was evaluated using cell viability assays to calculate the concentration required to inhibit cell growth (IC50).

In the presence of a magnetic field, nanoparticle uptake was significantly faster at two hours (mean intensity 49.8AU vs 1.7AU,  $p < 0.01$ ). Conjugation of a targeting antibody resulted in an increased rate of uptake (mean intensity at 2 hours

9.83AU vs 0.14AU,  $p < 0.01$ ). The inhibitory concentration was significantly improved in antibody-targeted particles (IC50 904nM vs 4,122nM,  $p = 0.046$ ), successfully demonstrating targeted drug delivery. Magnetically targeted drug release showed significant reduction of cells at the area of greatest magnetic force (3 cells/mm<sup>2</sup> vs 92 cells/mm<sup>2</sup>,  $p < 0.001$ ).

We have developed a novel nanoparticle capable of targeting antigen expressing pancreatic cancer cells using a specific antibody or non-antigen expressing cells using a focused external magnetic field. When loaded with modified



Nanoparticle (red) accumulation inside antigen (green) expressing pancreatic cancer cells

gemcitabine, these nanoparticles act as drug delivery vehicles capable of intracellular drug release. This could provide the opportunity to reduce off-target effects and increase the efficacy of chemotherapy agents. The next stage is to assess these properties in animal models.

# CONTRAST ULTRASOUND FOR STROKE PREDICTION

Carotid surgery (removal of atherosclerosis inside the carotid artery) in older, asymptomatic persons is unaffordable and cost-ineffective in stroke prevention. The effort would be better spent on primary preventative medical therapy

## FELLOWSHIP/SPONSOR

Joint RCS/Dunhill Medical Trust Fellowship

## SUPERVISOR

Professor Alun Davies and Professor Edward Leen

## SITE OF WORK

Imperial College London

## PUBLICATIONS

1. Thapar A, Jenkins H, Mehta A, Davies A H. Clinical review: carotid atherosclerosis. *BMJ* 2013; **346**: f1,485.
2. Thapar A, Garcia-Mochon L, Epstein D, Shalhoub J, Davies A H. Modelling the cost-effectiveness of asymptomatic carotid endarterectomy. *Br J Surg* 2013; **100**: 231–39.

## PRESENTATIONS

1. Thapar A, Zheng Y L, Dharmarajah B, et al. *Dynamic contrast-enhanced ultrasound for assessment of perfusion and ulceration within carotid plaque*. Radiological Society of North America, Chicago 2012.
2. Thapar A, Garcia-Mochon L, Epstein D, Shalhoub J, Davies A H. *Cost-effectiveness of asymptomatic carotid endarterectomy*. London Surgical Symposium.

## PRIZES

1. EFSUMB European Young Investigator 2012
2. Graham-Dixon Prize for Cardiovascular Surgery 2012

## FURTHER FUNDING

Circulation Foundation, MS Trust for one year



**ANKUR THAPAR**

My PhD focused on two areas of relevance to older people with carotid atherosclerosis.

Firstly, I worked with the health economists to create a health economic model for carotid surgery. This suggested that operating on young women was the most cost-effective strategy. Projecting these results into the future, with improved medical therapy, it is likely that surgery will soon lose its cost-effectiveness in men and older women. I then modelled the cost per stroke saved with surgery ( $\approx$ £75 000). Testing high-risk groups in the UK would not only be unaffordable but would also save only a handful of strokes. The money could be spent more effectively on preventative medication.

Secondly, I scanned 140 patients with carotid atherosclerosis with the new technique of contrast-enhanced ultrasound, a bedside test for plaque vascularity. The results showed that the assessment of small blood vessels within plaques was unreliable in identifying high risk-plaques in stroke patients. However there was potential benefit in identifying damage to the plaque surface (ulceration), another recognised marker of risk.

Men with asymptomatic carotid artery disease are best served by having basic risk factors such as blood pressure and cholesterol controlled and should avoid routine carotid ultrasound and surgery. Young women may still benefit from surgery.



Ankur scanning a carotid artery patient with supervisor Professor Alun Davies and colleague Joseph Shalhoub to identify the presence of a plaque

# DESIGNING A TACROLIMUS-ELUTING POLYMER NERVE GUIDANCE CONDUIT

Approximately 6,000 cranial and peripheral nerve injuries are reported per year in England

## FELLOWSHIP/SPONSOR

Enid Linder Foundation Research Fellowship

## SUPERVISOR

Professors Martin A Birchall and AM Seifalian

## SITE OF WORK

University College London Centre for Nanotechnology and Regenerative Medicine, Royal Free Hospital

## PUBLICATIONS

1. Toll EC, *et al.* The role of immunophilin ligands in nerve regeneration. *Regen Med* 2011; **6**: 635–52.
2. Toll EC, *et al.* The effect of low-dose tacrolimus on recurrent laryngeal nerve regeneration in pigs: A pilot study. *Archives of Clinical and Experimental Surgery*. [in press]

## PRESENTATIONS

1. Toll EC, *et al.* *The functional and myologic effects of tacrolimus on recurrent laryngeal nerve regeneration.* Otorhinolaryngological Research Society Spring Meeting 2011, London, UK.
2. Toll EC, Sedaghati T, Whiting S, Birchall MA, Seifalian AM. *A tacrolimus-releasing nanocomposite for peripheral nerve regeneration.* Accepted April 2013 for presentation at 25th European Conference on Biomaterials, Madrid, 2013.

## PRIZES

1. Otorhinolaryngological Research Society Pump Priming Research Grant awarded March 2013

## FURTHER FUNDING

Otorhinolaryngological Research Society one-off grant for research consumables



**EDWARD  
TOLL**



Ed examines a sheet of polymer coated with tacrolimus before sterilisation



Ed uses the ultrasonic atomisation machine to coat sheets of polymer with tacrolimus



Ed in the tissue engineering laboratory at the UCL Centre for Nanotechnology and Regenerative Medicine, Royal Free Hospital

Peripheral and cranial nerves are the hard wiring that permits movement to occur. Injuries to these nerves can profoundly change patients' lives. Current treatment methods and outcomes have changed little over the last 30 years and have important disadvantages.

The aim of my project is to speed up the regrowth of nerves following injury and guide nerve growth over a zone of injury. I have designed a nerve repair conduit: a plastic tube that is fixed in position between the cut ends of an injured nerve. Conduits have been used in nerve repair for several years, but the conduit that I have designed is fabricated from a unique type of biodegradable polymer that has been shown to support the growth of nerve cells and does not cause a significant immune reaction. Additionally, the polymer is combined with a drug called tacrolimus, resulting in a material that slowly releases the drug whilst the nerve fibres are regrowing. Tacrolimus is a licensed anti-rejection drug used

in organ transplantation and has been shown to have potent effects of accelerating nerve regrowth.

During this research fellowship the fabrication and sterilisation processes and sustained release profile of the tacrolimus-releasing nerve conduit have been optimised. Efficacy in supporting and enhancing the growth of nerve cells has been demonstrated *in vitro*, with enhanced cell survival. Further large-scale experiments to confirm efficacy are planned, including combining the use of stem cells with the conduit. Important questions on the use of tacrolimus in nerve regeneration have been answered by this study, and further experiments will help bring this device towards clinical trials. When this device is used clinically, it is anticipated that resultant muscle function will be more complete and occur earlier than with standard nerve repair techniques, maximising the rehabilitation potential of patients who have suffered nerve injuries and limiting the effect on their quality of life.

# FUNCTIONAL INVESTIGATION OF NOVEL BIOMARKERS IN HEAD AND NECK CANCER

Head and neck cancer is the sixth most common cancer and if as a patient you develop a spread to the neck (lymph node metastasis) survival falls by half

## FELLOWSHIP/SPONSOR

Enid Linder Foundation Fellowship

## SUPERVISOR

Professors MT Boyd and TM Jones

## SITE OF WORK

Cancer Research Centre, University of Liverpool

## PUBLICATIONS

1. National Cancer Research Institute Conference, Liverpool, UK, November 2012.
2. American Head and Neck Society, Toronto, July 2012.

## FURTHER FUNDING

A consumable grant from Cancer Research UK and an Academic Clinical Fellowship to cover my salary part time for three years.



**NAVDEEP SINGH UPILE**



Navdeep examining a patient



Navdeep in theatre

Our goal is to analyse whether a gene called TP53 is mutated in 200 head and neck tumours. Earlier work suggests that mutation of TP53 is important in the development of tumour spread. Once this is done, we can analyse this data together with the clinical outcome data to confirm the effect of this gene on survival and spread of disease. While there have been many large studies into this area, unlike breast cancer for example, there is no marker that can help predict if a patient's disease is likely to spread.

Should this gene prove to be important there will be on going work in order to understand how it can cause cancer cells to spread. By understanding the mechanisms in the short term we can predict which patient's disease is likely to

spread. But in the longer term we can try and target these mechanisms with new medicines or treatments.

Treating patients is a delicate balance between aiming to cure them of their disease, without inflicting the side effects from the treatment itself. If we are able to more accurately predict how a patient's cancer is to behave, we could personalise and therefore optimise their treatment. This would help us from over treating patients with diseases that are unlikely to spread, for example saving them from having a neck dissection operation, but equally importantly we can increase the treatment to patients with a disease that is likely to behave poorly, and try to improve their life expectancy.

# MINIMALLY INVASIVE SENTINEL LYMPH NODE BIOPSY IN OESOPHAGEAL ADENOCARCINOMA

The UK has the highest reported incidence of oesophageal adenocarcinoma in the world

## FELLOWSHIP/SPONSOR

College Research Fellowship

## SUPERVISOR

Professor S Michael Griffin

## SITE OF WORK

Royal Victoria Infirmary, Newcastle upon Tyne

## FURTHER FUNDING

BUFA Foundation for two years



**SHAJAHAN WAHED**

Oesophageal cancer in the UK is on the increase and over 8,000 people are diagnosed with it each year. Over two-thirds of oesophageal cancer in the UK is adenocarcinoma. The only potential for cure is surgery to remove most of the oesophagus and all the surrounding lymph nodes. The nodes are removed routinely as there is no way of knowing whether cancer cells have spread to them. There are new techniques using endoscopy to remove the very earliest forms of oesophageal cancer and keyhole techniques of the surgery have been developed in the hope that the recovery is quicker and the associated risks of surgery are reduced.

The sentinel node concept is that if the first lymph nodes draining a cancer are clear of cancer cells, then the remaining nodes should also be clear. Our study is looking at whether injection of a tracer using an endoscope and a keyhole operation to detect the tracer can identify these sentinel nodes. We can compare the sentinel nodes with all the other nodes as we are studying our technique when patients are having their standard radical operation. We are still recruiting for the study at present although the results so far appear encouraging. By the end of the study we will be able to say whether this novel technique in oesophageal adenocarcinoma is accurate.

If the results show that the technique works, it has the potential for us to tailor treatment for individual patients and reduce the risks from surgery. Patients with very early adenocarcinoma who have clear sentinel lymph nodes might be able to have the cancer removed with an endoscope, avoiding the need for surgery to remove the oesophagus. The status of the sentinel nodes could help us make decisions about whether an individual is suitable for a keyhole operation to remove the cancer.



Shajahan with the keyhole gamma probe and monitor



Shajahan using the keyhole gamma probe to identify the sentinel nodes

# JOINT ROYAL COLLEGE OF SURGEONS/CANCER RESEARCH UK CLINICIAN SCIENTIST FELLOWS

This fellowship, of up to five years in duration, was established in 2007 and provides Fellows with an opportunity to gain postdoctoral experience in cancer research and consolidate research skills.

Cancer Research UK is one of the world's leading cancer research organisations and is committed to developing the next generation of leaders in cancer research through a programme of research fellowships. Cancer Research UK supports their clinician scientist fellows by appointing an independent clinical mentor, whose role is to advise them on their career, ease their transition to an independent research role and support them as they balance the clinical and research commitments. They also hold an annual clinical fellow's meeting, where clinical fellows, at all levels of seniority, meet each other to hear research talks, attend career workshops, and talk to senior clinical academics.

## IN SITU CHARACTERISATION OF STEM CELLS AND THEIR FATE IN THE AGEING HUMAN PROSTATE

**SUPERVISOR**  
Professor Doug Turnbull and  
Professor Robert Taylor  
**SITE OF WORK:**  
University of Newcastle



**RAKESH HEER**

Identification of prostate stem cell markers have been compromised with culture-based approaches leading to deviations from phenotypes observed *in vivo*. Combined with the previous inability to trace stem cells *in situ* we do not have a clear understanding of stem cell fate. This is of clinical relevance as abnormal regulation of stem cell fate is thought to be critical to cancer pathogenesis. To overcome these issues, I aim to identify stem cells *in situ* within benign ageing human prostate tissue.

Changes in stem cell homeostasis can lead to a proliferative imbalance and is considered a central mechanism to benign prostate hyperplasia and prostate cancer. It is first essential to accurately characterise stem cell processes in the aging prostate before we can reliably establish the critical transforming differences present in cancer stem cells.

- » Characterisation of the location and fate of human prostate stem cells *in situ*



- » Characterisation of stem cell specific markers and regulatory pathways
- » *In vitro* and *in vivo* study of the identified putative stem cell markers to complete comprehensive functional validation of new stem cell molecular signatures

Mitochondrial DNA (mtDNA) mutations occur within stem cells, and I will characterise the location and fate of human prostate stem cells using 3D gland reconstructions with mitochondrial enzyme-histochemistry and immunohistochemistry. Laser capture microdissection of epithelial stem cell niche will allow comprehensive transcriptome characterisation using RNA microarray analysis. Functional validation of identified stem cell markers will be undertaken using primary culture and xenografts in mice.

