Surgical Research Report

2019 – 2020

Contents

Chairman's introduction

Last year was the 25th anniversary of the Research Fellowship Scheme founded by Professor Sir Norman Browse and initiated by Professor Sir Peter Morris in 1993. A scheme that is regarded as a real feather in the cap of the College's activities. More than 750 prestigious fellowships have been awarded during this time supported by a large array of charities, foundations and individuals. The scheme continues to attract new fellowships including the UK Stem Cell Foundation, Professor Don Low at Virginia Mason hospital in Seattle, the Institute of Child Health at Great Ormond Street, the Circulation Foundation and most recently the Moondance Foundation, whose munificence is concentrating on improving bowel cancer outcomes in Wales. Blond McIndoe have this year linked with the RCS on plastics surgical projects and we have also seen renewed support from the Freemasons fund, the Enid Linder Foundation, the Shears family, the Newman Foundation, the Rosetrees Trust and the National Joint Registry. In total an astounding £40 million has been donated and administered by the RCS since the scheme's inception.

Professor Tim Rockall
Chair, Research Committee.

This document contains brief reports intended for the lay reader from more than 60 trainee surgeons who have been supported by the award of a Royal College of Surgeons of England Research Fellowship grant during the past two years. They show the breadth of research in all fields of surgery including trauma, cancer and perioperative care with projects in every surgical specialty. They include research into genomics, oncology, immunotherapy and basic sciences as well as clinical outcomes research and investigation of new technologies. Cutting edge fields of research such as stem cells, 3D bioprinting, artificial intelligence and remote monitoring are all well represented. These grants support a salary and some research costs and will often kick-start a project that goes on to attract more funding support from major grant giving bodies such as the Wellcome Trust, Cancer Research UK (CRUK) and National Institute for Health Research (NIHR) to name a few. Fellows are supported in their research aims at major academic centres but also in smaller hospital environments where truly valuable research is being undertaken. The Research Fellowship grants are extremely competitive and each year are considerably over subscribed. The best applications are invited to present their research plan in the form of a poster and the applicants are rigorously challenged by a wide spectrum of examiners to determine those most worthy of support. It is hugely encouraging to observe the impressiveness of the applicants and their projects. It is always the case that we wish we could support more of the projects than we do as they are almost all deserving of support.

There are also reports from six recipients of pump priming grants that aim to support surgeon researchers at the beginning of their academic career to allow them to foster a programme of research with some 'seed corn' funding.

The Clinical Effectiveness Unit (CEU) at the RCS was established in 1998 as an academic collaboration with the Health Services Research Unit of the London School of Tropical Medicine and Hygiene. The five-year partnership agreement has been renewed, which will enable the CEU to continue its role in providing trainee surgeons with research and training opportunities. The CEU produces clinical research that helps to inform health policy and audits practice in the UK. Trainee surgeons are appointed into research posts to undertake large audit projects under the direction of the CEU and its director Professor David Cromwell. Over the years the unit has continued to expand its portfolio of large scale national projects.

In 2019 Professor Dion Morton steps down from his role of Clinical Director of the Surgical Trials Initiative. His energy, dynamism and vision in this role will be missed. He has initiated and overseen a hugely successful programme of developing and supporting surgical trials units to expand the number of randomised controlled trials in surgery. There are now seven trials units across the UK and there is enough funding in place to support eight chairs of surgical trials dedicated to this aim, which we hope to appoint by mid 2019. This has been achieved through incredibly generous support from the Rosetrees Trust, The Freemasons, Mary Kinross, The Enid Linder Foundation and The George Drexler Charitable Foundation. The first appointment was Professor David Jayne from Leeds supported by Bowel Cancer UK and more recently there have been three further appointments – Professor David Beard and Professor Michael Douek in Oxford and Professor Joy Adamson in the Hull/York centre.

Professor Dion Morton will continue to work with Globalsurg, which is supported by the RCS. Professor Derek Alderson, President of the RCS and previous Chair of Research, chairs an International Policy Implementation Committee, which aims to ensure the results of these international surgical trials are implemented across low- and middle-income countries (LMICs). Sixty-five countries currently participate in this international surgical research effort with more joining on a regular basis.

There are a number of other people to thank who have been involved with the research activities of the RCS – Penny Egan, outgoing Executive Director of US-UK Fulbright Commission. Natasha Stern of McKinsey for continuing to host surgical trainees undertaking clinical leadership fellowships. Professor Cliff Shearman for his role as chair of the research committee of the RCS prior to his election to Vice President of this College. Martyn Coomer and his staff, who among a number of other roles, continue to lead the RCS' fundraising for research activities and has done a fantastic job in expanding our ability to offer research grants to our training surgeons and coordinating the selection of recipients of these fellowships. Thanks also to the great work of the development office for their ongoing fundraising efforts for research.

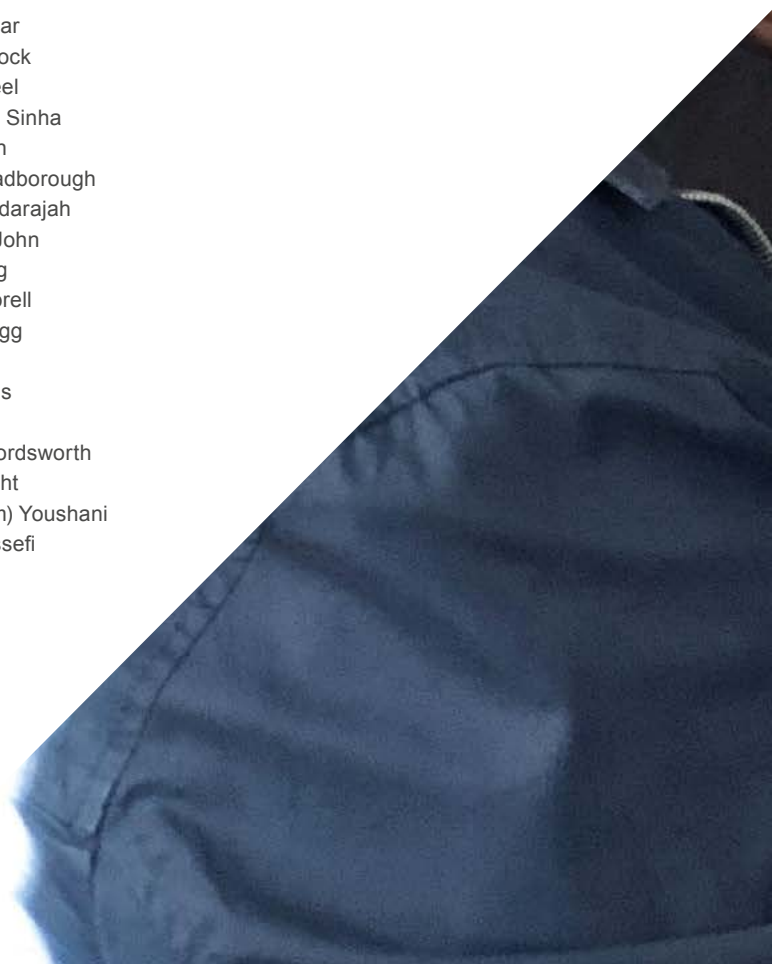
The future of surgical research in the UK is bright thanks in no small part to the activities of the RCS and its research fellowship scheme, which depends so much on its generous and enlightened supporters. The RCS and the surgical community in general is greatly indebted.

Fellows are supported in their research aims at major academic centres but also in smaller hospital environments where truly valuable research is being undertaken.

Research Fellows' Reports

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

Muneer Ahmed
Ali Al-Hussaini
Natalie Allen
Saira Alli
James Barnes
Thomas Barnes
Damiano Barone
Andrew Beamish
Ruth Benson
Jemma Bhoday
Timothy Biggs
Oliver Boughton
Vanessa Brown
Pankaj Chandak
Sumita Chhabra
Jun Seok Cho
Mohammed Chowdhury
Emman Combellack
Prita Daliya
Philip Dobson
Candice Downey
Georgios Garas
Nicholas Hamilton
Philip Herrod
Daniel Hipps
Ray Hsu
Amel Ibrahim
Laura Jackson
Zita Jessop
Yazan Khaled
Tanvir Khan
Jennifer Kingston
Rebecca Llewellyn-Bennet
Robert MacFarlane
Max Marsden
James Masters
Scott McCain
Emma McGlone
Rory Morrison
Ankur Mukherjee
Wee Ngu
Hannah Nieto
Katherine Oakland
Rachel O'Connell
Sarah Onida
Mahim Qureshi
Mustafa Rashid
Peter Rees
Geoffrey Roberts
Patrick Garfjeld Roberts
Olamide Rominiyi
Holly Roy
Kapil Sahnan
Ali Salamat
Kit Sampat
Hema Sekhar
Anna Sharrock
Andrea Sheel
Rohitashwa Sinha
Henry Smith
Philip Spreadborough
Nish Srikandarajah
Edward St John
Sean Strong
Simon Timbrell
Victoria Twigg
Navin Vig
Tom Wiggins
Mark Wilkie
Matthew Wordsworth
Naomi Wright
Amir (Samm) Youshani
Pouya Youssefi



Magnetic occult lesion localization in breast cancer

Muneer Ahmed

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

SUPERVISORS:
Professor M Douek

SITE OF WORK:
King's College London (Guy's Campus)

PUBLICATIONS:
1. Ahmed M, Woo T, Ohashi K *et al.* Magnetic sentinel lymph node biopsy in a murine tumour model. *Nanomedicine.* 2016; **12**: 1,045–1,052

2. Ahmed M, Anninga B, Goyal S *et al.* Magnetic Sentinel Node and Occult Lesion Localization in breast cancer (MagSNOLL trial). *Br J Surg.* 2015; **102**: 646–652

PRESENTATIONS:
1. M Ahmed. *Magnetic Occult Lesion Localization (MOLL) in breast cancer.* Presented at: Association of Breast Surgery; 16 May 2016; Manchester

2. M Ahmed. Magnetic sentinel node and occult lesion localization in breast cancer: The first 50 patient experience in the MagSNOLL trial. The 23rd annual meeting of the Japanese breast cancer society, 2-4th July 2015, Tokyo International forum, Tokyo, Japan

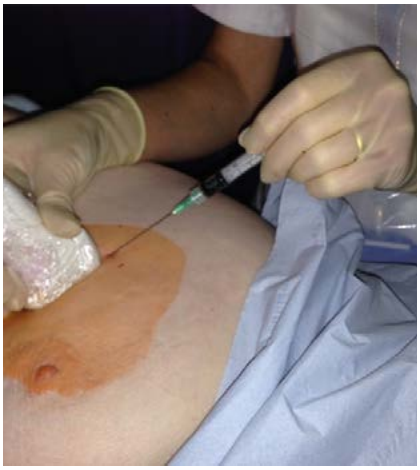
PRIZES:
1. Rosetrees Essay Prize Winner (2016), RCS

2. Ethicon Foundation Fund Travel Grant (2016–17), RCS

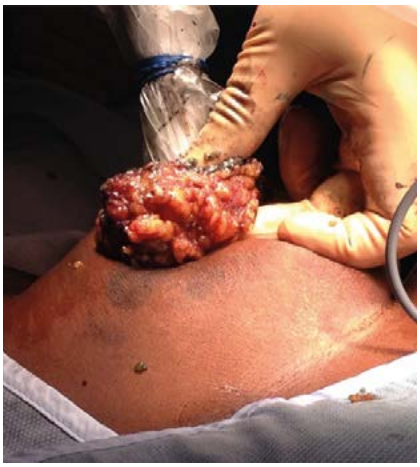
FURTHER FUNDING:
Association of Breast Surgery Research Development Grant

Annually 50,000 women are diagnosed with breast cancer within the UK and of this, one-third present completely asymptomatically via the National Breast Screening Programme. Such early diagnosis of breast cancer poses unique problems for the breast surgeon, who is unable to clinically feel the cancer during excision. Current techniques for localisation result in a conservative estimate of 20 per cent of patients requiring a second operation for incompletely clear surgical excision. The aim of my research was to develop a novel localization technique to reduce the need for surgical re-excisions.

Our unit in collaboration with the University of Tokyo developed a novel localization technique based upon the use of a magnetic tracer and a handheld magnetometer, which could be used in conjunction to successfully localize and excise clinically non-palpable breast cancers. This technique avoids the use of radiation, with its associated handling and disposal issues. It allows avoidance of cumbersome wires, which have to be placed external to the skin, meaning that they have to be introduced on the day of surgery for risk of migration and make for little intraoperative surgical guidance. The magnetic technique was successfully demonstrated to reduce re-excision rates to under 10 per cent and also to allow localization with the magnetic tracer to be performed up to a week before surgery, with consequent logistical benefits. We have now progressed to developing a solid marker and to antibody-label the magnetic tracer to allow for more precision guided surgical excision and look forward to reporting the outcomes of this research shortly.



The injection of magnetic tracer into the tumour using ultrasound.



The surgical excision guided by the handheld magnetometer.

We hope that this ongoing research from our magnetic nanotechnology collaboration will move forward in alleviating the significant physical and emotional morbidity experienced by patients diagnosed with breast cancer who then have to receive the news that their cancer has been incompletely excised and a second operation is required.

One in five of all women undergoing breast conserving surgery (lumpectomy) will require a second operation due to incompletely excised cancer.

Investigating the role of the novel cytokine IL-35 in the regulation of anti-tumour immunity against head and neck cancer

Ali Al-Hussaini

FELLOWSHIP/SPONSOR:
RCS Research Fellowship

SUPERVISORS:
Dr Xiaoqing Wei

SITE OF WORK:
Oral and Biomedical Sciences Unit, Dental School, Cardiff University

PUBLICATIONS:

1. Al-Hussaini A, Xu R, Jones A *et al.* Investigating the role of the novel cytokine IL-35 in the regulation of anti-tumour immunity against head and neck cancer. *J Laryngol Oto.* 2016; **130**: e6

2. Al-Hussaini A, Xu R, Jones A *et al.* Investigating the role of the novel cytokine IL-35 in the regulation of anti-tumour immunity against head and neck cancer. *Oral Oncol.* 2015; **51**: e44-45

PRESENTATIONS:

1. Investigating the role of the novel cytokine IL- 35 in the regulation of anti-tumour immunity against head and neck cancer. IFOS ENT World Congress. Paris. 28/06/2017

2. *The role of the novel cytokine IL-35 in the regulation of macrophage-mediated anti-tumour immunity against head and neck cancer.* Presented at: Royal Society of Medicine Rhinology and Laryngology Section. February 2017; London

PRIZES:

1. International ENT Masterclass Trainee's Gold Medal (28/01/2017)

2. ENT Wales Senior Academic Prize (07/10/2016)

FURTHER FUNDING:
RCS/Saven Research and Development Programme consumables grant, Cancer Research Wales grant and Velindre Cancer Centre Head and Neck Research consumables grant

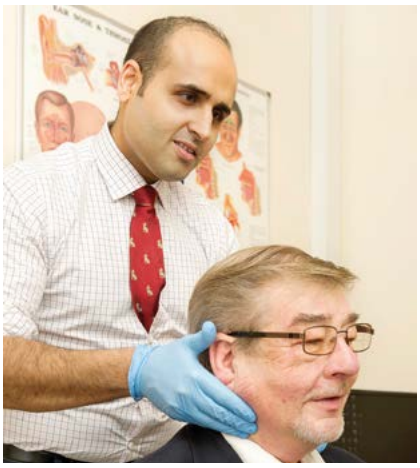
Fibreoptic nasendoscopy for surveillance of head and neck cancer.

The interaction between the immune system and cancer is fascinating. It is well known that the immune system recognises cancer cells and mounts an attack to eliminate them. However, what is incredibly interesting is the ability of cancer cells to respond to this immune attack by causing immunosuppression and manipulating the immune system to their advantage. Not only do the immune cells in tumour tissue change to a cancer-tolerant phenotype, but they also express growth factors, which serve to promote tumour survival and proliferation.

We hypothesised that a relatively novel immune-modulating mediator: Interleukin 35 (IL-35), may play a role. By co-culturing head and neck cancer and immune system cells such as macrophages, and using various laboratory techniques, we investigated the production of IL-35 and other mediators at the genetic expression and protein secretion levels.

We found that head and neck cancer cells produce IL-35 and this is increased in response to pro-inflammatory mediators. Furthermore, head and neck cancer cells reduce the pro-inflammatory immune mediators secreted by macrophages and this is associated with increased production of IL-35. Additionally, macrophages decrease expression of immune-activation genes and are polarised to cancer tolerant and supportive tumour-associated macrophages.

These are promising preliminary findings, which demonstrate IL-35 is secreted by head and neck cancer cells as well as macrophages and builds on previous knowledge that IL-35 is an immune suppressing mediator produced by regulatory T cells of the immune system. It can be postulated that IL-35 is a factor in promoting cancer escape from the immune system and its antagonism may be a novel therapeutic target. Further research will explore whether patients with head and neck cancer have higher levels of IL-35 in their blood and in cancer tissue specimens and if this correlates with the stage of cancer, site of origin and response to treatment.



Ali conducting a neck examination.

Head and neck cancer is the sixth most common cancer with an overall five-year survival of 50%.

Functional significance of altered Myoepithelial Cell Phenotype in DCIS

Natalie Allen

FELLOWSHIP/SPONSOR:
Frances and Augustus Newman Foundation Fellowship

SUPERVISORS:
Professor Louise Jones

SITE OF WORK:
Barts Cancer Institute

PRESENTATIONS:
1. *The development of an immunohistochemistry panel for DCIS risk stratification using markers alectin-7 and ß6- making breast screening more acceptable.* Presented at: UK/Oncoplastic and Reconstructive Breast Surgery; September 2018; Nottingham

2. *Myoepithelial Cell-Associated Galectin-7: Functional and Clinical Relevance in DCIS Progression.* Presented at: Pathological society/ Royal Society of medicine meeting; January 2018; London

PRIZES:
The RCS/Saven Research and Development Programme, 25/01/18

Each year in the UK approximately two million women undergo breast screening. Breast screening aims to improve outcomes for women diagnosed with breast cancer by detecting disease at an earlier, more treatable stage. It is highly effective, now detecting pre-invasive breast cancer, known as Ductal Carcinoma *in-situ* (DCIS) in up to 30% of women with breast cancer. However, it is now evident that only around half of all DCIS will ever progress to life-threatening disease, though currently all are treated in the same way. There is a need to distinguish between DCIS that will progress and that which will not.

The aim of this project is to contribute towards the development of a risk stratification tool that can be used in clinic. This will offer a more personalised approach and help prevent unnecessary surgery. Our work has focused on myoepithelial cells. In normal breast ducts the myoepithelial cells have tumour suppressor properties. The changes in the myoepithelial cells in DCIS may be key in risk stratification. We have used two groups of patient samples; a low-risk model and a high-risk model (already has associated invasive breast cancer). In these tissues we have assessed the expression of Galectin-7. There is a significantly higher loss of Galectin-7 in the high-risk model, indicating Galectin-7 in DCIS is a good prognostic marker. The upregulation of ß6 has been shown to be a poor prognostic marker in DCIS.

As part of the ongoing project, RNA sequencing has been performed to assess the effect of silencing myoepithelial Galectin-7. This has identified other markers that will be investigated in the development of the DCIS risk signature. This risk signature will allow us to have a more personalised approach in the management of DCIS.

Natalie consenting to recruit for tissue.

One in two patients with DCIS will never progress to invasive breast cancer.

Using MRI Guided Focused Ultrasound (MRgFUS) for drug delivery in Diffuse Intrinsic

Saira Alli

FELLOWSHIP/SPONSOR:
Harry Morton Fellowship

SUPERVISORS:
Dr James Rutka, Dr Heiko Wurdak and Prof Susan Short

SITE OF WORK:
The Arthur and Sonia Labatt Brain Tumour Research Centre, Toronto, Canada

PUBLICATIONS:
1. Alli S, Figueredo C, Rutka JT *et. al.* Brainstem Blood Brain Barrier Disruption using Focused Ultrasound: A Demonstration of Safety and Enhanced Doxorubicin Delivery. *J Controlled Release*. 2018; **10**: 281: 29–41

2. Alli S, Isik S, Rutka JT. Microscopic removal of craniopharyngioma: endoscopic and transcranial techniques for complication avoidance. J Neuro-oncology. 2016; **130**: 299–307

PRESENTATIONS:
1. MRI guided focused ultrasound. A demonstration of safety in the brainstem. Presented at: Society of Neuro-oncology Paediatric Meeting; June 2017; New York

2. MRI guided focused ultrasound as a delivery method for DIPG. Presented at: International Society of Paediatric Neuro-oncology; June 2016; Liverpool

PRIZES:
1. International Society of Paediatric Neuro-oncology 2016, Cure Starts Now Snap Grant

2. DIPG Collaborative Grant, 2017

Saira and Dr Rutka being awarded a grant by members of the DIPG Collaborative.

Diffuse Intrinsic Pontine Glioma (DIPG) is a devastating brainstem tumour that occurs predominantly in young children and results in a near 100% fatality rate within two years of diagnosis. Its diffuse growth pattern and eloquent location precludes surgical resection. Our current best standard of care is radiation therapy, which provides temporary relief of symptoms but minimal gains in life expectancy. Despite chemotherapy agents demonstrating efficacy in cell culture, numerous clinical trials of chemotherapeutic agents have failed to demonstrate an improvement in prognosis or survival. A contributing factor to these findings is the preservation of the blood brain barrier (BBB), which limits the penetration of drug therapeutics to the site of the tumour.

Targeting low frequency ultrasound to a site in the brain while intravenously administering microbubbles has led to the transient opening of the BBB without tissue injury. It is the interaction between the ultrasound energy and microbubbles that results in a temporary disruption of the BBB for between four to six hours.

My work has been focused on the safety and feasibility of using focused ultrasound in the rodent brainstem. Our published work has demonstrated that BBB disruption in the brainstem can be performed without histological tissue injury, cardiorespiratory changes or a decline in motor function. Furthermore, we have shown the efficacy of the chemotherapy agent doxorubicin against patient derived DIPG cell lines and the ability to achieve a 40-fold increase in doxorubicin concentration in the brainstem when delivered with MRgFUS. This is particularly significant given the poor BBB permeability of doxorubicin.

As a result of this work, we are currently seeking ethical approval to conduct a Phase I/II clinical trial of MRgFUS and doxorubicin delivery in children with DIPG at The Hospital for Sick Children in Toronto, Canada.

Saira participating in the annual Meaghan's Walk charity event.

DIPG results in a near 100% mortality rate within two years of diagnosis.

Donor-derived skin grafts to detect rejection in pancreas transplantation

James C H Barnes

FELLOWSHIP/SPONSOR:
Frances and Augustus Newman Foundation Fellowship

SUPERVISORS:
Professor Peter Friend

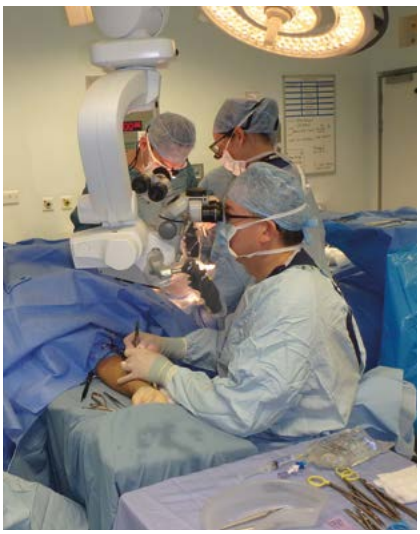
SITE OF WORK:
Oxford Transplant Centre

PUBLICATIONS:
Barnes J, Issa F, Vrakas G *et al.* The abdominal wall transplant as a sentinel skin graft. *Curr Opin Organ Transplant*. 2016; **21**: 536–540

PRESENTATIONS:
The project is not complete yet, but it will be presented at both a national and international level in 2018 (eg BTS and ESOT)

FURTHER FUNDING:
Oxford NIHR Biomedical Research Centre, Oxford Medical Research Fund, Oxford University Hospitals NHS Foundation Trust for one year

All patients with diabetes are susceptible to complications, but a minority experience a markedly more aggressive form of the disease. Some patients find their lives dominated by erratic glycaemic control despite best medical therapy. Others develop advanced complications that are extremely disabling, including heart disease, strokes, renal failure, blindness, and limb amputation.

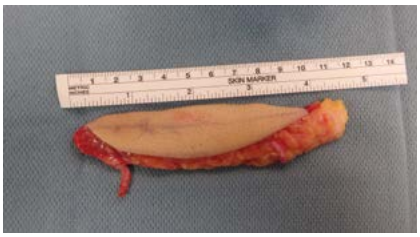


James doing sentinel skin flap transplantation simultaneously with pancreas transplantation.

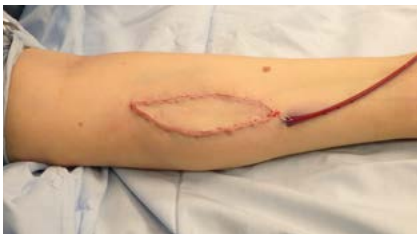
Pancreas transplantation is a well-established and highly-effective therapy for some patients with the most severe complications of diabetes. It is the only treatment that can cure diabetes, providing insulin independence and significant improvements in both quality of life and mortality.

The benefits of pancreas transplantation require the graft to function for many years, but medium-term graft loss is common because there is no effective way to monitor the graft for rejection until the damage is irreversible. The experience from hand, face and abdominal wall transplantation suggests that transplanted skin rejects at the same time or earlier than other transplanted tissues. Therefore, direct access to donor skin tissue in pancreas transplantation should enable daily inspection and, where necessary, early biopsy and treatment of rejection before significant graft injury occurs. The sentinel skin graft acts as a visual barometer of rejection that patients can assess on a daily basis.

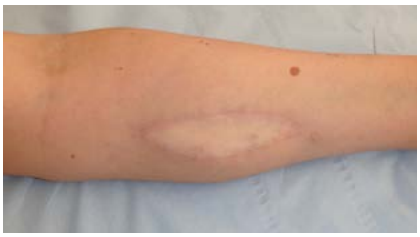
The aim of this pilot study is to establish whether donor-derived skin grafts can aid in the diagnosis and monitoring of rejection in pancreas transplantation. So far, we have recruited 15 of the planned 20 patients and we have not observed any cases of pancreas/kidney rejection in the absence of sentinel skin rejection. The sentinel grafts have been very well received by patients in the study who have described an added sense of daily reassurance when their sentinel graft is normal.



The sentinel skin flap before transplantation.



The sentinel skin flap immediately after transplantation.



The sentinel skin flap after one year.

Up to 50% of pancreas transplants will fail by five years due to our inability to identify rejection or graft dysfunction before irreversible damage has occurred.

Uses of near infra-red light to provide real-time image guided surgery

Thomas Barnes

FELLOWSHIP/SPONSOR:
RCS Research Fellowship

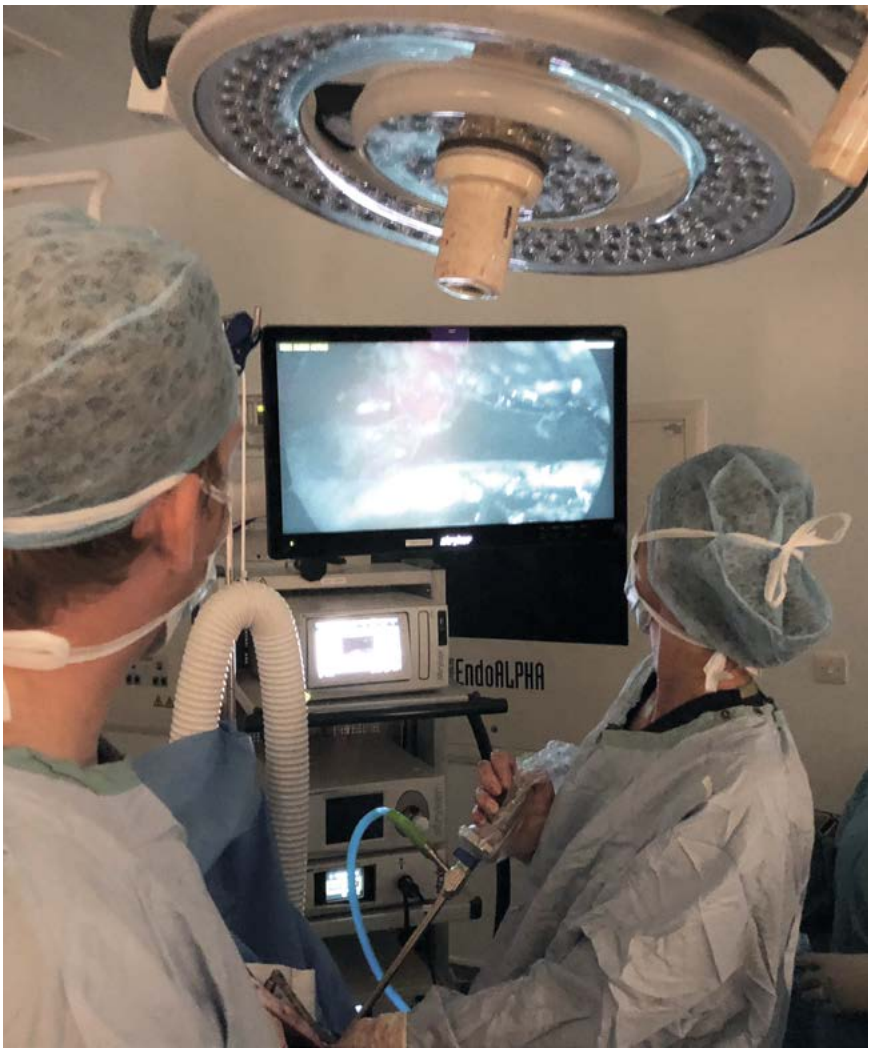
SUPERVISORS:
Professor N Mortensen

SITE OF WORK:
Nuffield Department of Surgery

PUBLICATIONS:

1. Barnes TG, Hompes R, Birks J *et al.* Methylene blue fluorescence of the ureter during colorectal surgery. *Surg Endosc* 2018; **32**: 4,036–4,043

2. Barnes TG, Volpi D, Cunningham C *et al.* Improved urethral fluorescence during low rectal surgery: a new dye and a new method. 2018. *Tech Coloproctol.* 2018; **22**: 115–119



Intraoperative use of real-time fluorescence guided imaging using a commercially available laparoscope.

Injury to key structures is still a feared consequence of surgery for both patients and surgeons. Using near infrared light and fluorescence technology, the work from the research fellowship has developed methods of highlighting important structures for surgeons to avoid their injury.

Near infrared fluorescence works by using a molecule that emits light in the near infrared spectrum when excited by light at a specific wavelength. Near infrared light penetrates through thicker tissue than white light and therefore once a fluorophore is in a 'key structure' then it is more easily seen.

One of our major projects has been investigating ureteric fluorescence. The ureter is a key part of the urinary tract. Our work has outlined the technique, dosing and timing to allow real-time fluorescence of the ureter during colorectal surgery. Not only is this likely to reduce injury to the ureter, but we also realised that it may help surgeons to operate quicker and in the correct area of dissection – making surgery easier.

Further work will be developed on this area including a randomised controlled trial to further clarify the safety benefits of this technology.

Injury to the ureter occurs in approximately one per cent of keyhole abdominal operations.

Targeting the molecular mechanism of foreign body reaction to neural interfaces

Damiano Giuseppe Barone

FELLOWSHIP/SPONSOR:
RCS Research Fellowship

SUPERVISORS:
Professor James Fawcett and Professor Clare Bryant

SITE OF WORK:
John Van Geest Centre for Brain Repair, University of Cambridge

PRESENTATIONS:
1. Preliminary results of this research have been presented to North American Neuromodulation Society Meeting, Las Vegas (US), 2017 and International conference on Nanoscience and Nanotechnologies (Greece), 2018 (Invited lecture)

PRIZES:
Wellcome Trust for three years

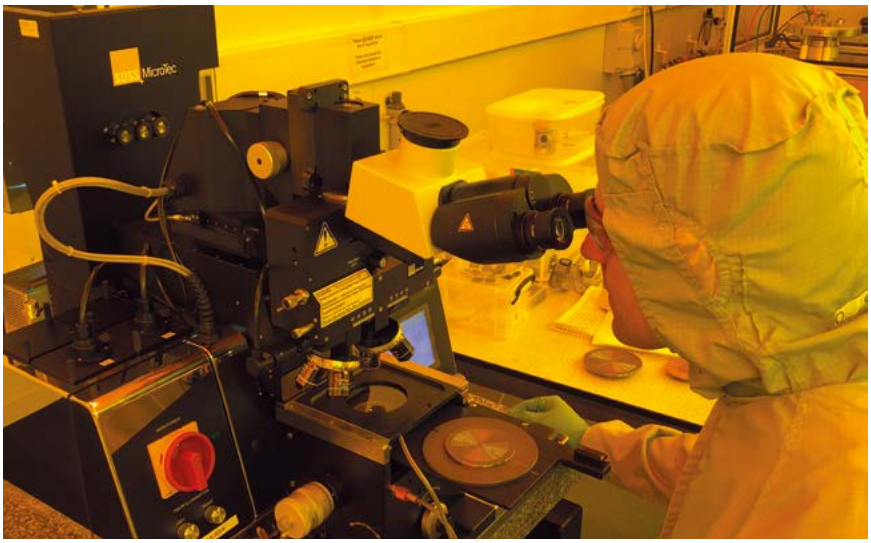
Damiano in the molecular biology laboratory to run tests on tissue samples.

In experimental settings, neural interface technology has been able to restore movement and sensation in animal models and patients suffering with long term paralysis (eg following spinal cord injury or neurodegenerative disease). However, this technology has never reached the clinical stage due to complex biological and engineering challenges.

A major challenge is the body rejecting the implanted bioelectronics, by developing a thick scar tissue and stopping the device from functioning in the long term (the process is called 'foreign body reaction' – FBR). The aim of the project is to understand better the molecular pathways involved in FBR in order to find the best and most effective therapeutic targets.

The project involved the use of nanotechnology, molecular biology and next generation sequencing techniques. The different experiments were carried out in animal models, with final testing planned in FBR tissue from human donors (scar tissue around implants removed at the time of surgery). The genetic, protein and tissue experiments have all demonstrated the fundamental role of innate immunity in the foreign body reaction process. Our immune system fights infections and external injury in two stage, called innate and adaptive immunity. The first is the initial and more general reaction, highly conserved in evolution and across species, while the second comes in action later and involve the recognition of specific markers. Within the innate immunity, we have targeted a particular pathway with both knock-out animals (animal not expressing certain genes) and experimental drugs (not yet available on the market) and the preliminary results show a dramatic reduction in the thickness of the scar tissue, offering a real and concrete solution to the problem.

Our aim is to validate these results in humans and translate them in strategies to use finally neural interface technology in clinical practice and potentially revolutionise the life of the millions of people suffering from paralysis or other neurological disabilities.



Damiano in the nanotechnology suite fabricating neuro-prosthetics devices.

More than one billion people worldwide suffer from a neurological disability and yet there is no treatment available to reverse lost neurological functions.