## MOLECULAR PATHOLOGY OF COLORECTAL CANCER: THE ROLE OF MICRORNAs IN COLORECTAL CANCER PATHOGENESIS AND PROGRESSION

**SUPERVISOR**  
Professor Graham Packham  
**SITE OF WORK**  
University of Southampton



**ALEX MIRNEZAMI**

Metastases are the principal cause of death in colorectal cancer (CRC). However, the mechanisms influencing metastasis in CRC remain unclear. MicroRNAs (miRNAs) are powerful regulators of gene expression strongly implicated in initiation and progression of cancer. However, little is known about their role in CRC. This project aims to identify miRNAs of importance in CRC progression.

I am analysing miRNA expression profiles in validated cell models of CRC progression alongside tumours of different stage. RNA samples are analysed with miRNA microarrays containing over 650 probes. An outstanding tissue series of human CRC with five-year follow up data in conjunction with CRC liver and lung metastases is available. Normal mu-

cosa will be compared with matched Stage I/II and Stage IV tumours; and stage II tumours with and without recurrence will be compared. Laser Capture Microdissection (LCM) will be used for tumours to reduce stromal and immune cell contributions. Array results are validated by qRT-PCR. Targets of candidate miRNAs are identified bioinformatically and tested experimentally. Biological consequences of interactions will be tested by overexpression or knockdown of miRNAs and assessed by standard *in vitro* assays.

A total of 112 miRNAs are overexpressed and 37 under-expressed in cell models of CRC progression. High scoring candidates have been verified by qRT-PCR *in vitro* and in LCM of tumour specimens. Targets of candidate miRNAs have been identified bioinformatically and are being evaluated experimentally.

MiRNAs differentially expressed in metastatic and non-metastatic cancers may help improve staging, guide therapy, and represent novel therapeutic targets.

## ANALYSIS OF ALTERNATIVE SPLICING IN PROSTATE CANCER METASTASIS REGULATED BY THE RNA-BINDING PROTEINS SAM68 AND HNRNP A2/B1

**SUPERVISOR**  
Professor Hing Leung  
**SITE OF WORK**  
University of Glasgow



**PRABHAK AR RAJAN**

Many men with prostate cancer (PCa), the second leading cause of male cancer-related deaths, have ‘incurable’ (locally advanced/metastatic) disease at diagnosis and a poor prognosis despite treatment. This observation may be due, in part, to a functional complexity of the cancer cell transcriptome primarily as a result of alternative mRNA isoforms, fusion transcripts, and non-coding RNAs. In addition to expression changes, metastasis may be mediated by structurally/functionally differing protein isoforms produced by alternative pre-mRNA splicing (AS), controlled by RNA-binding proteins (RBPs). Our and others’ work has implicated interacting-RBPs Sam68 and hnRNP A2/B1 in PCa, epithelial-mesenchymal transition (EMT), and metastasis.

We propose a systematic evaluation of Sam68/hnRNP A2/B1 and mRNA targets in PCa by: (i) Examining expression of Sam68/hnRNP A2/B1 in primary tumours/metastases; (ii) Studying the role of these RBPs in EMT/metastasis of PCa cells; and, (iii) Developing a model of transcriptome-wide AS regulated by Sam68/hnRNP A2/B1 in metastasis.



A prostate

Expression of Sam68/hnRNP A2/B1 will be compared in primary/metastatic clinical PCa by immunohistochemistry, and correlated with clinico-pathological parameters. The functional role of Sam68/hnRNP A2/B1 in EMT/metastasis will be studied by RNA interference in PCa cell lines and *in vivo* models. Alternatively spliced mRNA targets for Sam68/hnRNP A2/B1 in metastases will be identified by next-generation sequencing methodologies. Using computational genomics, an integrative model for RBP-orchestrated AS in PCa metastasis will be developed.

The above approach will enumerate several Sam68 and/or hnRNP A2/B1 target mRNA isoforms in PCa metastasis, furthering our understanding of RBP-driven metastasis. By specifically disrupting key RBP-mRNA isoform interactions in cancer cells, PCa-specific AS may be modulated as a potential targeted therapy. We hope that mRNA targets identified in this study will help to delineate therapeutic strategies for ‘incurable’ PCa in clinical trials.



Prabhakar Conducting a laparoscopic nephrectomy (removal of a kidney)

# FULBRIGHT RESEARCH AWARDS

Three years ago the College was approached by the Fulbright Commission to discuss potential partnerships and this has resulted in the following awards.

Subsequently, each year one Fulbright Research Award is offered in conjunction with The Royal College of Surgeons of England to a surgeon, trainee surgeon or specialist to pursue research (that does not include clinical work, laboratory-based or otherwise) into the development of new operative techniques, improvements in patient care and recovery, and/or the causes of surgical conditions and how to treat them, at any accredited US higher education institution. The award is for a period of 3–12 months and the funding is intended as a contribution towards institutional fees, travel to/from the US and general maintenance costs while in the US and UK clinical salary costs.

## TRAUMA: DAMAGE RESPONSE AND RECOGNITION

Half of the patients with severe injuries develop multiple organ failure and even with modern intensive care treatment, only two out of three survive

### FELLOWSHIP/SPONSOR

Inaugural RCS England Fulbright Scholars Award

### SUPERVISOR

Prof Timothy Billiar and Prof Karim Brohi

### SITE OF WORK

UPMC Presbyterian Hospital, Pittsburgh



**JO  
MANSON**

My project this year built upon findings from my PhD studying human trauma patients. My overall goal is to determine how the immune system responds to traumatic injury and understand why it may impair rather than expedite recovery. My work forms part of a long-term research strategy for my London-based department. Very few people in the world investigate this aspect of surgical disease. If successful, we may be able to amend treatment strategies or develop therapeutics that speed recovery or improve outcomes. It is also possible that findings from this field may be of benefit to other surgical specialties.

For my year as a Fulbright Scholar, I joined a lab in Pittsburgh with substantial expertise studying the mechanics of the immune response in mice. Use of murine models enables targeted study of the immune response in a way that is not possible in patients. The year has been extremely valuable. It has provided me with excellent training, access to vast research infrastructure and experience of academic surgery in America.

My focus has been on Natural Killer cells,  $\gamma\delta$  T cells and Natural Killer T cells; all of which are implicated as key players in the first phases of immune system activation. These cells share a common property: they can all become activated after direct exposure to 'harmful substances'. This is useful during invasion by bacteria or viruses or after abnormal

growth of cancerous tissues. After traumatic injury it may be an impediment, as the 'harmful substances' originate from the patient's own tissues. Activation of these immune cells may therefore be 'inappropriate' and may lead to organ damage. Detailed investigations are required if we are to provide evidence for the processes involved in this response. Over the next few years, I hope to continue this research alongside my clinical training.



UPMC Presbyterian Hospital

# DEVELOPING A NEW APPROACH TO INTESTINAL SURGERY

By 2050, the number of individuals aged 65 or older will increase by 135%

## FELLOWSHIP/SPONSOR

RCS Fulbright Scholar Award/H&S Charitable Trust Award

## SUPERVISOR

Dr J Milsom

## SITE OF WORK

Weill Cornell Medical College, New York, New York

## PUBLICATIONS

1. Lee E, *et al*. Endoscopic Submucosal Dissection for colorectal tumours. *Surg Endosc* 2013.
2. Brigid *et al*. A systematic review regarding the feasibility and safety of endoscopic full thickness resection (EFTR) for colonic lesions. *Surg Endosc* 2013. [epub ahead of print]

## PRESENTATIONS

1. *Novel Endoluminal Therapies*. Gastrointestinal Diseases Conference, UCLA, LA, USA. July 2013.



**SAMEER SHARMA**

Diseases of the large intestine are some of the most common disorders requiring surgery (eg cancer and inflammation of the intestine). In the western world, these diseases affect a large number of people and in developing countries the number of affected individuals are increasing at an alarming rate.

The elderly disproportionately bear the brunt of these diseases. The proportion of the elderly that exists in our society is set to increase dramatically in the coming years as life expectancy increases. Those aged 65 or older will increase by 135% by 2050.

Current surgical treatment of colonic disease usually requires major surgery either in the form of open operations (large abdominal incisions) or as minimally invasive operations (several small incisions and use of a camera). Surgical treatment is the mainstay of therapy for nearly all cancers of the large intestine, and for serious manifestations of many other intestinal diseases. These operations carry a significant risk of complications as well as the possibility of death.

The aims and objectives of this project are to develop the technology to perform surgery within the lumen (inside) of the intestine. By designing and producing these tools a shift will occur in how we plan and perform intestinal operations.

This project will focus on the further development and perfection of these operative techniques and associated medical devices in models and live animals. Ultimately we envisage that patients, particularly the elderly and those with serious disease (eg heart disease, diabetes, etc), will benefit from this new technology and techniques. By having the least minimally invasive operation as possible, avoiding general anaesthesia, decreasing the number of days spent in hospital (or even just as a day-case procedure) and eventually leading to the safest possible outcome.



Top: Testing the new devices in the laboratory

Bottom: Some of the excellent team that makes this work possible



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.

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# TEMPORAL CHANGES IN ENERGY EXPENDITURE AND GLUCOSE HOMEOSTASIS ASSOCIATED WITH RESTRICTIVE AND MALABSORPTIVE METABOLIC SURGERY

Bariatric (metabolic) surgery is the most effective treatment for morbid obesity, resulting in significant weight loss and reducing obesity-related comorbidities and mortality



**JONATHAN BARRY**

## SITE OF WORK

Clinical Research Unit, Morriston Hospital, Swansea

## CURRENT POSITION

Consultant laparoscopic bariatric surgeon and honorary senior lecturer

## SPECIALTY

Bariatric surgery

## PRESENTATIONS

Current work from this thesis is still undergoing analysis and will be submitted to the American Diabetes Association, where Royal College of Surgeons will be acknowledged.

## FURTHER FUNDING

BUPA Foundation for one year

## PUBLICATIONS

1. Mallipedhi A, Prior SL, Dunseath G, *et al.* Temporal changes in inflammatory biomarkers after laparoscopic sleeve gastrectomy compared to malabsorptive bariatric surgery: A non-randomised prospective study in participants with impaired glucose tolerance and Type 2 diabetes. *Int J Obesity*. [Submitted July 2013]
2. Mallipedhi A, Prior SL, Dunseath G, *et al.* Temporal changes in insulin and glucose homeostasis after laparoscopic sleeve gastrectomy compared to malabsorptive bariatric surgery: A non-randomised prospective study. *Ann Surg*. [Submitted June 2013]

Diet-induced weight loss results in an adaptive decrease in energy expenditure (EE), which may explain the difficulty in maintaining weight loss in the long term. Conversely, patients undergoing bariatric surgery often experience sustained weight loss years after surgery. Changes in postoperative EE could explain this sustained weight loss. Surgery results in decreased total EE, principally owing to reduced resting EE and explained by a decrease in both fat-free mass and fat mass.

The measurement of oxygen uptake ( $VO_2$ ), together with carbon dioxide production ( $VCO_2$ ) and expired ventilation (VE), are commonly performed in many laboratories in order to assess cardiorespiratory fitness and the metabolic demands of various activities. Previously, these measurements were obtained in laboratory conditions using the Douglas bag method (DBM). More recently, automated computerised metabolic gas analysis systems have superseded the time-consuming DBM in most labs. Metamax 3B possesses virtually all the data-collection powers of their lab-based counterparts,



Jonathan, Akhila Mallipedhi and patient on Metamax device

including recording or telemetering breath-by-breath and heart rate.

Our aim was to study the impact of bariatric surgery on total EE, resting EE, and diet-induced thermogenesis (DIT) in obese patients and to compare these variables between restrictive and malabsorptive surgery. All patients were studied before surgery and at one and six months postoperatively. Initial results have been encouraging and hence assessment of all patients undergoing surgery is mandatory.

This project has complemented established ongoing research within Morriston Hospital and Swansea University. Investigating the mechanisms by which physiological improvements occur in relation to EE will provide an evidence base for metabolic surgery and may aid in the selection of appropriate patients if rationing criteria are in place.



Jonathan performing laparoscopic sleeve gastrectomy

# ASSESSMENT OF MITOCHONDRIAL FUNCTION AND PHYSICAL ABILITY IN PATIENTS WITH CRITICAL LIMB ISCHAEMIA

Critical limb ischaemia (CLI) is becoming an increasing problem within the UK (affecting 40 per 100,000 population), and is associated with poor functional outcomes

## SITE OF WORK

Addenbrookes Hospital, Cambridge

## CURRENT POSITION

Consultant vascular surgeon

## SPECIALTY

Vascular surgery



**PATRICK  
COUGHLIN**



Patrick examining a patient with CLI on the ward

CLI presents with either constant pain in the foot or the presence of ulcers/gangrene due to insufficient amount of blood getting to the peripheries of the lower limb. This is due to severe narrowing/blockages within the arteries of the leg that often require opening using balloon treatment (angioplasty) or by formal bypass procedures that have associated morbidity. Patients with CLI have severe physical impairments, causing poor physical and socioeconomic outcomes. The aim of this study was to attempt to determine whether or not the energy-producing components of muscle (called the mitochondria) in patients with such severe ischaemia correlated with preoperative and postoperative physical function. Determining this will reveal whether they are a potential target for pharmacological intervention.

Pre- and postoperative markers of daily physical function were measured, specifically looking at specific facets of walking and lower limb strength. Biopsies of calf muscle were taken at surgery and mitochondrial function determined.

Initial results confirm that CLI is associated with poor physical function. As yet it is too early to link this with mitochondrial function.

Increasingly CLI patients are concerned with outcomes after treatment that relate not only to limb salvage but also function, allowing them to return to an independent way of life. This study forms one facet of a number of clinical and laboratory-based studies with the aim of optimising rehabilitation of such patients to meet such favourable outcomes.

# INCREMENTAL BENEFIT OF 3T PELVIC ARRAY DIFFUSION-WEIGHTED MRI FOR STAGING PRIOR TO RADICAL PROSTATECTOMY

Surgery is an important modality of treatment for prostate cancer, with over 4,000 operations performed annually. For many men surgery can offer complete cure

## SITE OF WORK

Addenbrookes NHS Trust and University of Cambridge

## CURRENT POSITION

University lecturer in uro-oncology and consultant urological surgeon

## SPECIALTY

Urology

## PRESENTATIONS

1. Lawrence EM, *et al.* Correlating prospective and histology-matched ADC histograms with extra-capsular extension in prostate cancer. The International Society for Magnetic Resonance in Medicine's 20th Annual Meeting, Melbourne, Australia. May 2012.
2. Lawrence EM, *et al.* Analysis of intermediate/high-risk prostate cancer with diffusion kurtosis at 3T. RSNA 2012.

## PUBLICATIONS

1. Lawrence EM, *et al.* The emerging role of diffusion-weighted MRI in prostate cancer management. *Nat Rev Urol* 2012; **9**: 94–101.



**JEYASEELAN  
GNANAPRAGASAM**

Increasing numbers of men are choosing surgery for treatment of prostate cancer. In the UK many of these men will be found to have a more significant burden of cancer than initially suspected. If surgery is unable to clear the cancer (leaving a positive margin) then a patient may need additional radiotherapy and potentially also hormonal therapy. Both these treatments can have side effects that are debilitating. Hence, being better able to detect where cancer has spread and planning surgery accordingly would reduce the need for this additional treatment and improve the patient's quality of life. An important tool to help better planning of surgery is a preoperative MRI (magnetic resonance imaging) scan. The aim of this study was to investigate if a new more precise form of MRI called diffusion-weighted MRI (DW-MRI) could improve the prediction of whether cancer has spread outside the prostate lining at the time of surgery. We undertook a pilot study to test this and successfully recruited 40 men to have a normal MRI and DW-MRI before surgery. We then compared how good the normal MRI and the DW-MRI was in predicting spread of the cancer outside the prostate lining when surgery was done and the prostate removed. We have been able to demonstrate that:

1. DW-MRI is better overall than standard MRI in detecting cancer that has spread
2. DW-MRI makes it easier for a radiologist to detect this spread outside the prostate
3. DW-MRI can be done easily, quickly and is reproducible in standard clinical care.

This is the first study that has focused on the use of DW-MRI in prediction of cancer spread outside the prostate before surgery. Our results justify a future larger randomised study with many other units. The critical aim would be to test if DW-MRI can help improve surgeons planning for surgery

and therefore reduce the incidence of incomplete clearance of cancer at surgery.



Vincent Gnanapragasam delivering the Hunterian Lecture in 2008



Vincent Gnanapragasam with two of his clinical PhD students

# TARGETING AND UPTAKE OF TUMOUR-SPECIFIC NANOPARTICLES FOR DIAGNOSTIC AND THERAPEUTIC USE

7,600 new cases of pancreatic cancer are diagnosed each year, with approximately the same number of deaths annually in the UK



**CHRISTOPHER  
MICHAEL HALLORAN**

## SITE OF WORK

University of Liverpool/Royal Liverpool University Hospital

## CURRENT POSITION

Clinical senior lecturer/consultant surgeon

## SPECIALTY

Pancreato-biliary surgery

## FURTHER FUNDING

The Royal and Broadgreen University Hospitals, The Royal College of Surgeons of England for research fellows and Cancer Research UK for consumables (£255,000) until 2014.

## PRESENTATIONS

1. European Pancreatic Club, Prague, Czech Republic.
2. American Pancreatic Association, Miami, USA.

## PUBLICATIONS

1. Olariu CI, Yiu HHP, Bouffier L, *et al.* Step-by-step preparation of Fe<sub>3</sub>O<sub>4</sub> nanoparticles with multi-functionality for targeted bi-modular imaging of pancreatic cancer (Targeted bi-modular imaging of pancreatic cancer with multifunctional Fe<sub>3</sub>O<sub>4</sub> nanoparticles). *J Mater Chem* 2011; 21: 12650.
2. Sykes PD, Neoptolemos JP, Costello E, Halloran CM. Nanotechnology advances in upper GI, Liver and pancreatic cancer. *Expert Rev Gastroenterol Hepatol* 2012; 6: 343–56.



Surgical treatment for pancreatic cancer

Pancreatic cancer is a devastating disease. Surgical resection with follow-on chemotherapy is the mainstay of treatment in those 20% of patients who present early enough for treatment. Future advances require novel approaches to better diagnosis and improved treatment strategies.

The aims and objectives are to develop a novel nanoparticle system that can seek and destroy pancreatic cancer. Targeting will be achieved by attaching molecules to the nanoparticle so that specificity for pancreatic cancer is increased; namely antibodies to surface proteins of the cancer (CA 19.9 and CEA). This will allow more specific and accurate treatment of the cancer with fewer side effects for the patient.

- » Using unique chemical functionalisation, two binding domains have been added to the polymer. First, an amine group to bind a marker signal. Second, a carboxyl group to bind the targeting antibody.
- » These particles have been extensively examined for toxicity to cell lines. No apparent effect at the quantities used in these experiments has been identified.

- » We have successfully conjugated two different antibodies to the nanoparticles, whose antigens are over-expressed by pancreatic cancer cells (CEA or CA19.9).
- » It has been demonstrated that such nanoparticles-antibody complexes appear to undergo enhanced uptake into pancreatic cancer cell lines compared with nanoparticles lacking attached targeting molecules.

## Chemotherapy release:

We have developed a method of reversibly binding gemcitabine (a chemotherapy agent) with the polymer surrounding the nanoparticles so that it should be released only after the nanoparticle has entered a cell; this is achieved by a pH breakable bond.

This work is still in a laboratory phase, but results so far indicate that these nanoparticles will provide a strong foundation for the development of a vehicle capable of targeted chemotherapy release in patients with pancreatic cancer. This will result in reducing the off-target effects that are currently commonly associated with chemotherapy agents. This epitomises a personalised medicinal approach for this disease.

# DEVELOPMENT OF NEW PATIENT-REPORTED OUTCOME MEASURES (PROMS) FOR PATIENTS WITH AORTIC ANEURYSMS

Aortic aneurysm-specific patient-reported outcome measures will help patients and doctors to decide upon best treatment, as well as ensuring that improvements in care are focused on those areas that are most important to patients

## SITE OF WORK

St George's Vascular Institute

## CURRENT POSITION

HEFCE Clinical senior lecturer/honorary consultant vascular surgeon

## SPECIALTY

Vascular surgery

## PUBLICATIONS

1. Peach G, Holt P, Loftus I, Thompson MM, Hinchliffe R. Questions remain about quality of life after abdominal aortic aneurysm repair. *J Vasc Surg* 2012; **56**: 520-27.



**ROBERT  
HINCHLIFFE**

Morbidity and mortality have traditionally been used as key markers of surgical outcome. However, as complication rates associated with abdominal aortic aneurysm (AAA) repair decrease, subjective measures such as quality of life (QoL) are increasingly recognised as important indicators of treatment efficacy and quality of care.

At present, little is known about how AAA and its treatment affect patients' QoL and the data relating to the relative effects of open repair and endovascular aortic repair on QoL have been conflicting. It is thought that this may be owing to the lack of any 'disease-specific' tool for patients with AAA and the fact that all previous studies have used generic tools to measure QoL, which may not identify the issues that are most relevant to these patients.

During this study we have designed a new set of tools to measure QoL, symptoms and treatment satisfaction in patients with AAA. These have been based upon information gathered in focus groups and one-to-one interviews with patients who are under surveillance or who have had open or endovascular repair of their aneurysm.

In developing these tools it has become clear that there may be previously unrecognised factors that adversely affect QoL in these patients. These tools are currently undergoing linguistic and psychometric validation in preparation for a larger-scale prospective study that will clarify the true prevalence of different symptoms in patients with AAA and the impact of these on QoL.

Surgical treatment for an aortic aneurysm



# ENDOTHELIAL INJURY AND THE MOLECULAR PATHWAYS IN PROMOTING AND PREVENTING STENOSIS IN VASCULAR ACCESS FOR HAEMODIALYSIS

Dialysis using a central venous catheter rather than an arteriovenous fistula (AVF) has a higher risk of death but up to 40% of fistulas fail to mature



**NICHOLAS  
G INSTON**

## SITE OF WORK

Queen Elizabeth Hospital and University of Birmingham Medical School

## CURRENT POSITION

Consultant surgeon

## SPECIALTY

Renal surgery

## PRESENTATIONS

1. Hemodialysis XIII Symposium. VASA (Vascular Access Society of the Americas). May 10–11 2012. Orlando, USA.
2. Prize Session European XXVI Annual Meeting, European Society for Vascular Surgery. 19–21 September 2012. Bologna, Italy.

## FURTHER FUNDING

Two years from the University Hospitals Birmingham charitable funds



Assessing flow with Doppler ultrasound in healthy arteries with research fellow Yazin Marie

scribed in large arteries but never in veins or AVFs. When we identified this in the vein segment of AVFs the outcomes are better than when it is absent. In addition, the observation that veins are capable of generating spiral flow has led us to study the structure of blood vessels and revealed that the muscle fibres lie in an angular arrangement, providing a potential generator for spiral flow. These observations are leading to further studies on these effects on the cells (endothelium) that line the vessel walls.

The pathways linking normal (protective) and abnormal (pathological) flow with intimal hyperplasia in arteries and veins are poorly understood and our current research is to gain a greater understanding of the important molecules in this balance, which may allow us to develop strategies and treatments to reduce VNH and vessel disease.

Kidney failure is a common disease that is increasing. Apart from transplantation the only other option is dialysis. Haemodialysis requires regular access to the blood stream. The best way of doing this is with an arteriovenous fistula (AVF), where a vein is connected surgically to an artery. Unfortunately AVFs have a high early failure rate (up to 40%), owing to a process called venous neointimal hyperplasia (VNH) for which the scientific basis is poorly understood. VNH also occurs with AV grafts, central venous catheters and even pacemaker wires. The aim of this study was to explore the mechanisms leading to VNH. Previous studies have shown that the character of flow through blood vessels can result in vessel wall changes or remodelling, which can be favourable or pathological.

By assessing patterns of blood flow in newly formed and established AVFs, we identified a pattern of flow that is termed spiral laminar flow. This has been previously de-

Performing kidney transplants as part of a transplant links mission



# REDUCING BLOOD TRANSFUSION REQUIREMENTS FOLLOWING CARDIAC SURGERY

One in four of our patients coming to cardiac surgery is anaemic, resulting in a high risk of needing a blood transfusion at time of surgery

## SITE OF WORK

Department of Cardiac Surgery, Royal Sussex County Hospital

## CURRENT POSITION

Consultant cardiac surgeon and honorary senior lecturer

## SPECIALTY

Cardiothoracic surgery



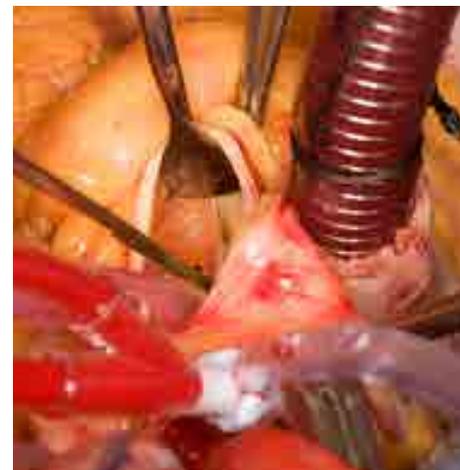
**MICHAEL  
EDWARD LEWIS**



A perfusionist running the heart lung machine



A fibroelastoma before excision



Heart surgery in progress

At least one quarter of patients coming forward for cardiac surgery are anaemic. Anaemic patients need more blood transfusions and have a higher risk of dying and developing complications at the time of their surgery. The aim of our study is to see if we can reduce the need for blood transfusion in this group of patients.

We have designed a trial looking at treating anaemic patients with two drugs (intravenous iron and Darbepoetin) prior to surgery. These patients will be compared with a group offered standard treatment and the effect upon blood transfusion and the development of complications will be examined. We aim to recruit 300 patients to our study during the next two years.

Blood transfusion is lifesaving in many circumstances. However, there is a growing body of evidence in many spheres

of medicine that would suggest that if blood transfusion could be avoided this may have a positive impact on patients. Also cardiac surgery uses a large proportion of blood bank stocks. Blood is becoming a scarce resource. Our ability to continue to provide safe, effective surgery is likely to be dependent on our ability to prevent blood transfusion wherever possible.

This work builds on our experience of dealing with anaemic patients. There have been no other trials looking at this particular question in cardiac surgery.

Our clear objective is to improve outcomes for our patients. This study is part of our overall research programme looking at our ability to optimise patients prior to the major insult of undergoing cardiac surgery.