Adolescent Bariatric Surgery in Sweden

Andrew James Beamish

FELLOWSHIP/SPONSOR:
David Johnston International Bariatric Fellowship

SUPERVISOR:
Associate Professor Torsten Olbers

SITE OF WORK:
Department of Gastrosurgical Research, Sahlgrenska University Hospital, Gothenburg, Sweden

PUBLICATIONS:
1. Olbers T, Beamish AJ, Gronowitz E *et al.* Laparoscopic Roux-en-Y gastric bypass in adolescents with severe obesity: a prospective five-year Swedish nationwide study (AMOS). *Lancet Diabetes Endocrinol.* 2017; **5**: 174–183

2. Beamish AJ, Olbers T, Kelly AS *et al.* Cardiovascular effects of bariatric surgery. Nat Rev Cardiol 2016; **13**: 730–743

PRESENTATIONS:
1. Beamish AJ, Gronowitz E, Mårlid S. *et al.* The Adolescent Morbid Obesity Surgery (AMOS) study: five-year outcomes following laparoscopic Roux-en-Y gastric bypass in a Swedish nationwide study. Presented at: The European Obesity Summit; June 2016; Sweden

2. Beamish AJ. Adolescent obesity surgery: the AMOS experience. Presented at: invited keynote lecture, International Federation for Surgery for Obesity; August 2015, Austria

PRIZES:
1. Bioscientifica Trust Research Award for research in endocrinology. Dec 2016

2. Best Oral Presentation Prize at British Obesity and Metabolic Surgery Society (BOMSS) 6th Annual Meeting, Newcastle. Jan 2015

FURTHER READING:
From University of Gothenburg for one year

Severe obesity in adolescence is associated with reduced life expectancy and impaired quality of life. Long-term benefits of conservative treatments in adolescents are limited and evidence of their effectiveness is scarce. Despite this, lifestyle and dietary interventions, often expensive, remain the mainstay of obesity treatments. We conducted the first prospective controlled study reporting five-year outcomes following Roux-en-Y gastric bypass (RYGB) surgery in adolescents, where excellent outcomes have previously been described in adults.

British Obesity and Metabolic Surgery Society (BOMSS) presentation.

Our Swedish national study compared surgical treatment of 81 adolescents (13–18 years) with severe obesity, with lifestyle treatment in a matched adolescent group. Our work has demonstrated that the safety and effectiveness of this intervention persist into the long term. During a period of five years, adolescents undergoing surgery achieved more than 25% total body weight loss, while control participants actually gained weight.

Andrew with his supervisors Torsten Olbers and Hans Lönroth.

Five years after surgery, type two diabetes, prediabetes and high blood pressure had resolved in all patients. Abnormal blood fats and abnormal liver function resolved in 83% and 92% respectively. Physical domains of quality of life improved significantly and most patients would recommend surgery to their peers.

However, surgery is not without risk. Obesity itself is associated with vitamin and mineral deficiencies and bariatric surgery reduces absorption of some micronutrients. This leads to higher rates of deficiencies and reinforces the need for compliance with dietary supplements. We also observed a 25% risk of needing additional surgery, a problem that research in Swedish adults has shown can likely be halved following significant advances in technical and medical procedures.

Future work is necessary to determine which procedure should be used in adolescents and to explore surgery as a treatment for diabetes, irrespective of obesity. International multicentre randomised controlled trials in these areas are needed, along with an adolescent bariatric service for these vulnerable adolescents in the United Kingdom.

A close supportive relationship with patients is essential to an effective adolescent obesity programme.

Adolescent bariatric surgery reduces body weight by a quarter and resolves cardiovascular risk factors in 75% to 100%.

Postoperative cognitive decline following endovascular aortic aneurysm surgery: A prospective clinical study

Ruth Alison Benson

FELLOWSHIP/SPONSOR:
Welton Foundation Fellowship

SUPERVISOR:
Professor Ian M Loftus

SITE OF WORK:
St George's Hospital, London

PUBLICATIONS:

1. Benson RA, Loftus IM. Subclinical neurological consequences following aortic aneurysm surgery. Vascular and Endovascular Controversies 2016 edition

2. Benson RA, Hogue CW, Everett AD *et al.* The role of GFAP, Neurogranin and BDNF as novel markers of microembolic neurological damage following endovascular aortic aneurysm repair – A pilot study. *BJS* 2016; **103**: S3; p1–56

PRESENTATIONS:

1. Benson RA, Loftus IM. *Neurological consequences of EVAR and TEVAR*. Presented at: Charing Cross Vascular symposium; April 2016. London

2. Benson RA, Matthews D, Ozdemir BA *et al. Postoperative Cognitive Decline following endovascular aortic aneurysm surgery: A prospective clinical pilot study.* Presented at: Vascular Society; November 2015; Bournemouth

PRIZES:

Certificate of Merit for excellent abstract presentation, Charing Cross International symposium, London. April 2015

Postoperative cognitive decline (POCD) is a well-recognised neurological complication of major surgery. Its significance lies in its links to worse long-term health and reduced quality of life. However, compared with the field of cardiothoracic surgery, the incidence following surgery for aortic aneurysms, a common and deadly ballooning of the major blood vessel in the body, is poorly researched. This is despite equivalent co-morbidity and operative complexity. This study aimed to investigate the effect of endovascular repair (EVAR) on cognitive function in the months following surgery.

The hypothesis was tested using two patient cohorts. The first recruited patients with an aortic aneurysm scheduled for surgery. The control group recruited patients with an aneurysm who were not scheduled for surgery. Both groups underwent identical cognitive tests at baseline, and again three months after surgery (or from baseline for the control group). Operative patients underwent additional peri-operative brain monitoring and serial blood testing with the aim of mapping out individual brain physiology and detect markers of cerebral damage.

10% of the operative cohort demonstrated a significant drop in cognitive scores compared with 0% in the control group, confirming the role of surgery. Interestingly, patients' risk rose if they performed poorly on preoperative intelligence scores. Poorer function was also linked to longer intensive care and inpatient stays.

Fellowship support of the project has enabled me to continue testing patients out to one year, which crucially will allow me to evaluate the longer-term impact on cognitive function. This is important, as cardiothoracic research suggests that patients often demonstrate a greater decline again at one year resulting in patients needing admission to nursing homes, and increased risk of death. Our results suggest that further drops in scores will be seen at one year with a significant impact on patient's level of activity and independence.

Ruth using Doppler ultrasound to look at cerebral blood flow via the middle cerebral artery through patients' temporal window, checking for interruptions to the blood flow caused by small particles of debris dislodged from the aorta during surgery.

Up to 10% of patients who have keyhole surgery for their aortic aneurysms suffer from cognitive decline, compared with patients that don't have surgery for the same condition.

Treatment induced cell death in rectal cancer

Jemma Bhoday

FELLOWSHIP/SPONSOR:
Joint RCS/Dunhill Medical Trust Fellowship

SUPERVISOR:
Professor Gina Brown

SITE OF WORK:
Royal Marsden NHS Trust, Imperial College London

PUBLICATIONS:
1. Bhoday J, Smith F, Siddiqui MR *et al.* Magnetic Resonance Tumor Regression Grade and Residual Mucosal Abnormality as Predictors for Pathological Complete Response in Rectal Cancer Postneoadjuvant Chemoradiotherapy. *Dis Colon Rectum*. 2016; **59**: 925–33

2. Siddiqui MR, Bhoday J, Battersby NJ *et al.* Defining response to radiotherapy in rectal cancer using magnetic resonance imaging and histopathological scales. *World J Gastroenterol*. 2016; **22**: 8,414–8,434

PRESENTATIONS:
1. Results of a Prospective RCT, 6 vs. 12: is greater tumour down-staging observed on post-treatment MRI, if surgery is delayed to 12-weeks vs. 6-weeks after completion of neoadjuvant CRT in rectal cancer? Bhoday J, Evans J, Tekkis P, Swift RI, Brown G. Presented at: ESMO, Oct 2016; Copenhagen

2. Can Magnetic Tumour Regression Grade (mrTRG) predict patterns of local regrowth and distant metastases in patients with locally advanced rectal cancer post chemoradiotherapy? Bhoday J, Siddiqui M, Brown G.ESCP, Sept 2016; Milan

FURTHER FUNDING:
Croydon University Hospital Research Grant, Dec 2015 for project costs

Operations performed to remove rectal cancers are not without risk. It is major surgery and is associated with considerable morbidity, including multi-organ failure and mortality. A significant proportion of these patients are left with a permanent stoma, which they may not be able to manage independently. For patients, this can mean the difference between living on their own and having to move to a nursing home or needing full-time care.

Jemma performing a colonoscopy, a test used to diagnose bowel cancer.

Part of the treatment for rectal cancer is preoperative chemoradiotherapy. Research has already shown that up to 30% of patients may have a 'clinical complete response' to treatment, ie there are no longer any viable cancer cells left. To perform a major operation on an elderly patient that no longer has a cancer evident is difficult. But what the surgeon needs to be sure of, before taking such a decision to 'watch and wait', is whether it is safe to not operate and whether the cancer could come back.

Our research has focussed on developing new techniques to accurately identify those patients that have had a complete response and uses a novel MRI (mrTRG) grading method. With this new system we have shown that we can identify ten times as many patients with a complete response than methods that have been used previously. Our research has also shown that by waiting 12 weeks (instead of 6, which is the current standard) after chemoradiotherapy before operating, we can significantly improve tumour shrinkage and therefore, in time, be able to offer 'watch-and-wait' to more patients.

We hope that the multicentre, prospective, randomised clinical TRIGGER trial (CRN 4326), where patients will be randomised between a standard of care that does not re-evaluate tumour stage after chemoradiotherapy, versus an mrTRG based approach that offers watch-and-wait to favourable mrTRG patients, will be able to answer many of the remaining questions.

Jemma in theatre operating on a patient with bowel cancer.

Rectal cancer surgery performed at 12 weeks (instead of 6) after chemoradiotherapy significantly increases tumour downstaging.

Intracellular *Staphylococcus aureus* within mast cells – The trojan horse of chronic rhinosinusitis?

Timothy Briggs

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

SUPERVISORS:
Mr Rami Salib, Dr Sylvia Pender and Dr Andrew Walls

SITE OF WORK:
Academic Unit of Clinical and Experimental Sciences, Faculty of Medicine, University of Southampton

PRESENTATIONS:
1. Biggs TC, Abadalkareem RS, Hayes SM *et al. Sensitisation of mast cells promotes the survival of S. aureus – Implications for chronic rhinosinusitis.* Presented at: The European Rhinology Society Meeting; April 2018; London

2. Biggs TC, Hayes SM, Harries PG *at al. The role of S. aureus in chronic rhinosinusitis; mechanisms aiding nasal polyp formation.* Presented at: The European Rhinology Society Meeting; April 2018; London

PRIZES:
1. Best original scientific paper, European Rhinologic Society (ERS) clinical research prize, April 2018

2. Travelling fellowship prize, Foundation Rhinology of Utrecht, April 2018

FURTHER FUNDING:
British Rhinological Society (BRS) Research Grant for one year and Rosetrees Trust Research Grant for three years

Chronic rhinosinusitis (CRS) is a chronic inflammatory condition affecting the lining of the nose and paranasal sinuses. It is the second most common chronic disease worldwide, has a significant impact on patients' quality of life and healthcare resources. Some patients with CRS go on to form nasal polyps, bags of inflammatory tissue that fill the nose and cause blockage and infection. No one knows why nasal polyps form, but bacteria are thought to play an important role.

Nasal polyp removed for a patient with chronic rhinosinusitis.

Growing evidence supports the presence of bacterial biofilms (antibiotic-resistant groups of bacteria) in patients with CRS, which when present are associated with failure of medical and surgical treatments. Recently, *S. aureus* (the most common bacteria found in CRS patients) has been found within mast cells in patients with nasal polyps. Mast cells are normally associated with allergic reactions, and therefore this research was conducted in order to understand whether *S. aureus* was using mast cells as a survival strategy.

We have discovered that *S. aureus* is able to survive within mast cells, and re-populate eradicated bacterial populations. We have also shown that mast cells contribute towards inflammation when exposed to *S. aureus*. Thus, not only is *S. aureus* able to survive within a protected intracellular environment, it also contributes to inflammation and potentially the formation of nasal polyps.

This research has highlighted the ability of bacteria to survive and cause ongoing inflammation in CRS patients. It has emphasised the importance of trying to clear bacterial infections, and that novel strategies are required to kill bacteria that are 'hiding' within mast cells. Surface bacteria are likely to be the tip of the iceberg, and targeting intracellular bacteria will aim to improve the quality of life of afflicted patients as well as improve the effectiveness of future treatments.

Tim receiving the basic science research prize, from Professor Fokkens, at the 2018 European Rhinological Society Conference, photo taken by Monique Kooijmans.

Chronic rhinosinusitis affects up to 15% of the population, and approximately 20% of these patients will develop nasal polyps (bags of inflammatory fluid that fill the nose causing blockage and infection) at some point in their lifetime.

Optimising surgery using bone quality metrics

Oliver Richard Boughton

FELLOWSHIP/SPONSOR:
Joint RCS/Dunhill Medical Trust Research Fellowship

SUPERVISOR:
Professor Justin Cobb

SITE OF WORK:
The MSk Lab,
Imperial College London

PUBLICATIONS:
1. Boughton O, Ma S, Zhao S *et al.* Measuring Bone Stiffness Using Spherical Indentation. *PLoS One.* 2018; **13**: e0200475

2. Zhao S, Arnold M, Ma S *et al.* Standardising Compression Testing for Measuring the Stiffness of Human Bone: A Systematic Review. *Bone Jt Res.* 2018; **7**: 524–538

PRESENTATIONS:
1. *Cortical Bone Spherical Indentation Modulus Correlates with the Elastic Modulus from Compression Testing and CT-measured Porosity. Presented at: British Orthopaedic* Research Society Annual Meeting; September 2018; Leeds

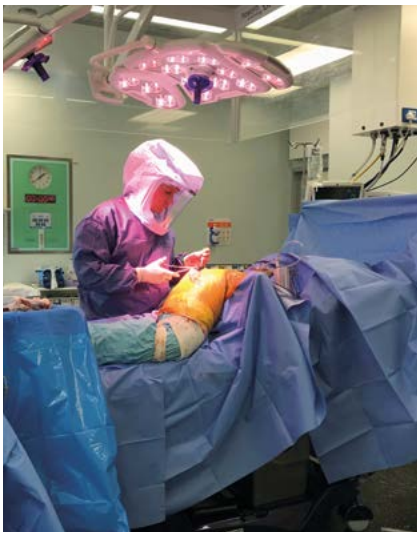
2. *Femoral Neck Cortical Bone Stiffness, as measured by Resonant Ultrasound Spectroscopy, Correlates with its Porosity.* Presented at: World Congress of Biomechanics; July 2018; Dublin

PRIZES:
1. British Orthopaedic Research Society (BORS) Young Investigator Award (£200) for 'Resonant Ultrasound Spectroscopy for Measuring Bone Stiffness', BORS Annual Meeting, London, 5/09/17

2. Best Poster Prize for 'Optimising Surgery using Bone Quality Metrics' at the Imperial Academic Trainees Annual Research Symposium, Hammersmith, 15/06/16

FURTHER FUNDING:
BORS/BRJ Travelling Fellowship to the USA

This research fellowship focussed on reducing risk in joint replacement surgery by personalising hip replacement based on patients' individual bone quality. The challenge of measuring a patient's bone quality was first addressed.



Oliver closing a wound following a hip replacement procedure.

Multiple techniques for measuring the mechanical properties of human bone were assessed. Of these techniques, high resolution computed tomography (CT) was highly predictive of bone mechanical properties, and ultrasound techniques were also good determinants of bone quality. Indentation was found to be a moderate predictor of bone quality. Following this work, a trial using an ultrasound device to measure bone quality is beginning at Imperial in January 2019.

The research next addressed how surgery can be optimised once a patient's bone mechanical properties are known. The optimal force used to seat a hip replacement implant was investigated in a cadaver study and a special testing rig was developed using this data. This rig is being used now to develop and test new implant designs as well as improve surgical technique. A hip impaction device to use in surgery is also currently being developed with the help of the testing rig.

The second part of optimising the surgery is optimising the implant being inserted. An animal model was used to investigate four bone implants of varying stiffness. Bone is responsive to its local mechanical environment and bone was found to grow more into scaffolds of low stiffness. Directly following this research, a project grant was submitted to the Wellcome Trust to translate this research into the clinic by developing implants that are stiffness matched to individual patients.

These research projects combine to make joint replacement surgery safer, reducing the chance of fracture at the time of surgery as well as improving the long-term durability of the implant and procedure.

Oliver with Dr David Polly, Spinal Surgeon, and two other travelling fellows, Jerry Tsang and Thomas Kurien at the University of Minnesota, USA.

With 80,000 patients undergoing hip replacements every year in the UK and 3 in 100 of these patients suffering fractures of their bones during surgery, this research addresses the issue of bone quality during surgery.

Does nitrate supplementation improve postoperative recovery in colorectal cancer?

Vanessa Brown

FELLOWSHIP/SPONSOR:
Freemasons' Fund for Surgical Research

SUPERVISOR:
Professor Tim Rockall

SITE OF WORK:
MATTU, Royal Surrey County Hospital, Guildford

PRIZES:
1. Shortlisted for Moynihan Prize. International prize presentation at ASGBI May 2017 in Glasgow, UK

2. KSS West and South West Thames Prize Day 2017, Frimley park hospital, 23/7/2017

Bowel cancer is the second most common cause of cancer death in the UK, with more than 40,000 new diagnoses a year. Every year approximately 16,000 people die from bowel cancer. Surgery is the most effective way of curing bowel cancer, but patients with colorectal cancer are often elderly and unfit. Fitter patients recover after surgery faster and suffer fewer complications.

Beetroot juice contains nitrates that have been proven to improve performance in professional athletes. Surgery for cancer is often described as 'running a marathon'.

Will giving beetroot juice to patients with bowel cancer, before and after surgery, improve their recovery? This research aims to investigate whether we can improve patients' fitness before surgery and therefore speed up recovery after an operation and improve patient outcomes.

Patients awaiting surgery for colorectal cancer performed an exercise test and were then given seven days of beetroot juice (high in nitrates) or placebo beetroot juice (without nitrates). The exercise test was then repeated. Patients then continued on their assigned juice before and after surgery until they were discharged home after their surgery.

Seven days of beetroot juice significantly improved patients' fitness before major surgery for colorectal cancer. The level of fitness did not change in patients who received the placebo juice. There was a tendency towards a lower rate of complications within the group of patients who received beetroot juice when compared with the placebo group.

Beetroot juice is widely used in the sports world to improve fitness, but only a few studies have been conducted in patients. This is the first study conducted in patients undergoing surgery.

Major surgery for colorectal cancer can be exhausting and some patients may take months to recover. Seven days of beetroot juice improves patients' fitness before surgery, which will hopefully improve and shorten their recovery.

Vanessa's patient after his operation, discharged on day four.

Mr M – Patient quote

"I was struck not just by your and the team's obvious dedication to, and enthusiasm in this project, but also as an extension of that commitment, by your interest in me as a patient and your encouragement and reassurance during my trial sessions. This type of surgery is pretty daunting, and that support was very helpful.

As to how being involved in the project affected me, I would say that for me at least, I was glad to have an opportunity to make a difference, and naturally keen to partake in something that might further enhance recovery from this type of surgery. I also wanted to contribute something to RSCH having regard to the excellent care and attention I'd been receiving from all involved right from the outset."

Mrs LM – Patient quote

"Having had the devastating news of being diagnosed with bowel cancer and then further investigations highlighting a kidney tumour I felt that if I participated in your research it could be a positive contribution that can only help in further treatments. I felt valued being part of a team seeking to expand medical knowledge and it did have some distraction benefits in the weeks prior to my surgery which was obviously a difficult time.

I felt little affect whilst taking the beetroot juice, I suppose sometimes a little inconvenient having to take it at the same time every day so remembering to always have it with you! The removal of certain foods from my diet caused no issue at all. I was happy to attend the hospital for the fitness tests. Although it was not significant to your research, my heart showed signs of stress before it impacted me physically so that was beneficial to me knowing I should not push my heartrate above your recommended level when exercising. This would not have come to light had I not been involved with the research.

Another fact I was very pleased with was when it was thought I had never smoked, I had in fact been a smoker for 10 years or so stopping in 2001. There were apparently no signs of the damage that could have been caused. Again I would not have got this information if I had not participated.

After my surgery I recovered remarkably quicker than I expected which was essential as my nephrectomy was planned for 6 weeks later. My recovery from that operation was much slower, probably to be expected....or did the beetroot juice work wonders!!"

Overcoming immunological and anatomical barriers in complex transplantation

Pankaj Chandak

FELLOWSHIP/SPONSOR:
The Wellington Hospital RCS Research Fellowship

SUPERVISORS:
Professor Nizam Mamode and Professor Anthony Dorling

SITE OF WORK:
King's College London

PUBLICATIONS:
1. Chandak P, Byrne N, Newton V *et al.* Classification of abdominal vascular anomalies and use of 3D printing to support complex renal transplantation in children. *Lancet* 2017; **389**: S32

2. Chandak P, Kessaris N, Callaghan CJ *et al.* Insights in Transplanting Complex Paediatric Renal Recipients with Vascular Anomalies. *Transplantation* 2017; **101**: 2,562–2,570

PRESENTATIONS:
1. Presented at: International Paediatric Transplant Symposium; Nov 2016; Shanghai, China

2. *3D printing in healthcare.* Presented at: The Royal Society; July 2017; London

PRIZES:
1. The Royal College of Surgeons of England Arnott Lecture and Medal. Lecture delivered at the British Transplant Society Congress, 24 Feb 2016

2. The British Science Association Charles Darwin Award Lecture 2017. Lecture delivered at the British Science Festival, Brighton 8 Sept 2017

FURTHER FUNDING:
Rosetrees Trust for two years

Transplantation is the treatment of choice for patients with kidney failure, however, significant barriers remain. Imagine a small child in desperate need of a kidney transplant who has complex abnormalities with the blood vessels and no blood group compatible living donor available. The child remains on the waiting list for a deceased donor kidney (may take months or years depending if the right matched kidney arrives). A major challenge is trying to place an adult sized donor kidney into a small (<20 kg) child with anatomical abnormalities making the feasibility of transplantation uncertain at times. Furthermore, we are increasingly being offered elderly deceased donor organs of marginal quality that may not function immediately after transplant. Such organs maybe 'discarded' and therefore contributing to the widening hiatus between the number of patients on the waiting list and the number of organs available due to a chronic shortage. The aims of my work were two-fold; firstly, to use patient-specific 3D printed models of the baby's abdomen and the adult donor kidney to help plan complex surgery; secondly, to use a novel organ bypass system (called *ex-vivo* normothermic perfusion, where we perfuse kidneys outside the human body with warm oxygenated blood) to develop an experimental model of human antibody mediated rejection. This will then be used to help overcome immunological barriers (eg blood group incompatibility) by protecting the donor kidney before the transplant. This will be by infusing locally acting drugs via the bypass machine, so the kidney is protected against rejection – before performing the transplant itself. This may mean in the long term, you could potentially perform a transplant using any kidney of any blood type for any recipient.

To date, I have successfully translated my idea of using 3D printing to aid surgeons in the planning of complex paediatric transplantation, which is routine clinical practice in our hospital and abroad. We have successfully transplanted a number of highly challenging paediatric transplants where the feasibility was uncertain based on conventional radiological planning. With respect to the second aim; I have managed to induce rejection in human kidneys by adding antibodies into the bypass machine circuit which is connected to the kidney. The next step is to introduce therapeutic drugs into the bypass machine to protect the kidney against rejection.

Pankaj and his supervisor, Professor Mamode, and the team, the official handover of the 3D models to the Science Museum for permanent display in the new Medical Galleries 2019. The models were used to help with the planning of a transplant of Chris Boucher's kidney into his daughter Lucy (pictured).

30% of patients on the transplant waiting list may not get a transplant due to the presence of antibodies and /or anatomical barriers.

Analysis of the behaviour and control of enteric nervous system progenitor cells isolated from aganglionic bowel in Hirschsprung's disease

Sumita Chhabra

FELLOWSHIP/SPONSOR:
Joint RCS/BAPS Research Fellowship with the support of the Harold Bridges Bequest

SUPERVISORS:
Mr Simon Kenny, Miss Sarah Almond, Professor David Edgar, Professor Patricia Murray and Dr Bettina Wilm

SITE OF WORK:
University of Liverpool, Department of Women's and Children's Health, Alder Hey Children's Hospital

PRESENTATIONS:
1. *Modulating the canonical Notch signalling pathway in aganglionic bowel to promote neurogenesis: A step towards autologous therapies for children with Hirschsprung's disease.* Presented at: Enteric Nervous System conference; April 2018; Boston, USA

2. *The role of Notch signalling in aganglionic Hirschsprung's bowel: A step towards autologous therapies for children with Hirschsrung's disease.* Presented at: British Association of Paediatric Surgeons conference; July 2018; Liverpool, UK

FURTHER FUNDING:
Medical Research Council (MRC Clinical Research Fellowship) for two years

Every other day in the UK a newborn child is diagnosed with Hirschsprung's disease, a congenital gut motility disorder characterised by a lack of nerve cells in the bowel. Despite surgical removal of the affected bowel, up to 30% of children suffer from long-term problems of constipation or incontinence, and 10% of children require a life-long colostomy. These problems significantly affect the child's psychosocial and physical wellbeing and have an impact on the family.

Obtaining consent to collect specimens from a patient with Hirschsprung's disease due to undergo a pull-through operation.

The joint RCS and BAPS fellowship funded the first year of my PhD in which I aimed to characterise the expression of nerve cell markers and components of the Notch signalling pathway, a key pathway regulating the development of nerve cells from stem cells in the bowel.

Human bowel samples were collected during elective surgical procedures and bowel was digested using enzymes to isolate individual cells. Stem cells were grown in tissue culture as aggregates, known as neurospheres. Sections of bowel, neurospheres and dissociated single cells were analysed using immunofluorescence to detect biomarkers of neural and stem cells. We could show that stem cells from normal and affected Hirschsprung bowel turned into nerve cells in culture, indicating they have potential to be used for therapeutic purposes. Components of the Notch signalling pathway were found in the affected bowel and in cultured neurospheres.

Thus, my current research is focused on manipulating the Notch signalling pathway and other important signalling pathways during stem cell culture to determine whether we can direct the formation of nerve cells from stem cells isolated from the affected bowel, while preventing any uncontrolled cell growth.

The ultimate goal is to develop a novel topical therapy targeting the affected bowel, using the patient's own stem cells to compensate for the lack of nerve cells, as a replacement or adjunct to surgery, thereby improving outcomes.

Sumita with her supervisor Mr Kenny prior to obtaining a bowel specimen from a patient with Hirschsprung's disease.

Up to 30% of children with surgically corrected Hirschsprung's disease suffer from long-term constipation or incontinence and 10% of children require a life-long colostomy.

Role of Neuropilin-1 expression on monocyte/macrophages in the ischaemic limb

Jun Seok Cho

FELLOWSHIP/SPONSOR:
Joint RCS/BSET Endovascular Research Fellowship with the support of the Fletcher Legacy

SUPERVISOR:
Professor Bijan Modarai

SITE OF WORK:
Academic Department of Vascular Surgery, School of Cardiovascular Medicine and Sciences, BHF Centre of Research Excellence, St Thomas' Hospital, King's College London

PRIZES:
Patey Prize Winner, SARS 2018

Jun performing part of a femeropopliteal bypass surgery with the vascular team.

Critical limb ischaemia (CLI) is a condition characterised by intractable pain or gangrene as a result of blocked arteries. Current treatment options include bypass surgery or the use of balloons/stents to improve blood flow to the limb. Despite recent advances in treatment modalities, it's estimated that 20–40% of patients with CLI are not suitable for treatment or have failed procedures due to existing medical frailty or unfavourable anatomy of disease. Patients with CLI have severely reduced quality of life, mainly due to pain, and up to one in three patients will undergo a major amputation within one year of diagnosis. This highlights the urgent need for new treatment strategies.

Delivering cells in order to stimulate growth/enlargement of blood vessels in the ischaemic limb has been proposed as an alternative treatment option for CLI patients. Cell therapy has shown promising results in the laboratory but the results of clinical trials using unselected mixture of cells have had modest efficacy to date. The aim of this research was to identify a potent sub-group of cells to maximise vessel growth and improve clinical outcomes.

We investigated the role of Neuropilin-1 expressing monocytes/macrophages (NEMs) in restoring blood flow of the ischaemic limb through bench side laboratory experiments, as well as a validated animal model of limb ischaemia. My experiments showed that injection of NEMs into the ischaemic muscle accelerated blood flow restoration. Conversely, deleting Neuropilin-1 protein from monocytes and macrophages significantly impaired vessel growth, demonstrated by reduction in the number and size of blood vessels in the ischaemic muscle. Therefore, delivery of large numbers of NEMs may represent an effective cell therapy for CLI patients. This has the potential to reduce major amputation rate and offer treatment to patients who are too frail for conventional treatment options.

One in three patients diagnosed with critical limb ischaemia would require a major limb amputation within a year.

Multi-modality imaging to determine the role of calcification and inflammation on restenosis rates following lower limb angioplasty – the CIRLA Study

Mohammed M Chowdhury

FELLOWSHIP/SPONSOR:
Freemasons' Royal Arch Fellowship

SUPERVISORS:
Mr Paul Hayes, Mr Patrick Coughlin and Dr James Rudd

SITE OF WORK:
University of Cambridge and Cambridge University Hospital Trust

PUBLICATIONS:
1. Chowdhury MM, Tarkin JM, Evans NR *et al.* PA 18F-FDG Uptake on PET/CT in Symptomatic versus Asymptomatic Carotid Disease: a Meta-Analysis. *Eur J Vasc Endovasc Surg* 2018; **56**: 172–179

2. Tarkin JM, Joshi FR, Evans NR *et al.* Detection of Atherosclerotic Inflammation by 68Ga-DOTATATE PET Compared to 18F-FDG PET Imaging. J Am Coll Cardiol 2017; **69**: 1,774–1,791

PRESENTATIONS:
1. Presented at: British Society of Endovascular Therapy – National conference first author); 2015; UK

2. Presented at: American Heart Association AGM – International conference (third author); 2016; USA

PRIZES:
1. The British Journal of Surgery Prize Vascular Society Annual Scientific Meeting 2018 Glasgow

2. Jay D. Coffman PVD Young Investigators Award 2018 Winner at International Young Investigator session, American Heart Association Scientific Session AGM, Chicago

FURTHER FUNDING:
BHF for three years

Atherosclerosis (hardening of the blood vessels with fatty substances) is linked with both inflammatory and calcification processes occurring at the vessel wall. Novel imaging techniques, such as positron emission tomography-computed tomography (PET/CT) have been developed to assess this using specialised tracers such as a bone tracer (radio-labelled sodium fluoride – 18F-NaF) to detect calcification and a sugar tracer (radio-labelled glucose – 18F-FDG) to detect inflammation, both in the blood vessel. This study is the first to prospectively utilise PET/CT analysis to determine renarrowing or restenosis after angioplasty in patients with symptomatic peripheral arterial disease (PAD).

18 patients (11 men, median age 69) with superficial femoral artery disease underwent PET/CT scans. Patients were imaged at baseline and 6-weeks post angioplasty. Over a median follow-up 8 months, 7 patients developed renarrowing. These patients showed no difference in tracer uptake between baseline and 6-week readings. However, those that did not suffer from renarrowing (*n*=11) demonstrated a decrease in both 18F-FDG and 18F-NaF readings. Furthermore, baseline tracer readings were higher for both 18F-FDG 18F-NaF in the restenosis versus no-restenosis group.

This study is the first to prospectively validate PET CT analysis in patients with symptomatic PAD. Further work is required to correlate this with systemic biomarkers.

This is an extremely novel method of imaging diseased arteries, and so its use in PAD has never been used. This forms the fellow's PhD and results thus far pertain to the fellow's first year report.

PAD affects 5% of males over the age of 65 years, and an estimated 202 million patients globally. PAD patient can present with claudication, night pain or tissue loss. This research could help identify 'high-risk' patients and help reduce their restenosis risk.

Mo presenting at the Vascular Society of GB & Ireland AGM where he was awarded the BJS prize for best scientific paper.

50% of patients will develop renarrowing (or restenosis) after a simple femoral balloon angioplasty (inflation of balloon in the artery to help improve blood supply to the leg) within 12 months. These patients face the risk of disease progression, which can ultimately lead to limb loss and increased cardiovascular mortality.

Interaction of Adipose Stem Cells (ADSC) & MCF-7s in the breast microenvironment: A pilot study

Emman Combellack

FELLOWSHIP/SPONSOR:
RCS Research Fellowship with the support of the Blond McIndoe Fund

SUPERVISORS:
Professor Shareen Doak and Professor Iain S Whitaker

SITE OF WORK:
The Reconstructive Surgery & Regenerative Medicine Research Group (ReconRegen), Institute of Life Sciences, Swansea University Medical School and the European Centre for NanoHealth, Institute of Life Science, Swansea University Medical School

PUBLICATIONS:
1. Combellack EJ, Jessop ZM, Naderi N *et al.* Adipose regeneration and implications for breast reconstruction: update and the future. *Gland Surg* 2016; **5**: 227–241

2. Naderi N, Combellack EJ, Griffin M *et al.* The regenerative role of adipose-derived stem cells (ADSC) in plastic and reconstructive surgery. *Int Wound J* 2017; **14**: 112–124

PRIZES:
1. Stephan and Anna Galeski Travel Fellowship 2017

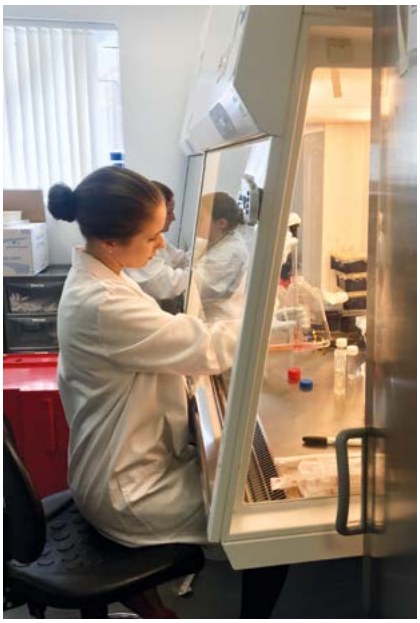
2. Rex and Jean Lawrie Travel Fellowship 2017

Breast cancer occurs in 1:8 women worldwide. Breast reconstruction is an important part of the recovery process, often seen as 're-building what has been lost'. As fat transfer has become an increasingly popular choice for patients and surgeons as a method of improving the breast shape following excisional surgery, understanding its safety profile and how it affects patients' prognosis and outcome is crucial.

Em teaching on an international surgical skills workshop in Yogyakarta, Indonesia.

Within the transferred fat, there are a population of stem cells (ADSCs), which primarily serve to respond to, and repair damage. When put into the same environment as cancer they can have a different effect and support the cancer to grow and develop more rapidly. Building on current scientific research, demonstrating the potential of fat grafts to promote cancer progression, this study set out to establish baseline differences between fat taken from two different patient populations and investigate how they affected cancer growth and progression.

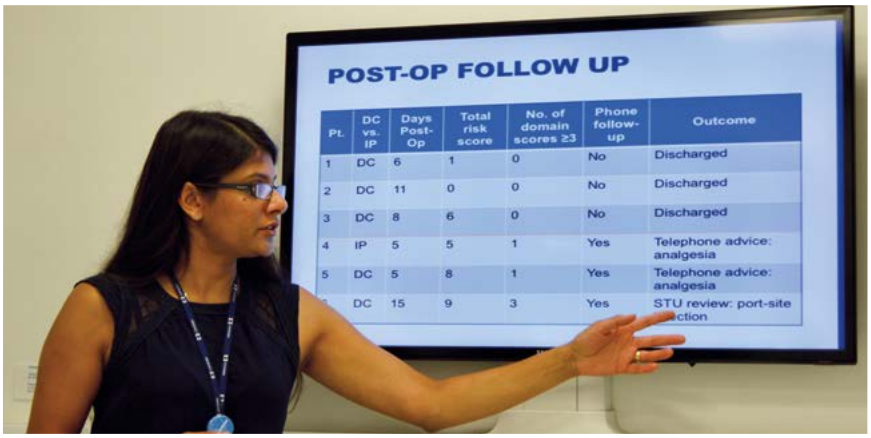
To date, we have been able to examine stem cells taken from six patients and evaluate how they affect the growth and movement characteristics of a breast cancer cell line (MCF-7). The two different groups of patients have demonstrated a difference in terms of their fat affecting the cancer. This is important because it adds to the understanding as to what factors affect the stem cells and how they might interact with any residual cancer that remains. Furthermore, this has allowed the design of the second stage of the research project, which will examine the co-culture of these cell populations in more detail. Overall, this will contribute to the understanding of safety of fat grafting enabling patients to not only make a more informed choice but to support potential regulation and recommendation of this procedure within the surgical community.



Em in the lab working on the Primary ADSC lines taken from breast cancer patients.

Breast cancer is the most common cancer in women in the UK, with more than 54,900 new cases every year.

Multimedia informed consent and PROMs in laparoscopic cholecystectomy



Prita presenting her research to additional study sites to expand recruitment.

Prita Daliya

FELLOWSHIP/SPONSOR:
RCS/EIDO Joint Research Fellowship

SUPERVISORS:
Mr Simon L Parsons and
Professor Dileep N Lobo

SITE OF WORK:
Nottingham Digestive Diseases Centre and National Institute for Health Research (NIHR) Biomedical Research Centre, Nottingham University Hospitals NHS Trust and University of Nottingham

PRESENTATIONS:
1. Presented at: Association of Surgeons of Great Britain and Ireland; May 2017; Glasgow

2. Presented at: East Midlands Surgical Society; June 2017

PRIZES:
1. Second prize – East Midlands Surgical Society, June 2017

2. First prize – Nottingham University Postgraduate Research Forum, June 2017

Gallstones are a common problem affecting 5 to 25% of adults worldwide. Affected patients can experience debilitating episodes of pain, in addition to a number of other serious complications.

Definitive treatment involves keyhole surgery to remove the gallbladder (laparoscopic cholecystectomy). Patients are normally informed of their diagnosis and this treatment in an outpatient clinic setting. These appointments are often time-limited, and can be overwhelming for patients to fully assimilate and understand the implications of surgery. This is less than ideal when ensuring informed consent.

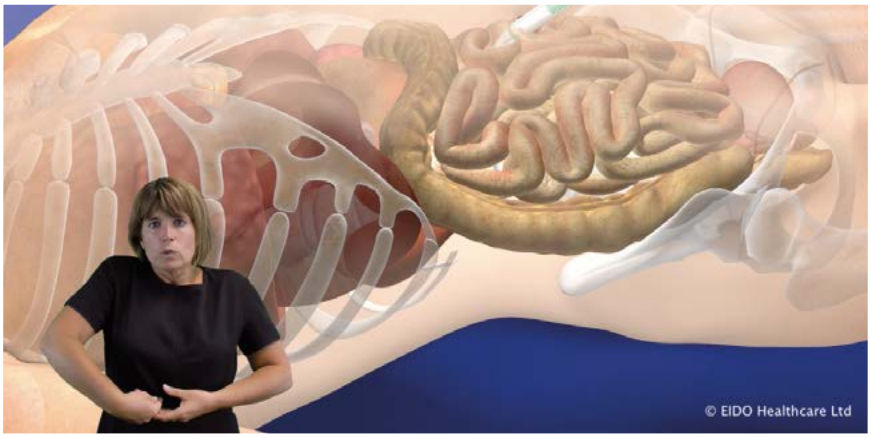
Although more than 60,000 cholecystectomies are performed annually in the UK, little is still known about its impact on a patient's quality of life. Patient reported outcome measures (PROMs) are validated questionnaires used to collect quality-of-life information on patients before and after surgery. They provide valuable information from the patient's perspective and are known to improve clinical services, yet they are not routinely recorded.

The aim of this study was to design and implement a secure patient-facing website into routine clinical care to:

- measure health *gain* in adult patients undergoing laparoscopic cholecystectomy
- improve the informed consent process and delivery of relevant patient information
- provide an alternative postoperative follow-up process
- improve communication and shared decision-making

Although this study is currently ongoing, preliminary data has demonstrated positive responses from patients who are keen to be involved and willing to engage with an online platform to support information sharing.

By providing a means to routinely collect pre- and postoperative PROMs, this research could provide valuable feedback to help hospitals review their clinical practice, monitor changes, and improve patient outcomes. The provision of timely information for patients, available with better accessibility, also has the potential to improve the quality of consultations for patients and clinicians, and provide a framework to encourage shared decision-making.



Accessibility options available from the aboutmyop.org website, designed as part of the research project.

More than 60,000 cholecystectomies are performed annually in the UK, yet little is still known about the impact of this surgery on a patient's quality of life.

The effects of mitochondrial dysfunction on bone density, osteoblasts and osteoclasts

Philip Francis Dobson

FELLOWSHIP/SPONSOR:
Shears Northern Research Fellowship

SUPERVISORS:
Professor Sir Doug Turnbull and Professor David Deehan

SITE OF WORK:
Wellcome Trust Centre for Mitochondrial Research, Medical School, Newcastle University

PUBLICATIONS:
Dobson PF, Rocha MC, Grady JP *et al.* Unique quadruple immunofluorescence assay demonstrates mitochondrial respiratory chain dysfunction in osteoblasts of aged and PolgA$^{-/-}$ mice. *Sci Rep* 2016; **24**: 31907

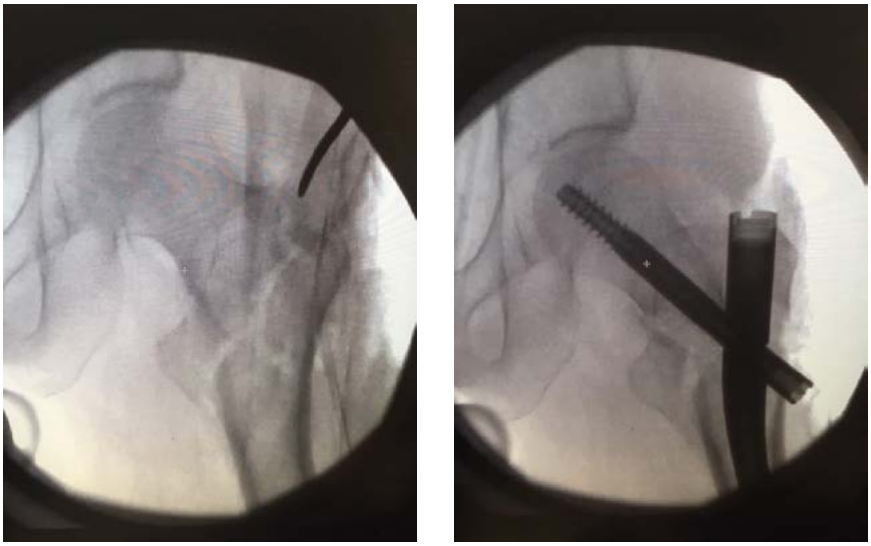
PRIZES:
University of Glasgow, September 2016

Mitochondria are the battery packs contained within all of our cells and are vital for normal cellular function. As we get older, we accumulate mutations in our mitochondrial DNA, which can impair cellular function. Evidence suggests these mutations may be causative in the process of ageing. I have used a mouse model that accumulates mitochondrial DNA mutations at an accelerated rate to assess the effects on bone biology.

I used a micro CT scanner to study lumbar spine and femoral bone to show that accelerated bone loss occurs in the presence of increased mitochondrial dysfunction. I developed a new microscopic technique, using immunofluorescent probes to target mitochondria within osteoblasts and osteoclasts, to show that increasing numbers of abnormal mitochondria occur with advancing age in normal mice and at increased levels in mutant mice, but that osteoblasts appear to be particularly vulnerable to the process. I extracted cells from the mice and differentiated them into osteoclasts and osteoblasts to show that severe functional impairment occurs in both cell types in the presence of mitochondrial dysfunction.

Current and extensive research into the pathogenesis of osteoporosis proposes various theories, but the concept that mitochondrial dysfunction could play a significant role is a relatively new one. This is the first work to show that mitochondrial dysfunction significantly impairs osteoblast function.

Humans accumulate mitochondrial DNA mutations over a much longer time period, albeit at a slower rate than the mutator mice, and it is highly likely that this will have a direct, detrimental effect on human bone biology. Further investigation in humans is underway. The disease burden is huge. Hip fracture data shows that only 30% of patients fully recover, with 50% being left permanently disabled to some degree and 20% dying due to the enhanced risk of complications such as pneumonia or thromboembolic disease.



Xrays of an osteoporotic proximal femur fracture which has been surgically treated by Philip with an intramedullary nail.

The incidence of hip fractures was 70,000 per year in 2006 but with an ever ageing population, this figure is projected to rise to 101,000 per year in the UK by 2020.

Making surgery safer: Can a wireless monitoring patch detect complications early?

Candice Downey

FELLOWSHIP/SPONSOR:
RCS Research Fellowship

SUPERVISOR:
Professor David Jayne

SITE OF WORK:
St James's University Hospital, Leeds

PUBLICATIONS:
1. Downey CL, Tahir W, Randell R *et al.* Strengths and limitations of early warning scores: A systematic review and narrative synthesis. *Int J Nurs Stud* 2017; **76**; 106–119

2. Downey CL, Brown JM, Jayne DG et al. Patient attitudes towards remote continuous vital signs monitoring on general surgery wards: An interview study. Accepted for publication in the *Int J Med Inform*

PRESENTATIONS:
Making Surgery Safer. Presented at: NHS Health and Care Innovation Expo; September 2017; Manchester

PRIZES:
1. Rosetrees Trust Essay Prize for 'Making surgery safer: Will a wireless patch detect complications earlier?' (December 2017)

2. The Worshipful Company of Cutlers' Surgical Prize 2018, 'Making surgery safer: Continuous remote monitoring via a wearable wireless patch for the early detection of surgical complications'

FURTHER FUNDING:
National Institute for Health Research Doctoral Research Fellowship for three years

Despite advances in patient care, major surgery remains high risk. Up to 30–40% of patients will experience a serious complication. Identifying complications early is crucial to avoid a longer stay in hospital, another operation or even death.

The most common way to detect complications is by monitoring patients' vital signs. The nurse looking after the patient will see them every few hours to measure their blood pressure, pulse, breathing rate and temperature. The problem with these intermittent observation rounds is that patients can deteriorate in between checks, leading to delayed recognition of complications.

A wireless monitoring patch could solve this problem. Worn on the patient's chest, it monitors their heart rate, breathing rate and temperature continuously. The patient's nurse is alerted immediately if the vital signs change.

The aim of my research was to discover if this new way of monitoring leads to earlier detection of complications and improves the outcome of major surgery for patients.

I tested the patch on two general surgical wards at St James's Hospital, Leeds, between January and June 2017: 140 patients received the new patch alongside normal monitoring and 210 received usual monitoring alone.

The patched patients tended towards a shorter stay in hospital and were half as likely to be readmitted to hospital once they were home. This might be because their complications were picked up earlier, which is supported by the fact that patients in the patch group tended to receive antibiotics faster when they got an infection, compared with those in the normal monitoring group.

The results suggest a trend in favour of the continuous monitoring patch when compared to traditional monitoring alone. The findings of this project have been used to design a feasibility trial funded by the National Institute of Health Research.

Candice highlighting patient deterioration using the continuous vital signs tracings.

Patients who wore the continuous monitoring patch tended towards a shorter stay in hospital and were half as likely to be readmitted to hospital once they were home.

Enhancing healthcare value though surgical innovation metrics

Georgios Garas

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

SUPERVISORS:
Professor Thanos Athanasiou and Professor Lord Ara Darzi

SITE OF WORK:
St Mary's Hospital, Imperial College London

PUBLICATIONS:
1. Garas G, Cingolani I, Panzarasa P *et al*. Beyond IDEAL: A call for surgical innovation metrics. *Lancet* 2018 [in press]

2. Garas G, Cingolani I, Panzarasa P et al. Network analysis of surgical innovation: measuring value and the virality of diffusion in robotic surgery. *PLoS One* 2017; **12**: e0183332

PRESENTATIONS:
1. Presented at: Annual Meeting of the American Head and Neck Society – Combined Otolaryngology Spring Meeting; April 2018; USA

2. Presented at: International Surgical Congress of the Association of Surgeons of Great Britain and Ireland; May 2017; Glasgow

PRIZES:
1. Alexander S. Onassis Public Benefit Foundation Fellowship 2018

2. Best E-Poster Prize, Surgical Simulation and Technology Category, Association of Surgeons of Great Britain and Ireland, International Surgical Congress 2017

FURTHER FUNDING:
Alexander S. Onassis Public Benefit Foundation and Imperial College London for three years

George performing transoral robotic surgery (TORS) as part of his surgical innovation studies.

The NHS is experiencing a radical transformation driven by pressures to reduce costs. An ageing population has ever increasing healthcare needs with patient expectations growing. Measuring healthcare innovation value is more important than ever.

Currently, the rate of innovation occurring in surgery is beyond our systemic capacity to quantify, with several methodological and practical challenges. Existing frameworks are limited to qualitative models. Big data, involving the capture and analysis of large, complex (multidimensional) datasets using machine learning remain underutilised in surgery.

Award of Poster of Distinction Prize by the American Head and Neck Society in New York.

The RCS Research Fellowship provided me with the opportunity to focus on addressing these limitations. With my supervisors and collaborators, we described the surgical innovation funnel and using network analysis developed the first surgical innovation metrics: the innovation index and structural virality. These were subsequently validated using big data from the real world that exceeded seven million hospital stays per year (NIS®). These novel ideas and findings were published in some of the world's most prestigious peer-reviewed scientific journals including *The Lancet*.

My research offers an exciting new perspective for understanding how the innovation process originates and evolves in surgery and how it can be measured in terms of value and virality, a priority for the RCS, NHS and wider surgical community. The ability to measure value and rank innovations is expected to play a fundamental role in guiding policy, strategically direct research funding, and uncover innovation barriers and catalysts. This will ensure participation in the forefront of novel surgical technology and lay the scientific foundations for the development of improved healthcare models and services to enhance the quality of healthcare delivered.

I will be taking this forward by analysing global surgical collaboration networks to demonstrate how this approach can be used to devise effective strategies towards the establishment of partnerships that can enhance innovation and advance patient care.

At a time when the NHS is experiencing a radical transformation driven by pressures to reduce costs, there is a growing sense of urgency to develop rigorous surgical innovation metrics, crucial for optimising patient care.

Tissue engineering airway mucosa

Nicholas Hamilton

FELLOWSHIP/SPONSOR:
RCS Research Fellowship

SUPERVISOR:
Professor Martin Birchall

SITE OF WORK:
Rayne Institute, UCL

PUBLICATIONS:
1. Hamilton NJ, Birchall MA. Tissue-Engineered Larynx: Future Applications in Laryngeal Cancer. *Curr Otorhinolaryngol Rep* 2017; **5**: 42–48

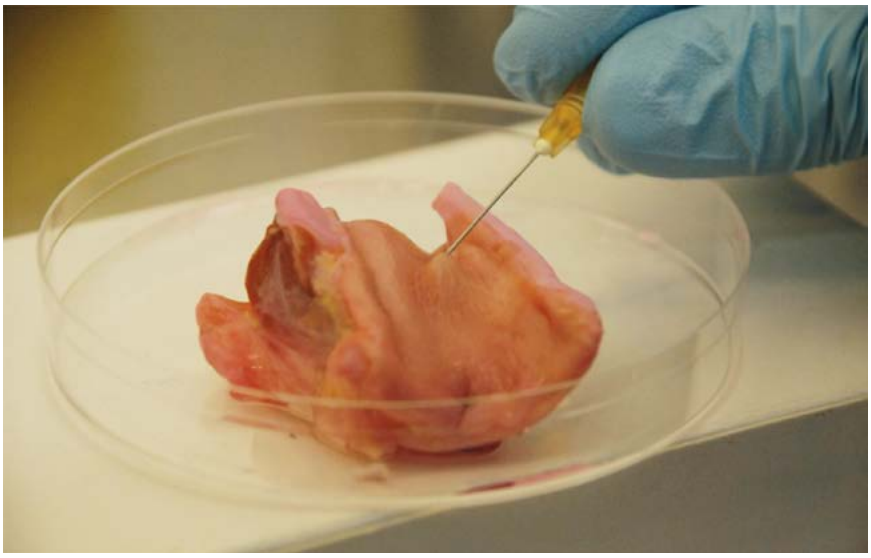
2. Hamilton NJ, Kanani M, Roebuck DJ *et al.* Tissue-engineered tracheal replacement in a child: a 4-year follow-up study. *Am J Transplant* 2015; **15**: 2,750–2,757

PRESENTATIONS:
1. *Tissue engineering airway mucosa using a decellularised dermis scaffold.* Presented at: Academy of Medical Sciences Spring Meeting; Feb 2017; London

2. *Tissue engineering airway mucosa.* Presented at: American Academy of Otolaryngology-Head & Neck Surgery; Sept 2016; San Diego

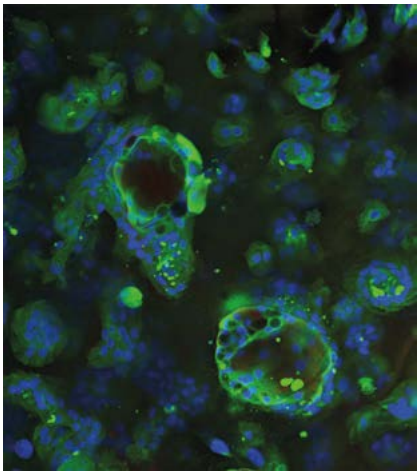
PRIZES:
Alice Maud-Hall Travel Prize (2013)

FURTHER FUNDING:
Medical Research Council for three years



Respiratory epithelial cells embedded within a collagen gel.

The safety and effectiveness of tissue-engineered transplants within the upper airways of the throat and windpipe are limited by the absence of an effective method to regenerate the lining. Airway lining is crucial as it provides a barrier against infection and has a number of specialised functions such as mucus secretion and clearance. My research aimed to regenerate upper airway lining in the laboratory and develop techniques to graft the new lining as part of an upper airway transplant.



Tracheal segment following grafting of regenerated mucosa.

Cells from patients' upper airways were taken and grown in a laboratory before seeding them onto collagen based scaffolds. Using a specialised culture environment, a lining that secreted mucus and had small hair cells that beat to clear secretions was regenerated. The lining was then grafted onto sections of windpipe to test integration. While the lining successfully grafted in the short term, the mucus secreting and hair cells degenerated in the long term. This led to the development of a new method for embedding cells within a collagen gel resulting in long-term cell survival following grafting.

The findings of this research have paved the way for a new therapy that can reline the upper airway of humans suffering from complex scarring disorders of the throat and windpipe. The ability to regenerate lining within other parts of the upper airway, such as the nose and ear, may also unlock a number of other novel therapies to address a range of conditions for which conventional treatments are ineffective.

Exploring time-efficient strategies to improve fitness for surgery in older adults

Philip James Joseph Herrod

FELLOWSHIP/SPONSOR:
Joint RCS/Dunhill Medical Trust Fellowship

SUPERVISORS:
Mr JN Lund and Dr BE Phillips

SITE OF WORK:
University of Nottingham at the Royal Derby Hospital

PUBLICATIONS:

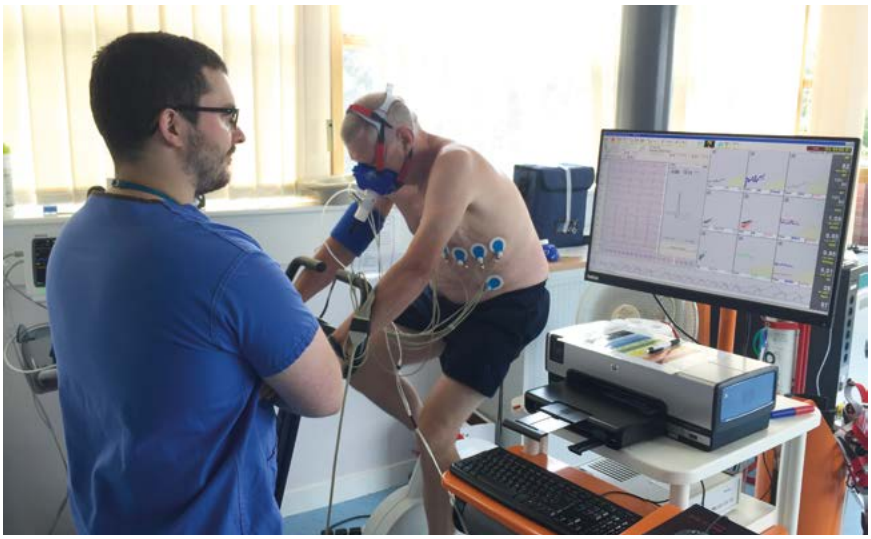
1. Herrod PJJ, Doleman B, Blackwell JEM *et al.* Exercise and other nonpharmacological strategies to reduce blood pressure in older adults: a systematic review and meta-analysis. *J Am Soc Hypertens* 2018; **12**: 248–67

2. Blackwell JEM, Doleman B, Herrod PJJ *et al.* Short-Term (<8 Weeks) High-Intensity Interval Training in Diseased Cohorts. *Med Sci Sports Exerc.* 2018; (in press)

PRESENTATIONS:

1. Herrod PJJ, Lund JN, Phillips BE. *Exploring time efficient strategies to improve fitness for surgery in older adults: A randomised trial.* Presented at: SARS; January 2018; Nottingham

2. Herrod PJJ, Doleman B, Blackwell J et al. *Non-pharmacological strategies to reduce blood pressure in older adults: a systematic review and meta-analysis.* Presented at: UK Public Health Science Meeting; November 2017; London



Phil supervising a cardiopulmonary exercise test.

The majority of diseases that can be treated by surgery become more frequent in older patients. Unfortunately people tend to become less fit as they get older and previous research has shown that people who are less fit are at increased risk of a complication during or after an operation. This is increasingly leading to more people being turned down for elective surgery as they are not fit enough to have an operation.

Setting up a cardiopulmonary exercise test.

Exercise interventions have the potential to reverse some of the decline in cardiovascular fitness associated with ageing and may improve the older patients' 'fitness for surgery'.

My research involves running a randomised controlled trial in healthy volunteers aged 65–85, investigating three time-efficient interventions to improve various aspects of fitness over 6 weeks. The interventions have all shown promise in pilot studies in younger individuals but have yet to be tested thoroughly in older adults. The interventions are high-intensity interval training on an exercise bike, isometric handgrip training (squeezing a hand gripper tightly) and remote ischaemic preconditioning (using a blood pressure cuff to intermittently cut off blood flow to a limb).

My trial is currently over its halfway point and aims to finish recruiting in early 2019. The interim results suggest that all three interventions may reduce a patient's blood pressure and improve other markers of fitness with six weeks of training. If after the trial is completed these simple and low cost interventions are demonstrated to work, then they have the potential to benefit many older patients who need an operation. Because these methods are simple and require very little equipment, they could also possibly be carried out in a patient's own home.

The peak incidence of bowel cancer is in those over 85. However, less than 8% of operations to cure bowel cancer happen in the over 85s. (NBOCA report 2017 and Cancer Research UK).

Mitochondrial dysfunction in the pathogenesis of osteoporosis

Daniel Hipps

FELLOWSHIP/SPONSOR:
Shears Northern Research Fellowship

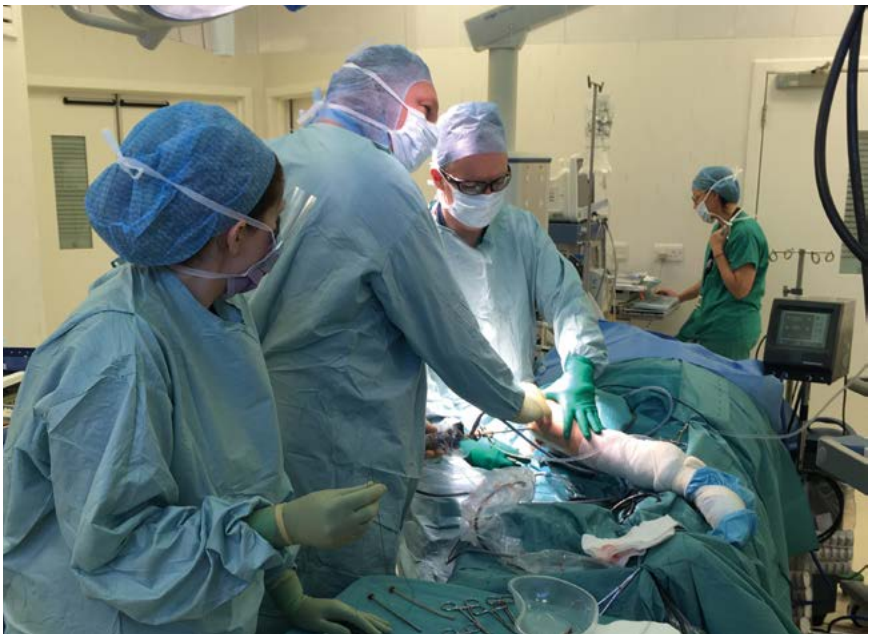
SUPERVISOR:
Professor Sir Doug Turnbull

SITE OF WORK:
Wellcome Centre for Mitochondrial Research, Newcastle University

PUBLICATIONS:
1. Dobson PF, Rocha MC, Grady JP *et al.* Unique quadruple immunofluorescence assay demonstrates mitochondrial respiratory chain dysfunction in osteoblasts of aged and PolgA$^{-/-}$ mice. *Sci Rep* 2016; **6**: 31,907

PRESENTATIONS:
1. Presented at: American British and Canadian (ABC) Travelling Fellowship Academic Day at Hexham General Hospital; May 2017; Northumbria

FURTHER FUNDING:
Biomedical Research Centre Newcastle for one year



Dan taking bone marrow samples for use as controls from a paediatric patient undergoing an ACL reconstruction with Professor Deehan.

The aims of this research are to show the links between DNA mutations or faults found in the energy making parts of cells (mitochondria) and osteoporosis or brittle bones. Osteoporosis leads to increased risks of fractures and complications associated with these. Osteoporosis is currently not fully understood and is thought to be multifactorial.

This work builds upon a mouse model that showed a clear link between these DNA mutations and osteoporosis. By taking samples of human bone and bone marrow at the time of routine orthopaedic surgery, we have been able to isolate cells from these samples. Using these cells, we have been able to grow bone in the laboratory and analyse these cells for DNA faults using a number of techniques.
We then can correlate these findings to show how DNA faults influence cell ability to produce bone and lead to the development of osteoporosis.

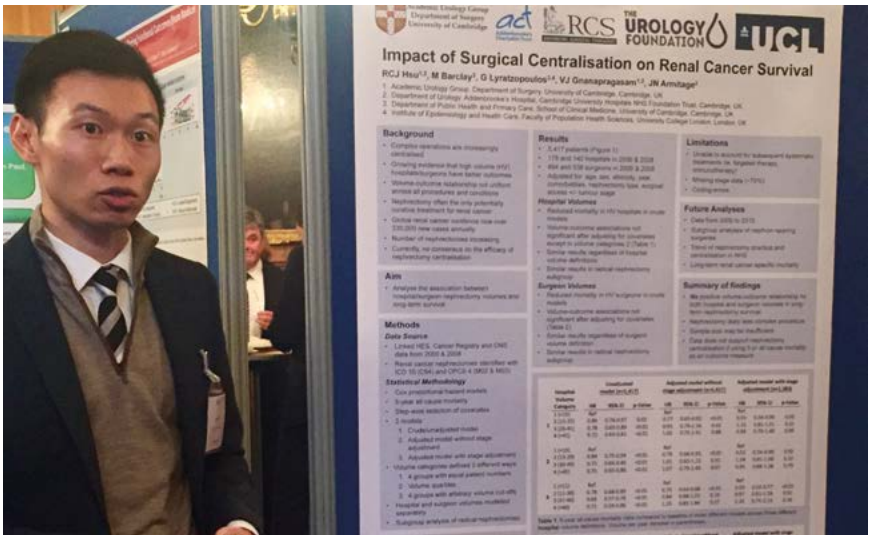
This research is the first of its kind to demonstrate a link between osteoporosis and mitochondrial DNA mutations. Moving this research forwards and further clarifying the link that mitochondria play in the cause of osteoporosis is the first step to developing new lines of treatment.

Osteoporosis is a global problem, which is increasing every year. Understanding the true cause of osteoporosis is the first step in developing new treatments. Effective treatment for osteoporosis will reduce the risks of fracture. Reducing the risks of fracture will reduce complications including death resulting from those injuries. Ultimately, this could have a significant impact on the elderly population of whom the vast majority have osteoporosis.
It also has the potential to benefit the healthcare system financially and by changing practice, which is also important given the current economic climate.

Dan and Professor Sir Doug Turnbull at the Wellcome Centre for Mitochondrial Research.

Osteoporotic fragility fractures cost the UK somewhere in the region of £2 billion per year.

The role and impact of surgical centralisation on renal cancer survival



Ray presenting at a British Association of Urological Surgeons meeting.

Ray Hsu

FELLOWSHIP/SPONSOR:
The RCS/ACT Research Fellowship with the support of the Starritt Legacy

SUPERVISORS:
Mr James Armitage, Mr Vincent Gnanapragasam and Professor Georgios Lyratzopoulos

SITE OF WORK:
University of Cambridge

PUBLICATIONS:
1. Hsu RCJ, Salika T, Maw J *et al.* Influence of Hospital Volume on Nephrectomy Mortality and Complications: A Systematic Review and Meta-Analysis Stratified by Surgical Type. *BMJ Open*. [In press]

PRESENTATIONS:
1. *The Volume–Outcome Relationship in Nephrectomy: A Systematic Review and Meta-Analysis*. Presented at: Public Health England Cancer Data and Outcomes Conference; June 2016, Manchester

2. *Trend and Impact of Nephrectomy Centralisation in England*. Presented at: British Association of Urological Surgeons Annual Scientific Meeting; June 2017; Glasgow

FURTHER FUNDING:
The Urology Foundation for one year

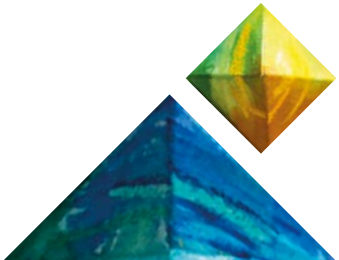
Kidney cancer is the seventh most common cancer in the UK affecting more than 12,000 new patients each year. This number is growing year-on-year partly due to the widespread use of radiological imaging detecting small asymptomatic tumours and also, to the increasing prevalence of common risk factors, such as obesity. The majority of patients are diagnosed with localised disease, which is typically managed with nephrectomy, the surgical removal of the kidney.

There is emerging evidence that complex operations carried out by hospitals performing a high annual number of the same procedure are more likely to result in better outcomes. However, this may not be applicable to all conditions and operations due to differences in disease biology and surgical complexity.

Our initial systematic review and meta-analysis of published studies showed that there is currently some, albeit limited, evidence favouring high volume hospitals with reduced risks of surgical complications and death within 30 days of nephrectomy. The majority of the studies were, however, from healthcare systems that are very different to that in the UK and the results may not be directly transferrable. In addition, little is known about how hospital volumes affect patient survivals at one and five years after nephrectomy. It is therefore essential that further research is carried out to understand the potential benefits of centralising surgical care for kidney cancer. At the same time, assessing the balance between the benefits and the disadvantages associated with service reconfiguration, such as the inconvenience to patients to travel to regional centres and the loss of physician skills and training opportunities at local district general hospitals.

Our objectives will be achieved by using various databases containing routinely collected data including the Hospital Episode Statistics and National Cancer Data Repository. These databases contain a wealth of information and are well suited for our project as they contain details on patient demographics, tumour characteristics and organisational features. They also benefit from unbiased whole population coverage with long-term follow up enabling us to answer questions that were previously not possible.

The results from our study will provide unique insights into the management of kidney cancer in England and will inform government agencies, health service providers and healthcare professionals to drive policy and service changes that have direct improvements on patients care.



More than 330,000 people per year are diagnosed with kidney cancer worldwide. Surgical removal of the kidney offers patients the best chance of a cure, but the effects that service provision and organisational factors have on patient outcomes remain unclear.

Patient-specific craniofacial reconstruction of congenital midface deformities using virtual surgery computer modelling

Amel giving a talk entitled 'Rewriting the Future – Changing the Discourse on Biotechnology' outlining her vision for the future of biotechnology in healthcare, which can be viewed on YouTube.

Amel Ibrahim

FELLOWSHIP/SPONSOR:
RCS Fulbright Scholar Award with the support of the Saven Research and Development Programme

SUPERVISOR:
Dr Roberto Flores

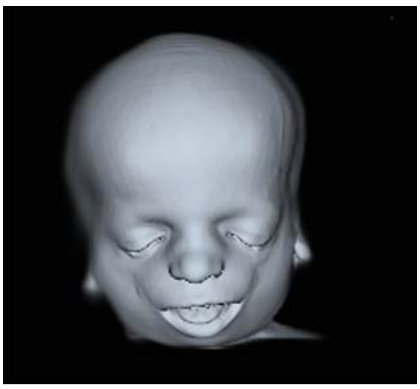
SITE OF WORK:
Hansjorg Wyss department of Plastic and Reconstructive surgery, New York University Langone Health

PUBLICATIONS:
This work is being prepared for submission to *Plast Reconstr Surg*

PRESENTATIONS:
Since this was a six-month scholarship, there have only been local presentations so far. I will be submitting this work for presentation at an international craniofacial surgery conference, and to the American Association of Plastic and Reconstructive Surgeons

FURTHER FUNDING:
New York University for 12 months

Children born with facial deformities can suffer from breathing, feeding and speech difficulties, which require multiple invasive surgeries throughout childhood. This research applies computer modelling to better understand these diseases, the extent of the deformities and identify more optimal treatments for these children.



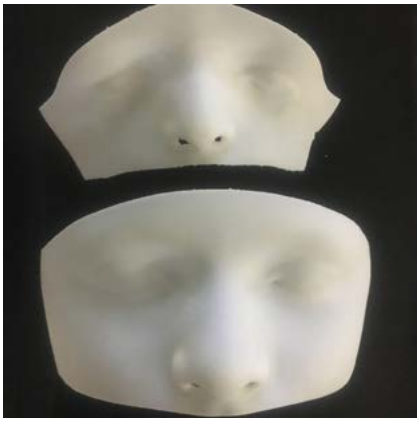
3D reconstruction of a facial scan from a child with a facial birth defect.

There is scarce data on normal facial growth and in children born with deformities. This work builds on my previous research which, for the first time modelled normal growth of the face and compared it with children suffering from two causes of facial deformities.

The aim of this project was to undertake research at New York University (NYU) to create a more advanced computer model that helps better understand facial deformities in children and increases the accuracy of surgical planning.

The study used facial scans from children treated at NYU Langone Health to build the computer model the face. The new model provided more information on normal facial growth and in children suffering from the four most common causes of facial defects. It has also been used to model the outcome of different surgical procedures. This information builds the foundations for developing surgical planning software that will enable a more accurate approach to planning treatment in these children.

This project has created a collaboration between New York University and University College London, which will enable further data collection and serve as the preliminary data for preparing an application for research funding from the National Institute of Health. I was asked to stay at NYU to direct a human stem cell and disease modelling program. In this role, I will continue to develop this work to create a surgical planning tool. I intend to combine this project with tissue engineering research to create a precision medicine approach to reconstructing childhood facial deformities.



3D printed faces from the computer model of a face with Treacher Collins Syndrome (top) and the aim after correction of the defect (bottom).