# PROSPECTIVE EVALUATION OF CHANGE IN LIVER FUNCTION IN PATIENTS WITH COLORECTAL LIVER METASTASES UNDERGOING LIVER RESECTION

Five to ten per cent of patients undergoing a liver resection develop postoperative liver failure



**DEREK O'REILLY**

## SITE OF WORK

Department of Surgery, North Manchester General Hospital

## CURRENT POSITION

Consultant hepatobiliary and pancreatic surgeon and honorary senior lecturer

## SPECIALTY

Hepatobiliary and pancreatic surgery

## PRESENTATIONS

1. *Digital determination and predictors of hepatic steatosis in patients undergoing resection for colorectal liver metastases.* Poster presentation at the ASGBI. 2013.
2. *The impact of steatosis on oncological outcome in chemotherapy-naïve patients undergoing liver resection for metastatic colorectal cancer.* Best oral presentation session (liver) at the International Hepato-Pancreato-Biliary Association. Paris. June 2012.

## PUBLICATIONS

1. Parkin E, *et al*, and the LiverMetSurvey Centres. The effect of hepatic steatosis on survival following resection of colorectal liver metastases in patients without preoperative chemotherapy. *HPB (Oxford)* 2013; **15**: 463–72.
2. Parkin E, *et al*. Body composition and outcome in patients undergoing resection of colorectal liver metastases. *Br J Surg* 2012; **99**: 1021–22.

## FURTHER FUNDING

Magnetic Resonance Imaging Facility grant, University of Manchester, for funding for a pilot study measuring preoperative liver fat levels in 10 patients using MRI scans

Indocyanine green (ICG) is a chemical dye used by surgeons in the Far East to measure how well the liver is working in patients who are suspected of having poor liver function due to hepatitis. Preoperative ICG clearance is not routinely measured in the UK, despite up to 10% of patients developing postoperative liver failure (the major cause of death following liver surgery). We aimed to expand on the technique of ICG clearance established in the Far East, taking into account other factors known to influence liver function, such as chemotherapy and fatty liver disease, to assess whether this method could identify patients at risk of liver failure in a UK hospital setting.

Twenty-nine patients scheduled for liver resection for colorectal cancer metastases were recruited prospectively over an 18-month period. ICG dye was injected intravenously at a dose of 5mg/kg; ICG clearance was measured using a LIMON monitor. The two blood tests that define postoperative liver failure according to international guidelines (day 5 INR and



The hepatobiliary surgical team at North Manchester General Hospital

bilirubin) were recorded. A novel digital histology technique was used to quantify the amount of fatty liver disease present in the resection specimen.

Relationships between preoperative ICG clearance, chemotherapy, fatty liver disease, international normalised ratio (INR) and bilirubin were assessed using Spearman's rank correlation coefficient. Preoperative ICG clearance correlated well with postoperative day 5 bilirubin ( $\rho=0.57$ ,  $p=0.0087$ ) but there was no significant relationship with chemotherapy or fatty liver disease.

These findings suggest that as a standalone test, preoperative ICG clearance can predict postoperative liver function in a UK population and thus can be used to guide decision making before surgery (for example, whether to proceed with a major resection in the presence of low ICG clearance). We are therefore planning to incorporate ICG clearance in to the preoperative assessment protocol in our department.



Liver surgery being undertaken at North Manchester General Hospital

# REGIONAL INTRATUMOURAL HETEROGENEITY OF PATHOLOGICAL FEATURES IN GLIOBLASTOMAS: A MULTIMODAL IMAGING STUDY

Despite accounting for only 2% of malignancies, brain cancer is the leading cause of cancer death in children, women below the age of 35 years and men below the age of 45

## SITE OF WORK

University of Cambridge

## CURRENT POSITION

Honorary consultant neurosurgeon and National Institute of Health Research clinician scientist

## SPECIALTY

Neurosurgery

## PRESENTATIONS

1. British Neurosurgical Research Group Meeting, Manchester, March 2013.
2. British Neuro-oncology Society Meeting, Durham, July 2013.

## FURTHER FUNDING

Cambridge Biomedical Research Centre (to develop <sup>11</sup>C-Temozolomide PET) for two years



**STEPHEN PRICE**

Glioblastomas are the commonest and most malignant primary tumour of the brain. Even with surgery, radiotherapy and chemotherapy, they invariably progress within months and most patients die within a year. Recent trials of new drugs have failed to show any improvement in survival and no other new treatments are on the horizon. This means there is a real need to go back to basics and better understand these tumours.

We are beginning to realise that glioblastomas encompass a large range of tumour subtypes with different behaviours. Differences between patients (intertumoural heterogeneity) mean that one treatment will not be suitable for all, and we desperately need to understand this variation. Within a single patient's tumour there are areas with different appearances. This intratumoural heterogeneity suggests that different regions of a single tumour will respond differently to a treatment. My group is interested in studying this regional variation using advanced imaging methods. These can probe differences in tumour pathology and provide an excellent way of looking at changes over time.

There had been some suggestion that areas with high vascularity (high relative cerebral blood volume [rCBV] measured using perfusion MRI) and high cellularity (low apparent diffusion coefficient [ADC] measured using diffusion MRI) respond better to chemotherapy. We studied 50 patients with glioblastomas by imaging them preoperatively. Imaging included perfusion and diffusion MRI. These images were coregistered so we could identify regions with low ADC and high rCBV.

When measuring the area of these regions we found great variation – from 1% to 58%. We would expect patients with large areas to respond better to chemotherapy but our results suggest this is not the case. These patients had a worse survival,



Stephen Price training a junior to resect a frontal lobe tumour

al, suggesting these areas are more aggressive. MR spectroscopy confirms that these areas are metabolically more malignant. We plan to explore this by biopsying these regions.

The question is whether these areas fail to respond to chemotherapy or the drugs don't get into them. We are working on imaging methods to look at regional response to therapy and will study drug uptake by imaging labelled chemotherapy drug (<sup>11</sup>C-temozolomide polyethylene terephthalate [PET]).

# DELINEATING THE RELATIONSHIP BETWEEN DEVELOPMENTAL DYSPLASIA OF THE HIP AND OSTEOARTHRITIS

A genome-wide association study of infant hip dysplasia in the UK

## SITE OF WORK

UCL Institute of Child Health

## CURRENT POSITION

Reader, UCL Institute of Child Health

## SPECIALTY

Paediatric orthopaedics

## FURTHER FUNDING

NIHR CLRN for two years.



**ANDREAS  
ROPOSCH**

This award was received in support of a genome-wide association study of infant hip dysplasia in the UK. Such a study will need to recruit 2,200 affected patients. The award was to support a pilot study that included recruiting patients at Great Ormond Street Hospital for Children, to establish a network of collaborating orthopaedic surgeons in the UK and to collect data in support of a definite grant application. In addition, some of the pump prime funding was in support of a feasibility study for a randomised clinical trial of the surgical treatment of hip dysplasia.

We have recruited 220 patients from Great Ormond Street Hospital and established a network of 9 participating orthopaedic units who have in total collected 400 DNA samples so far. The funding was primarily used to cover costs for DNA collection kits and processing. There is an increasing awareness of this popular study among paediatric centres in the country, with many more centres wanting to sign up. Sixteen consultant orthopaedic surgeons have signed up for this study to date. The national network is growing. The study is a National Institute for Health Research (NIHR) Portfolio study and additional funding has been received from the NIHR Comprehensive Local Research Network (CLRN) in support of the study.

Furthermore, the feasibility study for a randomised clinical trial was important and helped to plan the trial adequately – a team of investigators from UCL and Southampton University have submitted a full application to NHIR Health Technology Assessment in support of a multicentre clinical trial. The outcome of this application is pending.



Andreas examining a patient at Great Ormond Street Hospital

# INVESTIGATION OF NOVEL ADJUVANT THERAPIES IN THE ERADICATION OF BACTERIAL BIOFILMS IN CHRONIC RHINOSINUSITIS

Chronic rhinosinusitis (CRS), with or without polyps, is an extremely common condition affecting up to 15% of the UK population

## TITLE OF FELLOWSHIP

Pump Priming Award

## SITE OF WORK

University Hospital Southampton NHS Foundation Trust

## CURRENT POSITION

Senior lecturer in rhinology and consultant in otorhinolaryngology

## SPECIALTY

Otorhinolaryngology

## PRESENTATIONS

1. *Characterisation of bacterial biofilms in nasal polyps*. Biofilms 5 International Conference. Paris. December 2012.
2. *Characterisation of bacterial biofilms in nasal polyps*. British Academic Conference for Otolaryngology & Expo. Glasgow. 2012.



**RAMI SALIB**

The impact of chronic rhinosinusitis is often underestimated, with afflicted patients having a significant impaired quality of life. Despite the millions of pounds of antibiotic and surgical procedures prescribed for this condition, there appears to be a subset of patients who remain resistant to established treatments. To this day, we know little about the underlying causes of this disease.

Our research project has focused on the emerging field of bacterial biofilms (complex colonies of bacteria with resistance to antibiotics) as potential mediators of the ongoing inflammation in CRS. The aim of our project was first to identify and characterise these bacterial biofilms in the tissue lining the sinuses and then to develop and test new therapies to help eradicate them.

Using imaging techniques, we successfully identified and characterised bacterial biofilms on the tissue lining the sinuses, then compared with tissue from patients not affected by the condition. In patients with nasal polyps (boggy swellings of the nose and sinus lining), we made the novel finding that these bacterial biofilms appear to migrate beneath the tissue lining and conceal themselves within the patient's own cells in a bid for survival, creating an environment where chronic inflammation can ensue. Work on eradicating these bacterial biofilms using novel therapies is ongoing and preliminary results are promising.

We hope that, if successful, these therapies could help to prevent infective exacerbations and reduce the overall antibiotic burden and the requirement for multiple operations in these patients. This would make significant financial savings for the NHS and have a positive impact on patients' quality of life.



Rami with a clinical research fellow (Stephen Hayes) in the operating theatre at University Hospital Southampton NHS Foundation Trust

# NOVEL THERAPEUTIC TARGETS IN GASTRIC CANCER: THE INSULIN-LIKE GROWTH FACTOR SIGNAL TRANSDUCTION PATHWAY

We have discovered a potential target for treatment that some stomach cancer cells rely on for their ability to survive and spread; in the UK, only about 15 out of every 100 people (15%) live for 5 years after being diagnosed with stomach cancer

## TITLE OF FELLOWSHIP

Pump Priming Award

## SITE OF WORK

Royal Victoria Infirmary, Newcastle upon Tyne, and Northern Institute for Cancer Research, University of Newcastle

## CURRENT POSITION

Consultant general and oesophago-gastric surgeon

## SPECIALTY

General and upper gastrointestinal



**JONATHAN SHENFINE**

The aim of this study was to develop our understanding of stomach cancer with a view to identifying potential new treatment targets and ultimately to improve the outcome for patients with this disease.

Stomach cancer is a devastating disease; 8,000 new patients are diagnosed with stomach cancer every year in the UK. Unfortunately, most patients present with inoperable, incurable disease and it can be very difficult to manage their symptoms. Survival is very limited in this situation so it is important to identify new treatment targets that would allow these patients to receive more effective drugs to control their symptoms and maintain their quality of life for as long as possible.

In our research we investigated if stomach cancer cells are particularly responsive to a specific growth factor. We developed a laboratory test that allows us to study what happens to stomach cancer cells that lose their normal interactions with the tissue that surrounds them. When normal cells lose these attachments they die, but cancer cells develop ways to survive and are able hence to spread throughout the body. We found that some stomach cancer cells are kept alive after loss of these attachments because of this growth factor. We hope to develop this research further to understand why some stomach cells depend on the growth factor whereas other stomach cancer cells do not. Drugs that inhibit this response are available and could be used to treat patients with stomach cancer but this has not been used as a target before. These novel drugs would have the potential to relieve patient symptoms and to prolong their lives.



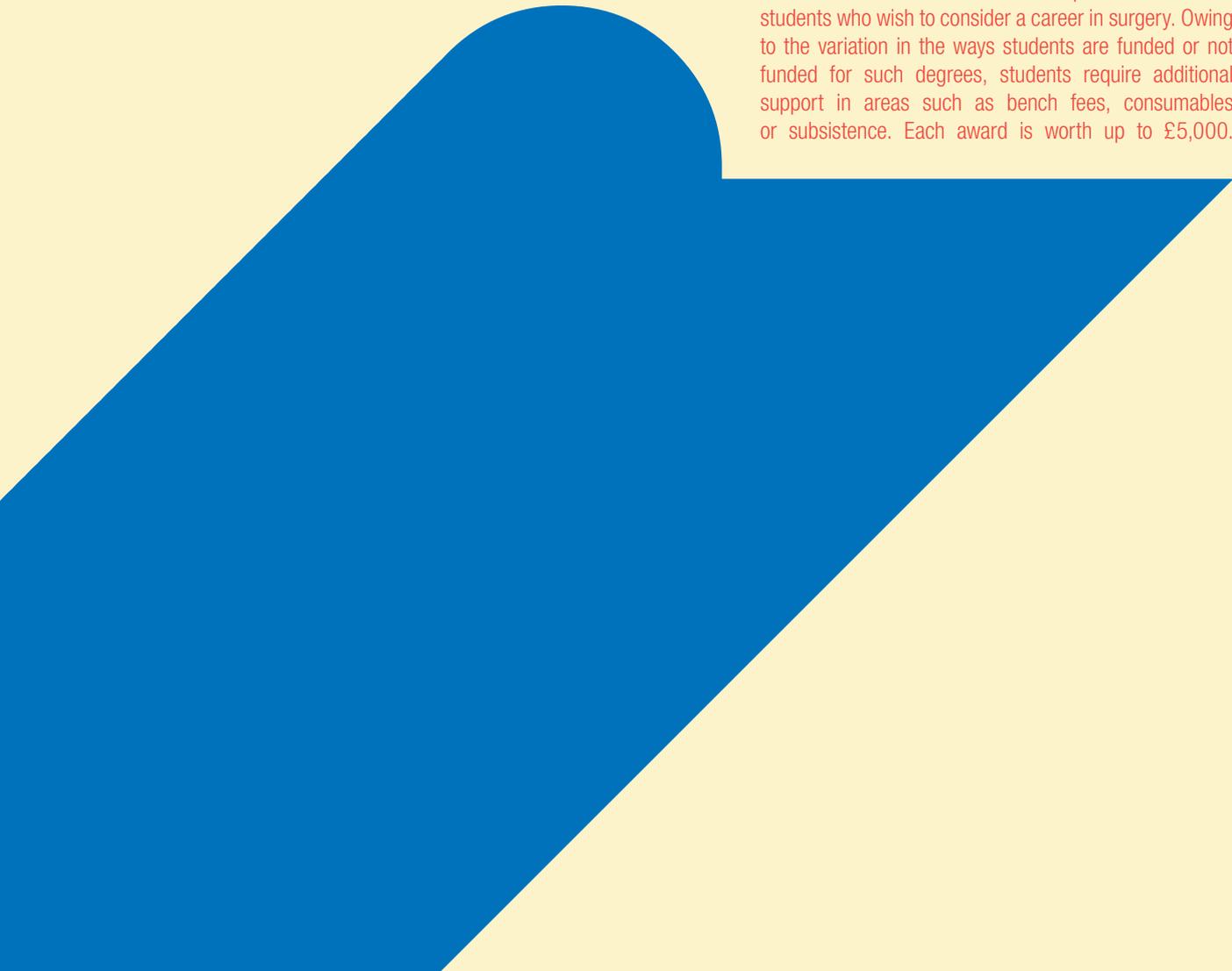
Counselling a patient and their partner preoperatively for an oesophageal resection



Communicating the management plan with a nursing colleague.



Documentation of the consultation



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

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## THE RELATIONSHIP BETWEEN TUMOUR ASSOCIATED MACROPHAGES, COLLAGEN, AND CLINICAL OUTCOME IN PANCREATIC DUCTAL ADENOCARCINOMA

JOHN CONNELLY

School of Medicine, University of Glasgow

Pancreatic cancer is associated with a 5-year survival of less than 5% and there is a pronounced deficit of molecular biomarkers to predict prognosis or response to therapy. Thus, our ability to stratify interventions is hampered considerably. Pancreatic ductal adenocarcinoma (PDAC) is characterised



Mr Nigel Jamieson (left), John Connelly (right) at the entrance to CRUK Beatson Institute, where the laboratory research was conducted

by a stroma (fibrous scarring and immune cell infiltration) that is actively protumoural and a barrier to drug delivery.

We used human PDAC tissue associated with prospectively-maintained clinicopathological data to investigate the prognostic impact of immune cell infiltrates and to explore the putative association between these immune cells and the fibrous matrix. We are now developing this in genetically engineered mouse models.

I wish to thank the College for this award, which facilitated these laboratory studies. I will graduate with first-class honours in cancer sciences and I hope to develop my interests in hepatopancreaticobiliary surgery and translational cancer research in the future.

## IS WISP 2 EXPRESSION ASSOCIATED WITH COLORECTAL CANCER CELL INVASIVENESS?

KATHRYN FREWER

Cardiff University School of Medicine

The Royal College of Surgeons award helped fund my intercalated BSc degree in cellular and molecular pathology. My research project (supervised by Miss Rachel Hargest and Professor Wen Jiang) focused on understanding the role of a gene (WISP-2) in colorectal cancer (CRC). Patients with CRC do not die from the initial primary tumour itself but from the spread of cancer cells around the body, most commonly to the liver. My research project assessed how inhibiting the expression of WISP-2 in CRC cells effected cell invasion, growth, adhesion and migration (characteristics associated with cancer cell spread).

I have been awarded first class honours for my BSc intercalated degree. I have recently submitted abstracts to the British Association of Surgical Oncologists conference (for my project on CRC) and the San Antonio Breast Cancer Symposium (for a project on breast cancer). I will soon be submitting manuscripts of my research for publication.



(Left to right) Mr Jared Torkington (Consultant Surgeon), Miss Rachel Hargest (Consultant Surgeon), Kathryn Frewer, Natasha Frewer, Professor Wen G Jiang (Head of Research Department)

## DOES INTERLEUKIN-24 HAVE AN EFFECT ON THE PROCESS OF LYMPHANGIOGENESIS?

NATASHA FREWER

Cardiff University School of Medicine

The RCS award supported me through my intercalated BSc degree in cellular and molecular pathology, for which I have been awarded first class honours. My research project (supervised by Mr Jared Torkington and Professor Wen Jiang) broke new ground in the investigation of the effect of Interleukin-24 (an anti tumour cytokine) on lymphangiogenesis (the formation of new lymphatic vessels). The lymphatic vasculature serves as a major route for the dissemination of malignant cells from solid tumours to regional lymph nodes and therefore may in the future be an important factor that can be manipulated to reduce cancer spread.

My participation in exciting high quality research with MARG (the Metastasis and Angiogenesis Research Group) has enabled me to submit abstracts as first author to two international conferences, the British Association of Surgical Oncologists and the San Antonio Breast Cancer Symposium. I will shortly be submitting my research findings for publication.

## VALIDATION OF A FUNCTIONAL KNEE STABILITY ASSESSMENT SYSTEM USING BODY WORN SENSORS

**HENRY GOODIER**

Imperial College London

The RCS award supported my intercalated BSc at the MSK (Musculoskeletal) lab in Charing Cross Hospital with Dr Jeroen Bergmann and Professor Alison McGregor. The aim of my project was to further research in qualitatively measuring stability. We created a new polymer-based sensor, and integrated it into normal clothing. This allowed measurements to be taken at the knee, and creates a platform for a sensor that could be worn at home. The new system was compared



Henry (left) and his supervisor Jeroen Bergmann holding the new Imperial QMU polymer sensor

to Vicon (a lab-based optical tracking system) and was shown to yield similar results.

I am very grateful for the support I received and for the opportunity to experience a more scientific aspect of clinical medicine. It gives me an insight into the effort required to make incremental gains towards evidence-based therapy, and inspires me to contribute more towards research.

## CLINICAL ANATOMY OF THE PSOAS AND ILIACUS MUSCLES

**MATTHEW GRAY**

University of Leeds

In receiving the College's generous award I was given the invaluable opportunity to undertake an intercalated BSc in anatomy, which I recently completed at the University of Leeds.

As part of a research project in collaboration with Sheffield Children's Hospital, I studied the clinical anatomy of the hip flexors, in particular the surgical treatment of contrac-



Having a 'humerus' time! Matthew (right) and his supervisor Dr James Pickering (left) at the Institute of Membrane and Systems Biology, University of Leeds

tures in cerebral palsy patients. Surgical approaches were observed in patients and reproduced in the cadaver where structures at risk were identified.

Additionally, I was fortunate enough to benefit from training in the theory and practice of medical education and was given the opportunity to formally teach students in their first and second year of study.

I greatly enjoyed the year of study, which reinforced my interests in both surgery and research. I am extremely grateful for the College's support.

## TOMORROW'S SURGEONS: BALANCING THE PUBLIC AND PRIVATE INTERESTS OF MEDICAL STUDENTS

**HARRIETT LATHAM-CORK**

University of Bristol



Harriett at her graduation

I am very grateful to the College for the generous award. It provided invaluable financial assistance towards my living and training during my intercalated BSc in bioethics. Intercalation allowed me to pursue my interest in medical ethics and medical law, deepen my knowledge base, improve my research skills and interact with experts in the field.

My project focused on the ethical and legal issues of the active participation of medical students in surgery. I am currently co-authoring a paper based on my dissertation with the course director, with an aim to publish in the coming year and present post-publication.

## FACTOR XIII VAL34LEU AND DIABETES IN MALE SUBJECTS WITH ABDOMINAL AORTIC ANEURYSM

HANNAH LEE EVANS

University of Leeds

The RCS award allowed me to investigate the prevalence of FXIII Val34Leu polymorphisms within abdominal aortic aneurysm (AAA) and control groups and the correlation with diabetes mellitus. The effect of the polymorphism on AAA survival was assessed. Real-time polymerase chain reaction determined the phenotype and the results were compared with the clinical data collected through the Leeds Aneurysm Development Study.

I found that there were more subjects with diabetes mellitus and at least one leucine allele than subjects with diabetes mellitus and no leucine alleles in the AAA group. I also found that the survival of AAA subjects was worse in the subjects with at least one leucine allele. Together, my data suggest that possession of at least one leucine allele may lead to a worse outcome and may be an additional risk factor for AAA patients. These results may help to develop a better understanding of AAA disease progression.



Hannah in the laboratory with her supervisor, Dr Robert Airens

## COMPARATIVE ANALYSES OF THE NEURAL STEM/PROGENITOR CELLS NICHE IN THE SPINAL CORD OF ADULT HUMAN AND MOUSE

NICK MANI

The University of Sheffield Medical School

As a part of Bachelor of Medical Sciences degree, I carried out a research project, which was funded by RCS, titled *Comparative Analyses of the Neural Stem/Progenitor Cells Niche in the Spinal Cord of Adult Human and Mouse*. From carrying out such research, I established and optimised a novel tissue culture system for studying the neural stem/progen-



Nick (right) with supervisor Mr Laurence O'Connor-Read (Neurosurgeon SpR)

itor like cells niche in adult human spinal cord *ex vivo*, which is very likely to be published. My preliminary analyses of the adult human and mouse spinal cord tissue cultured by such system demonstrated that, once stimulated, neural stem/progenitor like cells have the potential to proliferate and migrate away from their niche. In the year, I also improved my statistical analyses as well as increasing my understanding of research principles, including ethics.

## GAIT CHARACTERISATION OF OSTEOARTHRITIC PATIENTS USING AN INSTRUMENTED TREADMILL

ROSALIND MARSHALL

Imperial College London

Over the past year I have been researching the change in function following knee arthroplasty, and how best to present these data. I recruited and assessed 42 patients preoperatively (21 TKA, 21 UKA) using the instrumented treadmill at the Charing Cross MSk lab. I presented a poster on this preoperative work at the British Association of Surgery of the Knee annual meeting.

Twenty-eight patients (12 TKA, 16 UKA) returned for a six-month postoperative re-assessment. Results showed significant improvement following surgery towards normal. My work also confirmed that an instrumented treadmill may be used to compare the efficacy of different interventions. In addition, I developed a method of easily visually analysing multiple ground reaction force data from the treadmill. This novel method, which creates a 3D graph of a patient's performance at different speeds and times, has been taken on in the lab, and is being developed further.



Rosalind (right) and fellow treadmill researcher, Victoria Manning

## A STUDY INTO THE USE OF WEARABLE TECHNOLOGY TO MONITOR AND AID COMPLIANCE WITH KNEE REHABILITATION CLASSES

**DENISE OSEI-KUFFOUR**

Imperial College London



Supervisors Professor Alison McGregor (far left) and Dr Enrica Papi (left) with Denise (right)

I am grateful to the College for their financial support during my Inter-calated BSc in surgery and anaesthesia at Imperial College. With funding from the College, I was able to undertake a study in the

Department of Surgery and Cancer, Charing Cross Hospital, investigating the use of body-worn sensor devices to monitor the performance of knee osteoarthritis rehabilitation exercises. The accuracy and reliability of two novel sensors designed by bioengineers at Imperial were compared with commercial sensors and validated against gold standard tools.

The results are promising and so we will be conducting further research into the material properties of the sensors alongside patient focus meetings to maintain a future patient-centred design. My first exposure to the research environment has been an enjoyable one. I've been introduced to new software and research techniques and feel motivated to pursue a future career in research.

## CHARACTERISATION OF ANTIBODY RESPONSES TO GAL POSITIVE AND GAL FREE BIOLOGICAL HEART VALVES

**NEHA NATASHA PASSI**

University College London

I am extremely grateful both for the generous award from the RCS and for the teaching and guidance I received from my supervisors, Professor Christopher McGregor and Dr Guerard Byrne, which have enabled me to have a successful and enjoyable iBSc research project.

My project contributed to ongoing research looking at the role of the major xenogeneic antigen  $\alpha$ Gal (galactose,  $\alpha$ ,1,3 galactose), expressed on all currently used replacement biological heart valves, in mediating antibody responses to valve tissue. These antibody responses may in turn contribute



Neha with her supervisors Professor Christopher McGregor (left) and Dr Guerard Byrne (right)

to valve degeneration. Overall, a better understanding of the mechanisms responsible for valve degeneration may lead to the development of better, more durable replacement valves for patients.

I hope that this wonderful learning experience serves as a platform for a future career in academic medicine.

## THE USE OF ROBOTIC ENDOVASCULAR CATHETERS IN THE FACILITATION OF TRANSFEMORAL AORTIC VALVE IMPLANTATION

**RADOSLAW A RIPPEL**

Imperial College London

Trans-femoral aortic valve implantation (TAVI) allows replacement of heart valves through the arterial system without opening the patient's chest but recent trials have raised concerns that TAVI may increase risk of stroke.

This project looked at a potential to reduce the risk of stroke by using a surgeon-guided robotic catheter. We used a silicone model to simulate the TAVI procedure and asked surgeons of varied experience to perform the simulation using robotic and conventional techniques. Overall, the time taken for passage to the valve using a robotic catheter was increased



Radoslaw with his project supervisor Mr Colin Bicknell

and the distance travelled was not different. The number of wall hits decreased implying the method may reduce the risk of dislodging particles into the brain. During crossing the valve there was no difference between techniques.