1 in 1,000 children is born with a disfigurement affecting the face or head.

Do aquaporins predict and protect against renal damage in PUJ obstruction?

Laura Jackson

FELLOWSHIP/SPONSOR:
Joint RCS/BAPS Research Fellowship with the support of the Carol Rummey Legacy

SUPERVISORS:
Professor Richard Coward, Mr Mark Woodward and Dr Gavin Welsh

SITE OF WORK:
Bristol Renal, Dorothy Hodgkin Building, University of Bristol

PUBLICATIONS:
1. Jackson L, Woodward M, Coward RJ. The molecular biology of pelvi-ureteric junction obstruction. *Pediatr Nephrol* 2017; **13**: [Epub ahead of print]

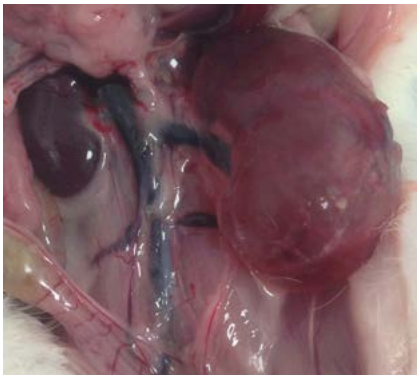
PRESENTATIONS:
1. *Do aquaporins predict and protect against renal damage in PUJ obstruction?* Presented at: Young Urology Meeting; September 2014; Bristol

FURTHER FUNDING:
David Telling Charitable Trust for one year

Laura performing surgery to create kidney obstruction in a two-day old rat pup.

A major challenge for paediatric urologists is deciding which children with antenatally detected kidney obstruction (termed PUJ obstruction) require surgery to relieve the blockage. This is because two thirds of children don't sustain kidney damage and grow out of the condition. It is not known why some children have 'damaging' and others have 'safe' obstruction. Additionally, there is no completely reliable method to distinguish these two groups. Children undergo repeated radiological tests to guide management, acknowledging the risk of declining function in the affected kidney while under observation.

This continuing research aims to address these issues. It has involved developing a neonatal rat model of PUJ obstruction alongside designing, implementing and coordinating a childhood study of PUJ obstruction at Bristol Children's Hospital.



A swollen left kidney resulting from neonatal rat kidney obstruction.

Recruitment to this study is ongoing. These complementary studies are enabling us to analyse the expression and urinary excretion of water channels, known as aquaporins, by the blocked kidney and drainage tube of both rats and humans.

Similar to limited previous studies, this research confirmed that rat kidney aquaporins are reduced in severe PUJ obstruction. Importantly, this research demonstrated for the first time the range of aquaporins found in rat kidney drainage tubes. It also established that aquaporins within kidney drainage tubes are reduced in rats with moderate and severe, but not mild PUJ obstruction.

These results have exciting implications. They indicate that aquaporins lining the kidney drainage tubes, as mediators of water re-absorption, may release pressure above the blockage protecting the growing kidney. Aquaporins may thus explain the difference between 'safe and 'damaging' obstruction. Ongoing research involves the creation of neonatal PUJ obstruction in a special mouse engineered without aquaporin channels in the kidney drainage tubes. This will demonstrate whether aquaporins are essential in protecting the blocked neonatal kidney, potentially bringing us significantly closer to developing new diagnostic tests and therapies for this condition.

1 in 200 babies has a swollen kidney on antenatal ultrasound scan.

3D bioprinting cartilage for facial reconstruction

Zita Jessop

FELLOWSHIP/SPONSOR:
RCS Fulbright Scholar Award with the support of the Sorab (Soli) Jamshed Lam Legacy

SUPERVISOR:
Professor Donald Ingber and Professor Iain Whitaker

SITE OF WORK:
Wyss Institute for Biologically Inspired Engineering, Harvard University

PUBLICATIONS:
1. Jessop ZM, Al-Sabah A, Gao N *et al.* Assessment of Crystal, Fibril and Blend Nanocellulose-Alginate Bioinks for Extrusion 3D Bioprinting with Nasoseptal Chondrocytes. *Biofabrication;* [Accepted 2018]

2. Thomas D, Jessop ZM, Whitaker IS. *3D Bioprinting for Reconstructive Surgery.* London: Elsevier, 2017

PRESENTATIONS:
1. *Development of a Novel Bioink to 3D Bioprint Cartilage for Facial Reconstruction.* Presented at: British Association of Plastic and Reconstructive Surgeons Scientific Meeting; November 2018; London

2. *The Chondrogenic potential of Nanocellulose-Alginate in Combination with Nasoseptal Chondrocytes for Tissue Engineering Purposes.* Presented at: Tissue Engineering and Regenerative Medicine International Society World Congress; September 2018; Kyoto

PRIZES:
1. BAPRAS Travelling Bursary for Presentation Overseas 2018

2. RCS Cutlers' Surgical Prize for Innovation 2017

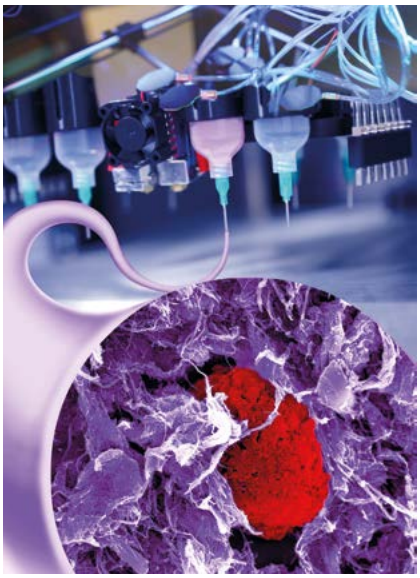
Zita with a patient following partial ear excision for squamous cell carcinoma.

Significant facial deformity can result following trauma, burns, skin cancer and congenital conditions with a profound effect on quality of life. Reconstruction of facial cartilage defects currently uses the patient's own cartilage or synthetic implants, resulting in complications related to cartilage harvest, in addition to infection and/or extrusion.

Worldwide research attempts to engineer cartilage focus on combining synthetic scaffolds with non-specific stem cells, which have led to well publicised failures involving regenerative medicine therapies. One of the reasons is a lack of a suitable natural biomaterial and tissue specific stem cells to replicate native tissue architecture. 3D bioprinting, which aims to more accurately replicate native microarchitecture, has been gaining traction to transition from theory into practice and allow surgeons to print customised and anatomically accurate replacement tissue using the patient's own cells.

Our laboratory was the first to successfully extract 'stem cells' from cartilage in the nose and demonstrate they can secrete cartilage matrix in the laboratory. This project builds on this, by combining these cells with a natural material for printing using a specialised 3D bioprinter. One of the major challenges in bioprinting is a bioink that is printable, capable of holding its structure, and able to provide an environment in which cells can thrive. Our initial results show that pulp derived nanocellulose bioink offers a number of advantages over other biomaterials for bioprinting applications.

Bioprinting has the potential to make personalised manufacturing of biological implants the gold-standard option for patients, removing the need for donor sites or long-term immunosuppression of transplantation. Spending my RCS Fulbright Scholarship at the Wyss Institute at Harvard University allowed me to learn about the integration of surgical research and industry, and the steps involved towards commercial and clinical translation of life science products and devices.



3D bioprinting of chondrocytes in natural bioink – illustration by Steve Atherton.

Significant facial disfigurements, including ear and nasal defects following trauma, burns, skin cancer resection and congenital conditions requiring reconstruction affect 1 out of 111 people in the UK.

Theranostic silica nanoparticles against colorectal cancer

Yazan S Khaled

FELLOWSHIP/SPONSOR:
RCS Research Fellowship

SUPERVISOR:
Professor David Jayne

SITE OF WORK:
University of Leeds

PUBLICATIONS:
1. Khaled YS. *Theranostic CEA-Affimer functionalised silica nanoparticles allow specific in vitro fluorescent imaging of colorectal cancer cells.* Presented at: British Association of Surgical Oncology meeting; 2017; Liverpool

2. Khaled YS. *Theranostic Foslip Loaded and Cea-Affimer Functionalised Silica Nanoparticles for Fluorescent Imaging and Photodynamic Therapy of Colorectal Cancer.* Presented at: SARS meeting; 2017; Nottingham

PRIZES:
1. Ronald Raven Prize for best oral presentation at the British Association of surgical Oncology 2017

2. Yorkshire Regional Surgical Club Prize, Huddersfield, 2018 Prize

FURTHER FUNDING:
MRC for three years

Yazan leading a group discussion on the applications of nanotechnology for colorectal cancer.

Surgery is the main treatment for colorectal cancer. It involves removal of the cancer together with any cancer cells that have spread along draining channels (lymphatics). This strategy of radical surgery minimises the risk of the cancer recurring, but subjects all patients to high-risk surgery; one-third of patients will suffer a complication with one-in-twenty patients dying as a result. In addition, only 30% of patients will truly benefit from radical surgery, as the remaining 70% will not have spread beyond the cancer meaning that removal of the draining lymphatics is unnecessary – they would have been cured by simple removal of the cancer alone.

A strategy is needed whereby the extent of surgery is tailored to the spread of the cancer and the fitness of the patient. Central to such a strategy is the ability to distinguish those patients that have cancer spread to lymphatics, who will benefit from radical surgery, from those without spread to the lymphatics, who will be adequately treated by a much less extensive operation to remove the cancer alone. Unfortunately, current imaging methods are only 50% accurate in determining cancer spread to the lymphatics – no better than tossing a coin.

We have manufactured a small particle (nanoparticle) that can be injected into patients and will specifically concentrate in cancer due to the incorporation of a targeting molecule (anti-CEA Affimer) on the particles surface. The nanoparticle was tested on a range of colorectal cancer cells and in a small animal model. The results from these tests are encouraging and demonstrated that the nanoparticle was able to target and kill colorectal cancer cells.

The findings of this study will lead to further pre-clinical studies to determine how best to bring the nanoparticle into clinic. The nanoparticle contains a fluorescent molecule (photosensitiser) allowing it to be easily detected at laparoscopic (keyhole) surgery, where a light is shone into the abdomen. For the first time, this will allow cancer images taken before surgery (MRI scan) to be matched to the images obtained at the time of surgery (laparoscopic fluorescence). This will enhance the surgeon's ability to be sure of the location and spread of the cancer. In addition, the fluorescent molecule in the nanoparticle has been chosen so that it has cancer-killing properties when it is activated by light, adding another important anti-cancer feature.

Colorectal cancer can be cured by surgery in 50% of cases but 25% will develop local recurrence.

The epidemiology of periprosthetic femoral fractures in total hip arthroplasty

Tanvir Khan

FELLOWSHIP/SPONSOR:
Joint RCS/NJR Research Fellowship

SUPERVISOR:
Mr Ben Ollivere

SITE OF WORK:
University of Nottingham

PUBLICATIONS:
1. Khan T, Grindlay D, Ollivere BJ *et al.* A systematic review of Vancouver B2 and B3 periprosthetic femoral fractures. *Bone Joint J.* 2017 **99-B**: 17–25

PRESENTATIONS:
1. *The Epidemiology of Periprosthetic Fractures in Total Hip Arthoplasty.* Presented at: British Orthopaedic Association Annual Congress; September 2017; Liverpool

2. *Cementless Femoral Stem Design in Total Hip Arthroplasty and the Risk of Revision for Periprosthetic Femoral Fracture.* Presented at: American Academy of Orthopaedic Surgeons; March 2018; New Orleans

Tanvir discussing the epidemiology of total hip arthroplasty modes in the outpatient clinic.

The overall aim was to perform an epidemiological study of periprosthetic femoral fractures (PFF) around total hip arthroplasties (THA) in England and Wales. The key objectives were to examine the trends in the incidence of revision surgery for periprosthetic femoral fractures (PFF) after THA, to determine the risk factors and predict individual risk and to investigate the outcomes after treatment.

The National Joint Registry is the largest register of joint replacements in the world with detailed data on all hip replacements performed in England and Wales since 2004. Novel flexible parametric competing risk models were developed and applied to investigate risk factors for fracture and quantify their influence of fracture probability.

A key finding is that the incidence of revision for PFF is increasing. Increasing age, male gender, cementless prosthesis and loaded taper cemented designs were associated with a higher risk of revision for PFF. Furthermore, there was a higher risk of mortality and further revision surgery following revision for PFF compared with other indications for revision hip replacements.

Although there are smaller cohort studies, this is the largest investigation of periprosthetic femoral fractures at national level and as it is UK based its findings are directly relevant to our hip replacement population. PFF leads to significant morbidity and mortality and this work has suggested strategies to lower the risk of its occurrence. There is ongoing work in this area looking in more detail at patient factors and risk of PFF.

The number of revision hip replacements in the UK is projected to reach over 137,000 with a broken bone around the implants as the second most common cause after 4 years.

The potential role of Coxsackievirus A21 in combination with radiotherapy as a treatment of metastatic colorectal cancer

Jennifer Kingston

FELLOWSHIP/SPONSOR:
Freemasons' Fund for Surgical Research

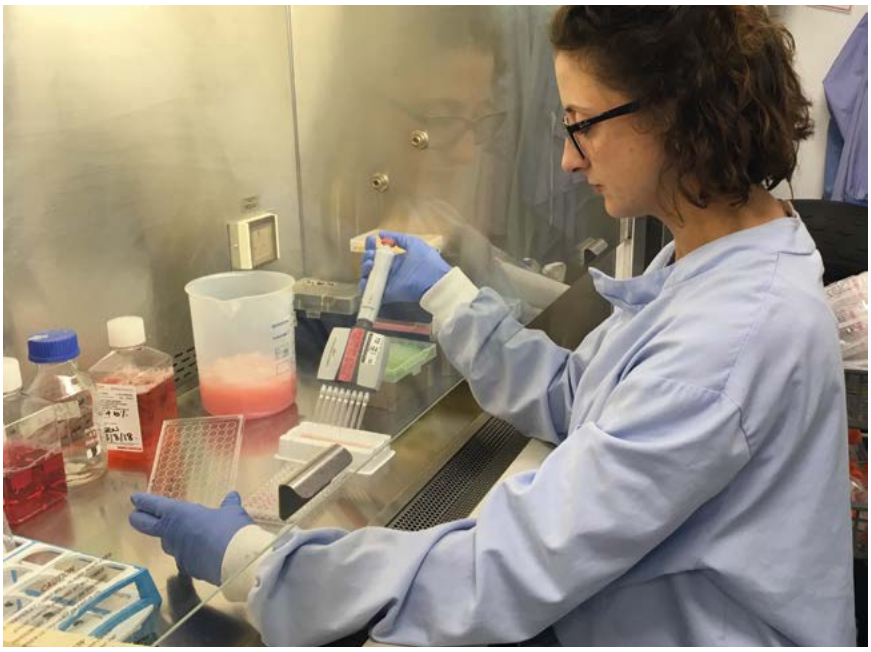
SUPERVISORS:
Dr F Errington-Mais and Professor G Toogood

SITE OF WORK:
Leeds Teaching Hospitals NHS Trust, The University of Leeds

PUBLICATIONS:
1. ASGBI, International Surgical Congress, Liverpool, 2018

2. International Conference of Immunotherapy Radiotherapy Combinations; September 2017; New York

FURTHER FUNDING:
Rays of Hope Charitable Foundation have provided additional bench fees during the full two and a half years of this research



Jennifer treating donor blood samples with Coxsackievirus A21 to assess immunological response to therapy.

Oncolytic Viruses (OVs) are an emerging treatment in the fight against cancer, with one, T-VEC, recently approved for use in melanoma. OVs selectively target and destroy cancerous cells without causing harm to the patient. Cancer cells are more prone to infection, due to abnormal changes that occur during their development. Viral infection and death of cancer cells leads to activation of the immune system and the development of an anti-cancer immune response.

The aim of our research was to investigate how one such OV, Coxsackievirus A21 (CVA21) could be used alongside pre-existing therapies to treat metastatic colorectal cancer (CRC). CRC is common, with more than 34,000 new cases reported per year in England alone. Currently 25% of newly diagnosed CRC patients also have disease that has spread to other organs. The 5-year survival for these patients is only 10%. As such, successful new treatments could have a significant impact on the outcome for these poor-prognosis patients.

Using human models of CRC, we have shown CVA21 has the ability to infect, replicate in, and destroy CRC cells if the CVA21 entry receptor, ICAM-1, is present. Moreover, the sensitivity of CRC cells was dependent of the level of ICAM-1 surface expression. Importantly, using donor blood samples we have also demonstrated, that non-infected CRC cells can be destroyed by activation of the patient's immune cells after exposure to CVA21.

We have also established that using radiotherapy in combination with CVA21 results in a significant improvement in cell death compared to using either treatment alone. Furthermore, some preliminary data also suggests that this combination may be as, if not more, effective than a standard chemo-radiotherapy regimen. An animal study is now planned to confirm the cell-based studies we have undertaken, if successful, we hope that this combination will progress to an early phase clinical trial.

20% of patients presenting with colorectal cancer will already have metastatic disease, a further 25% will go on to develop metastases and only 10% of these will survive beyond five years.

The effect of carotid endarterectomy on lifetime stroke risk and incident dementia in ACST-1

Rebecca Llewellyn-Bennett

FELLOWSHIP/SPONSOR:
RCS Research Fellowship with the support of the Gwendoline Shrimpton Legacy

SUPERVISORS:
Mr Richard Bulbulia and Professor Alison Halliday

SITE OF WORK:
Clinical Trial Service Unit and Epidemiological Studies Unit (CTSU), Nuffield Department of Population Health (NDPH)

PUBLICATIONS:

1. Llewellyn-Bennett R, Bowman L, Bulbulia R. Post-trial follow-up methodology in large randomised controlled trials: a systematic review protocol *Syst Rev* 2016; **5**: 214

2. Llewellyn-Bennett R, Edwards D, Roberts N. Post-trial follow-up methodology in large randomised controlled trials: a systematic review. *Trials* 2018; **191**: 298

PRESENTATIONS:
1. Presented at: 7th Munich Vascular conference (MAC); December 2016; Munich

2. Presented at: Alzheimer's Society conference; May 2018; London

The research undertaken for the fellowship was in two parts. Firstly, a systematic review analysed and compared methods used in the long-term follow-up of participants from large randomised controlled trials. Our systematic review was published and concluded that a number of post-trial follow-up methods were used by different trials that were neither complementary nor cost-effective.

Rebecca's presentation on the progress of the ACST long-term follow-up study.

The second part of the research established the long-term follow up of a vascular trial called the Asymptomatic Carotid Surgery Trial (ACST); an international, randomised controlled trial of 3,120 participants. This trial showed that there were benefits of an operation that corrected the narrowing of the carotid artery (carotid endarterectomy-CEA) at five and ten years, with successful surgery halving the risk of future strokes.

The long-term follow-up of these participants is to assess whether there are lasting benefits of having this operation in terms of reducing stroke and dementia risk. We followed-up 1,601 participants remotely using electronic health records via NHS Digital (England/Wales), equivalent health bodies in Scotland and Northern Ireland and Socialstyrelsen (Sweden). The process of obtaining data from NHS Digital was time-consuming, due to sensitive data and a changing regulatory framework. In the UK, 89% of participants and 97% of participants in Sweden had their electronic data matched.

The preliminary results of the long-term follow-up showed that the beneficial effects on stroke risk reduction were maintained up to 15 years after a successful CEA. These benefits were seen in men and women and among participants receiving medical therapy (aspirin, anti-hypertensives and statins.)

The future results of the long-term follow-up of ACST participants will help doctors treat patients with this condition better. Analysis of rates of dementia in ACST-1 long-term follow-up is ongoing. If CEA is associated with a reduction in the risk of dementia then more patients may be considered for this operation.

Alzheimer's Society conference with ACST Project Manager Mary Sneade and Alzheimer's Society mentors.

The beneficial effects on stroke risk reduction were maintained up to 15 years after a successful carotid endarterectomy.

The generation of bio-inspired 3D mineralised cellular implants using human induced pluripotent stem cells for bone tissue engineering applications

Robert James MacFarlane

FELLOWSHIP/SPONSOR:
Joint RCS/Dunhill Medical Trust Fellowship

SUPERVISORS:
Professor Athanasios Mantalaris and Professor Eleftherios Tsiridis

SITE OF WORK:
Department of Chemical Engineering, Imperial College London

PUBLICATIONS:
1. Klontzas M, MacFarlane RJ, Heliotis M *et al.* Investigational drugs for fracture healing: preclinical and clinical data. *Exp Opin Invest Drug* 2016; **25**: 585–596

2. Gamie Z, MacFarlane RJ, Gamie Y *et al.* Skeletal Tissue Engineering using mesenchymal or embryonic stem cells: clinical and experimental data. *Expert Opin Biol Ther* 2014; **14**: 1,611–1,639

PRESENTATIONS:
1. Macfarlane RJ, Klontzas M, Heliotis M *et al. Two-stage mesodermal and osteogenic differentiation of human induced pluripotent stem cells.* Presented at: EFFORT; June 2017; Vienna

2. Macfarlane RJ, Klontzas M, Heliotis M *et al. Osteogenic differentiation of human induced pluripotent stem cells using simvastatin and atorvastatin.* Presented at: EFFORT; June 2017; Vienna

FURTHER FUNDING:
The Royal College of Surgeons for one year

Bone graft surgery is common in patients who have suffered trauma, severe arthritis or bone cancer, but current methods can be unreliable. This study was aimed at devising a new method for bone tissue production using human stem cells to improve the outcome of bone graft surgery. Stem cells were grown in a 3D culture system using a rotating microgravity bioreactor, and drugs such as statins were added to enhance the amount and quality of bone tissue produced. Drugs including Simvastatin, Atorvastatin, and Teriparatide were used to enhance the process, and the results demonstrated improved production of novel bone tissue using a simple and reliable method.

Several studies have previously reported on the use of drugs for bone graft production using stem cells. However, this is the first time these agents have been used to enhance bone tissue production from human induced pluripotent cells in a 3D culture system, which may now pave the way towards a technique for patient-specific bone graft production to combat the range of adverse effects of having bone defects. Failure of bone graft surgery in patients with large bone defects in their skeleton causes pain and a range of disabilities, and current techniques are unreliable. Sources of bone graft are limited and the techniques developed in this study represent an exciting new avenue for improving bone graft surgery outcomes and the range of symptoms in these patients.

Robert looking at an X-ray of a complex trauma case requiring bone graft surgery, which his research is aimed at treating.

Up to 70% of bone grafting procedures 10 years resulting in pain and disability.

Decision support for traumatic coagulopathy using Bayesian Networks

Max Marsden

FELLOWSHIP/SPONSOR:
Joint RCS/Military Research Fellowship

SUPERVISORS:
Colonel Nigel Tai and Professor Karim Brohi

SITE OF WORK:
Royal London Hospital

PUBLICATIONS:
1. Presented at: Military Health System Research Symposium; August 2017; Florida

2. Presented at: Centre for Blast Injury Studies Annual Conference; November 2017; London

PRIZES:
Centre for Blast Injury Studies Annual Conference 2017; Best of British, Oral Presentation

In 2003, a blood clotting disorder was discovered in 25% of severely injured trauma patients. This trauma induced coagulopathy (TIC) is associated with a one in four chance of death. Many of the treatment strategies for TIC are complex; improving outcomes in some patients, while exposing others to increased risk of adverse events.

The aim of this work is to create a clinical decision support tool to help identify patients with TIC before they arrive in hospital. Therapeutic interventions can then be targeted according to the individual patient's risk characteristics. We used a machine learning technique to combine prior knowledge and data called a Bayesian Network (BN). The BN uses information about the patient and their injury which is readily available in the prehospital environment. Information such as the mechanism of injury and the patient's heart rate, is used to predict the patient's individual risk of coagulopathy. The BN has comparable accuracy to laboratory tests of coagulation, without needing laboratory equipment and within shorter timescales. In addition, the BN is able to maintain the accuracy of its predictions with up to one third of predictor information missing.

To apply the results of the BN prediction to a treatment decision, the model was compared with clinicians in deciding which patients would require a large volume of blood products early in their resuscitation. In an analysis of more than 800 patients, the model performed in a similar manner to experienced trauma clinicians. The model demonstrated minor improvements in detection and less false positives compared to clinicians. Clinical decision making was augmented when the clinicians' decisions were combined with the model.

The next steps will be to test this relationship in a prospective trial. The premise is that earlier, accurate decision making will improve patient outcomes and decrease costs within the trauma system.

Max is collecting data in the prehospital environment with Kent Surrey Sussex Air Ambulance and is seen here, shortly after handing over a patient on the roof of King's College Hospital, London.

Worldwide, 6 million people die from injuries every year and about 40% of these deaths are due to bleeding.

Investigating surgical site infection after hip fracture surgery

James Masters

FELLOWSHIP/SPONSOR:
Joint RCS/Dunhill Medical Trust Fellowship

SUPERVISORS:
Matthew Costa and Andrew Judge

SITE OF WORK:
Kadoorie Centre, John Radcliffe Hospital, Oxford

PUBLICATIONS:
1. Masters JPM, Achten J, Cook J *et al.* Randomised controlled feasibility trial of standard wound management versus negative-pressure wound therapy in the treatment of adult patients having surgical incisions for hip fractures. *BMJ Open* 2018; **8**: e020632

2. Masters, JP, Nanchahal J, Costa ML. Negative pressure wound therapy and orthopaedic trauma. *Bone Joint J* 2016; **98-B**, 1,011–1,013

PRESENTATIONS:
1. *Randomised controlled feasibility trial of standard wound management versus negative-pressure wound therapy in the treatment of adult patients having surgical incisions for hip fractures.* Presented at: Wounds UK meeting November 2018; Harrogate

James discussing results of the trial with the trial management team.

Hip fractures are common injuries that affect elderly patients. The treatment is almost always an operation to allow the patient to get back on their feet. However, one of the most important complications of these operations is an infection in the wound. These are knows as surgical site infections (SSIs).

The consequences of an SSI may be profound after any operation. In orthopaedic surgery where metalwork is used to either fix or replace injured bones, SSI is devastating. Hip fracture surgery involves both metalwork and elderly frail patients. This means 1 in 3 patients who undergo surgery for a broken hip and also develop an SSI will die within 30 days of surgery.

The purpose of this study is to use different methods to understand the true rate of infection in the hip fracture population.

Phase 1 of this fellowship involved looking at all the published studies where infection after hip fracture was reported. This found a rate of around 3 in every 100 operations, but there was big variation in the number of infections reported.

Phase 2 involved looking at the routinely collected information from approximately 12,000 hip fracture patients across the UK. These data showed a rate of 2 infections in every 100 operations, but it is likely that this way of measuring infection misses a significant number.

Phase 3 was a multicentre randomised control trial that looked at infection after using different wound dressings in patients across five centres. This phase showed a rate of 5 infections in every 100 operations.

These three strands of work combined to give us the best and most up-to-date understanding of this problem and serve as the foundation for future work to reduce this critical problem.

Infection after hip fracture surgery may be as common as 5 in every 100 operations.

Informed consent for general surgery

Scott McCain

FELLOWSHIP/SPONSOR:
RCS Research Fellowship

SUPERVISOR:
Professor Mike Clarke

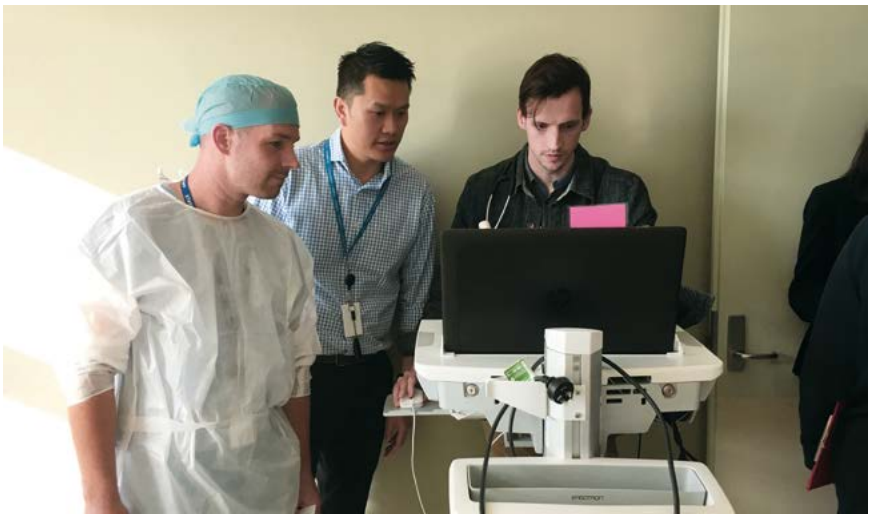
SITE OF WORK:
Ulster Hospital, Belfast and Queen's University Belfast

PUBLICATIONS:
1. A systematic review of randomised trials of interventions to improve informed consent for invasive procedures. [Submitted to *BMC Med Res Methodol*]

2. Patient experiences of informed consent and wishes for an ideal consent process

PRESENTATIONS:
1. Presented at: SARS; 2017, Dublin

2. Presented at: ASGBI; 2017, Glasgow



Scott on the surgical ward round.

My research aimed to assess informed consent for general surgery and I did this in several ways. Firstly, a systematic review of current literature found that trials measuring consent do so in many different ways and they are subject to bias. As a result, the findings of the trials cannot be compared meaningfully, highlighting the need for researchers to measure consent in a consistent way.

Recall and understanding of consent information was examined in 200 patients. Patients were only able to recall and understand half of the information provided to them by doctors during consent discussions.

To attempt to improve consent, an iPad application was developed to provide patients with information in a more easily understandable way. As part of the process of piloting the app to design a trial, several stakeholder (patient, doctor, lawyer) focus groups identified that stakeholders viewed consent differently and there was a need to further examine the concept of informed consent to ensure patients' needs were met.

A larger patient survey of more than 800 patients confirmed that patients' wishes for informed consent vary widely and demonstrated the need for patient tailored consent with regard to the amount and type of information provided. It also described the existing variation with regard to decision-making responsibilities of the patient and doctor within such a process. Some patients continue to prefer a paternalistic view of their treatment decisions.

Informed consent is a vital component of good medical practice. This work is therefore being taken forward by our research group. Firstly, a core outcome set for informed consent trials will be developed to ensure researchers are measuring consent in the same way. Thereafter, a patient tailored informed consent process will be developed, aiming to improve the informed consent process for all.

Scott taking a preoperative history from a patient.

Patients only understand half of the information given by doctors during consent discussions.

Prediction of diabetes resolution following bariatric surgery using ursodeoxycholic acid

Emma Rose McGlone

FELLOWSHIP/SPONSOR:
Enid Linder Foundation Research Fellowship

SUPERVISORS:
Steve Bloom, Tricia Tan and Ahmed Ahmed

SITE OF WORK:
Hammersmith Hospital, Imperial College

FURTHER FUNDING:
MRC Clinical Research Training Fellowship for 30 months

Emma consenting a volunteer.

Six million people in the UK have type 2 diabetes, of which 90% are overweight or obese. Diabetes is a chronic condition which has severe complications including blindness, nerve damage and kidney failure. Most patients require multiple medications.

Bariatric surgery (eg gastric bypass) is the only cure for this condition, but it is not successful in all cases. At present, we have no personalised ways of predicting which patients undergoing bariatric surgery will experience cure of their diabetes. My research aims to develop a simple test that would help patients and their doctors decide whether bariatric surgery is right for them.

Change in the body's release of gut hormones is key to the improved sugar control seen after bariatric surgery; 'poor responders' to bariatric surgery secrete fewer of these hormones. In recent years it has been shown that bile acids, which are natural detergents released by the liver to digest food, also stimulate gut hormone release. In my study we are using bile acid tablets to measure the gut hormone release potential of patients preoperatively. We then follow up patients for one year after bariatric surgery to see if patients with higher bile acid stimulated gut hormone release are more likely to experience diabetes cure.

Based on my preliminary data we have slightly modified the structure of the test and are now in the second phase of recruitment. The test is simple and involves drinking a nutritional milkshake with bile acid tablets, and then having some blood tests. The research takes place in the NIHR/Wellcome Trust Imperial Clinical Research Facility.

Emma preparing a milkshake for the test.

Although there has been lots of research into the role of gut hormones in diabetes and bariatric surgery, this is a novel approach that will potentially help many patients. Final results are eagerly anticipated in around 18 months' time.

Bariatric surgery cures diabetes, but only in one in three cases.

VASO (Vitamin D and Arthroplasty Surgery Outcomes)

Rory John McGillivray Morrison

FELLOWSHIP/SPONSOR:
Shears Northern Research Fellowship

SUPERVISORS:
Professor Mike Reed and
Mr Kenneth Rankin

SITE OF WORK:
Northumbria Healthcare NHS Foundation Trust, South Tees Hospitals NHS Foundation Trust and Newcastle University

PUBLICATIONS:
1. Morrison RJM, Bunn D, Gray WK *et al.* VASO (Vitamin D and Arthroplasty Surgery Outcomes) study – supplementation of vitamin D deficiency to improve outcomes after total hip or knee replacement: study protocol for a randomised controlled feasibility trial. *Trials* 2017; **18**: 514

PRESENTATIONS:
1. Presented at: 21st International Workshop on Vitamin D; May 2018; Barcelona

2. Presented at: Society of Academic and Research Surgery; January 2018; Nottingham

3. Presented at: British Orthopaedic Association Congress; September 2018; Birmingham

PRIZES:
1. George Feggetter medal, Northern England Surgical Society Meeting, Newcastle May 2018

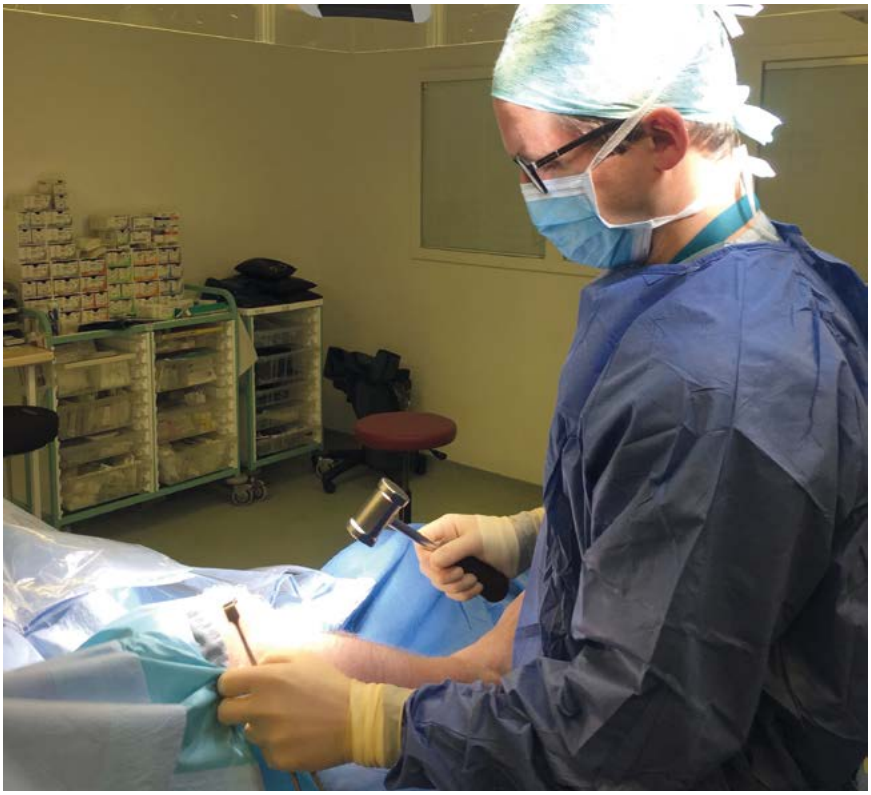
2. Best Poster Award, British Orthopaedic Association Congress, Birmingham, September 2018

FURTHER FUNDING:
Orthopaedic Research UK for two years

There are 200,000 hip and knee replacements performed each year in the UK, but up to 20% of patients are dissatisfied following surgery. Low vitamin D levels have been reported as a possible cause of a poor outcome, including longer length of stay, increased infection rates, and lower satisfaction scores on patient-reported questionnaires. However, nobody yet has proved whether a low vitamin D level causes a poor outcome, or if it is not actually related at all. One way to demonstrate this would be to give supplements to patients with a low vitamin D level, and see if their outcome improved, but to date, nobody has done this.