Use of robotic technology is feasible in the initial stages of TAVI and some parts of the procedure may be safer.

# INVESTIGATING THE EFFECT OF DECORIN ON GLIOBLASTOMA MULTIFORME GROWTH AND ANGIOGENESIS

HANNAH SHEREEF

University of Birmingham

Glioblastoma multiforme is the commonest and most aggressive brain cancer in adults. There is no cure; the treatments currently available can prolong life by only a few months and can have serious side effects. Surgery can be done to remove the tumour, but owing to its branching nature, it is impossible to remove all the cancer cells.

Decorin is a drug that specifically targets growth factor molecules that are abundant in glioblastoma but not in normal cells.

The RCS award helped to fund my laboratory-based research project, which showed that decorin reduced the growth and formation of new blood vessels in a cancer model of glioblastoma.



Hannah plating glioblastoma cells isolated from patient tumours for cell culture

My work will help set up a clinical trial to test the drug in patients with glioblastoma. It is hoped that by stopping the growth of the remaining cancer cells, decorin will improve the survival of patients after surgery without causing many side effects.

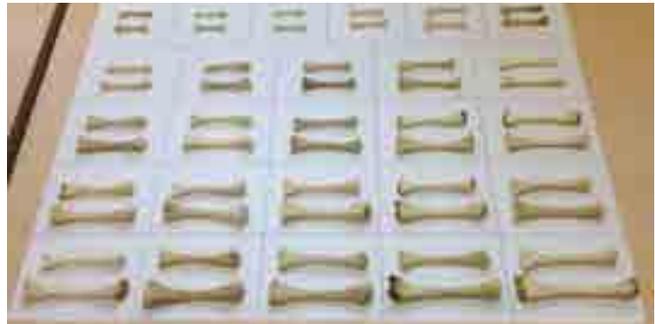
# FOETAL LIMB BONE TRABECULAR ARCHITECTURE IS NOT SEXUALLY DIMORPHIC

CHARISON TAY

Imperial College London

Even before menopause, women have an increased fracture risk owing to poorer trabecular microarchitecture and bone quality. My project investigated whether this difference is already present during in utero development. Understanding when this sexual divergence in trabecular microarchitecture occurs is important as it could allow scientists to identify the factors that influence this pattern of trabecular development and introduce measures to reduce fracture occurrence in later life. I scanned 52 fetal humeri and femora of male and female specimens from a range of gestational ages using micro-computed tomography and compared the trabecular structure using 6 structural bone parameters: bone volume fraction, thickness, number, structure model index, connectivity and anisotropy.

I am grateful for the generous grant, which paid for the scans and the transportation cost of the fetal specimens. An abstract has also been accepted as a poster presentation at the Bone Research Society / British Orthopaedic Research Society Joint Conference in Oxford 2013.



Collection of fetal specimens from the University of Liverpool

# TRAINING OF SURGICAL AND ANAESTHESIA STAFF IN SIERRA LEONE: A DESCRIPTIVE STUDY

EMILY VAUGHAN

University of Birmingham

This research project investigated the training of surgical and anaesthesia staff in the west African nation of Sierra Leone. This post-war, donor-dependent nation of 6 million has a critical shortfall in surgical and perioperative care with previous research demonstrating an unmet surgical burden of 25%, and an extreme lack of equipment and resources. This study was the first investigating the training and skill set of both surgical and anaesthesia staff.



Operating room, half in the open air



Emily outside one of the provincial hospitals being surveyed

The research team (consisting of a UK and Sierra Leonean medical student with support from the Johns Hopkins team in Sierra Leone) travelled to 10 out of the 23 government hospitals across the country interviewing staff and distributing questionnaires. Overall 51% of surgical staff and 55% of anaesthesia staff in government hospitals nationally were accessed in this study. Results have provided an evidence base for healthcare policy makers and the future of surgical training in Sierra Leone.

# CREEP DEFORMITY OF VERTEBRAL BONE

ELEANOR FRANZISKA ZIMMERMANN

Peninsula College of Medicine and Dentistry

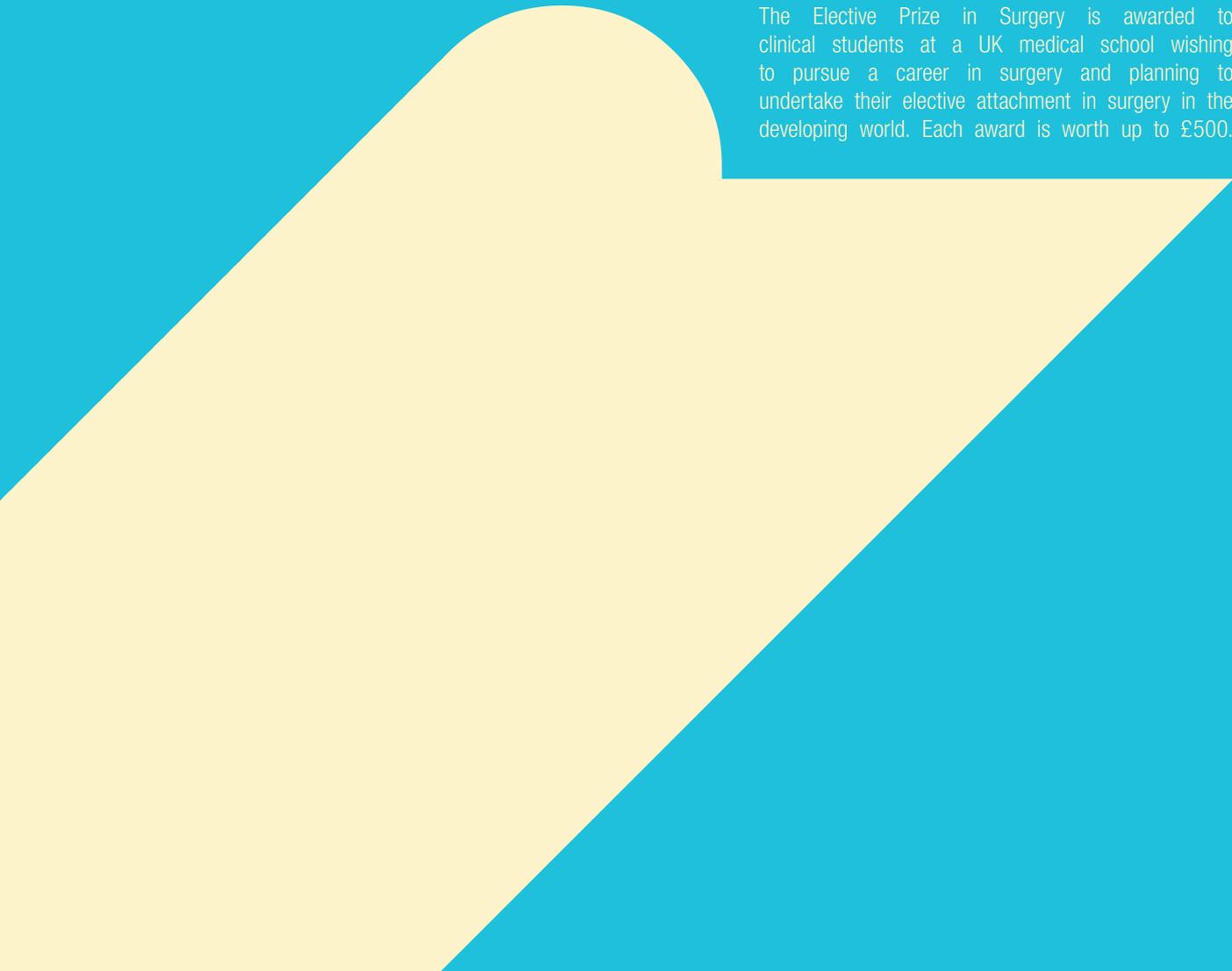
This grant was awarded towards my musculoskeletal research, which I carried out under the supervision of Professor Michael Adams and Dr Phil Pollintine at the University of Bristol.

My research focused on the micro-architectural properties of creep deformity in human vertebral bone, which can contribute to vertebral deformity including senile kyphosis. Creep deformity is a time-dependant deformity thought to be caused by small fractures in bony architecture. We further tested a novel staining method using barium precipitation and microCT analysis and we are preparing to publish our research in a peer-reviewed journal.

I have found it invaluable to gain direct research experience under expert supervision and I have thoroughly enjoyed my time here. The skills I have developed over these months will undoubtedly benefit my future surgical training in which research will play an integral role, and I am extremely grateful to the RCS for this generous award.



Eleanor Zimmermann (far right) and the research team: Mr Priyan Landham, Dr Trish Dolan and Professor Micheal Adams



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.

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## TRAUMA AND ORTHOPAEDICS IN THE DEVELOPING WORLD

### ADAM MOHSAN ALI

MEDICAL SCHOOL: University of Oxford  
SITE OF WORK: Kilimanjaro Christian Medical Centre, Moshi, Tanzania

My elective period in the Department of Orthopaedics at Kilimanjaro Christian Medical Centre (KCMC), Tanzania, was a truly amazing experience. The variety of cases was astonishing, from victims of crocodile and buffalo attacks to road traffic accidents and children who sustained fractures after falling out of mango trees. I was able to assist in many operations and learnt how to apply plaster casts and manage a variety of wounds. Moreover, I came to appreciate some of the immense challenges faced by surgeons in the developing world, both in terms of the operative equipment available and the facilities for pre- and postoperative care.



Wound management (Adam dressing the wound of a patient with a complex fracture)



Adam assisting in the operating theatre (this patient was one of the many arriving daily at KCMC with serious injuries following a road traffic accident)

## TRAUMA SURGERY IN SOUTH AFRICA

### MELANIE BUCHMANN

MEDICAL SCHOOL: Newcastle University  
SITE OF WORK: Chris Hani Baragwanath Hospital, Johannesburg, South Africa



Melanie (second on left) and her colleagues after a 30-hour night shift.



Sign at the entrance of the trauma unit.

I organised my elective at Chris Hani Baragwanath Hospital (Bara) in Johannesburg. Bara is the largest hospital in the southern hemisphere and is famous for its exposure to a great variety of trauma cases. My tasks ranged from inserting chest drains, suturing stab wounds on my own and assisting during trauma and skin graft surgery. I also attended the *Advanced Trauma Life Support*<sup>®</sup> (ATLS<sup>®</sup>) course during my elective in order to refine my acquired surgical skills. I gained plenty of experience and would truly recommend an elective such as this to others. My elective consolidated my aspiration to become a trauma surgeon working in challenging environments.

## ELECTIVE IN SURGERY WITH THE CINTERANDES FOUNDATION IN ECUADOR

**SALMA KAMALEDEEN**

MEDICAL SCHOOL: King's College London School of Medicine  
 SITE OF WORK: The Cinterandes Foundation, Cuenca, Ecuador

I spent my elective with the Cinterandes Foundation in Ecuador, a non-governmental, non-profit organisation, which operates a mobile surgical unit that transcends economic and geographical barriers to health. The team, composed of local volunteer surgeons, an anaesthetist and assisting medical students, travels to an impoverished Ecuadorian town to perform procedures such as laparoscopic cholecystectomies (removal of the gallbladder) and hernia repairs in an operating theatre in a converted truck. It was inspiring and refreshing to witness a successful solution to the problem of lack of access to surgical care that can, with similar dedication and good organisation, be applied elsewhere in the developing world.



Salma with the team in front of the mobile surgical unit after a day of surgeries (third from left)



Salma assisting with surgery inside the surgical truck (far right)



A patient is brought down from the surgical truck following their operation

## ELECTIVE IN JOHANNESBURG

**SAM KYUNG MIN LEE**

MEDICAL SCHOOL: University of Southampton  
 SITE OF WORK: Chris Hani Baragawanth, Johannesburg, South Africa

South Africa is a popular destination for medical electives and was full of jobs for elective students. As hospitals were short of staff and frequently overcrowded, interns were very glad when elective students offered help. Theatre was the first place I headed towards when not required on the wards, and I gained some experience of assisting with operations. I was on call at least twice a week with weekends included, and was given the chance to manage the patients. Bloods, imaging, simple suturing and admission documentations were skills I quickly picked up at Baragawanath hospital. I would thoroughly recommend this experience to those who wish to be hands-on during their elective.



Top: Sam clerking a patient

Bottom: Sam with other elective students

## SURGERY AND OPHTHALMOLOGY IN KENYA AND A SQUAMOUS CELL CARCINOMA TRIAL

**ESME REBECCA LONGBOTTOM**

MEDICAL SCHOOL Barts and the London Medical School, QMUL  
 SITE OF WORK Kenyatta National Hospital, Nairobi, Kenya



Patients waiting at the outreach clinic

During my placement in Kenya my time was spent in general surgery and ophthalmology, in clinics, theatre and the wards. I also attended an outreach surgical visit to a hospital in a rural area of Kenya. The team primarily performed cataract surgery. The density of the cataracts before seeking treatment was markedly more advanced than in the UK. I was also involved in helping set up sample collection for a clinical trial for conjunctival squamous cell carcinoma, which has a high incidence in east Africa. The project involves investigating samples for HIV and HPV infection with particular interest in HPV genotype of infection.