We designed the VASO trial – Vitamin D and Arthroplasty Surgery Outcomes. This was a feasibility study at two hospitals in the North East of England, where half of patients with a low vitamin D level were given supplements before surgery, and the other half were not. A feasibility study means we look at trial 'processes' such as how many patients drop out of the trial, if patients take their vitamin D supplements, and which is the best outcome measure to use. This means we can work out how many patients are needed for a full-scale trial to confidently answer the research question, and helps find any potential problems on a small-scale, before running a large trial with more significant costs.

Through the feasibility trial involving 102 patients, we have shown that; we can recruit patients to the study; that giving vitamin D supplements increases a patient's vitamin D level; and that those patients who received vitamin D supplements had better outcome scores than those who didn't. This work will contribute to the design of a larger trial.



Rory operating on a patient's knee.

Up to 80% of adults have low vitamin D levels, and this may have a relation to poor outcomes following total hip or knee replacement.

Investigating an innovative self-care model for patients with prostate cancer

Ankur Mukherjee

FELLOWSHIP/SPONSOR:
Shears Northern Research Fellowship

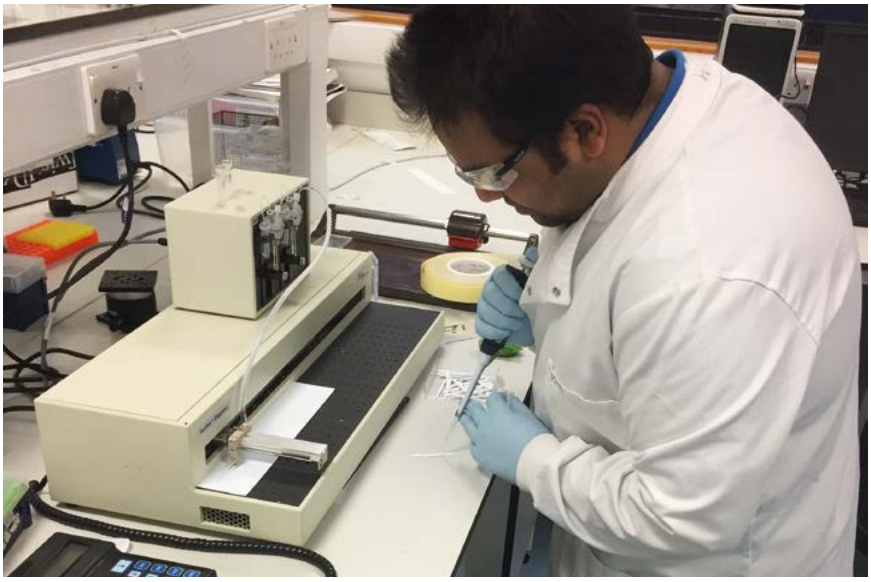
SUPERVISORS:
Dr Stuart McCracken

SITE OF WORK:
NICR and Institute of Cellular Medicine

PRESENTATIONS:
1. Presented at: the North of England Urological Society (NEUS) Meeting; November 2016; Durham Cricket Club

PRIZES:
Awarded the JGW Patterson Foundation Research Grant – April 2018

FURTHER FUNDING:
Patterson Foundation Research Grant for one year

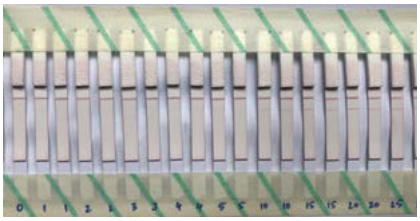


Ankur at work in the Diagnostic and Therapeutic Technologies Research Group Laboratory, Newcastle University, constructing the lateral flow immunoassay strips.

Prostate cancer (PCa) is the commonest cancer in men. 215,000 men are living with a diagnosis of PCa in England, with 39% prescribed hormone therapy. These men need regular blood test monitoring for their Prostate Specific Antigen (PSA) levels. The follow-up cost to the NHS for this method of cancer monitoring is around £250 million/yr. By 2040, the total number of PCa survivors is projected at 831,000. There is an urgent need for an effective new model that integrates 'well survivors' back into the community, providing cost-effective support. Furthermore, this leads to excessive follow-up that lacks individualised care.

The aim of our research is to assess if PCa patients can be monitored and managed at home, with benefits to their quality of life. We will design a reliable, rapid 'home test', which could be linked to mobile communication to report values to the clinic, instructing patients to amend their treatment dose or schedule a clinic appointment. Such an information and communications technology (ICT) connected 'home test' currently does not exist.

Using near-to-market technology, the device would enable PSA measurements through a finger pin-prick and compare its analytical performance with standard hospital laboratory tests. This will involve development of a one-step lateral flow immunoassay (LFIA), for the detection of PSA levels in blood, which would be imaged and quantified using a mobile smartphone.



Lateral flow immunoassay at work showing varying concentrations of PSA solutions (0-25ng/mL; numbered in blue below each strip) – note the gradient in colour intensity of the test lines with varying PSA concentrations.

This project encompasses three vital elements in designing and evaluating a point-of-care device for clinical application. Firstly, the technology that plays a vital part in delivering a reliable device; secondly, patient responsiveness to this new technology in monitoring their disease by way of validated patient acceptability studies; thirdly, the cost effectiveness of this care delivery model through economic health-model analysis. I will look to apply for further funding with the ultimate aim to facilitate a multi-centre study.

Currently 215,000 men are living with a diagnosis of prostate cancer with a projected figure of around 830,000 by 2040.

Improving adenoma detection rate with Endocuff Vision™

Wee Sing Ngu

FELLOWSHIP/SPONSOR:
RCS Research Fellowship

SUPERVISOR:
Professor Colin J Rees

SITE OF WORK:
South Tyneside NHS Foundation Trust

PUBLICATIONS:
1. Ngu WS, Bevan R, Tsiamoulos Z *et al.* Improved adenoma detection with Endocuff Vision: The ADENOMA Randomised Controlled Trial. *Gut* 2018; **23**; [Epub ahead of print]

2. Bevan R, Ngu WS, Saunders BP et al. The ADENOMA Study. Accuracy of Detection using Endocuff VisionTM Optimization of Mucosal Abnormalities: study protocol for randomized controlled trial. *Endosc Int Open* 2016 **4**: E205–E212

PRESENTATIONS:
1. Ngu WS, Bevan R, Tsiamoulos Z *et al. The ADENOMA Study: Accuracy of Detection using Endocuff Optimisation of Mucosal Abnormalities.* Presented at: Digestive Diseases Week; May 2017; Chicago

2. Ngu WS, Bevan R, Tsiamoulos Z *et al. Improved adenoma detection with Endocuff Vision – a multi-centre randomised controlled trial.* Presented at: United European Gastrointestinal Week; October 2016; Vienna

PRIZES:
1. Presentation Award: Best Abstract Award 2016 for, 'Improving adenoma detection with Endocuff Vision', 4th Northern Region Endoscopy Group (NREG) Symposium, Gateshead. 28 November 2016

2. Shire Award for Gastrointestinal Excellence (SAGE) Award 2016: Joint 1st prize Gastrointestinal, Research Team SAGE Awards Ceremony, Liverpool. 1 June 2016

Colonoscopy is the gold standard investigation for the large bowel. However, colonoscopy is imperfect due to variation in operator-dependant adenoma detection rates. High adenoma detection rates are associated with a lower incidence of post-colonoscopy colorectal cancers. A new device called Endocuff Vision™ has shown to improve adenoma detection rates in pilot studies. Endocuff Vision™ is attached to the end of the colonoscope and works to improve views of the bowel wall during colonoscopy by holding back folds.

Our study was a prospective, multi-centre, randomised controlled trial across seven NHS hospital trusts and the main aim was to ascertain if there was a difference in adenoma detection rate in patients undergoing Endocuff Vision™ assisted colonoscopy compared with standard colonoscopy. It was the first trial to evaluate the use of Endocuff Vision™ in patients having colonoscopies who were referred via clinic, via surveillance and via the bowel cancer screening programme.

A total of 1,772 patients were recruited to the study and no patients were lost to follow up. We found that Endocuff Vision™ increased adenoma detection rates globally by 4.7%. This was driven largely by a 10.8% increase in adenoma detection rates in patients attending for colonoscopy via the bowel cancer screening programme. These group of patients have already undergone faecal occult blood testing and found to be positive. Consequently, they may have higher rates of pathology compared with other patients. This suggests that Endocuff Vision™ improves visualisation and detection of adenomas in a population where they are more prevalent. Our study demonstrated that Endocuff Vision™ is a safe device, which improves adenoma detection rate, speeds up procedures and is generally well tolerated by patients. Our study has led to the development of another randomised controlled trial looking at the use of Endocuff Vision™ in the bowel scope screening programme.

Team photo for winning the 1st prize for the best gastrointestinal research team at the SAGE Awards.

Endocuff Vision™

A 1% increase in adenoma detection rate is associated with a 3% reduction in post-colonoscopy colorectal cancer and a 5% reduction in risk of death due to post-colonoscopy colorectal cancer.

Novel biomarkers in recurrent thyroid cancer

Hannah R Nieto

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

SUPERVISORS:
Professor Chris McCabe, Professor Jean-Baptiste Cazier and Professor Hisham Mehanna

SITE OF WORK:
IMSR, University of Birmingham

PUBLICATIONS:
1. Nieto H, Boelaert. Thyroid-stimulating hormone in thyroid cancer: does it matter? *Endocr Relat Cancer* 2016; **23**: T109–T121

2. Read ML, Fong JC, Modasia B *et al.* Elevated PTTG and PBF predicts poor patient outcome and modulates DNA damage response genes in thyroid cancer. *Oncogene* 2017; [Epub ahead of print]

PRESENTATIONS:
1. *Novel biomarkers in recurrent thyroid cancer.* Presented at: The Society for Endocrinology BES; November 2017; Harrogate

FURTHER FUNDING:
1. The Institute of Translational Medicine starter fellowship 2015–2016: PhD stipend year 1

2. The Midland Institute of Otology consumables

3. Get A-Head Charity 2017–2018: PhD stipend year 3 and consumables

Worldwide, around 300,000 new cases of differentiated thyroid cancer are reported per year and thyroid cancer now represents the most rapidly increasing cancer in the US and in the UK. In general terms, outcomes are good (10-year survival >90%). However, up to 25% of patients develop local or regional recurrences, and have a significantly reduced life expectancy. We hypothesise that thyroid tumours that subsequently recur display a distinct pattern of driver mutations, and that understanding these can have an impact on patient prognosis and treatment.

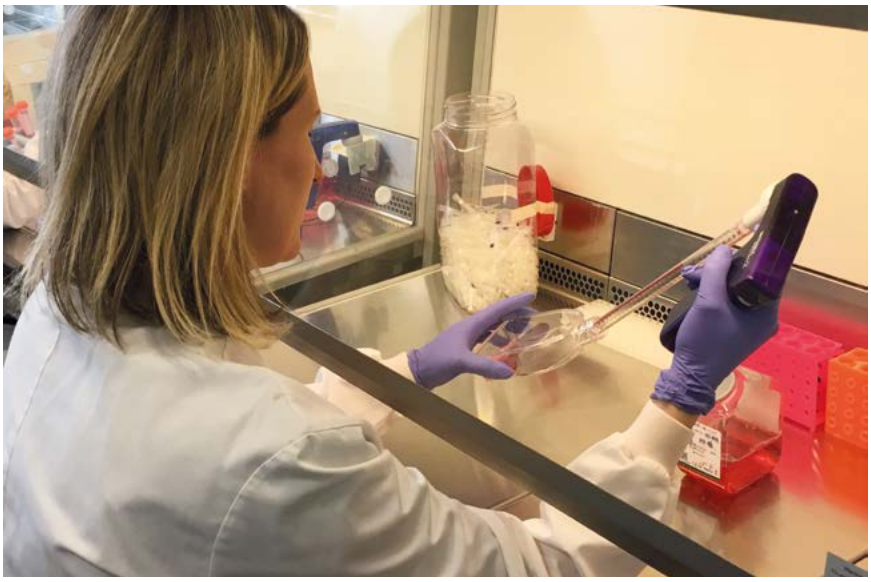
Hannah researching into the effects of mutations on thyroid cancer cells.

Using next generation sequencing data and high performance computing analysis, we located several genes with mutations in recurrent cancer patients.

We have also located genes that are overexpressed, with raised amounts of the corresponding messenger RNA in the tumours.

Transfecting these genes into cancer cell lines (growth of tumour cells in a controlled lab setting) allowed assessment of how the mutations affect cell behaviour, and therefore how they potentially affect patients. One particular gene called DICER1 had a mutation that affected how invasive the tumour cells are. Interestingly, several local patients have a syndrome related to other mutations in this gene, which I am now investigating, replicating these mutations in the lab.

Next in the project is to look at patients locally who have had thyroid cancer and recurrence of the cancer, and to assess the presence and expression of our genes of interest in their tumours. Through the use of personalised medicine, this information will inform us as clinicians as to the impact expression levels and mutations have in certain genes. This can then lead on to helping understand the likelihood of recurrence of thyroid cancer in future patients, amending their treatment and follow up accordingly.



Hannah growing thyroid cancer cells.

Up to 25% of patients with differentiated thyroid cancer go on to get recurrent disease, even after successful treatment; at present it is not known who is likely to get recurrent disease.

Acute lower gastroinestinal bleeding in the United Kingdom

Kathryn Oakland

FELLOWSHIP/SPONSOR:
Saven Research and Development Programme

SUPERVISOR:
Professor Mike F Murphy

SITE OF WORK:
NHS Blood and Transplant, Oxford

PUBLICATIONS:
1. Oakland K, Guy R, Uberoi R *et al.* Acute lower gastrointestinal bleeding in the UK: patient characteristics, interventions and outcomes in the first nationwide audit. *Gut* 2018; **67**: 654–662

2. Oakland K, Guy R, Uberoi R *et al.* Study Protocol: First nationwide comparative audit of acute lower gastrointestinal bleeding in the United Kingdom. *BMJ Open* 2016; **6**: e011752

PRESENTATIONS:
1. Oakland K. *Lessons Learned from the National Lower Gastrointestinal Bleeding Audit.* Research and audit in the emergency setting session Presented at: ACPGBI; July 2016; Edinburgh

2. Oakland K, Guy R, Uberoi R *et al. Blood Transfusion in Lower Gastrointestinal Bleeding: Results From a National Study in the United Kingdom.* Presented at: AABB International meeting; October 2016; Orlando

FURTHER FUNDING:
The Bowel Disease Research Foundation and NHS Blood and Transplant for two years

Blood donor: Gastrointestinal bleeding is the second most common reason for blood transfusion and requires thousands of donations a year.

Lower gastrointestinal bleeding (LGIB) is a common medical emergency worldwide. Despite this, there are a lack of data supporting interventions to treat the bleeding and patient outcomes. The aim of this research is to describe the type of patient who develops LGIB in the UK, appraise clinical interventions and develop a risk score to avoid unnecessary hospital admission.

I conducted a nationwide study of patients admitted with LGIB to UK hospitals during two months in 2015, collecting data on treatments (including blood transfusion) and outcomes (further bleeding, complications, death).

Of 174 acute hospitals in the UK, 143 (82.2%) participated, providing data on 2,528 cases of LGIB. This is the largest study of its kind anywhere, to date. Most patients were elderly with other medical problems. The use of blood-thinning medications was very common. Despite this, most patients did not develop severe bleeding, and treatments to stop bleeding (such as emergency surgery) were incredibly rare. Blood transfusion was common, used in 25% patients. Nearly half of all patients were not investigated for their bleeding, and often patients unnecessarily stayed in hospital for several days.

The data from this study were used to design a risk score that could be used to identify patients who can safely be discharged from Accident and Emergency (A&E), and treated as an outpatient. The score uses patient characteristics, examination findings and a simple blood test. Overall, 68.5% patients with LGIB were suitable for discharge from A&E.

In the UK, LGIB is a disease of older patients, one quarter receive red cell transfusion, but only a minority require treatment for bleeding, or come to harm. By avoiding unnecessary hospital admission these patients can receive the benefit of investigation without exposure to the risks of hospital stay. In the current climate of financial pressures, increasing outpatient treatment has organisational and financial benefits. Economic modelling suggests that the use of the risk score could save the NHS £18.7m per annum on the cost of hospital stay alone.

Blood recipient: LGIB has many causes, including haemorrhoids, diverticular disease and cancer, and can be a complication of cancer treatments, such as radiotherapy.

One in two patients with acute lower gastrointestinal bleeding are unnecessarily admitted to hospital.

The use of three dimensional surface imaging in the assessment of aesthetic outcome after oncological breast surgery

Rachel O'Connell

FELLOWSHIP/SPONSOR:
Saven Research and Development Programme

SUPERVISORS:
Miss Jennifer Rusby and Professor Nandita deSouza

SITE OF WORK:
Royal Marsden NHS Foundation Trust/Institute of Cancer Research

PUBLICATIONS:
1. O'Connell RL, Di Micco R, Khabra K *et al.* The potential role of three-dimensional surface imaging as a tool to evaluate aesthetic outcome after Breast Conserving Therapy (BCT). *Breast Cancer Res Treat* 2017; **26**; [Epub ahead of print]

2. O'Connell RL, DiMicco R, Khabra K *et al.* Initial experience of the BREAST-Q breast-conserving therapy module. *Breast Cancer Res Treat* 2016; **16**; [Epub ahead of print]

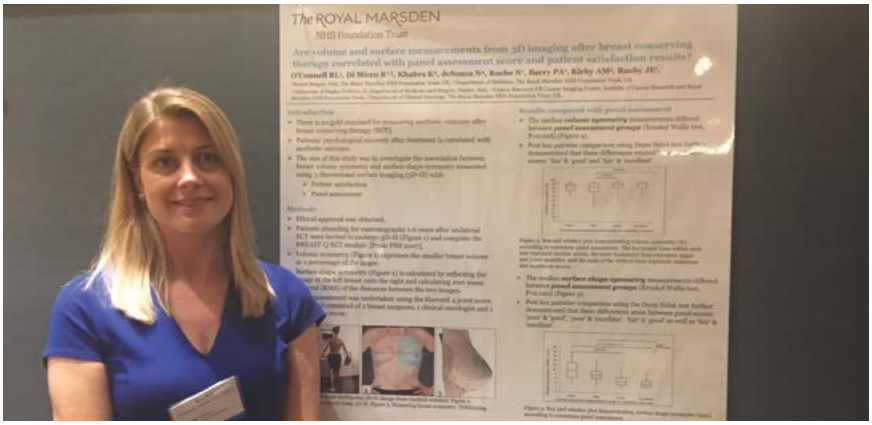
PRESENTATIONS:
1. O'Connell RL, DiMicco R, Khabra K *et al. Timing of DIEP flap reconstruction with respect to radiotherapy. Results of panel assessment and patient reported outcomes.* Presented at: British Association of Plastic, Reconstructive and Aesthetic Surgeons; June 2017; Helsinki

2. O'Connell RL, DiMicco R, Khabra K *et al. Can an objective outcome measurements from 3 dimensional imaging convey the subjective opinion of a panel assessment or patient satisfaction?* Presented at: American Society of Breast Surgeons; April 2017; Las Vegas

PRIZES:
1. Royal Society of Medicine, Sylvia Lawler Oncology prize, Best poster, 2016

2. Rome Breast Surgery Symposium, International abstract competition, oral presentation, 2016

FURTHER FUNDING:
A generous grant from the Biomedical Research Centre (BRC)



Rachel presenting her research at the American Society of Breast Surgeons.

The long-term success of breast cancer surgery is measured primarily by disease-free survival, which is easily measured. Now that breast cancer patients are likely to survive their disease (87% 5 year survival), the physical and psychological effects of treatment, especially long-term effects, are very relevant. Psychological recovery after breast cancer surgery is associated with aesthetic outcome. Despite this, there is no gold standard for measuring appearance after surgery.

The VECTRA XT™ is a 3D photographic image capture system, which can make detailed measurements of the breasts, including the volume of the breasts and the symmetry of the shape of the operated breast, compared with the non-operated breast. The aim of this research was to investigate whether 3D-SI could be used as a tool to objectively record aesthetic outcome, so that it can be used in research studies evaluating new surgical and radiotherapy techniques.

The research funded by RCS built upon my earlier work in which I had developed a protocol developed to measure breast volume and symmetry in a pilot study of 16 women. I found that the measurements were reliable.

3D imaging correlates with surgeons' and patients' satisfaction after breast cancer surgery.

I then recruited 200 women who had undergone breast conserving therapy and measured volume symmetry and surface symmetry. We investigated whether the volume or symmetry scores were associated with patient satisfaction or with the opinion of a panel of clinicians. Surface symmetry better correlated with panel assessment and patient reported 'satisfaction with breasts' than comparing the volume of the operated and non-operated breast.

We also investigated the value of 3D-SI in 167 women who have undergone DIEP flap breast reconstruction after mastectomy. We found that there was a moderate correlation between shape symmetry and panel assessment, and noted that the evaluation of a breast reconstruction is more complex than breast conservation.

The project is ongoing to develop an objective tool to assess the aesthetic outcome after oncological breast surgery, to ultimately try to improve the quality of life of women who have been treated for breast cancer.

The epidemiological and metabolic profiling of chronic venous disease

Sarah Onida

FELLOWSHIP/SPONSOR:
The Annie Julia Speight Fellowship

SUPERVISOR:
Professor Alun Davies

SITE OF WORK:
Charing Cross Hospital/South Kensington campus

PRESENTATIONS:
1. Onida S, Bergner R, Lees H *et al. The Metabolic Phenotyping of Chronic Venous Disease*. Presented at: XVIII World Congress of the Union Internationale de Phlébologie; Feb 2018; Melbourne

2. Onida S, Bergner R, Lees H *et al. Nuclear Magnetic Resonance Spectroscopic Analysis of Biofluids from Patients with Chronic Venous Disease*. Presented at: American Venous Forum Annual Meeting; Feb 2018; Arizona

PRIZES:
Servier Travelling fellowship from the American Venous Forum (see presentation two above)

FURTHER FUNDING:
NIHR for 4 years as an Academic Clinical Lecturer

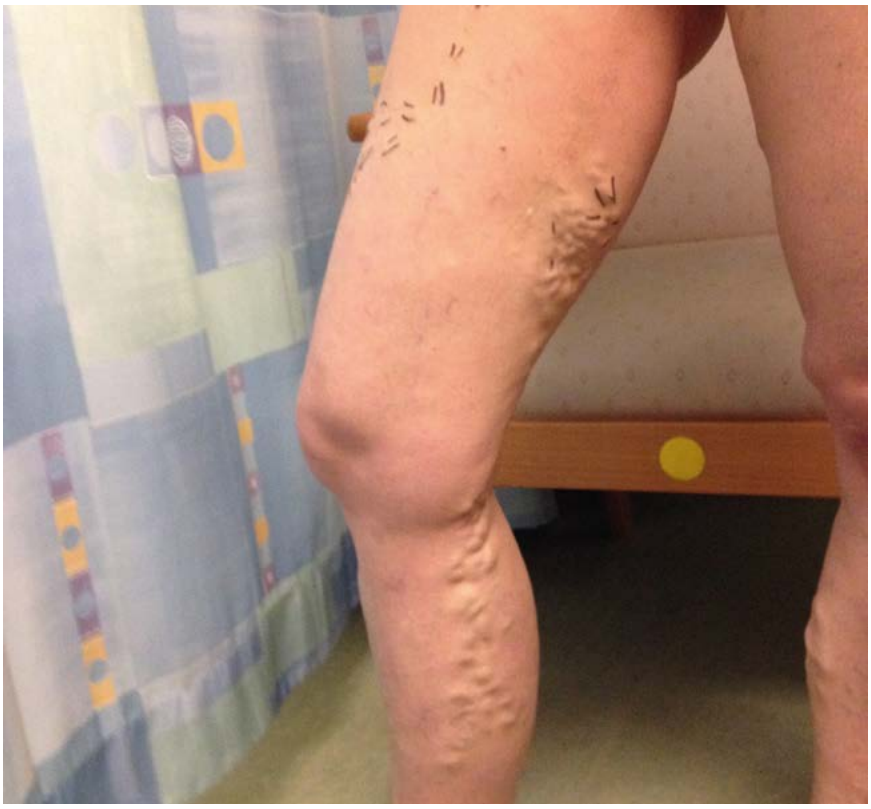
Venous disease, including varicose veins and ulcers, affects a large proportion of the population and causes pain, swelling and venous ulceration (open sores in the legs), and poor quality of life. Although effective treatments exist, the veins can come back and their condition can progress, ultimately risking the development of ulceration.

The development and progression of venous disease is poorly understood. Improved knowledge in this area would help researchers identify ways of predicting who is likely to progress, who is likely not to respond to treatment and, perhaps, discover new treatments. This would help deliver the best management to that individual, helping improve symptoms and quality of life. Ideally, this should be done via simple test, like a blood or a urine test.

Metabonomics, the study of small chemicals (metabolites), is new, advanced technology that detects tiny molecules. Previous departmental work has shown that varicose veins have different metabolites compared with non-varicose veins. The aim of this study was to identify molecules that were associated with disease severity, setting the foundation for further work. The project also aimed to perform a large-scale epidemiology study to assess how common venous disease is; this work is currently being completed.

Blood and urine samples were collected from 517 patients with venous disease and 105 controls. Samples were stored in -80 degrees and experiments performing using Nuclear Magnetic Spectroscopy (NMR) and Mass Spectrometry (MS) technology.

The NMR results showed that molecules associated with energy metabolism (Kreb's cycle) were more common in the group of people with severe disease, such as ulcers. Interestingly, in the urine, the opposite was true; the molecules decreased with increasing disease stage. This demonstrates that energy metabolism is affected in venous disease, likely more so in the ulcer patients. This work is currently being continued with the MS statistical analysis.



Varicose veins and venous ulceration.

Alterations in energy metabolism are increasingly important in patients with worsening venous disease severity.

Biomarker research in thromboembolic stroke

Mahim Irfan Qureshi

FELLOWSHIP/SPONSOR:
Joint RCS/Dunhill Medical Trust Fellowship

SUPERVISOR:
Professor Alun H Davies

SITE OF WORK:
Charing Cross Hospital and Sir Alexander Fleming Building (South Kensington Campus)

PUBLICATIONS:
1. Qureshi MI, Grecco M, Vorkas P *et al.* AH The application of metabolic profiling to aneurysm research. *J Proteome Res* 2017, **16**: 2,325– 2,332

2. Qureshi MI, Vorkas P, Coupland A *et al.* Lessons from metabonomics on the neurobiology of stroke. *Neuroscientist* 2016 23: 1073858416673327

PRESENTATIONS:
1. Qureshi MI, Vorkas P, Kaluarachchi M *et al. Metabolic Profiling of Carotid Atherosclerosis.* Presented at: European Society of Cardiovascular Surgery; Apr 2018; Strasbourg

2. Qureshi MI, Vorkas P, Kaluarachchi M *et al. Biomarker Research in Thromboembolic Stroke.* Presented at: European Stroke Conference; May 2017; Berlin

Approximately 45 national/ international presentations achieved during my PhD

PRIZES:
1. UK Stroke Forum Prize for Translational Research 2016

2. The Graham-Dixon Prize for Surgery 2016

Total 14 prizes, awards and grants since RCS fellowship awarded.

FURTHER FUNDING:
Imperial College Private Healthcare

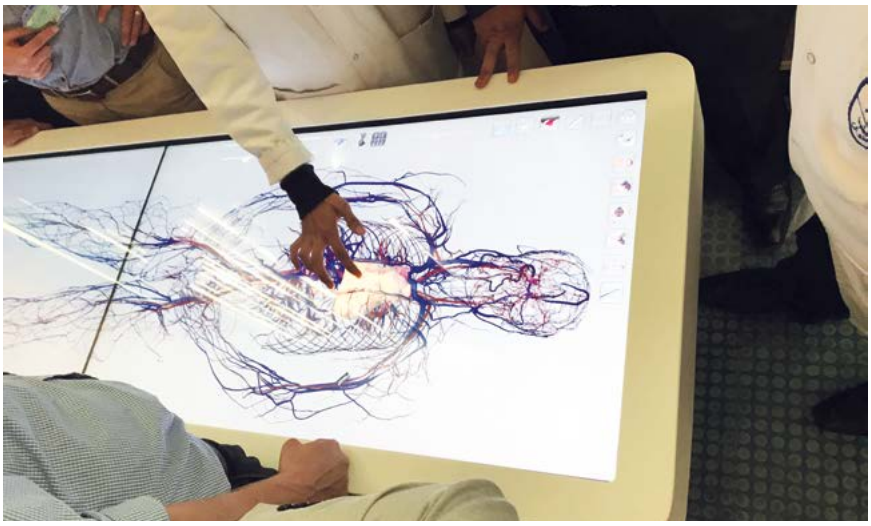
Stroke is a leading cause of death and disability. Approximately one-third of strokes are due to carotid artery fatty plaques. It is estimated that 130,000 people in the UK have significant carotid plaques, but we are unable to predict who will suffer a stroke. It is possible to surgically remove the plaques, but this operation itself carries a risk of stroke. If we were to operate on every individual with carotid plaques, we would cause as many strokes as we would prevent.

This study aimed to determine the biochemical changes in blood and urine of patients with carotid plaques, looking for the molecules that indicate a patient is at risk of a stroke, and ensure that any distinguishing molecules would still separate high-risk carotid disease from other forms of arterial disease.

I recruited 150 patients with symptomatic or asymptomatic carotid artery disease, strokes or mini strokes of non-carotid origin, normal controls, as well as patients with leg artery disease or aneurysmal disease. Blood and urine were collected from all patients and analysed using a biochemical profiling technique called ‘metabonomics’, which had not previously been applied to study carotid disease. Each analysis can determine the presence of hundreds of molecules. Thirteen different metabonomic experiments were performed.

The results were particularly strong for urinary analysis, and showed it was possible to distinguish high-risk carotid disease from other forms of arterial disease based on the presence of key molecules. Little is published about several of the molecules discovered.

Important lessons were learned about metabonomic experimental design that are invaluable to the ongoing research I have set up, pertaining to stroke, leg artery and aneurysmal disease. But to conclude this research, it is the first to demonstrate urinary markers of high-risk carotid disease, and a step forward in personalised medicine to help prevent stroke.



Simulated vascular teaching model at Helwan University Cairo.

One-third of all strokes are due to carotid artery disease, but three quarters of these were previously asymptomatic.

Augmentation strategies in rotator cuff repair

Mustafa Rashid

FELLOWSHIP/SPONSOR:
Freemasons' Fund for Surgical Research

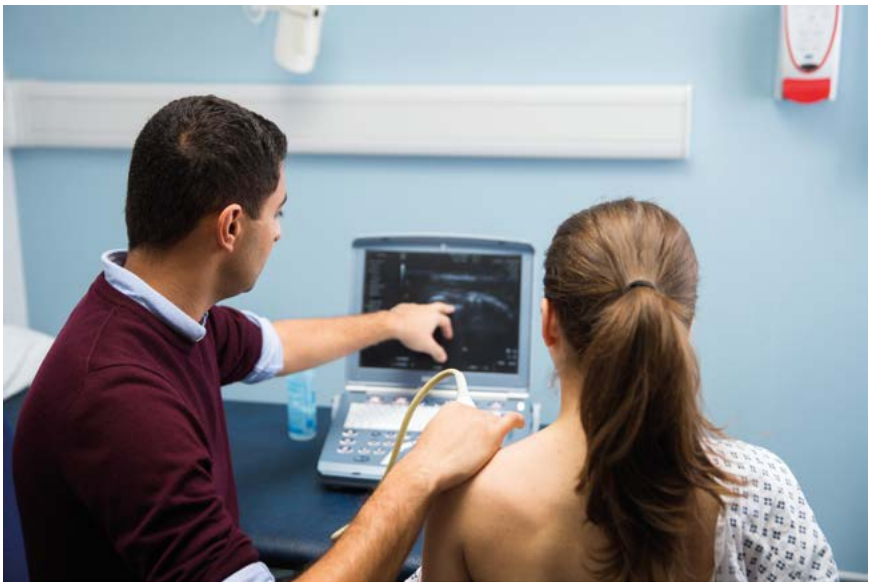
SUPERVISOR:
Professor Andrew Carr

SITE OF WORK:
Nuffield Department of Orthopaedics, Rheumatology, and Musculoskeletal Sciences

PUBLICATIONS:
1.Rashid MS, Cooper C, Cook J *et al.* Increasing age and tear size reduce rotator cuff repair healing rate at 1 year. *Acta Orthop* 2017; **88**: 606–611

PRESENTATIONS:
1. Presented at: British Elbow and Shoulder Surgeons (BESS) Annual Scientific Meeting; June 2017; Coventry

2. American Academy of Orthopaedic Surgeons (AAOS); March 2017; Orlando



Mustafa demonstrating the rotator cuff on shoulder ultrasound scan.

My project involved identifying a problem with healing, or lack thereof, of the rotator cuff tendon following surgical repair. 1 in 3 patients aged over 65 years will have a rotator cuff tendon tear of the shoulder. A tear is often painful, leading to significant impact on quality of life, and disability in performing daily activities. More than 15,000 patients a year undergo rotator cuff surgery in the NHS. I began by determining the influence of age and tear size on the healing rate. I then developed a predictive model for healing that allows surgeons and patients to better understand the likelihood of healing following surgery.

Having discovered that this tendon fails to heal in 40% of all patients undergoing surgery, and in even lower rates in older patients, I focussed on evaluating a common strategy to aid healing. I tested the response of the tendon when a reinforced patch, made of human or porcine skin, is applied on top of the repair.

I found this method of augmenting the repair produces negative changes to the tendon architecture, and may instigate a harmful response from the recipient's immune system.

Having concluded that these patches may not improve healing, I then evaluated two novel implants, developed in Oxford. These implants have been purposefully designed to stimulate the human tendon to heal after surgery. I tested these implants, a suture and a patch, in sheep. I found that tendons healed following application of these implants. They did not cause any safety concerns, and promoted the host tissue to integrate within them. At three months, these implants had completely integrated into the sheep tendons, promoting them to heal. The next steps will include testing these implants in a first-in-man clinical trial. The goal is to bring these strategically-designed implants to all patients undergoing rotator cuff repair.

1 in 3 people aged over 65 years old will have a rotator cuff tendon tear of the shoulder.

The role of extrinsic clotting pathway activation in the colorectal cancer microenvironment

Peter Adam Rees

FELLOWSHIP/SPONSOR:
The Black Fellowship

SUPERVISOR:
Ms Cliona Kirwan

SITE OF WORK:
Manchester Cancer Research Centre, University of Manchester

PUBLICATIONS:
1. Rees PA, Couston HW, Duff SD *et al.* Colorectal cancer and thrombosis. *Int J Colorectal Dis* 2018; **33**: 105–108

2. Clouston HW, Rees PA, Lamb R *et al.* Effect of tissue factor on colorectal cancer stem cells. *Anticancer Research* 2018; **38**: 2,635– 2,642

PRESENTATIONS:
1. PA. Rees, HW. Clouston, H. Shaker, S. Duff CC. Kirwan Incidence of VTE amongst patients undergoing curative resection for colorectal cancer – an underappreciated clinical entity. Presented at: ACPGBI Annual Meeting; July 2017; Bournemouth

2. P.A. Rees, H.W. Clouston, H. Shaker, J. Castle, S. Duff, C.C. Kirwan Preoperative systemiccoagulation factors as biomarkers in colorectal cancer. Presented at: 9th International Conference on Thrombosis and Haemostasis Issues in Cancer; April 2018; Bergamo

PRIZES:
1. Dukes' Club top trainee presentation finalist. Association of Coloproctology of Great Britain and Ireland Annual Congress. July 2017

2. Best Trainee Presentation. Manchester Regional Association of Surgeons Meeting. April 2018

Adam with a patient.