Rebecca on outreach visit in theatres assisting with cataract surgery

## PROJECT HARAR COMPLEX FACIAL RECONSTRUCTION SURGICAL MISSION 2012, ADDIS ABABA,

**FIONA MCCLENAGHAN**

MEDICAL SCHOOL Barts and the London School of Medicine and Dentistry  
 SITE OF WORK Yekatit 12 Hospital, Addis Ababa,

I travelled to Ethiopia with a charity providing treatment for young people with complex facial deformities. I was able to assist in theatre but my main role was in coordinating post-operative care. Working as the only medic, often without water or electricity, was challenging. The trip highlighted something often overlooked in undergraduate surgical training; the importance of good nutrition, wound dressing and dealing promptly with infection in order to avoid surgery failing postoperatively. This experience enabled me to see the breadth of conditions within maxillofacial surgery and has confirmed my ambition to pursue a career in this specialty.



In the operating theatre at Yekatit 12 Hospital, Addis Ababa, with Dr Anisha Sukha (FY2 UCH).



Mandibular distraction of a three-year-old patient at Yekatit 12 with Professor McGurk (OMFS Consultant Guy's Hospital)



Some patients after surgery



Farewell party with the Ethiopian nursing staff and some of the postoperative patients

## MEDICAL ELECTIVE IN MBARARA, UGANDA

**JAMES O'DONOVAN**

MEDICAL SCHOOL: Newcastle Medical School  
SITE OF WORK: Holy Innocents Children's Hospital and MUST, Mbarara, Uganda



Checking sutures from the previous day

The Preiskel Prize awarded by the RCS allowed me to spend my elective placement in Uganda, gaining hands-on experience in paediatric surgery. The majority of my time was spent in theatre and outpatient clinics; however, I also spent time with a surgical outreach team where we visited local villages to provide medical support. The team were all extremely welcoming and very helpful, providing teaching opportunities and allowing me to assist in surgery. By the end of my visit I felt I had a much greater insight into the challenges faced by surgical services in Uganda. My experience has strengthened my desire to work in the developing world and I would highly recommend Uganda as an elective destination to anyone with an interest in surgery.



Emergency tracheostomy on a baby girl

## FIVE MOMENTS FOR HAND HYGIENE

An audit investigating hand hygiene compliance in Southern Regional Hospital, Belize, compared with World Health Organization (WHO) guidelines

**OLIVER SHASTRI**

MEDICAL SCHOOL: Newcastle Medical School  
SITE OF WORK: Southern Regional Hospital, Dangriga, Belize

Belize is a developing country with a limited medical infrastructure. During my elective I worked in obstetrics and gynaecology, assisting in theatre and delivering medical care within available resources. Hand hygiene is the most cost-effective means of preventing infectious disease.

I conducted a hand-washing audit to review compliance, with a view to help reducing hospital infections. Initial results indicate that the adoption of recommended WHO hand hygiene guidelines would be of significant benefit.

By practising medicine in the developing world, I have undoubtedly broadened my clinical perspective and hope to apply these skills after I qualify.

Top left: Oliver assisting in an emergency Caesarean section  
Top right: A wash basin adjacent to outpatients



## COMPLICATIONS OF VENTRICULOPERITONEAL SHUNTS IN A TEACHING HOSPITAL

**ERDINC SOYLU**

MEDICAL SCHOOL Barts and The London School of Medicine and Dentistry  
SITE OF WORK Hacettepe University Hospital, Ankara, Turkey

I organised my elective at Hacettepe University Hospital, which is one of the largest neurosurgery units in central Turkey. During my elective I was able to attend clinics and accident and emergency to help clerk the great variety and high volume of patients, most of whom travelled as far as 600 miles from socioeconomically deprived areas of the country. I was able to assist in neurosurgical operations, including tumour resections and insertion of ventriculoperitoneal shunts, allowing me to gain skills in suturing and the use of neurosurgical microscopes. This was a unique opportunity for me to experience the practice of neurosurgical care in one of the emerging economies of the world.



Neurosurgery intensive care unit, running at near full capacity



Residential area, Ulus, located within a half mile distance from Hacettepe University Hospital



Erdinc (left) with Dr Sahin Khaniyev (neurosurgery resident)

## MOBILE SURGERY IN ECUADOR

**SEBASTIAN MIGUEL TOESCU**

MEDICAL SCHOOL Bristol  
SITE OF WORK Cuenca, Ecuador

I worked with the Cinterandes Foundation in Ecuador, which has a long-established history of performing mobile surgery across the country. A custom-built mobile operating theatre is used to perform simple but timely and effective operations. I assisted the travelling surgeons in many cases, and I came to know the villagers and their stories well. I really enjoyed my time spent working with the foundation; not only was it an excellent learning experience for basic surgical technique, but it was also a privilege to witness the gratitude with which medical care is received in parts of the developing world.



Sebastian (right) assisting with an elective umbilical hernia operation



Sebastian (left) closing an elective inguinal hernia operation

# GENERAL SURGERY IN VIETNAM

## ELEANOR FRANZISKA ZIMMERMANN

MEDICAL SCHOOL Peninsula College of Medicine and Dentistry  
SITE OF WORK Cho Ray Hospital, Ho Chi Minh City, Vietnam



Eleanor being taught how to close a laparotomy

My time in Cho Ray Hospital was divided between assisting in theatre and attending postoperative ward rounds while I collected prospective data for an audit on postoperative complications. The financial implications of a hospital admission for the families of patients and limited health education means late-stage malignancy is the most common elective presentation, and sadly the patient care is largely guided by the cost, not availability, of resources. This elective provided an invaluable insight into the challenges of healthcare provision, as well as offering an outstanding hands-on experience, and I would thoroughly recommend it to any student with a passion for surgery.



A typical afternoon on a busy postoperative ward

# 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 our Development Office on 020 7869 6086, or by email at [fundraising@rcseng.ac.uk](mailto: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

Arthritis Research Trust  
Ballinger Charitable Trust  
Bedford Memorial Trust  
Bowel Disease Research Foundation  
CA Redfern Charitable Foundation  
Cancer Research UK  
Cardy Beaver Foundation  
DBP Trust  
Dunhill Medical Trust  
Enid Linder Foundation  
Facial Surgery Research Foundation (Saving Faces)  
Family of the late Stefan and Anna Galeski  
Frances & Augustus Newman Foundation  
Fullbright Commission  
George Drexler Foundation  
George Dudley Herbert Charitable Trust  
Golden Bottle Trust  
Grand Lodge of Freemasons 250th Anniversary Fund  
Henry Lumley Charitable Trust  
H&S Charitable Fund  
Joseph Strong Frazer Trust  
Leeds Surgical Research Trust  
Mary Kinross Charitable Trust  
Orthopaedic Research UK  
Philip King Charitable Settlement

Rosetrees Charitable Trust  
Royal Arch Masonry  
Shears Foundation  
Worshipful Company of Cutlers  
Wyndham Charitable 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  
Elizabeth Rashleigh Legacy  
Geoffrey G T Fletcher Legacy  
Guyatt Legacy – Sir Alan Parks Research Fellowship  
Gwendoline Shrimpton Legacy  
Harold Bridges Bequest  
Harry S Morton Fund

Jeanette Denker Legacy  
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  
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)  
Cancer Research UK (CRUK)  
Get-A-Head Charitable Trust  
Prostate Cancer UK



# 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: [fundraising@rcseng.ac.uk](mailto:fundraising@rcseng.ac.uk) or call 020 7869 6086.**

# PRIZES AND 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.

## **Anna and Stefan Galeski Travelling Fellowship 2013**

The fellowship paid for the two winners to go to the RCS triennial presidential trip to Brazil and Peru to teach skills and give papers from 18 May to 2 June 2013.

### **Recipients**

Julia Blackburn  
Mekhola Mallik



Julia Blackburn (second from left) teaching in a skills workshop in Rio



Mekhola Mallik (fourth from right) teaching on skills workshop in Rio

## **Ethicon Foundation Fund**

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

### **Recipients May 2012**

Ravinder Natt  
David Bunting  
Behrad Elmiyeh  
Hussain Anthony Kazi  
Ivan Timofeev  
William Townley

### **Recipients October 2012**

Siong-Seng Liao  
Philip Clamp  
Andrew Choong

### **Recipients May 2013**

Nick Howells  
Hesham Al-Khateeb  
Nigel D'Souza

## **Colledge Family Memorial Fellowship Fund**

The Colledge Memorial Travelling Fellowship was established by 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 study for a period overseas.

#### Recipients 2012

James Wolfe Rainsbury  
Sukhbir Ahluwalia  
Behrad Elmiyeh

#### Sir Ratanji Dalal Research Scholarship

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

#### Recipients 2012

Caris Elizabeth Grimes  
James A Turner

#### HJ Windsor Prize

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

#### Recipients 2012

Andrew Choong

#### Ronald Raven Barbers Award

The Ronald Raven Barbers Award was established by the generosity of The Worshipful Company of Barbers (at Ronald Raven's bequest). The award is aimed at assisting trainee surgeons going abroad to develop their individual skills by special education or training of an innovative nature. Particular weight is given to the excellence of the applicant, the innovative qualities of the work to be done and the relevance

of such work to the ultimate benefit of patient care.

#### Recipients 2012

Naren Basu  
Siong-Seng Liao  
Ravinder Natt

#### Recipients 2013

Alan Cheung  
Nikolas Jagodzinski and Alistair Philips

#### The Rosetrees Trust Prize

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

**Winner:** Neil Barua: *Direct delivery of drugs to the brain: a novel strategy for the treatment of Alzheimer's Disease.*

**Runner up:** Arul Ramasamy: *Saving Private Tom: Preventing amputation from blast injury.*

**Runner up:** Christopher Ray: *Novel techniques in transplantation: – oxygenation and a new era for solid organ preservation.*



Neil, Arul and Christopher receiving their prizes at the College Diplomates' Ceremony on Wednesday 23 January 2013

# LECTURES DELIVERED IN 2012–2013

## Hunterian, Arris and Gale, Zachary Cope, Kinmonth & Lionel Colledge Memorial Lectures

Hunterian	Mr Aaron Ranasinghe, Society of Cardiothoracic Surgery, 20 April 2012 <i>Metabolic and hormonal substrate support in cardiac surgery</i>
Hunterian	Mr Alan Osborne, BSG/DDF, 18 June 2012 The impact of gut hormones and metabolic surgery
Hunterian	Mr Andrew Renehan, ACPGBI, 02 July 2012 <i>The role of obesity in risk of incidence and progression of surgical cancers</i>
Hunterian	Mr Alexander Fitzgerald O'Connor, BACO, 04 July 2012 <i>Laser doppler vibrometry: the interface between micromechanics and surgical otology</i>
Hunterian	Mr Daniel Perry, BOA, 12 September 2012 <i>A century of Perthes' Disease: unravelling the enigma</i>
Kinmonth	Professor Peter Rothwell, Vascular Society Meeting, 30 November 2012 <i>Carotid interventions: past, present and future</i>
Zachary Cope	Professor David Neal, SARS, 01 January 2013 <i>The androgen receptor and prostate cancer</i>
Arris & Gale	Mr Aziz Momin, SCTS, 19 March 2013 <i>Exploring the role of leptin and C-reactive protein in saphenous vein endothelial dysfunction</i>
Lionel Colledge Memorial Lecture	Mr James Russell Tysome, Royal Society of Medicine, 12 April 2013 <i>360° skull base surgery: a US perspective</i>

# 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](http://www.transplantevidence.com)).

The CET has been involved in a number of projects since its creation, one of which has been to establish a registry of all randomised controlled trials (RCTs) 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*, which was replaced by the *Transplant Library* in January 2008.

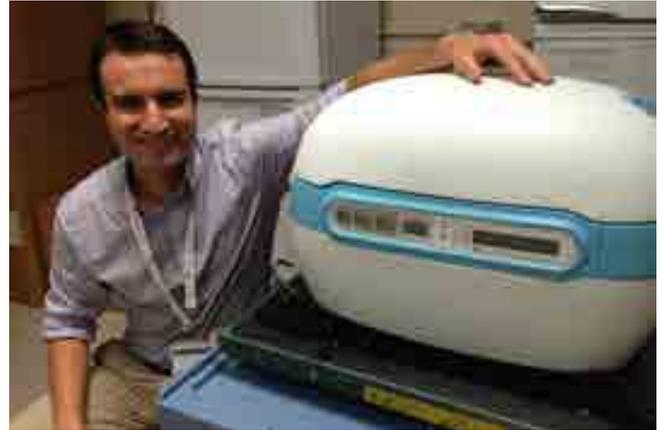
The *Transplant Library* is an electronic library of all RCTs in solid organ transplantation from 1970 to the present, including systematic reviews that are regarded as being of reasonable quality. The development of an electronic library has been a major project and includes all RCTs in solid organ transplantation. It became available to all members of the European Society of Transplantation, the British Transplantation Society, Scottish NHS libraries and various other medical school libraries.

More recently, Evidentia Publishing has taken on the library and is currently in the process of marketing and providing free trials to expand awareness of the *Transplant Library*.

It is often asked why we need an electronic library in transplantation. If we remember that RCTs and systematic reviews and meta-analyses of RCTs are level-one evidence in any medical discipline then the aim is to develop an 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 and subspecialist libraries of RCTs some 30 years ago. This is the first!