More than 40,000 patients are diagnosed with bowel cancer every year in the UK. It is the second leading cause of cancer death. Patients diagnosed with bowel cancer are at increased risk of developing blood clots in the leg (deep vein thrombosis) or the lungs (pulmonary embolism), particularly when they undergo surgery to remove the cancer. Patients developing a blood clot are more likely to die, not just from the blood clot itself, but also from more aggressive bowel cancer. Patients who survive can be left with chronic pain and are at high risk of developing further clots. Identifying patients at increased risk of developing blood clots is difficult and many are not recognised.

Our clinical research has focussed on patients developing blood clots around the time of their surgery for bowel cancer. We have shown that blood clots following surgery occur in 7% of patients, more than double previous estimates, despite measures to prevent them. Additionally, we have found that 1 in 20 patients will already have an established blood clot before undergoing their operation. We have also identified factors that may lead to patients to be at increased risk of a blood clot for an extended period following their surgery. This work paves the way for more tailored measures to prevent blood clots in these patients.

Our laboratory work has shown that blood clotting factors promote key processes in the progression of bowel cancer, but that it may be possible to inhibit this progression using a widely available medication (dabigatran) that is commonly used to prevent and treat blood clots.

In the future, we will analyse whether factors involved in blood clot development can predict poorer outcomes in bowel cancer patients.

Adam performing experiments on bowel cancer cells in the laboratory.

Patients with bowel cancer who develop a deep vein thrombosis have a 20% increased risk of death after one year compared with patients who are clot free.

The metabolic consequences of oesophago-gastrectomy

Geoffrey Roberts

FELLOWSHIP/SPONSOR:
RCS Research Fellowship with the support of the Rosetrees Trust

SUPERVISOR:
Richard Hardwick

SITE OF WORK:
Institute of Metabolic Science, University of Cambridge

PUBLICATIONS:

1. Roberts G, Kay RG, Howard J *et al.* Gastrectomy with Roux-en-Y reconstruction as a lean model of bariatric surgery. *Surg Obes Relat Dis* 2018; **14**: 562-568

2. Roberts G, Hardwick R, Fitzgerald R. Decision making, quality of life and prophylactic gastrectomy in carriers of pathogenic CDH1 mutations. *Transl Gastroenterol Hepatol* 2017; **2**: 21

PRESENTATIONS:

1. Roberts GP *et al. Gut hormones explain early post-prandial symptoms, and severe hypoglycaemia is common, in gastrectomy patients.* Presented at: AUGIS; 2017; Cork

2. Roberts GP *et al. Glucagon-like peptide 1 is a key factor in early and late dumping syndrome after gastrectomy: A randomised, double-blind, placebo controlled crossover study.* Presented at: AUGIS; 2018; Edinburgh

PRIZES:
BJS presentation prize at AUGIS conference 2018 (September)

Discussing eating after surgery to remove the stomach with a research participant in Cambridge.

The only potentially curative treatments for cancer of the stomach and oesophagus are surgical removal. These operations however have a profound impact on how a person can eat, resulting in loss of appetite, unpleasant post-prandial symptoms, low blood sugar after eating and ultimately weight loss and reduced quality of life. At present, there is no effective treatment for these problems, and before this project there was very little active research in the field anywhere in the world.

We have investigated whether the hormones (chemical signals) released from the lining of the gut in response to food are changed by surgery, and whether this explains the negative symptoms experienced by post-surgery patients. Specifically, there is a very tightly controlled system by which hormones from the gut link how much a person eats to how full (or not) they feel, and how much of the sugar in their blood they store versus leaving available for use as energy. We found that blood levels of these hormones were far greater after a sugar drink in patients after gastrectomy (stomach removal) than in healthy volunteers.

To investigate the effects of high levels of one of these hormones (glucagon like peptide-1 [GLP-1]) we gave five post-gastrectomy patients an infusion of an agent that specifically blocked its effects and compared the participant's response to a sugar drink ingested either with the infusion of agent or a placebo. We found that when given the active agent, participants did not feel as full, had fewer symptoms and did not experience severe low blood sugar levels, in contrast to the placebo wing of the study.

This is very exciting – more patients are surviving long-term after treatment for stomach and oesophagus cancer, and this is the first evidence that a specific, targeted treatment may improve quality of life for survivors.

Improving simulation training in orthopaedics

Patrick Garfjeld Roberts

FELLOWSHIP/SPONSOR:
The Dinwoodie
Simulation Fellowship

SUPERVISOR:
Professor Jonathan L Rees

SITE OF WORK:
Botnar Research Centre and Nuffield Orthopaedic Centre, Oxford

PRESENTATIONS:
1. Presented at: RCS Annual Surgeon Educators' Day; March 2017; London

FURTHER FUNDING:
NIHR Oxford Biomedical Research Unit for one year

Patrick demonstrating high fidelity simulation in Oxford.

The aim of this project was to provide evidence that simulation in surgery has an impact on training and surgical technical skills. Though popular, and potentially costly, simulated training has not been shown to lead to the improvements in training outcomes in surgery that have been shown in other fields such as aerospace, motor sports and athletics.

This project focused on the development and validation of wireless elbow-worn motion sensors (see Image 2) that could be used in the skills lab and in theatre, which would for the first time allow the same objective measurement of markers of technical performance to be used in each setting. The preliminary results indicate that those trained on a simulator perform a keyhole examination of the knee joint in half as many hand movements, half the time, and twice as smoothly as their counterpart who received only traditional training.

This project supports previous subjective measures of intra-operative technical performance, such as 'global rating scales' (which require attentive monitoring by an independent observer), and enhances these methods by adding objective and less time-consuming measures of surgical performance.

Together, this demonstrates the objective and subjective case for the efficacy of simulation training in surgery.

This project has confirmed that simulation is acceptable and leads to learning, and demonstrated for the first time that it leads to real-world behavioural change. The next stages are to show this behavioural change leads to improvements in patient outcomes from surgery, and the project group will continue the work to this end at the conclusion of the fellowship.

Elbow-worn motion sensors.

Junior doctors who train on simulators perform keyhole surgery on the knee with half as many hand movements and twice as smoothly as their counterparts who received only traditional training.

3D models of glioblastoma stem cells to develop novel combination therapies

Ola Rominiyi

FELLOWSHIP/SPONSOR:
RCS/Freemasons' United Grand Lodge of England Research Fellowship

SUPERVISORS:
Dr Spencer Collis, Mr Yahia Al-Tamimi and Professor Anthony Chalmers

SITE OF WORK:
Academic Unit of Molecular Oncology (The University of Sheffield Medical School) and Department of Neurosurgery (Sheffield Teaching Hospitals NHS Foundation Trust)

PUBLICATIONS:
1. Rominiyi O, Gomez-Roman N, Lad D *et al.* Preclinical evaluation of combinations targeting the DNA damage response in 2D and 3D models of glioblastoma stem cells. *Neuro-Oncology* 2018; **20**: iii297

PRESENTATIONS:
1. *FA-based combinations to target the DNA damage response in glioblastoma.* Presented at: British Neuro-Oncology Society Meeting; July 2018
2. Presented at: 13th Meeting of the European Association of Neuro-Oncology; October 2018; Stockholm

PRIZES:
1. NC3R's Poster Presentation Competition Winner, 15 June 2018
2. Oral Presentation 2nd Prize at the University of Sheffield Medical School Research Meeting, 15 June 2018

FURTHER FUNDING:
Neurosurgical PhD Research Fellowship – Sheffield Hospitals Charity. Equipment grant for efficient generation of 3D models – Weston Park Hospital Cancer Charity for 12 months

From theatre to the laboratory: Ola working with 3D models generated using cells taken from a patient's tumour.

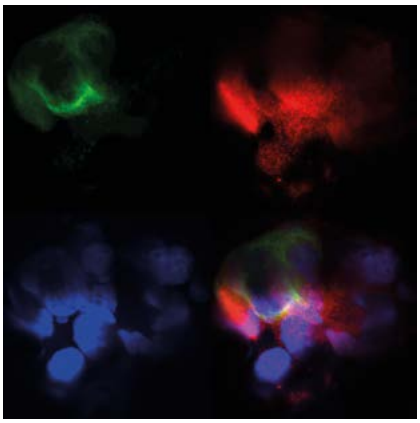
Glioblastoma is the most common malignant tumour arising from within the brain. Currently we use surgery to remove as much of the tumour as safely possible, followed by DNA-damaging treatments – chemotherapy and radiotherapy. In spite of this, most people diagnosed with a glioblastoma will only survive between one and two years.

Researchers have identified a population of cancer cells that are able to repair DNA damage more efficiently and divide with unlimited potential. Often described as 'glioblastoma stem cells' – these are considered to play a key role in the condition worsening. It seems rational that blocking the pathways these cells use to repair damaged DNA would make them more susceptible to present treatments. However, similar to a sat nav, when an important pathway is blocked in cancerous cells, they are often able to re-route – finding another way to the same destination. One way around this issue would be to block a combination of important DNA damage repair pathways simultaneously.

Another critical challenge in neuro-oncology research is to ensure the way we use cells to mimic or model cancer in the laboratory reflects the condition in patients as closely as possible.

Our research tackles these challenges by using part of the brain tumour taken during surgery to grow glioblastoma cells in the laboratory. We grow the cells within a 3D scaffold, which allows them to orientate themselves similarly to how they are arranged in a patient's brain tumour. Crucially, the 3D system is better at predicting which new treatments are more likely to treat cancer effectively in patients.

Our results highlight the role of a DNA damage repair mechanism called the 'FA pathway' in glioblastoma and provide proof of concept that blocking this pathway in conjunction with connected DNA repair mechanisms may represent an effective strategy to treat this devastating disease in the future.



Patient-derived glioblastoma cells (blue) expressing the stem cell markers – nestin (green) and CD133 (red) as viewed using 3D confocal immunofluorescence.

Patients with glioblastoma will, on average, experience worsening disease within seven months of diagnosis.

Bladder control in Parkinson's disease

Holly Roy

FELLOWSHIP/SPONSOR:
Joint RCS/Dunhill Medical Trust Research Fellowship

SUPERVISOR:
Mr Alexander Green

SITE OF WORK:
John Radcliffe Hospital, Oxford

PUBLICATIONS:
1. Roy HA, Aziz TZ, Fitzgerald JJ *et al.* Beta oscillations and urinary voiding in Parkinson disease. *Neurology* 2018; **90**: e1,530–e1,534

PRESENTATIONS:
1. *Modulation of autonomic nervous system function by deep brain stimulation of the subthalamic nucleus: comparison between outcome groups using a structural fingerprint technique*. Presented at: Joint German-British neurosurgical society meeting; May 2017; Magdeburg

2. *Subcortical local field potentials during micturition and related tasks*. Presented at: 5th International Neurourology Meeting; January 2017; Zurich

PRIZES:
1. SBNS travel award 2017

2. Shortlisted for the Swiss Continence Prize 2016/2017

Holly with a patient.

In this project, we used brain imaging and electrophysiological techniques to investigate the neural control of bladder function in Parkinson's disease (PD). Bladder problems, along with other non-motor symptoms, have an important impact on quality of life in PD, but these symptoms have historically been neglected. Research is needed to better understand how to improve this aspect of this disease.

My work focused on brain areas targeted clinically for deep brain stimulation (DBS) in patients with PD, including the subthalamic nucleus (STN) and pedunculopontine nucleus (PPN). The aim was to understand the effect that DBS at these brain areas had on bladder control, using a variety of means including questionnaire assessments, urodynamics, electrophysiology and functional MRI. We hoped to establish whether DBS at these different nuclei has a predictable effect on bladder function and whether this could be harnessed to benefit patients. A secondary aim was to understand the mechanisms of bladder control in PD, again to help understand pathophysiology and guide targeted intervention.

We used resting state functional MRI to measure connectivity between different brain regions in patients with PD in the full bladder and empty bladder state. We found that functional connectivity between the STN and a key posterior brain region in the bladder control network varied with bladder state (full vs empty). This suggests that the effects of STN on bladder function may be mediated via its connections with this region. The next step will be to investigate how this connection is related to the disease process occurring in PD and whether connectivity is altered by the presence of dopamine or by DBS. There have been very few functional brain imaging studies relating to bladder function in PD and we hope that this study will open the door for further research.

Non motor symptoms including bladder dysfunction are common in Parkinson's disease and may affect quality of life as much as or more than motor symptoms.

Perianal fistula: Improving the diagnosis and understanding

Kapil Sahnan

FELLOWSHIP/SPONSOR:
Crohn's and Colitis UK/RCS Research Fellowship with the support of the John Lawson Williams Legacy

SUPERVISORS:
Professor Robin Phillips, Professor Ailsa Hart and Professor Omar Faiz

SITE OF WORK:
St Mark's Hospital, London

PUBLICATIONS:
1. Sahnan K, Tozer P, Adegbola S *et al.* Developing a core outcome set for Fistulising Perianal Crohn's Disease. *Gut* 2018: [Epub ahead of print]

2.Sahnan K, Adegbola SO, Tozer PJ *et al.* Improving the understanding of perianal Crohn's fistula through 3D modelling. *Ann Surg* 2018; **267**: e105–e107

PRESENTATIONS:
1. Presented at: European Crohn's and Colitis Organisation; February 2018; Vienna

2. Presented at: European Society of Coloproctology; September 2017; Berlin

PRIZES:
Best Oral Presentation, 'Developing a core outcome set for fistulising Crohn's disease from the European Crohn's and Colitis Organisation'

FURTHER FUNDING:
Anson Charitable Trust, Rolfe Charitable Trust, For Crohn's Charity and Basil Samuel Charitable Trust for 12 months

Kapil painting the first fistula model prototype.

Anal fistulas (abnormal tunnels connecting the bowel to the adjacent skin on the buttock, arising close to the anus) occur in a third of patients with Crohn's disease (CD), a type of inflammatory bowel disease (IBD). They cause pain and discharge resulting in reduced quality of life. Treatment is challenging owing to the risk of damaging the anal sphincter, the muscles controlling continence. The disease course is often severe and disabling, with high recurrence rates.

Using a national administrative dataset we established incidence/prevalence for fistula, as well as using algorithms to determine that just under a fifth of patients presenting with an anal abscess develop a fistula and that 3 in every 100 patients presenting with an infection in anal region have an underlying diagnosis of CD.

The lack of standard outcomes amongst researchers hampers effective analysis and comparison of data when comparing treatments in fistulising perianal Crohn's disease. We worked with 228 stakeholders (surgeons, gastroenterologists, nurses, radiologists and patients) to develop a core outcome set (COS) for perianal Crohn's fistula. Application of the COS will reduce ambiguity in outcome reporting, thereby facilitating more meaningful comparisons between treatments, data synthesis and ultimately benefit patient care.

Using software packages, we created an MRI based scoring system to provide an objective/reproducible measure a range of 3D reconstructions. Fistulas can be very difficult to understand for patients and surgical trainees. We created a range of 3D reconstructions (images which can be rotated on a PDF viewer, animations, 3D models and an app based software to facilitate accessibility) to better serve (i) patients in clinic to improve the consenting process (ii) trainees to allow them to better comprehend complex disease and (iii) surgeons in pre-operating planning.

3D printed fistula model – sphincters in blue (internal), green (external) with the fistula in red.

One in three patients with Crohn's disease suffer from perianal disease, a distinct and aggressive phenotype of the disease.

Developing an engineered honey (Surgihoney RO) as a novel topical anti-MRSA treatment

Mr Ali A Salamat

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

SUPERVISOR:
Dr Sylvia LF Pender

SITE OF WORK:
University Hospital Southampton NHS Foundation Trust and University of Southampton

PUBLICATIONS:
1. Dryden MS, Cooke J, Salib RJ *et al.* Reactive oxygen: a novel antimicrobial mechanism for targeting biofilm-associated infection. J Glob Antimicrob Resist 2017; **8**: 186–191

PRESENTATIONS:
1. Presented at: British Rhinological Society; May 2016; Leeds

2. Presented at: European Rhinologic Society; July 2016; Stockholm

PRIZES:
1. British Rhinological Society (BRS) best oral presentation (1st prize), BRS, Armouries Museum, Leeds, May 2016

2. European Rhinologic Society (ERS) junior member travelling fellowship, Stockholm, July 2016

FURTHER FUNDING:
British Medical Association Helen H Lawson Grant for three years

Ali performing an ENT examination of a patient with chronic rhinosinusitis.

Our antibiotic armamentarium is being increasingly restricted in the face of a looming post-antibiotic crisis that the World Health Organisation has long warned about. *Staphylococcus aureus* is a common bacterium that affects our society at large, such as newborns, the elderly and surgical patients. MRSA is a resistant form of bacteria that can cause serious harm to these patients whether in hospital or the wider community. The financial burden on the NHS from MRSA is huge. It is estimated that MRSA costs the NHS and ultimately the taxpayer up to £1 billion a year.

Ali in theatre.

Our project has looked into whether a biologically engineered honey gel (Surgihoney RO™), which has been trialled in chronic wounds, could be a potential anti-MRSA treatment. Mupirocin is one of the few available treatments available used to clear (decolonise) patients of MRSA before an operation. There are concerns about MRSA resistance to Mupirocin.

Using a number of MRSA samples from our local laboratory and supplemented by resources provided by the RCS fellowship, we have extensively tested Surgihoney RO™ against a number of MRSA bacteria. These experiments have shown that Surgihoney RO™ is more effective than Mupirocin. This is a significant advance that we are still currently analysing prior to publishing.

How does this affect patients in the NHS? Well, we potentially have a new treatment that can be used to decolonise patients with MRSA, cleaning our hospitals, an alternative to current hand washes and as anti-septic before and after operations to prevent infections.

While these results are very encouraging, we should remain realistic about its use in the clinical arena until clinical trials, proving its use, safety and feasibility are performed.

One in three of the population will be colonised with *Staphylococcus aureus* such as MRSA.

Evaluation of novel combination drug protocols for neuroblastoma using advanced imaging in a chick embryo model

Keerthika Sampat

FELLOWSHIP/SPONSOR:
Joint RCS/BAPS Research Fellowship

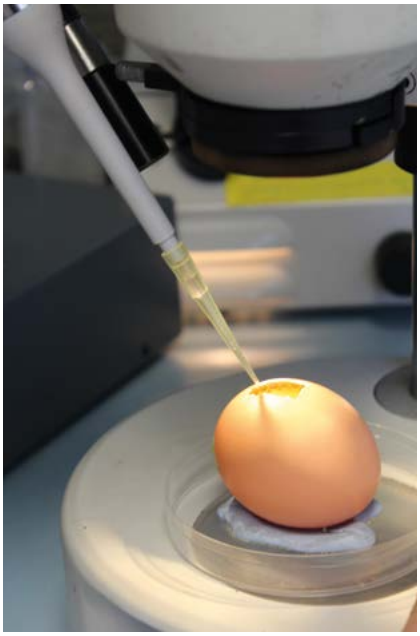
SUPERVISORS:
Professor Paul Losty and Dr Violaine See

SITE OF WORK:
University of Liverpool, Alder Hey Children's Hospital

PRESENTATIONS:
1. Presented at: Society of Academic and Research Surgery; January 2017; Dublin

PRIZES:
NIHR Academic Clinical Fellow Poster Prize (Winner), June 2017

FURTHER FUNDING:
North West Cancer Research for two years

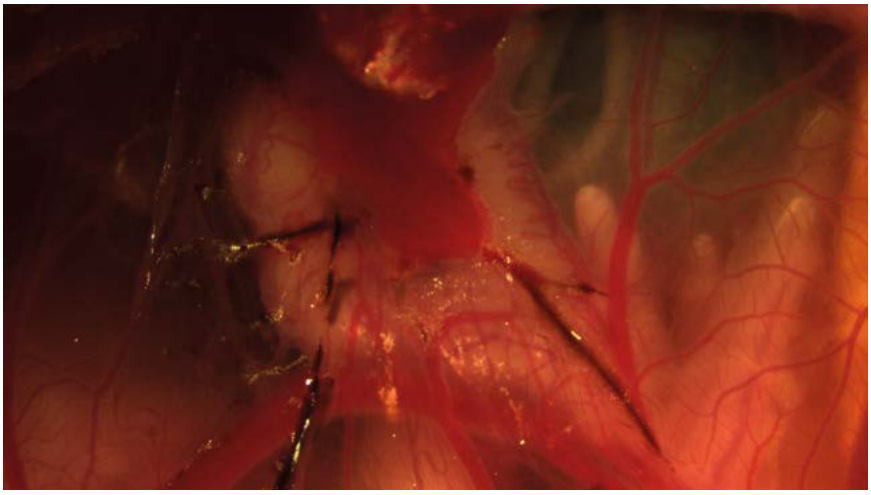


Injection of neuroblastoma cells into the chick embryo model.

Neuroblastoma is a childhood tumour affecting the developing nervous system. It is the most common extra-cranial solid tumour cancer of childhood. It can occur anywhere in the body, but predominantly is found in the abdomen. Children diagnosed with high grade neuroblastoma often have widespread cancer upon diagnosis. Unfortunately, there is currently no effective treatment for this type of neuroblastoma and as a result, the survival rate for children with high grade disease is very low. Discovery of new drugs to improve mortality rates is desperately needed, but this is often a long and expensive process. Our aim is to use a developing chick embryo as a drug testing platform, to identify new treatment options which may have a therapeutic benefit in neuroblastoma.

The chick embryo is a well-established Nobel Prize winning model. By placing neuroblastoma cells into the egg, we are able to develop a tumour, which then spreads into the developing chick, similar to how cancer cells spread in children. By analysing these tumours, we were able to identify multiple cancer-causing pathways, which could be targeted using drugs that are already approved for use in other cancers. In order to further characterise the drugs' effect on neuroblastoma, we are also developing an analysis protocol using a state of the art microscopy and live embryo imaging. This high throughput, high fidelity model will allow us to screen and identify multiple new drugs that may be beneficial in treating aggressive neuroblastoma. Moreover, this model is in keeping with the good ethics in animal research, by reducing and replacing the number of rodent models used. Preliminary findings have identified several drugs currently in use for adult cancers as potential candidates for further investigation.

If successful, the chick embryo model will serve as a valuable tool in expediting drug discovery in neuroblastoma.



Neuroblastoma tumour growing on the outer membrane of the chick embryo model.

Neuroblastoma is the third most common childhood cancer, and the most common cause of malignancy of infancy (<1 year old).

Large-scale (re)evaluation of the relationships between imaging, tumour and nodal staging and oncological outcome in patients with anal cancer

Hema Sekhar

FELLOWSHIP/SPONSOR:
RCS Research Fellowship

SUPERVISORS:
Professor Andrew Renehan and Professor Marcel van Herk

SITE OF WORK:
The Christie NHS Foundation Trust, Manchester Cancer Research Centre and The University of Manchester

PUBLICATIONS:
1. Sekhar H, Zwahlen M, Trelle S *et al.* Impact of nodal stage migration on prognosis in anal cancer: systematic review, meta-regression and simulation studies. *Lancet Oncol* 2017; **18**: 1,348–1,359

PRESENTATIONS:
1. *Temporal Trends and Impact on Survival after Chemoradiotherapy for Anal Cancer – A large single institute cohort over 25 years.* Presented at: Association of Coloproctology Great Britain and Ireland, BJS Prize Session; July 2016; Edinburgh

2. *Lymph node positivity in patients with anal cancer treated in the modern era: prognostic impact and patterns of locoregional relapse (L-NuANCE).* Presented at: Digestive Disorders Federation; June 2015; London

PRIZES:
1. Manchester Medical Society – Trainees' Presentation Prize – March 2017, Manchester

2. Margaret Pritchard Prize (runner up) – May 2017, University of Manchester

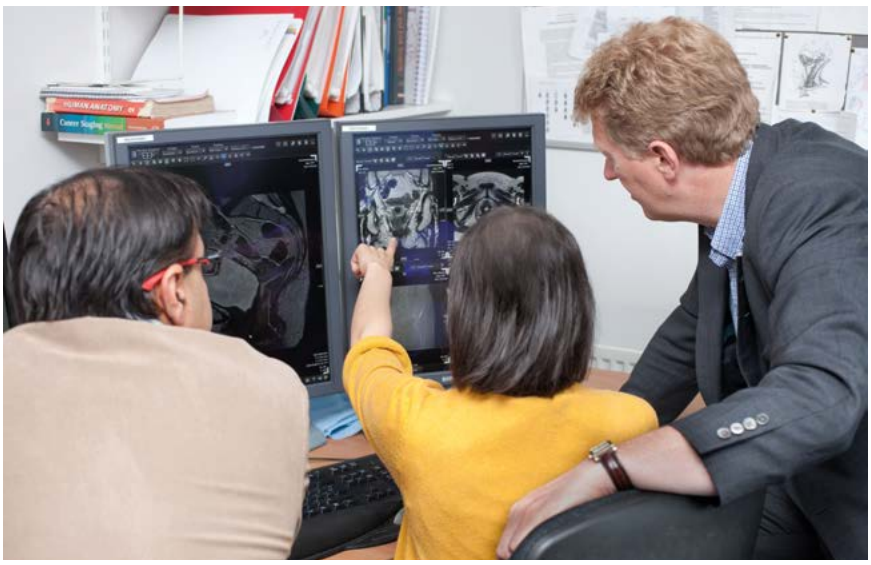
FURTHER FUNDING:
Two years of PhD funded by BDRF

The incidence of squamous cell carcinoma of the anus has increased three-to-four-fold in western populations during the past 30 years. Initial treatment is with a combination of chemotherapy and radiotherapy (chemoradiotherapy) but can lead to complications. For up to 20% of patients this treatment may not work and they will require extensive surgery. Being able to identify which patients are at risk of this would help to tailor treatment to improve outcomes in these patients.

By using detailed characterisation of disease on MRI scans in 265 patients, the largest series of this kind, I demonstrated novel tumour and nodal features on imaging that may help to predict which patients are at risk of treatment failure. These features included tumour volume, growth of the tumour along vessels, differences within the image texture of the tumour and the involvement of certain groups of pelvic lymph nodes.

Additionally, the patterns of disease recurrence were analysed in relation to the radiotherapy dose received at these sites which demonstrated a group of recurrences occurring despite adequate dose being delivered and a separate group of recurrence that occurred at sites above standard radiotherapy coverage.

Together, this information can further be used to find out which patients may benefit from receiving higher doses of radiotherapy (for example, as part of the dose-escalation arm of the national PLATO trial) and which ones may benefit from radiotherapy treatment of a wider field. The next step is to confirm these results with other data sets. The long-term goal of this work is to be able to provide personalised treatment to patients based on individual patient's risks of disease recurrence and their likely pattern of recurrence. This will allow improved cure rates while reducing the side effects of treatment in those found to be at low risk of recurrence.



The research team analysing MRI scans; from left to right: Dr Rohit Kochhar, Hema Sekhar and Professor Andrew Renehan.

The incidence of squamous cell carcinoma of the anus has increased during recent decades – there are now more than 1,000 new diagnoses per year in the UK.

The generation and function of microvesicles in blast injury

Anna Sharrock

FELLOWSHIP/SPONSOR:
Joint RCS/Military Research Fellowship

SUPERVISORS:
Professor S Rankin and
Sargent Captain Professor R Rickard

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

PUBLICATIONS:
1. Barnett-Vanes A, Sharrock A, Eftaxiopoulou T *et al.* CD43Lo classical monocytes participate in the cellular immune response to isolated primary blast lung injury. *J Trauma Acute Care Surg* 2016; **81**: 500–511

2. Eftaxiopoulou T, Barnett-Vanes A, Arora H et al. Prolonged but not short-duration blast waves elicit acute inflammation in a rodent model of primary blast limb trauma. *Injury* 2016; Vol: **47**: 625–632

PRESENTATIONS:
1. Sharrock AE, Remick K, Midwinter M, *et al. Rickard Combat vascular injury: Influence of mechanism of injury on outcome.* Presented at: Association of Trauma and Military Surgeons; May 2016. Belfast. Also presented at: American Association for the Surgery of Trauma; September 2016; USA

2. Sharrock AE, Amin HD, Harrison P *et al. Human endothelial microvesicle shedding in response to simulated blast trauma.* Presented at: International Society for Extracellular Vesicles meeting; May 2016; Rotterdam

PRIZES:
Richard Wiseman Medal, May 2016

FURTHER FUNDING:
The Drummond Foundation, The Royal Centre for Defence Medicine, and travel grants provide by the Royal British Legion Centre for Blast Injury Studies

The first aim was to study patients with arterial injuries from operations in Iraq and Afghanistan (2003–2014), to see if there were more complications (ie clotting, infections, survival) in explosive or ballistic (gunshot) injured patients. The second aim was to build models of explosive injury to study the effects on the structure and function of cells, particularly those lining blood vessels, with a focus on cell fragments (microvesicles, MV). These are present at low levels in body fluids and carry cargo from parent cells to aid cellular communication and maintain the body's status quo. Stressed cells (ie in trauma) shed more MV, which may be of a type to promote clotting abnormalities and inflammation. This may influence the development of organ failures and the chances of survival.

Patients from the UK and USA who had arterial injuries sustained in Iraq or Afghanistan were equally likely to have localised clotting problems and infections, and to die from their injuries whether they were injured by explosive or ballistic mechanisms.

Models for simulating explosive forces versus controls were developed at the Royal British Legion Centre for Blast Injury Studies, The Biomedical Engineering department, and The Institute of Shock Physics at Imperial College. In laboratory conditions, cells exposed to a blast wave generated more MVs within 24 hours and carried four times as much clot promoting protein (tissue factor). Platelets (involved in clot formation) also work less well after a blast wave exposure, but recovered within 24 hours.

Previously, it has been shown that civilian trauma patients have more clot forming MV, this however is the first study of MV in blast injuries. The project continues to develop through comparison with civilian patients. It is important to identify patients at particular risk of developing clotting problems, so that they may be a focus for treatment in a situation of mass casualty management in the future.

Anna presenting data at the Association of Trauma and Military Surgeons conference in 2015.

70% of combat casualties are injured by explosive means: complications occur more commonly in these, compared to penetrating mechanisms alone.

Biomarkers of disease progression in Chronic Pancreatitis

Andrea Rhiannon Glynne Sheel

FELLOWSHIP/SPONSOR:
RCS Research Fellowship with the support of the Rosetrees Trust

SUPERVISOR:
Mr Christopher Halloran

SITE OF WORK:
The Institute of Translational Medicine, The University of Liverpool

PUBLICATIONS:
1. Drewes AM, Bouwense SAW, Campbell CM *et al*. Guidelines for the understanding and management of pain in chronic pancreatitis. *Pancreatology* 2017; **17**: 720–731

PRESENTATIONS:
1. *Alcohol excess and continued smoking are risk factors for progression from minimal change chronic pancreatitis to established chronic pancreatitis*. Presented at: The Jubilee Meeting of the European Pancreatic Club; June 2018; Berlin

2. *Missed cancers in hereditary pancreatitis (HP) kindred indicate the importance of a systematic approach to secondary screening*. Presented at: 48th Annual meeting of the European Pancreatic Club; 2017; Budapest

PRIZES:
1. European Pancreatic Club Travel Scholarship July 2018

2. European Pancreatic Club Travel Scholarship July 2017

Andrea sitting on the panel at a special session of the combined meeting of the IAP/JPS/AOPA in Sendai, Japan 2016 entitled 'What is early chronic pancreatitis and why is diagnosis important?' Joined by esteemed Professors Whitcomb, Neoptolemos, Lerch, Hegyi, Kitano, and Pandol.

Chronic pancreatitis (CP) is a chronic inflammatory syndrome affecting around 50 per 100,000 people. Patients suffer recurrent pancreatic inflammation leading to progressive and irreversible destruction of pancreatic tissue. Typical symptoms include; chronic abdominal pain, malnutrition and diabetes. The severity of these symptoms and the resulting complications can be so great that patients' quality of life and life expectancy are significantly reduced. In addition, the risk of developing pancreatic cancer is increased. There is currently no cure, with treatments focused on easing the complications of the disease.

Andrea with her 12-week-old daughter and the President of the EPC Professor Markus. M. Lerch at the 50th Jubilee meeting of the European Pancreatic Club, Berlin 2018.

Advanced disease is often easy to diagnose using imaging and has historically been the focus of CP research, but at this stage the pancreas is all but destroyed. If CP can be diagnosed at an earlier stage then lifestyle modifications, medical treatments and novel therapeutic interventions may be able to halt, prevent or even reverse the damage to the pancreas.

My research aims to support clinicians in diagnosing CP earlier and identifying those patients at greater risk of having progressive disease. One major challenge that previously limited CP research prospects, novel therapeutic development and the initiation of clinical trials was the lack of consensus on classification of CP by stage. To address this, I coordinated an international panel of experts and together we produced the first consensus statements on early CP.

By analysing potential biomarkers such as imaging features, clinical information and novel protein markers found in blood, I have developed a model that can assist in identifying the patients at highest risk of disease progression and complications. I have also been the first to demonstrate that features traditionally used to diagnose 'early CP' during endoscopic ultrasound examination of the pancreas can in some cases completely resolve. This work furthers the diagnosis of early CP; allowing earlier interventions and improving patient outcomes.

A diagnosis of chronic pancreatitis carries a heavy burden; life expectancy following diagnosis is only 15 years, 1 in 3 patients are left unable to work, 3 out of 4 patients will require surgery in their lifetime and the risk of developing pancreatic cancer is increased 14-fold.

Impact of surgical brain injury

Rohitashwa Sinha

FELLOWSHIP/SPONSOR:
The Wellington Hospital RCS Research Fellowship

SUPERVISOR:
Mr Stephen Price

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

PRESENTATIONS:
1.*Impact of Surgical Brain Injury*. Presented at: the British Neurosurgical Research Group Meeting; February 2017; Birmingham

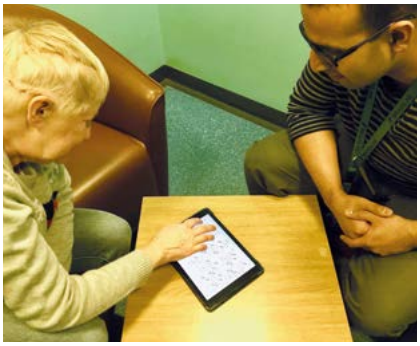
FURTHER FUNDING:
A Clinical PhD Fellowship for three years from Cancer Research UK via the Cambridge Cancer Centre

Keeping surgical skills active during research, Rohit operating on a patient with a brain tumour.

Patients with glioblastoma brain cancer often suffer difficulties with memory, attention and planning, collectively called cognition. This can mean they lose confidence in leaving the house alone, returning to work or enjoying social activities.

We aimed to study cognitive brain function in patients with glioblastoma before and after brain surgery to understand the effect of both the cancer and surgery.