## THE AIM IS TO DEVELOP A LIBRARY THAT COULD PRODUCE REFERENCES IN MINUTES RATHER THAN HOURS.

In an analysis of the methodology of RCTs 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



John O'Callaghan, research fellow in Oxford, with a kidney pump

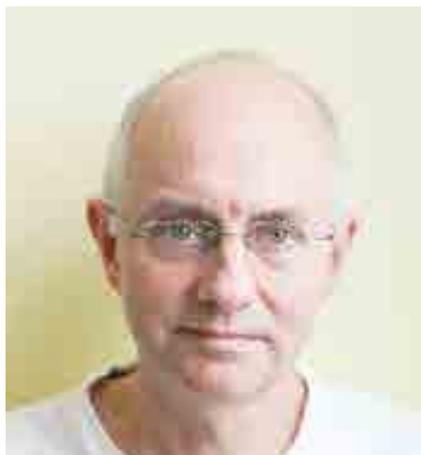
reached with European Society for Organ Transplantation (ESOT) that the CET would become the knowledge centre for ESOT and would offer advice in the design of RCTs, as well as provide assistance with the reporting of RCTs. Trials that were methodologically sound in design would be given ESOT/CET accreditation.

Some recent publications include *Hypothermic machine perfusion versus static cold storage for kidney allograft preservation: a systematic review and meta-analysis* (John O'Callaghan), *Compliance to the CONSORT statement of randomized controlled trials in solid organ transplantation: a 3-year overview* (Liang Liu) and *Alemtuzumab induction therapy in kidney transplantation: a systematic review and meta-analysis* (Robert Morgan).

Karina Pall joined the CET in February 2013 as a research associate. Simon Knight was appointed as an academic clinical lecturer within the Nuffield Department of Surgical Sciences, which will allow him more time for his research

activities during his continuing surgical training. John O'Callaghan secured a numbered training post in surgery (ST3) within the Oxford Deanery and will commence this appointment later this year. By this time he expects to have completed his DPhil thesis, which is currently on track. Robert Morgan, who is choosing the medical path, has secured a core training post in medicine in the London Deanery and Philip Macklin has been appointed to an academic training fellowship in Pathology within the Oxford Deanery.

# PAST FELLOWS: HOW RESEARCH AWARDS HAVE HELPED CAREERS



**Julian McGlashan**

Consultant Laryngologist and Head  
and Neck Surgeon  
Department of Otorhinolaryngology  
Queen's Medical Centre Campus  
Nottingham University Hospitals

I was lucky enough to be a recipient of the first Royal College of Surgeons GLAXO Research Fellowship twenty years ago. At the time I was senior registrar in otorhinolaryngology at Guy's and St Thomas' Hospital with a particular interest in laryngology. The fellowship paid for my basic salary and enabled me to obtain further funding, in the form of a small project grant from the Medical Research Council (MRC) for a research assistant and consumables.

The aim of my project was to explore the possibility of obtaining three-dimensional surface measurements of the mucosal wave motion of the vocal folds during phonation. Although the three-dimensional analysis element did not translate into a practical application, the research project did result in a commercial product: the Laryngostrobe (Laryngograph Ltd).

There is no question that the research fellowship played a major part in the development of my professional career. It allowed me to develop a much better understanding of vocal physiology and I would like to think has made a much better clinician as a result. I now head one of the leading comprehensive and multi-professional voice disorders services in the UK at the Queen's Medical Centre campus in Nottingham. I shall have a lifelong curiosity about the voice in both health and disease and I continue to have an active research portfolio, particularly in voice measurement, laryngeal endoscopic imaging and understanding the singing voice.

The fellowship also enhanced my appreciation of multi-professional collaboration and I still find the meetings and conferences where I can meet other voice specialists (such as speech therapists, singing teachers, osteopaths, engineers and scientists) to be the most stimulating and fruitful. I am forever indebted to the College, GLAXO, the MRC and all the colleagues I have had the privilege of working with over the years.

I was privileged to be awarded one of the first RCS research fellowships in 1993–1994. I undertook research at the Royal National Orthopaedic Hospital in Stanmore under the supervision of Professor George Bentley looking at joint replacement failure. It was a very stimulating year where I learnt much about the requirements for basic research. This has been very useful in my career as a consultant orthopaedic and hand surgeon.

I have continued to undertake research, particularly in the Centre for Orthopaedic Biomechanics at the University of Bath, and in conjunction with a range of other researchers in Bath and outside. We have made some useful progress studying wrist biomechanics including looking at how people fall and, from this, how they avoid distal radius (wrist) fractures. In particular the training I received taught me how to appraise and assess research papers. This has been especially useful now I am the Editor-in-Chief of the *Journal of Hand Surgery (European Volume)*.



**Grey Giddins**

Consultant Orthopaedic and Hand  
Surgeon

# CLINICAL EFFECTIVENESS UNIT

The Clinical Effectiveness Unit (CEU) was established in 1998 as an academic collaboration between the College and the Department of Health Services Research and Policy at the London School of Hygiene and Tropical Medicine (LSHTM). The CEU is largely self funded by external project grants and contracts, although it receives an annual contribution from the College's research funds and the College underwrites four senior academic posts within the school.

The CEU 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 specialty associations. The unit has 16 staff members, 8 of whom are academic staff members of the school. The staff have a variety of backgrounds (eg health services research, epidemiology, medical statistics, clinical medicine, public health and social science), which ensures a multi-disciplinary outlook and approach. David Cromwell, Senior Lecturer at the LSHTM, has been the CEU director since May 2011.

## Audit and research

The core activity of the CEU is to conduct national clinical audits and research projects. In each clinical audit, the aim is to assess specific standards of clinical practice, focusing on the structure, process and outcome of care. Many of these national audits are funded as part of the government's National Clinical Audit and Patient Outcomes Programme (NCAPOP).

The National Oesophago-Gastric Cancer Audit is one of the national clinical audits undertaken within the CEU. The audit was re-established in 2011 (the original audit ran from 2007 to 2010), and began collecting prospective data on patients diagnosed with oesophageal or stomach cancer from 1 April 2011. The audit also included patients diagnosed with oesophageal high-grade dysplasia from 1 April 2012. Its first annual report was published in June 2012. This described the findings of an organisational audit, as well as long-term outcomes among patients in the first audit that had undergone curative surgery. It found that considerable progress had been made in the reorganisation of services for oesophago-gastric cancer since the previous survey in 2007, with the majority of cancer networks and NHS hospitals having access to key therapies (surgery, oncology and therapeutic endoscopy). In addition, most cancer centres achieved the minimum number of surgeons performing surgical resections. This



The Clinical Effectiveness Unit, May 2013

standard reflected evidence that postoperative mortality was lower among patients treated in hospitals with larger surgical teams.

The 2012 annual report also gave estimates of one- and three-year survival after curative surgery for patients with different types of tumour.

- » For oesophageal squamous cell tumours, the proportion of patients undergoing curative treatment who survived for 1 and 3 years were 73% and 41%, respectively.
- » For oesophageal adenocarcinoma tumours, the proportion of patients who survived for 1 and 3 years were 78% and 46%, respectively.
- » For gastric tumours, the proportion of patients who survived for 1 and 3 years was 78% and 49%, respectively.

These results illustrate the relatively poor prognosis for these cancers compared with other types of tumour (eg breast cancer). However, the length of survival was found to be longer than reported in older studies, and highlights how the reorganisation of cancer services has improved the care delivered to patients.

Survival is an important outcome for patients undergoing surgery for cancer but it can be less relevant for procedures whose principal aim is to improve quality of life. The routine measurement of surgical outcomes such as quality of life is still developing within the NHS, and the CEU is continuing to contribute to this important area of work. In 2012, this contribution was most notable in relation to our collaborative work with colleagues at the LSHTM on using patient-reported outcomes to evaluate healthcare. One aspect of this work was to examine if assessments of performance were influenced

## BOX 1: MAJOR CEU AUDITS UNDERTAKEN IN 2012

### 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 2012 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's specialist commissioners involved in cleft care.

### UK and Ireland Liver Transplant Audit and the UK Intrathoracic Transplant Audit

These audits are carried out in collaboration with UK Transplant. They accrue and validate data from all transplant centres in the UK and Ireland since 1994 and 1995, respectively. The CEU is responsible for the analysis and interpretation of the data on post-transplant outcome for each participating centre stratified for major risk factors. The audits were funded by the NHS National Commissioning Group for Highly Specialised Services.

by the choice of patient-reported outcome measure (PROM). The study derived scores on disease-specific and generic PROMs for patients having hip replacement, knee replacement or varicose vein surgery, and examined the agreement between various risk-adjusted outcomes such as the mean postoperative score on a PROM, and the proportion of patients achieving a minimum clinically important health gain.

The study found that the proportion of healthcare providers that were rated as having above or below average performance differed considerably between the measures and across procedures. For 243 providers performing hip replacement surgery, whether or not a provider was identified as an outlier depended on which measure was used for 30% of providers. For knee replacement, the choice of measure affected 16% of providers and 40% of providers for varicose



Intraoperative view of oesophagogastrrectomy.

vein surgery. These findings highlight the care with which assessments of surgical outcomes need to be made, and suggest that it may be necessary to use several measures of outcome to describe provider performance. Alternatively, a decision is required on which outcome measure is seen as most important to patients.

A brief description of other major CEU projects undertaken in 2012 is given in **Box 1**.

### Use of routine data sources

During the past decade, the CEU has increasingly used routine data in its audits and for research projects. Much of our work has used the hospital episode statistics (HES) database, which contains records with diagnostic and procedure information for all NHS admissions in England (equivalent databases also exist in Scotland, Wales and Northern Ireland). The major advantage of these administrative databases is that they can provide a timely, national picture of clinical practice.

In 2012, we used HES data to examine reoperation rates among women undergoing breast-conserving surgery (BCS) for breast cancer. Few studies had examined reoperation rates after BCS, and estimated rates ranged from 17% to 68%. We identified 55,297 adult women who had BCS in 156 NHS trusts between April 2005 and March 2008. We found that among women with isolated invasive disease, 18.0% had at least one reoperation. Reoperation was more common among women with a carcinoma in situ (29.5%), and was also more common among younger women.

There was substantial variation among NHS trusts in their risk-adjusted reoperation rates (10th and 90th centiles 12.2%

and 30.2%). This raised questions about the uniformity of the selection criteria for both BCS and reoperation, and highlights the need for initiatives aimed at reducing the risk of reoperation. The current situation is unsatisfactory because a woman's experience of care will depend upon where she is treated, and also because around 40% of women who had a reoperation after BCS ended up having a mastectomy.

Various concerns have been expressed about the quality and completeness of the clinical coding in HES. A theme within various CEU projects has therefore been to combine it with clinical datasets, so that its information can be compared against an independent data source. In 2012, the CEU undertook some work for the National Hip Fracture Database (NHFD) that involved assessing the quality of HES coding for hip fractures. We looked at 40,094 linked NHFD–HES records and found good agreement in terms of the admission day, and the coding of the procedure, and the overall incidence of hip fracture. The reassuring agreement between HES and the NHFD meant that we were able to estimate the number of hip fractures treated in individual English NHS hospitals and their case ascertainment within the NHFD. It also enabled us to develop a method of defining total length of NHS inpatient stay ('superspell') that covered the whole period of acute and post-acute care.

### Teaching

Each year, the CEU runs a number of courses for surgeons and other healthcare professionals on statistics, clinical research methods and evidence-based surgery. They 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 2012

1. Ahmed HU, Hindley RG, Dickinson L, *et al.* M. Focal therapy for localised unifocal and multifocal prostate cancer: a prospective development study. *Lancet Oncol* 2012; **13**: 622–32.
2. Cromwell DA, Mays N. The NHS outcomes framework 2012–3. *BMJ* 2012; **344**: e1,080.
3. Fitzsimons KJ, Mukarram S, Copley LP, *et al.* Centralisation of services for children with cleft lip or palate in England: a study of hospital episode statistics. *BMC Health Serv Res* 2012; **12**: 148.
4. Grosse Frie K, van der Meulen J, Black N. Relationship between patients' reports of complications and symptoms, disability and quality of life after surgery. *Br J Surg* 2012; **99**: 1,156–63.
5. Jameson SS, Baker PN, Charman SC, *et al.* The effect of aspirin and low-molecular-weight heparin on venous thromboembolism after knee replacement: a non-randomised comparison using National Joint Registry Data. *J Bone Joint Surg Br* 2012; **94**: 914–18.
6. Jeevan R, Cromwell DA, Trivella M, *et al.* Reoperation rates after breast conserving surgery for breast cancer among women in England: retrospective study of hospital episode statistics. *BMJ* 2012; **345**: e4505.
7. Johal A, Mitchell D, Lees T, *et al.* Use of Hospital Episode Statistics to investigate abdominal aortic aneurysm surgery. *Br J Surg* 2012; **99**: 66–72.
8. Neuburger J, Hutchings A, Allwood D, *et al.* Socio-demographic differences in the severity and duration of disease amongst patients undergoing hip or knee replacement surgery. *J Public Health (Oxf)* 2012; **34**: 421–29.



1. Jagdeep Rai teaching skills at Birmingham Surgical Society
2. Jared Torkington addressing Welsh Barbers Society
3. The Rt Hon Ken Clarke delivering the opening address at the Brazilian College of Surgeons, Rio
4. Trevor & Lyn Shears with Raveen Sandher in the lab at Newcastle Fertility Centre
5. Chris Peach talking at the North West Surgical Society, Manchester
6. Nobel Prize Winner Sir Martin Evans receiving Honorary Fellowship
7. Liza Osagie teaching skills at Graveney School, Tooting
8. President with students at the Welsh Barbers Society
9. Julia Blackburn, Stefan and Anna Galeski Fellow at Machu Picchu
10. Professor Angelita Habr-Gama receiving Honorary Fellowship in Rio
11. Martyn Coomer and Otto Philipp Braun at skills workshop in Rio
12. Raveen, Trevor and Lyn Shears with supervisor Professor Mary Herbert



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