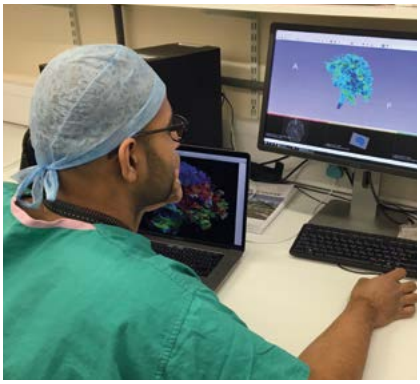
Insufficient cognition research has been done with these patients. Cognitive testing by clinical psychologists is scarce in the NHS. Where available, high rates of dropout occur in previous studies because patients find the conventional paper tests too burdensome.



Rohit performing a cognitive test with a patient using the tablet-based tool.

We used a tablet computer-based tool to test cognitive function before and after surgery. It uses standard tests from trained clinical psychologists, but by enabling other clinicians to perform them, it broadens patient access to efficient assessments.

Our preliminary findings confirm that more cognitive functions are impaired in patients by glioblastoma as compared with less aggressive brain cancers. Furthermore, surgery can worsen cognitive functions that were assessed as normal before the operation. These findings highlight this patient group in particular needs more research focus to protect their brain function during treatment.



Learning brain imaging analysis methods to study brain connection.

This fellowship has generated vital data on which to build future studies. We have fortunately secured further funding to continue this work by Cancer Research UK, in which we will also study the changes in brain scans that accompany cognitive problems. Our current findings will help patients to better understand the likely risks to their cognitive function from the cancer and surgery, empowering them to make more informed decisions about their treatment. In future research, we aim to build on this work by applying current findings to help target rehabilitation at the problems found by such cognitive testing to improve patient function and hence quality of life whilst undergoing surgery.

The majority of patients with glioblastoma brain cancer suffer problems with cognitive brain functions such as memory, attention and language, which can lead to a poor quality of life.

Combination immunotherapy to target metastases in extremity soft tissue sarcoma

Henry Smith

FELLOWSHIP/SPONSOR:
Saven Research and Development Programme

SUPERVISORS:
Mr Andrew Hayes and Professor Kevin Harrington

SITE OF WORK:
Institute of Cancer Research, Royal Marsden Hospital

PUBLICATIONS:

1. Wilkinson MJ, Smith HG, McEntee G *et al.* Oncolytic vaccinia combined with radiotherapy induces apoptotic cell death in sarcoma cells by down-regulating the inhibitors of apoptosis. *Oncotarget* 2016; **7**: **81**, 208–81,222

2. Wilkinson MJ, Smith HG, Pencavel TD *et al.* Isolated limb perfusion with biochemotherapy and oncolytic virotherapy combines with radiotherapy and surgery to overcome treatment resistance in an animal model of extremity soft tissue sarcoma. *Int J Cancer* 2016 **139**: 1,414–1,422

PRESENTATIONS:

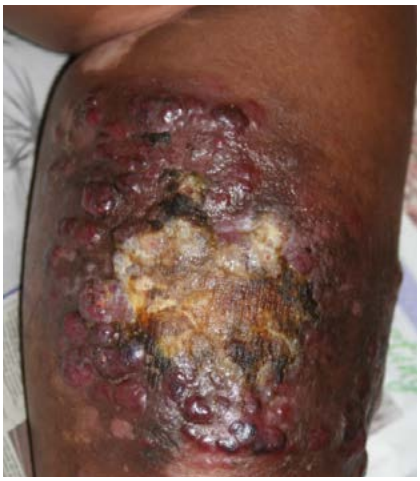
1. *Viral ILP combines with PD-1 blockade to improve local and distant disease control in extremity soft tissue sarcoma.* Presented at: Society of Surgical Oncology Congress; March 2018; Chicago

2. *Viral ILP augments the efficacy of PD1 blockade in a model of extremity soft tissue sarcoma.* Presented at: BASO/NCRI Conference; November 2017; Liverpool

PRIZES:
BASO Trainees Prize, BASO/NCRI Conference, Liverpool, November 2017

FURTHER FUNDING:
Sarcoma UK for 12 months

Soft-tissue sarcomas are rare cancers, most commonly developing in the limbs. Surgery is the standard of treatment for patients with potentially curable disease and prevents the cancer returning in the limb in three of every four patients. Despite this, one in every three patients develops disease elsewhere, known as metastases. Once metastases develop, there are few effective treatments and most patients survive less than 12 months.



An inoperable sarcoma that would be suitable for Isolated Limb Perfusion.

Henry presenting his research findings at the British Association of Surgical Oncology and National Cancer Research Institute Congress, Liverpool.

Treatments that stimulate our immune system to attack cancer, known as immunotherapies, have markedly improved survival from other cancers. Similarly to how vaccines protect against future infections, immunotherapies can 'vaccinate' patients against their cancer, preventing it from ever returning. However, immunotherapies have limited effects in sarcoma, as these cancers are better able to hide from our immune systems. Certain cancer treatments help our immune systems identify cancers and we hope that by combining one such treatment (cancer-killing viruses) with immunotherapies, we can improve responses to treatment.

Cancer-killing viruses specifically target cancer cells. Similar to a normal infection, viral infection of cancer attracts the attention of our immune system, helping it recognise previously undetected cancers. Our previous research suggests the best way to deliver virus to sarcoma is using a technique known as isolated limb perfusion (ILP).

Using an experimental model, we found that virus delivered by ILP provokes the immune system to attack sarcoma. Immunotherapies have little effect in this model when used alone, but when given after a viral ILP, marked improvements in treatment were noted. The combination of viral ILP and immunotherapy before surgery prevented any cancers returning to the limb and the development of metastases.

We will soon be opening a first-in-man trial combining cancer-killing viruses with ILP in patients with sarcoma. This novel treatment may allow patient to be 'vaccinated' against their sarcoma prior to surgery, markedly improving their survival.

Following surgery, one in three patients with soft-tissue sarcoma develop metastases for which there are few effective treatments.

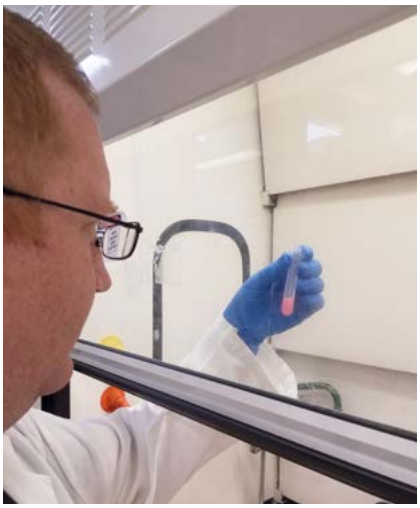
The effects of tourniquet associated ischemia reperfusion injury on the development of secondary organ injury and heterotopic ossification in blast related lower limb trauma

Philip James Spreadborough

FELLOWSHIP/SPONSOR:
Joint RCS/Military Research Fellowship

SUPERVISORS:
Dr Thomas Davis,
Captain Eric Elster USN and
Surgeon Captain Rory Rickard

SITE OF WORK:
Department of Surgery, Uniformed Services University of the Health Sciences (USUHS), Bethesda, MD, USA and the Department of Regenerative Medicine, Naval Medical Research Center (NMRC), Silver Springs, MD USA



Philip assessing RNA extracted to identify molecular gene markers of injury.

During conflicts in Iraq and Afghanistan, blast accounted for 70% of all mechanisms of injury. Blast injuries are increasingly relevant to the NHS, as evidenced in Manchester and London. Globally, landmines remain a significant source of blast-related lower limb injuries, indiscriminately resulting in death or injury to non-combatants long after conflicts have ceased.

Improved pre-hospital survival, in part due to tourniquets controlling bleeding, has meant that secondary injury as the result of a dysregulated excessive immune response following polytrauma is now a significant challenge. Development of multi-organ failure increases mortality 6-fold, while heterotopic ossification (HO), a debilitating condition characterised by abnormal bone formation in soft tissues, occurs in 65% of blast related traumatic amputees; many of whom had tourniquets applied during their initial care.

Blast wave exposure affects multiple organs in the body, with a complex interplay of local, systemic and cerebral responses. It induces tissue damage and cell stress, even without obvious external signs of injury. Tourniquets that are used to control bleeding do so at the expense of starving the limb of oxygen, causing further damage through an ischaemia reperfusion injury (IRI) if applied too long. This project will determine if blast wave exposure predisposes to an earlier or more exaggerated inflammatory response from tourniquet application if an ischemia reperfusion injury (IRI) occurs.

Our pilot study suggests that tourniquet application may increase the volume of HO formed, negatively affecting patient outcome. By examining how inflammatory mediators, gene expression and tissue biomarkers are affected by blast wave exposure and tourniquet application, we will better understand any synergistic mechanisms. An important component of early patient care is identifying those at greatest risk of deterioration. Injured tissues release warning signals termed 'DAMPs', which activate the immune system. These correlate with injury extent and survival in other medical conditions; we will assess if these biomarkers are effective at stratifying injury severity and outcome in blast related trauma.

Philip loading RNA Nano Chips to determine the quality of RNA from injured tissue samples.

During recent conflicts in Iraq and Afghanistan, blast accounted for 70% of all mechanisms of injury. Changes in global security has meant the management of blast associated injuries has become increasingly relevant to the both the NHS and wider society.

Developing research outcomes relevant to patients with Cauda Equina Syndrome

Nisaharan Srikandarajah

FELLOWSHIP/SPONSOR:
RCS Research Fellowship

SUPERVISOR:
Professor Tony Marson

SITE OF WORK:
University of Liverpool

PUBLICATIONS:

1. Srikandarajah N, Noble A, Clark S *et al.* Systematic Literature Review of Outcomes after Surgery for Cauda Equina Syndrome. *The Spine Journal*. 2017; **17(3)**: S26–7

2. Srikandarajah N, Boissaud-Cooke MA, Clark S, Wilby MJ. Does early surgical decompression in cauda equina syndrome improve bladder outcome? *Spine*. 2015; **40(8)**: 580–3

PRESENTATIONS:

1. *Qualitative Interviews of Patients who have had an operation for Cauda Equina Syndrome; The outcomes that are of importance to them.* Presented at: Society of British Neurological Surgeons; September 2017; Liverpool

2. *Developing a Core Outcome Set in Surgery for Cauda Equina Syndrome.* Presented at: Core Outcome. Measures in Effectiveness Trials VI; November 2016; Amsterdam

FURTHER FUNDING:
Medtronic for two years

Cauda Equina syndrome (CES) is a serious condition that occurs when the nerves located at the bottom of the spinal cord – known as the 'cauda equina' – become compressed which can cause severe disability if not managed and operated on as an emergency. CES can be caused by trauma, such as a car crash, herniated disk, spinal stenosis, tumours, inflammatory conditions, infectious conditions and medical treatment (such as surgical errors). The aim of this research was to find out what outcomes mattered to patients who had the condition.

Nish in theatre performing a lumbar microdiscectomy and removing sequestered disc material for a patient with CES.

We performed a comprehensive review of the literature and found that in CES research different outcomes were reported, not defined similarly and measured with different assessments. There was little consistency between the studies. As there has been no research into which outcomes matter the most to patients, we recruited and recorded one-to-one interviews with patients, with ethical approval. The transcripts were transcribed and analysed. Patients had varying severity of the condition.

There are a number of issues patients experience after the condition such as bladder, bowel and sexual dysfunction, back and leg pain, and mobility and psychological issues. We found that back and leg pain as well as mobility issues concerned patients the most, as opposed to bladder and bowel issues, which is what the current research is focused on. Important themes regarding future prognosis, return to work, feeling unsupported, isolation and the detrimental effect on family life were highlighted.

For the following year, we hope to run an iterative Delphi questionnaire and a consensus meeting with key stakeholders (patients and healthcare professionals) to identify which of these outcomes are the most important. This will develop with transparent methodology the minimum set of outcomes that should be reported for future CES studies. We hope to run a study analysing these outcomes which will allow for a stronger evidence base to help improve management and aftercare for this rare condition.

Nish with Claire Thornber, a CES patient and research partner in the study. Claire is the founder and actively involved in The CES Association, a patient-led international CES support group.

Over 1,000 emergency spine operations are done per year in England alone for Cauda Equina Syndrome.

Rapid evaporative ionisation mass spectrometry for examination of breast surgical excision margins

Edward St John

FELLOWSHIP/SPONSOR:
Enid Linder Foundation Research Fellowship

SUPERVISOR:
Professor Darzi, Mr Daniel Leff and Professor Takats

SITE OF WORK:
Charing Cross Hospital

PUBLICATIONS:

1. St John ER, Balog J, McKenzie JS *et al.* Rapid evaporative ionisation mass spectrometry of electrosurgical vapours for the identification of breast pathology: towards an intelligent knife for breast cancer surgery. *Breast Cancer Research.* 2017; **19**: 59

2. Leff DR, St John ER, Takats Z. Reducing the margins of error during breast-conserving surgery: Disruptive technologies or traditional disruptions? *JAMA Surg.* 2017; **152(6)**: 517–518

PRESENTATIONS:

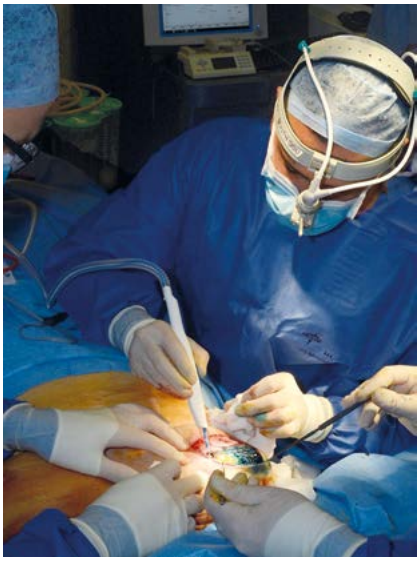
1. St John E, Balog J, McKenzie J *et al. Rapid Evaporative Ionisation Mass Spectrometry of surgical vapours towards an intelligent knife for precision breast surgery.* Presented at: Association of Breast Surgeons (ABS) Annual Conference; May 2017; Belfast

2. St John E, White E, Balog J *et al. An Intelligent Knife for Detection of Invasive Breast Cancer at Radial Margins: An Intraoperative Feasibility Trial.* Presented at: American Society of Breast Surgeons (ASBS); April 2017; Nevada, USA

PRIZES:

1. BJS prize for best oral presentation at ABS international conference, Breast Surgery (2017), Association of Breast Surgeons (British Journal of Surgery prize)

2. Mammary Fold Academic and Research Prize, Best Oral Presentation, Breast Surgery, Mammary Fold (2017), National Breast Surgical Trainees Group



Demonstrating the iKnife system in use during breast surgery.

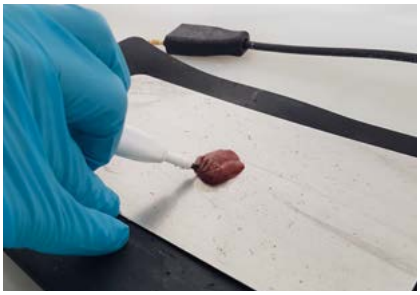
Unfortunately, in the UK breast cancer is the commonest cancer, affecting 1 in 8 women. The majority are now treated with breast conserving surgery (BCS) involving removal of the cancer lump while preserving the rest of the breast. Because cancer cells are not visible to the surgeon, 1 in 5 patients undergoing BCS require re-operation due to the presence of cancer at the specimen edge (positive margin) detected by the pathologist after surgery. Re-operation is costly, negatively affects cosmetic outcome and increases patient suffering. The aim of this project was to develop a novel technique called the 'iKnife' to assess the cancer margin during surgery.

Surgical aerosol produced as a by-product of standard electrosurgical dissection was analysed by a mass spectrometry technique known as Rapid Evaporative Ionisation Mass Spectrometry. Previous work has successfully demonstrated this concept in a broad range of surgical specialties but this was the first work focusing specifically on its use in breast surgery.

Surgical aerosol was collected from normal and cancer breast tissues in the laboratory, a tissue type database was created and significant differences were identified between the two groups. The technique was then used in the operating theatre for the classification of breast tissue during surgery. In these tests, the system performed well during surgery with results demonstrating that analysis is rapid and can correctly diagnose invasive cancer at the specimen edge with high accuracy.

In the future, this technique may enable more precise BCS and decrease the large number of patients requiring re-operations while reducing anxiety and suffering. Furthermore, this novel technique of analysing breast tissue could enable a greater understanding about the underlying metabolism of breast cancer, which may help further improve outcomes for breast cancer patients.

This research has led to the successful funding of a multicentre feasibility study funded by Cancer Research UK.



Close-up of a specimen being analysed by the iKnife in the laboratory.

1 in 8 women develop breast cancer; 20% of patients undergoing breast conserving surgery require a further operation due to positive cancer margins.

Understanding the role of teamwork in recruitment to randomised controlled trials in surgical oncology: an exploratory study

Sean Strong

FELLOWSHIP/SPONSOR:
Sir Alan Parks Research Fellowship

SUPERVISOR:
Professor Jane Blazeby

SITE OF WORK:
Centre for Surgical Research, School of Social and Community Medicine, University of Bristol

PUBLICATIONS:

1. Strong S, Paramasivan S, Mills N *et al.* The trial is owned by the team, not by an individual: a qualitative study exploring the role of teamwork in recruitment to randomised controlled trials in surgical oncology. *Trials.* 2016; **17**: 212

2. Paramasivan S, Strong S, Wilson C *et al.* A simple technique to identify key recruitment issues in randomised controlled trials: Q-QAT - quanti-qualitative appointment timing. *Trials.* 2015; **16**: 88

PRESENTATIONS:

1. Strong S, Paramasivan S, Donovan J, Blazeby J. *Effective teamwork is crucial to maximising recruitment to randomised controlled trials in surgical oncology.* Presented at: Society of Clinical Trials; 2017; Liverpool

2. Strong S, Paramasivan S, Donovan J, Blazeby J. *Understanding the role of teamwork in recruitment to randomised controlled trials in surgical oncology – results from an exploratory study.* Presented at: Society of Clinical Trials; 2014; Philadelphia

Clinical trials are important to the NHS and patients because they are the best way to evaluate surgical interventions. These trials however often have difficulties recruiting patients. Trials involving the comparison of very different treatments such as surgery and chemotherapy are known to be most challenging to recruit into. Close collaboration between different clinical and research teams is required to make such trials successful. This research used interviews to explore aspects of teamwork that were important for recruitment to such trials.

The aim of the research was to identify factors that facilitated and hindered teamwork in trials in surgical oncology. Three cancer trials in bowel, gullet and lung surgery were studied. Interviews and observations of teams in seven different centres were undertaken. Findings revealed the importance of the existing team culture within centres and the leadership of the study at each centre.

Teamwork was facilitated in situations where the team had worked together for longer periods of time or had experience of recruitment to previous randomised controlled trials. Centres with a collaborative approach to clinical care were able to reach team decisions regarding study participation and more easily integrate trial demands into standard clinical practice.

At a centre level, qualities of leadership that were desired included charisma and tenacity to overcome the many obstacles associated with trial recruitment. The insights gained into the team factors that may influence recruitment will serve as the basis for the development of interventions to optimise the process. In the future, it is hoped that this work will lead to the design, development, piloting and assessment of team workshops to address these issues.

Sean (top left) with the surgical research team in Bristol.

The cancer multidisciplinary team meeting was of central importance to aiding the development of interdisciplinary teamwork in relation to trial recruitment.

FAK: An invasive breast cancer target

Simon Timbrell

FELLOWSHIP/SPONSOR:
RCS Research Fellowship

SUPERVISOR:
Professor Nigel Bundred

SITE OF WORK:
Breast Biology Laboratory, Manchester Cancer Research Centre

PUBLICATIONS:
1. Timbrell S, Al-Himdani S, Shaw O *et al.* Comparison of local recurrence after simple and skin sparing mastectomy performed in patients with Ductal Carcinoma in Situ. *Ann Surg Oncol.* 2017

2. Al-Himdani S, Timbrell S, Tan K *et al.* Prediction of margin involvement and local recurrence after skin-sparing and simple mastectomy. *Eur J Surg Oncol.* 2016

PRESENTATIONS:
1. Timbrell S, Clarke R, Bundred N, Farnie G. *A role for Focal Adhesion Kinase in regulation of Invasive Ductal Carcinoma.* Presented at: European Network of Breast Development and Cancer; 9–11 March 2018; Weggis

2. Timbrell S, Al-Himdani S, Shaw O *et al. Local recurrence after mastectomy performed for pure DCIS.* Presented at: San Antonio Breast Cancer Symposium; 8–12 December 2015; San Antonio

FURTHER FUNDING:
Masons Medical Research Foundation for consumables for one year

Breast cancer is a significant clinical problem, with 50,000 women diagnosed each year and a need to identify new treatment strategies in young women with oestrogen, progesterone and *HER2* receptor negative breast cancer. These 'triple negative' patients have a poor prognosis and despite improvements in treatment, 12,000 women die as a result of breast cancer each year in the UK.

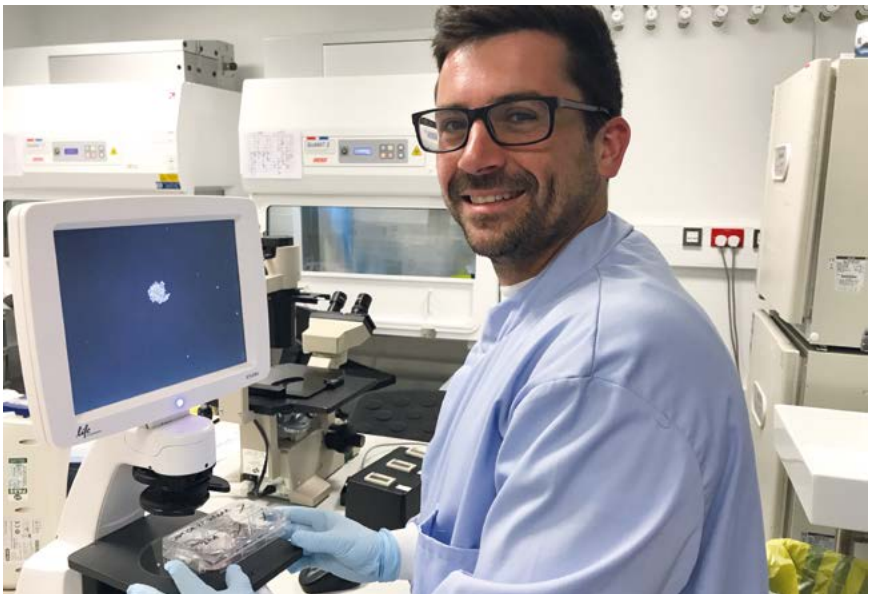
Simon in theatre during excision of a breast cancer.

Growing evidence supports the concept that breast cancers, particularly those with a poor prognosis, are sustained by a sub-population of cells termed Cancer Stem Cells (CSC) which are resistant to chemo, radio and endocrine therapy. It is important to inhibit CSC alongside current regimes in order to improve patient survival.

Focal Adhesion Kinase (FAK) is a protein that is over-expressed in breast and other cancers. We have previously shown that in the pre-invasive form of breast cancer, inhibition of FAK reduces CSC activity and increases sensitivity to radiotherapy.

My research aims to determine the role of FAK inhibitors on breast CSC activity using invasive breast cancer cell lines, human samples and mouse models. My first year of work has shown that pharmacological FAK inhibition reduces CSC activity in the difficult to treat 'triple negative' setting in multiple cell lines and patient tissue from surgical specimens.

We are taking this work forward to evaluate the role of inhibiting FAK *in vivo*, and are correlating FAK expression with CSC marker expression and patient outcome in 300 patient samples. Ultimately, this work aims to improve our understanding of the role of FAKs in invasive breast cancer, and provide evidence that will form the basis for a clinical trial. Such a trial would employ one of a number of FAK inhibitors currently available, with the aim of improving survival in the difficult to treat 'triple negative' patient group.



Simon evaluating CSC using the mammosphere assay.

Breast cancer affects 1 in 8 of women in the UK and despite improvements in patient survival, still results in 12,000 deaths per year.

1-year fellowship as National Medical Director's Clinical Fellow at RCSEng

Victoria Twigg

FELLOWSHIP/SPONSOR:
Haddock Fellowship

SUPERVISOR:
Martyn Coomer

SITE OF WORK:
The Royal College of Surgeons

PUBLICATIONS:
1. Twigg V. Training in the NHS needs to be tailored to 'Generation Y'. *BMJ Opinion*. 2017. Available at: http://blogs.bmj.com/bmj/2017/06/22/victoria-twigg-training-in-the-nhs-needs-to-be-tailored-to-generation-y/

2. Twigg V. We still need to do more to encourage the brightest and best female doctors to become surgeons. *RCS Eng Blogs*. 2016. Available at: https://www.rcseng.ac.uk/news-and-events/blog/encourage-female-doctors-to-become-surgeons/

PRESENTATIONS:
1. V Twigg. *Why do some medical schools graduate more aspiring surgeons than others? Results of a quantitative survey*. Presented at: Association of Otolaryngologists in Training meeting; 14 July 2017; Sheffield

2. V Twigg. *Does choice of medical school affect students' likelihood of becoming a surgeon?* Presented at: Association of Medical Education Europe conference; 28–30 August 2017; Helsinki

PRIZES:
1. Oral presentation prize (2017), Association of Otolaryngologists in Training

2. Stefan and Anna Galeski Fellowship

My time spent as a National Medical Director's Clinical Fellow at the RCS has been fruitful. The fellowship aims to introduce and enthuse surgical trainees about leadership within medicine, particularly at a national level. As well as learning the remit of the college, including observation of the function of council and how the college operates, I witnessed project work in action at the college and provided input to several work streams, including 'Improving Surgical Training' and the 'Extended Surgical Team' project which champions the use of extended role practitioners such as surgical care practitioners.
A large proportion of my fellowship was focused on the production of guidelines for end of life care in surgery, an area in which surgeons are often perceived to need improvement. It is hoped that these guidelines will both set a benchmark for surgeons to strive toward and also provide practical support to surgeons in achieving excellent patient care.

Victoria helping junior doctors and medical students learn basic surgical skills in Borneo, November 2016.

During my fellowship I have focused a great deal on investigating careers in surgery. The application rate for surgical posts has dropped dramatically over recent years. In order to ensure a consistent future supply of surgeons to meet the future rising demand, these reasons needed to be investigated.

Victoria speaking at a clinical fellows event hosted by Dame Clare Marx.

Findings from this work were that students perceive surgical careers as difficult and work-intense, are discouraged by the perceived poor work–life balance and are reluctant to work for surgeons that many students perceived as 'arrogant' and exhibiting 'bad attitudes'. The prime differences in universities that produce more surgeons compared to those that produce fewer surgeons were the focus on anatomy teaching (specifically through dissection), the length of time in surgical attachments and involvement in surgical procedures. The discovery of these gives both the college and educationalists a focus to target interventions in future.

In addition to this work, I have run workshops for school students to l earn more about surgical careers and applying to medical school, and have taught surgical skills to junior doctors and medical students in Malaysia and Borneo.

There have been several other outputs from this year so far, including blogs, presentations both internationally and nationally, and hopefully (subject to peer review) paper publications.

The biggest difference between medical schools which produce the most and least budding surgeons is the presence of anatomical dissection at the medical schools with more budding surgeons.

Investigation of the role of the amoeboid cell in oral cancer

Navin Vig

FELLOWSHIP/SPONSOR:
Frances and Augustus Newman Foundation Fellowship

SUPERVISOR:
Professor Ian Mackenzie

SITE OF WORK:
Blizard Institute, Queen Mary University of London

PUBLICATIONS:
1. Vig N, Mackenzie IC, Biddle A. Phenotypic plasticity and epithelial-to-mesenchymal transition in the behaviour and therapeutic response of oral squamous cell carcinoma. *J Oral Pathol Med.* 2015; **44(9)**: 649–55

PRESENTATIONS:
1. British Association of Oral and Maxillofacial Surgeons Annual Scientific Meeting; June 2017; Birmingham

2. The Academy of Medical Sciences Spring Meeting; February 2017; London

PRIZES:
1. The Paul Toller Research Prize (2016), British Association of Oral and Maxillofacial Surgeons

2. The Graduate Studies Prize (2016), Queen Mary University of London

FURTHER FUNDING:
British Association of Oral and Maxillofacial Surgeons

Faculty of Dental Surgery

Facial Surgery Research Foundation

Over the past 50 years, the chances of surviving 5 years after a diagnosis of oral cancer have only improved slowly and are currently only 3 in 5. One of the reasons for this is that cells in a tumour can escape and spread throughout the body. These cells are often better able to resist drugs too. Two types of cells are commonly described: the 'epithelial' and the 'mesenchymal'.

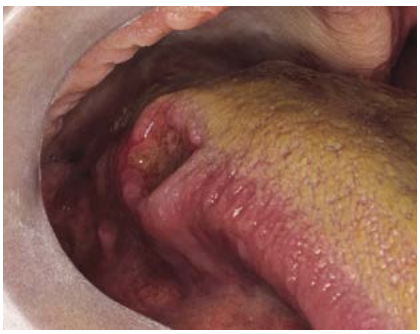
Navin operating on a head and neck procedure in Goa, India (second from left).

In our work, we have identified another type, the 'amoeboid', that might have an impact on the survival outcomes of patients with oral cancer. These cells arise from the cancer itself and form only a small number within each cancer.

Navin receiving the Paul Toller Research Prize from Mr Steve Dover, President of BAOMS.

However, the amoeboid cancer cells are much smaller, faster and spread more quickly than the other types. They are able to better resist certain drugs and have the ability to switch to the other types if required.

Using oral cancers from patients, I have been able to show that amoeboid cells can move more quickly and spread further than other oral cancer cells, survive in more adverse conditions and better resist certain drug treatments. I have also been able to identify the key genes behind the cell, giving us an idea as to how they survive and how they might be targeted. Using these genes as identifiers, or biomarkers, we appear to have identified amoeboid cells in oral tumour specimens. In addition, the top dozen amoeboid genes are associated with poorer outcomes for patients with breast, gastric and ovarian cancer. Our findings would suggest that amoeboid cancer cells play a role in the spread and treatment-resistance of not only oral cancer, but other cancers too.



An oral cancer of the tongue, presenting as a long-standing ulcer.

Further work will continue to explore the role of the amoeboid cell in oral cancer and other cancers, with the hope that some of the biomarkers might be able to predict clinical outcomes and offer ways to better eliminate cancer cells of all types, improving patient survival.

Approximately 7,000 people each year in the UK are diagnosed with oral cancer; despite big advances, only 3 in 5 will still be alive 5 years after treatment.

Investigation of phenol and amino acid metabolism dysfunction in gastro-oesophageal cancer

Tom Wiggins

FELLOWSHIP/SPONSOR:
RCS Research Fellowship with the support of the Gwendoline Shrimpton Legacy

SUPERVISOR:
Professor George Hanna

SITE OF WORK:
Department of Surgery and Cancer, Imperial College London

PUBLICATIONS:
1. Wiggins T, Kumar S, Markar SR *et al.* Tyrosine, phenylalanine, and tryptophan in gastro-oesophageal malignancy: a systematic review. Cancer Epidemiol Biomarkers Prev 2015; **24(1)**: 32–8

2. Sovova K, Wiggins T, Markar SR, Hanna GB. Quantification of phenol in urine headspace using SIFT-MS and investigation of variability with respect to urinary concentration. *Anal Methods*. 2015; **7**: 5134–41

PRESENTATIONS:
1. *Use of dried blood spot analysis to guide targeted molecular investigation of homogentisate 1,2-dioxygenase activity in esophageal cancer*. Presented at: International Society for Diseases of the Esophagus; 19–21 September 2016; Singapore

2. *Dysfunctional tyrosine metabolism in oesophago-gastric cancer and link to phenol production*. Presented at: Society of Academic and Research Surgery; 18–19 January 2017; Dublin

PRIZES:
1. Best Oral Presentation (2015), Imperial College London Division of Surgery Research Meeting

2. Best Oral Presentation (2016), North-East Thames General Surgery Regional Presentation Day

Cancer of the gullet (oesophagus) and stomach (together termed gastro-oesophageal cancer) affect over 21,000 patients per year in England and Wales. Oesophageal and gastric cancer have overall 5-year survival rates of only 15% and 19%, respectively, in the UK. Only 37.6% of patients can be treated with curative intent due to advanced disease at diagnosis.

Tom receiving training in mass spectrometry with one of the group's scientists.

The development of non-invasive biomarkers aims to identify patients at early stages of disease prior to disease spread. Previous studies have established phenol as a potential biomarker of gastro-oesophageal cancer in exhaled breath or urine. However, the biological mechanism responsible for these changes remains unknown.
This project aimed to identify how phenol production in gastro-oesophageal cancer may be linked to dysfunctional aromatic amino acid metabolism.

Analysis of dried blood spot samples from gastro-oesophageal cancer patients, using mass spectrometry, identified the specific area of aromatic amino acid breakdown that was dysregulated in these patients.
A targeted biological investigation of enzymes regulating this section of the metabolic pathway using quantitative PCR and immunohistochemistry was undertaken. Further mass spectrometry analysis established that phenol was produced from aromatic amino acids within the stomach and transported in the blood of gastro-oesophageal cancer patients. This indicated a transport mechanism for this compound from the area of production around the tumour to the lungs and kidneys for excretion, at which point it can be measured non-invasively in exhaled breath or urine.

By demonstrating the biological mechanism responsible for phenol production, this project has validated the potential use of this compound as a non-invasive marker of this disease in exhaled breath or urine. This will help to introduce the clinical use of phenol as a non-invasive marker for gastro-oesophageal cancer risk stratification. It is hoped that this will increase the proportion of patients diagnosed at early stages of disease and thereby improve survival.

A patient engagement event to introduce the breath test for detection of oesophageal and gastric cancer.

The UK has the highest incidence of oesophageal adenocarcinoma worldwide, with 62% of patients having incurable late-stage disease at the time of presentation.

Tumour metabolism in squamous cell carcinoma of the head and neck: Consequences and potential therapeutic implications of TP53 mutation

Mark David Wilkie

FELLOWSHIP/SPONSOR:
Saven Research and Development Programme

SUPERVISOR:
Professor Mark Boyd and Professor Terry Jones

SITE OF WORK:
University of Liverpool Cancer Research Centre

PUBLICATIONS:

1. Wilkie MD, Lau AS, Vlatkovic N *et al.* Metabolic signature of squamous cell carcinoma of the head and neck: consequences of *TP53* mutation and therapeutic perspectives. *Oral Oncol.* 2018; **83**: 1–10

2. Wilkie MD, Lau AS, Vlatkovic N *et al.* Tumour metabolism in squamous cell carcinoma of the head and neck: an *in vitro* study of the consequences of *TP53* mutation and therapeutic implications. *Lancet.* 2015; **305(S1)**: S101

PRESENTATIONS:

1. Otorhinological Research Society Spring Meeting; March 2017; Liverpool

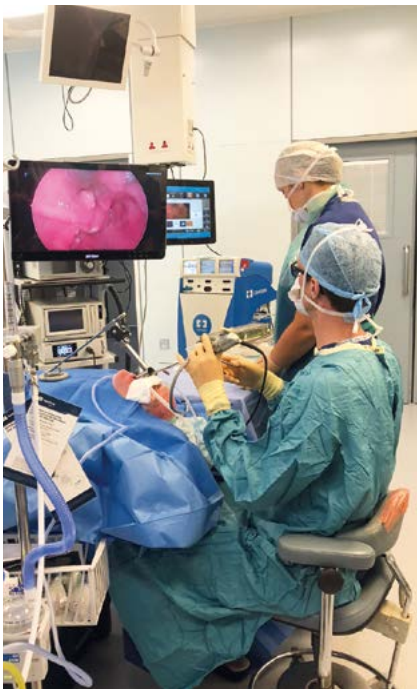
2. National Cancer Research Institute Annual Meeting; November 2015; Liverpool

PRIZES:

1. Best Oral Presentation (2015), Mersey Regional Annual Audit and Research Day

2. Best Oral Presentation Autumn Meeting, North of England Otolaryngology Society

FURTHER FUNDING:
Cancer Research UK for three years



Mark undertaking an endoscopic evaluation and biopsy of a patient with suspected head and neck cancer.

The failure to improve survival outcomes for head and neck cancer (HNC) in recent years can be attributed largely to failure of advanced disease to respond to currently available treatments. Radiotherapy remains a mainstay of treatment for HNC, with approximately 75% of patients recommended to receive radiotherapy during their treatment pathway. Consequently, a major objective is to identify means of sensitising these tumours to the effects of radiotherapy.

The ways in which cancer cells process energy sources (metabolism) typically differs from that in normal cells and is therefore a potentially attractive target for new treatments. Metabolism, however, can vary widely between different cancer types and has been a neglected area of study in HNC. Our principal aims, therefore, were to characterise the metabolic changes associated with HNC, and to determine whether these could be therapeutically targeted to enhance response to radiotherapy.

Advanced metabolic profiling experiments were performed on HNC cells grown in culture in the laboratory, and revealed that metabolism in HNC is consistently related to the tumour suppressor gene *p53*. Specifically, HNC cells carrying a mutation in the *p53* gene displayed reliance on two particular metabolic pathways (glycolysis and pentose phosphate pathway), while those without a *p53* mutation remained diverse in their use of metabolic pathways. Importantly, the metabolic changes in HNC cells harbouring a *p53* mutation were found to be targetable with anti-metabolic treatments. Drugs that inhibit glycolysis and pentose phosphate pathway enhanced the effects of radiation in mutant *p53* HNC cells only. This is of particular relevance to HNC given the frequency of *p53* mutation (implicated in approximately 60–70% of all HNCs), and the more aggressive, treatment-resistant disease typically associated with *p53* mutation. Future work will be directed toward translating these findings into the clinical setting with the aim of improving survival outcomes for HNC patients.

Mark examining a patient in the head and neck clinic.

Survival outcomes for most head and neck cancers have not improved over the past 20–30 years, still accounting for nearly 350,000 deaths annually worldwide.

The development and validation of a porcine peripheral nerve injury and regeneration model

Major Matthew Wordsworth

FELLOWSHIP/SPONSOR:
Joint RCS/Military Research Fellowship

SUPERVISORS:
Professor A Hart, Surg Capt R Rickard RN, Professor V Gorantla, Col M Davis and Col E Weitzel USAF

SITE OF WORK:
United States Army Institute of Surgical Research and the 59th Medical Wing, San Antonio, Texas, USA

PRESENTATIONS:
1. *Enhancing peripheral nerve regeneration after neurorrhaphy: a systematic review of animal models.* Presented at: American Society of Peripheral Nerves; January 2018; Arizona, USA

2. *Gait Analysis as a Functional Outcome Measure of Porcine Peripheral Nerve Injury.* Presented at: Military Health System Research Symposium (MHSRS); August 2017; Florida, USA

FURTHER FUNDING:
1. Drummond Foundation, UK

2. Congressionally Directed Medical Research Programme, USA

San Antonio Military Medical Centre.

Traumatic nerve injuries often cause long-term disability and uncertain outcomes. The surgical management has changed little in the past half century despite significant advances in our understanding of the neurobiology. Most animal work in enhancing recovery from nerve injury has occurred in the rat sciatic nerve model but failed to translate into clinical practice. This is due in part to the size and anatomical differences in rat nerves compared with human nerves. Pig models are the standard military trauma model but have been underused for the study of nerve injury and regeneration. This project is a two-year research degree to develop a model of pig nerve injury, and the second year will use the model to test a number of promising interventions to enhance nerve regeneration.

We have developed a model of pig nerve injury utilising the median and ulnar nerves of the forelimb accessible through a small incision. Functional outcomes from the injury and subsequent regeneration have been modelled using gait analysis and wearable sensors. Understanding the histology of the pig nerve and its regeneration has been developed with an international collaboration with the neuroscience department of Plymouth University. Our model has been presented at a number of conferences to both military and civilian audiences. We hope that the next phase of the research using three different locally delivered drugs will demonstrate significant benefit to nerve regeneration in this large animal model.

I have been very fortunate to be able to utilise the considerable military research infrastructure in San Antonio. I have also been working on a number of other surgical research protocols including limb transplantation, *ex vivo* limb preservation and locally delivered analgesia in nerve injury.

Pig forelimb nerves provide a useful model in the study of nerve injury and regeneration.

Paediatric surgery across sub-Saharan Africa: A multi-centre prospective cohort study

Naomi Wright

FELLOWSHIP/SPONSOR:
Freemasons' Fund for Surgical Research

SUPERVISOR:
Mr Andy Leather

SITE OF WORK:
King's Centre for Global Health and Health Partnerships in collaboration with 76 hospitals in 23 countries across sub-Saharan Africa

PRESENTATIONS:
The study was presented by Naomi and the study collaborators 30 times across the globe between July 2016 and March 2018 – below are just two

1. World Congress of Surgery; August 2017; Switzerland

2. Global Initiative for Children's Surgery (GICS) conference; January 2018; Vellore, India

PRIZES:
Professor BK Sandhu Prize for best oral presentation (2017), Commonwealth Association of Paediatric Gastroenterology and Nutrition (CAPGAN) conference in Lusaka, Zambia

FURTHER FUNDING:
Wellcome Trust for 3-year PhD

A newborn baby requiring surgery in sub-Saharan Africa.

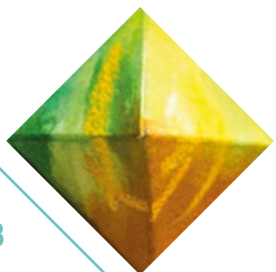
In 2015, it was reported that 5 billion people do not have access to safe, affordable, timely surgical care. In the same year, emergency and essential surgical care were incorporated into 'Universal Health Coverage' by the World Health Organization for the first time. As a result, many low and middle-income countries (LMICs) have started to produce national surgical plans with the potential to exponentially scale-up access to surgical care for their population. However, there is a dearth of research on children's surgical conditions, particularly in sub-Saharan Africa (SSA) where up to half of the population are below 15 years of age. Hence, there was a real risk that children would not be adequately represented in these plans to scale-up care.

My project involved establishing the 'PaedSurg Africa Research Collaboration', consisting of 220 children's surgeons and anaesthetists across SSA to collectively undertake the largest prospective cohort study of paediatric surgery in this region of the world. Data was collected on 1,407 children with 5 common paediatric surgical conditions. Death rates were significantly higher for all 5 conditions in SSA at 10%, compared to high-income countries where less than 1% would die. Gastroschisis, a birth defect where the intestines protrude through a hole in the abdominal wall, had the greatest disparity in outcome with above 75% mortality in SSA compared to less than 4% in the UK. Results from this study are now being used to advocate for much needed enhanced children's surgical services across SSA.

Map of collaborating centres.

Following on from this study, I have been awarded a Wellcome Trust PhD Fellowship, which will enable me to undertake an interventional study across multiple sites in SSA aimed at improving survival in babies born with gastroschisis.

I will also lead the first large-scale, geographically comprehensive study of birth defects across the world. This is vital since birth defects, which commonly require a surgical intervention, have risen to become the fifth leading cause of death in under-5-year-olds globally, yet there is very little research from LMICs where the majority of deaths occur. Such data will aid global health prioritisation and inform interventions to improve survival.



10% of children with common surgical conditions died in sub-Saharan Africa during this study; less than 1% would have died in the UK.

Characterisation of central *versus* peripheral tumour associated macrophages in Glioblastoma

Amir Saam Youshani

FELLOWSHIP/SPONSOR:
Freemasons' Fund for Surgical Research

SUPERVISORS:
Professor Brian Bigger and Mr Ian Kamaly-Asl

SITE OF WORK:
University of Manchester

PUBLICATIONS:
1. Yu KK and Youshani AS (joint first authorship), Wilkinson FL *et al.* A non-myeloablative transplant accurately defines microglia/macrophage contribution in glioma. *Neuropathol Appl Neurobiol.* 2018. [Epub ahead of print]

2. Youshani AS, Yu K, O'leary C *et al.* Characterisation of central versus peripheral tumour associated macrophages in glioblastoma multiforme. *Lancet Abstract.* 2016

PRESENTATIONS:
1. *International oral presentation.* Presented at: Society for Neuro-oncology (SNO) conference; 18 November 2017; San Francisco

2. *International poster presentation.* Presented at: Neuro-immune axis conference; 17–19 September 2017; Sitges, Spain

PRIZES:
Bursary award (2017), Society of Academic Research Surgeons (SARS)

Setting up brainlab calibration and trajectory positioning.

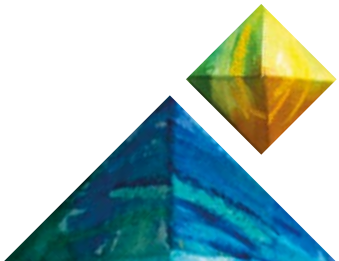
Glioblastoma (GBM) is an incurable primary brain cancer with devastating outcomes. Conventional therapies of surgery, chemotherapy (chemical substances used to eliminate cancer cells) and radiotherapy (high energy X-rays delivered to the brain) have failed to significantly improve survival in over 30 years. Furthermore, both disease and treatments reduce quality of life compared to any other cancer and place emotional burden on both patient and loved ones. In order to improve survival outcomes and treatments, it is essential to understand the cancer GBM environment and its interaction with our brain and immune cells to discover new target strategies that can kill cancer cells.

Immune cells found throughout the body are highlighted as potential therapeutic targets. Our current understanding shows that there are two main populations of immune cells that migrate to and infiltrate the tumour: bone marrow derived cells termed macrophages and resident brain cells called microglia. Approximately 30–50% of the GBM tumour consists of these two populations, collectively known as 'tumour-associated macrophages and microglia' (TAMM), but their individual functions remain contradictory due to similar appearances. Using mouse models, our aim was to accurately identify TAMMs in GBM and investigate their function at a cellular level to determine their role.

We initially developed a novel tool in mice to separate macrophages and microglia and results provided a new set of markers that can reliably track these two cell populations. Our research then focused on the function of TAMMs and using our marker sets, we have shown that macrophages originating from the bone marrow are vital for mouse survival and become manipulated by the GBM tumour, resulting in cancer progression.

In future studies, we hope to harness and exploit the 'anti-cancer' function of macrophages to target cancer cells more effectively and convert the incurable GBM into a chronic and curative disease.

Saam confirming the surgical trajectory against the neurosurgery navigation system.



Glioblastoma is the most common primary brain cancer in adults, with less than 5% survival at 5 years.

Bicuspid aortic valves and aortic aneurysms – the importance of wall shear: Stress and proteomic changes in the aortic wall

Pouya Youssefi

FELLOWSHIP/SPONSOR:
Saven Research and Development Programme

SUPERVISOR:
Professor M Jahangiri

SITE OF WORK:
St. George's Hospital, London

PUBLICATIONS:

1. Youssefi P, Gomez A, He T *et al.* Patient-specific computational fluid dynamics – assessment of aortic hemodynamics in a spectrum of aortic valve pathologies. *J Thorac Cardiovasc Surg.* 2017; **153(1)**: 8–20

2. Youssefi P, Sharma R, Figueroa CA, Jahangiri M. Functional assessment of thoracic aortic aneurysms – the future of risk prediction? *Br Med Bull.* 2016

PRESENTATIONS:

1. Youssefi P, Gomez A, He T *et al. Effect of Aortic Valve Morphology on Fluid Dynamics of the Thoracic Aorta.* Presented at: Society of Cardiothoracic Surgeons Annual Meeting; March 2016; Birmingham

2. Youssefi P, Gomez A, He T *et al. 'In Vitro' Comparison of Aortic Haemodynamics of Bicuspid and Tricuspid Aortic Valves Using Computational Fluid Dynamics.* Presented at: European Association for Cardiothoracic Surgery (EACTS); October 2016; Barcelona

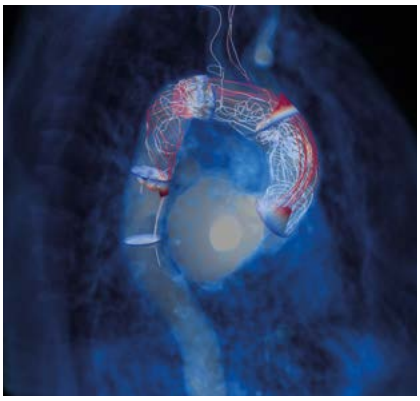
PRIZES:

1. Walton Lillehei Young Investigator Award (2015), EACTS

2. Ronald Edwards Medal for Best Scientific Presentation (2016), SCTS

The bicuspid aortic valve (BAV) is the most common congenital heart abnormality, affecting 1.2 million people in the UK, and it has been linked with aneurysms (abnormal enlargement) of the thoracic aorta.

The bicuspid aortic valve (BAV) is the most common congenital heart abnormality, affecting 1.2 million people in the UK, and it has been linked with aneurysms (abnormal enlargement) of the thoracic aorta.



Computational fluid dynamics of the thoracic aorta showing velocity streamlines and vectors.

We aimed to investigate the link between aneurysms and aortic valve disease, and find a new way of identifying patients at high risk of rupture. Patients with aortic valve disease and/or aneurysms of the aorta underwent magnetic resonance angiography of the thoracic aorta, with flow studies above the aortic valve. Patient-specific computational fluid dynamics analysis was carried out to measure wall shear stress and other haemodynamic parameters in different parts of the aorta. At the time of surgery, biopsies were taken at different parts of the aorta and correlated with haemodynamic parameters.

During the period of the Research Fellowship, we devised a novel method of performing patient-specific computational fluid dynamics analysis of the aorta, thereby calculating wall shear stress, oscillatory shear index, helicity and flow asymmetry in different parts of the thoracic aorta. Our preliminary results show that wall shear stress and helicity are increased in the aorta of patients with BAV, particularly in the greater curvature of the ascending aorta. This is the typical site of aneurysm formation in patients with BAV, thus indicating a link between shear stress and aneurysm formation. Proteomics analysis from aorta biopsies have shown changes in the ascending aorta of BAV patients, with protein changes involved in extracellular matrix degradation and remodelling, both involved in aneurysm formation.

Patients with aortic valve disease may suffer from severe breathlessness, chest pain or dizziness, making daily activities challenging. However, depending on the extent of valve disease, their symptoms may be milder or completely absent. Aneurysms of the aorta usually do not cause any symptoms until the point of dissection or rupture. Therefore, the timely diagnosis and management of this condition is vital in ensuring life-threatening complications do not occur. This research aims not only to investigate the link between aortic valve disease and aneurysms, but also to identify a new way of assessing and identifying patients at risk of aneurysm formation.

Pouya operating on a patient with a bicuspid aortic valve and aneurysm.

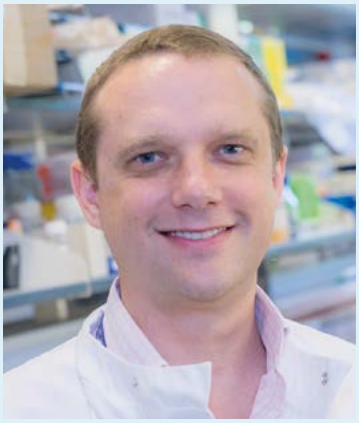
Aneurysms are life-threatening, killing over 50% of people when they rupture.

Pump Priming Reports

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

Simon Buczacki
Charles Evans
Joseph Hardwicke
Adel Helmy
Iain Whitaker
Gregory James

The role of PW1/Peg3 in intestinal homeostasis



Simon Buczacki

SPECIALTY:
Colorectal Surgery

CURRENT POSITION:
Honorary Consultant
Surgeon/Cancer Research UK
Clinician Scientist

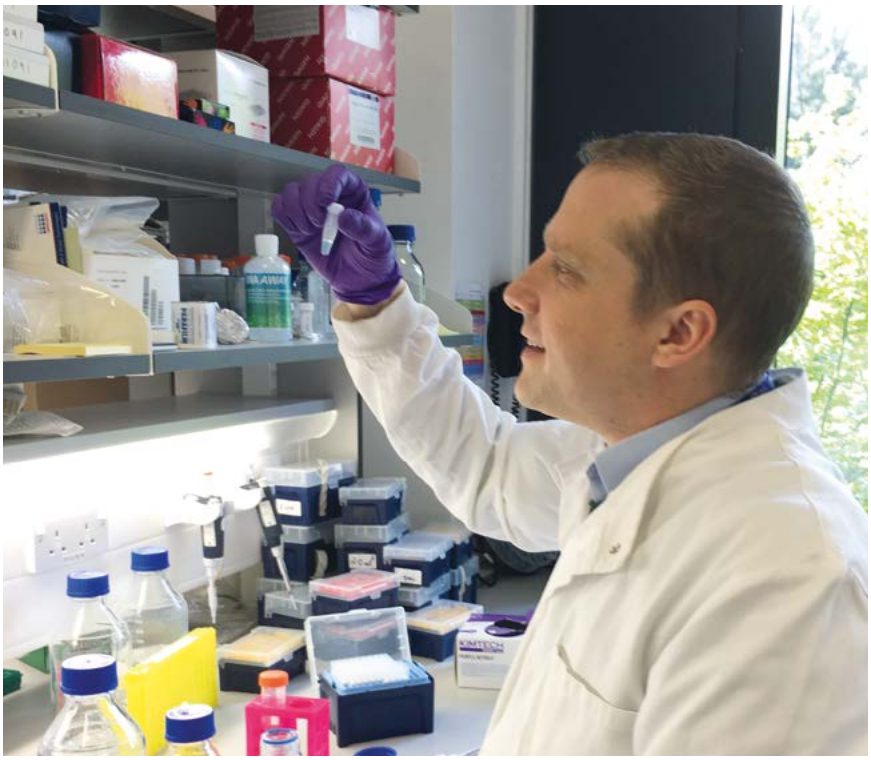
SITE OF WORK:
CRUK Cambridge Institute

PUBLICATIONS:

1. Buczacki SJ, Popova S, Biggs E *et al.* Itraconazole targets cells cycle heterogeneity in colorectal cancer. *J Exp Med.* 2018; **215**: 1,891–1,912

2. Buczacki, SJ *et al.* Mex3a Marks a Slowly Dividing Subpopulation of Lgr5+ Intestinal Stem Cells. *Cell Stem Cell.* 2017; **20**: 801–816.e7

3. Buczacki, SJ. *et al.* Intestinal label-retaining cells are secretory precursors expressing Lgr5. *Nature.* 2013; **495**: 65–69



Simon in his laboratory at the Cancer Research UK Cambridge Institute examining samples from PW1 deficient mice for intestinal tumour development.

We sought to investigate the role that the gene PW1 plays in controlling how the lining of the intestine develops and also ascertain whether the gene plays a role in bowel cancer (colorectal cancer). The lining of the bowel is generated by stem cells and it has also been shown that these are the cells from which bowel cancers develop. We have shown that PW1 marks a subset of intestinal stem cells that do not divide. We have also found that the levels of this gene are lost when bowel cancers develop suggesting it plays a role in tumour development.

Using animal models, we found that loss of PW1 causes stem cells to change the relative proportions of specialised gut cells that they generate as well as slowing down stem cell division rates. We have now been able to identify a panel of genes that similarly alter their expression when PW1 levels are altered. Many of these newly identified genes play a central role in bowel cancer.

Furthermore, the changes in the types of cells seen in the lining of the bowel in conjunction with loss of PW1 are often seen in colorectal cancers. We are now validating and expanding these findings using alternative experimental techniques.

Many genes have been shown to have altered levels and/or mutated in bowel cancer. One of the major thrusts of current research is determining which play a role in tumour development (driver genes) and which are just altered by chance (passenger genes). Here, we have developed a preliminary dataset strongly suggestive that PW1 is a driver gene in bowel cancer, a finding not previously been described. We will use these data to develop a rational hypothesis to further understand the mechanism behind how PW1 controls cell division and fate.

The gene PW1 determines how cells divide in the intestine.

Detection of colorectal cancer using a urinary protein marker test – Results of a pilot study

Charles Francis Mitchell Evans

SPECIALTY:
Colorectal Surgery

CURRENT POSITION:
Consultant Colorectal Surgeon

SITE OF WORK:
University Hospitals Coventry and Warwickshire NHS Trust (UHCW)

PUBLICATIONS:
1. Rajjoub Y, Metzger J, Evans C *et al. Novel urinary and blood peptide markers for detection of colorectal cancer – early results.* Colorectal Disease. 2018; **20**: 20

PRESENTATIONS:
1. *Novel urinary and blood peptide markers for detection of colorectal cancer – early results.* Presented at: ASGBI 2018; May 2018; Liverpool

2. Novel urinary and blood peptide markers for detection of colorectal cancer – early results. Presented at: ACPGBI 2018; July 2018; Birmingham

PRIZES:
Short Paper of Distinction Prize – ASGBI 2018

FURTHER FUNDING:
UHCW charitable trust to undertaken the additional histological work for four months

Charles in theatre operating robotically on a patient with colorectal cancer recruited to the study.

Colorectal cancer (CRC) is the second most common cause of cancer death in the UK. Outcomes are dramatically improved if the cancer is detected in its early stages. Current screening methods require testing faecal samples that are often not well accepted by patients. The study of proteins within a patient's urine has been used to assess for markers of other cancers but not CRC. This study aimed to examine the feasibility of a urinary protein-based test in the detection of CRC, using specialised hybrid techniques: capillary electrophoresis coupled with mass spectrometry (CE-MS).

CE-MS was used to obtain urinary protein-based patterns from 12 patients with CRC and 12 controls. A protein-based panel was used to establish a model for predicting the presence of CRC, which was trialled on the urine samples as a diagnostic test.

Protein-based sequencing identified proteins with a potential role in CRC disease development. Specialised staining methods were employed to determine the presence and intensity of one of these proteins, Meprin-alpha (MEP1A), at the colonic tumour site.

A statistical classification model derived from 26 surrogate CRC protein-based markers, differentiated the 12 CRC cases from 12 non-CRC cases with 100% sensitivity and 92% specificity. Nine key proteins within the raw urine data were identified. MEP1A staining was found in higher concentrations at the tumour (75%) compared with control (38%) and was located at the advancing margin of the tumour.

This early phase study has demonstrated the utility of a urinary protein-based test that correctly identifies CRC from patients without disease and could form the basis of a diagnostic test. Nine key proteins were identified with a potential role in CRC development. Further research is needed to investigate the role of MEP1A in cancer progression and whether it is an indicator of more aggressive tumours.

Charles with Professor R Arasaradnam and endoscopy team diagnosing patients before recruitment to the study.

A proof of principle model using the detection of key urine proteins can be used to identify patients with colorectal cancer with 100% sensitivity.

Olfactory Biosensors for Offensive Wound Evaluation (OBOWE study)

Joseph Thomas Hardwicke

SPONSOR:
Gwendoline Shrimpton Legacy

SPECIALTY:
Plastic and reconstructive surgery

CURRENT POSITION:
Consultant

SITE OF WORK:
University Hospitals of Coventry and Warwickshire/University of Warwick

Infected wounds can lead to devastating outcomes for patients. At present, diagnosing an infected wound requires laboratory analysis that can take up to 72h. By using an electronic nose sensor (eNose) that can detect compounds emitted by certain bacteria that are associated with either infected or necrotic wounds, an immediate insight can be obtained about the status of the wound. This preliminary study has collected and analysed wound dressings from infected wounds and non-infected wounds.

Joseph at the Plastic Surgery Dressing Clinic, UHCW NHS Trust.

The OBOWE project was designed to investigate gas phase biomarkers that emanate from an infected wound. Its main aim is to investigate if an infected wound generates odours than can be detected using the latest in gas analysis technology.

Twenty-four wound dressings were collected from patients attending the University Hospitals of Coventry and Warwickshire Plastic Surgery Dressing Clinic (Figures 1 and 2) with infected wounds, and healthy control wounds. Samples were analysed using a gas chromatography pre-separator and a drift-tube ion mobility spectrometer detector (Figure 3). Using this equipment, more than 20 new molecules were observed for an infected sample over a healthy control – from a large range of molecular weights.

Thus, are sensitivity and specificity were 100%. We believe that using this approach we are easily able to identify samples with infection and that in the future, it maybe be possible to identify specific conditions and strains of infective micro-organisms.

Sister Sunita Mahay and her team in the Plastic Surgery Dressing Clinic, UHCW NHS Trust.

This is the first study to analyse wound dressings in this way and it has helped to analyse the molecules of interest associated with wound infections. This has not only added to the current knowledge in this area, but also may help the earlier diagnosis of wound infection and could lead to improved patient outcomes in the future by stimulating earlier intervention, such as change of dressings, wound cleansing, surgical removal of dead tissues, and appropriate antibiotic therapy.

Collaborator, Prof James Covington at the University of Warwick School of Engineering.

An electronic nose accurately identified 100% of wounds that are showing signs of infection.

Neuroinflammation in traumatic brain injury

Adel Ezzat Helmy

SPONSOR:
Vandervell Research Fund

SPECIALTY:
Neurosurgery

CURRENT POSITION:
University Lecturer/
Honorary Consultant

SITE OF WORK:
Division of Neurosurgery, Department of Clinical Neurosciences, University of Cambridge

PUBLICATIONS:
1. Tsyben A, Guilfoyle M, Timofeev I *et al.* Spectrum of outcomes following traumatic brain injury-relationship between functional impairment and health-related quality of life. *Acta Neurochir.* 2018; **160**: 107–115

2. Thelin EP, Hall CE, Gupta K *et al.* Elucidating Pro-Inflammatory Cytokine Responses after Traumatic Brain Injury in a Human Stem Cell Model. *J Neurotrauma.* 2018; **35**: 341–352

PRESENTATIONS:
1. Elucidating Pro-Inflammatory Cytokine Responses after Traumatic Brain Injury in a Human Stem Cell Model. Presented at the International Neurotrauma Symposium, Toronto, August 2018.

2. Spectrum of outcomes following traumatic brain injury-relationship between functional impairment and health-related quality of life - presented at the International Neurotrauma Symposium, Toronto, August 2018.

PRIZES:
International Neurotrauma Symposium, Best Poster, August 2018

FURTHER FUNDING:
Addenbrooke's Charitable Trust, one year and Academy of Medical Sciences, two years, post-doctoral position

Traumatic brain injury (TBI) is a complex disease that causes both physical and neuropsychological problems. In 2012 in the European Union (EU) alone it is estimated that there were 1.5 million hospital admissions and 82,000 deaths. This doesn't account for the huge burden of morbidity in the cognitive, physical and psychological domains that has important social and economic impacts. It is estimated that in 2010, TBI cost the EU economy €33 billion. As TBI often affects young people, in 2013, 1.3 million life years were lost as a result of TBI in the EU alone. The first step in understanding how to reduce the injury to the brain and improve patient outcomes comes from finding the inflammatory mediators that cause the injury at a molecular level.

Our research work has focussed on measuring the inflammatory molecules, called cytokines and chemokines, in patients after TBI using a technique called microdialysis. The next phase of our research has focussed on two approaches. At one end of the spectrum we have used cell culture models to explore how these cytokines and chemokines affect individual cell types, such as neurones and astrocytes. Secondly, we are using anti-inflammatory cytokines given as drugs to dampen down inflammation in patients with TBI to see how this affects patient's outcomes.

This inflammation research is combined with ways of exploring how accurately we can measure a patient's outcome, and in particular the impact on TBI patient's quality of life. The existing measures for outcome are sometimes crude, and do not reflect the complexity of patient's recovery after a devastating injury.

We are about to start a further study of an anti-inflammatory drug, IL1ra, using what we have learned about inflammation and patient outcomes.

Adel teaching neuroanatomy (the anatomy of the nervous system).

Head Injury (Traumatic Brain Injury) is the commonest cause of death in those aged under 40 years in the developed world.

3D printing cartilage for facial reconstruction: Optimising the printability and biofunctionality of nanocellulose for extrusion based 3D bioprinting

Iain S Whitaker

SPONSOR:
Carol Rumney Legacy

SPECIALTY:
Plastic and Reconstructive Surgery

CURRENT POSITION:
Professor of Plastic and Reconstructive Surgery

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

PUBLICATIONS:

1. Jessop ZM, Al-Sabah A, Gao N *et al.* Printability of Pulp Derived Crystal, Fibril and Blend Nanocellulose-Alginate Bioinks for Extrusion 3D Bioprinting. *Biofabrication.* 2018

2. Jessop ZM, Manivannan S, Al-Sabah A *et al.* Tissue specific stem/progenitor cells for cartilage tissue engineering – A systematic review of the literature. *Applied Physics Reviews.* 2018

PRESENTATIONS:

1. *Combining Tissue Specific Stem Cells with a Natural Biomaterial to 3D Print Cartilage for Facial Reconstruction. 3D Bioprinting: Physical and Chemical Processes.* 2–3 May 2017; Winston Salem, NC, USA

2. *The potential of Tissue Engineering and 3D Bioprinting to Revolutionise Plastic Surgery. Followed by: Combining Tissue Specific Stem Cells with a Natural Biomaterial to 3D Print Cartilage for Facial Reconstruction.* Presented at: National Plastic Surgery Research Forum; 30 June 2018; London

PRIZES:

1. The Worshipful Company of Cutlers' Surgical Fellowship in Ear Reconstruction To visit Clinic Bizet, Paris (2018) and the Clarke Medal (2017)

2. Golden Scalpel Award (2017), Plastic Surgery Trainees Association (PLASTA)

FURTHER FUNDING:
Welsh Government (via the Welsh Clinical Academic Training pathway)

Oak Grove Foundation

Health and Care Research Wales/ ABMU Health Board Pathway to portfolio funds

Worshipful Company of Cutlers

British Association of Plastic, Reconstructive and Aesthetic Surgeons (BAPRAS)

The Scar Free Foundation for two years

Iain with a patient in a Microtia (little ear) clinic with Steve Key (Maxillofacial Surgeon) and Peter Evans (Senior Maxillofacial Prosthetist).

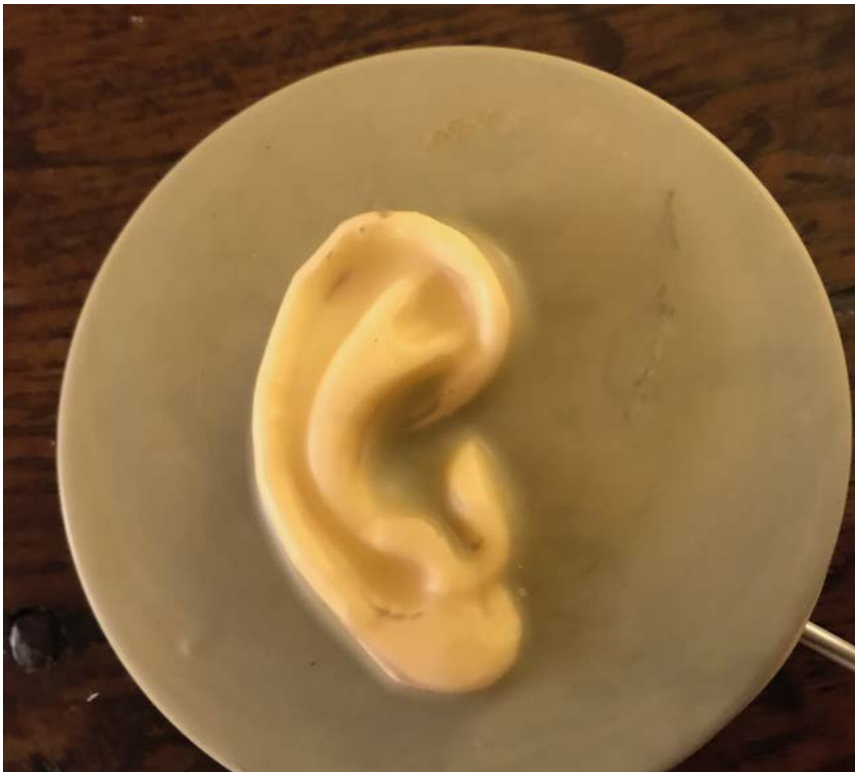
Over 500,000 people in the UK have significant facial disfigurement. The use of patients' own tissue or synthetic implants results in scarring and occasional infection, tissue death or implant rejection. Previous attempts to use synthetic scaffolds and non-specific stem cells to engineer tissue have failed. New approaches in tissue engineering combined with 3D bioprinting mean there is potential to remove the need for donor tissue for reconstruction.

My research is multidisciplinary, involving surgery, cell biology, rheology, engineering, computational modelling, imaging, biomaterial science and industry. This fits well with the UK government highlighting regenerative medicine as one of the 'eight great technologies' worthy of significant investment and one of the key areas which could provide a global competitive advantage for the UK. The MRC itself states tissue engineering 'holds the promise of revolutionising patient care in the twenty-first century'.

Dr Francois Firmin performing total auricular reconstruction with Iain in Paris, January 2018.

Learning from the failures of other approaches, my group is developing a novel strategy to combine tissue-specific stem cells from naso-septal cartilage with a natural biomaterial (patent pending) and to tailor this for 3D printing purposes. We have shown that stem cells protect the mature cells from converting into different cells types while enhancing cartilage growth. Via an exclusive collaboration with a US based company, we have characterised a novel biomaterial and modified it to enhance its ability to support cartilage growth, strengthen it enough to allow implantation in the human body and allow it to be 'printed'. The next stages of this work are animal studies and first-in-man trials.

This research has led to prestigious awards during this funding period, and the group have not only looked into ways to treat facial disfigurement using tissue engineering and 3D bioprinting, but also how to quantify the psychological and physical effects on patients using research modalities such as Patient Reported Outcome Measures (PROMs) and the use of big data.



An ear construct carved by Iain using the 'Firmin Trainer' at an ear reconstruction workshop run by Dr Francoise Firmin in Paris.

1 in 111 (542,000) people in the UK have a significant disfigurement to the face.

Endoscopic lavage for intraventricular haemorrhage in neonates (the ENLIVEN study)

Gregory Adam James

SPONSOR:
RCSE Fellows' Fellowship Fund

SPECIALTY:
Neurosurgery

CURRENT POSITION:
Consultant and Honorary Senior Lecturer

SITE OF WORK:
Great Ormond Street Hospital

Greg with a post-operative neurosurgical patient.

As perinatal care advances, more babies are surviving premature birth. A devastating problem faced by these infants is 'intraventricular haemorrhage' – bleeding in the brain. This often causes hydrocephalus – a high-pressure build-up of fluid in the brain.

The traditional technique of managing this condition is to insert a drainage tube into the ventricle allowing drainage of the fluid and relieve the pressure. However, the majority of children still require a permanent 'shunt' which requires lifelong follow-up, and many will be left with cerebral palsy or other long-term neurological problems.

Greg James, in partnership with colleagues at Great Ormond Street Hospital and UCL Institute of Child Health, is leading a research study called ENLIVEN. The study is examining whether washing out the bloody fluid from the brain with a tiny telescope (endoscopic lavage), before inserting the drainage tube, improves outcomes for these babies. Blood breakdown products create a cytokine-rich inflammatory 'soup' in the brain fluid, which should be crystal clear. Washing this 'soup' away with endoscopic lavage may protect the brain tissue from inflammation and secondary injury, reducing the need for a permanent shunt and improving brain development.

ENLIVEN is a randomised controlled trial comparing traditional treatment to endoscopic lavage in premature infants. The study aims to recruit a minimum of 50 babies over a 5-year study period, and will follow them up clinically, with special MRI scans and detailed developmental assessments.

The Royal College of Surgeons grant is supporting data collection and storage, and 'roadshows' to engage and educate referring neonatal units – as timely referrals are critical both to patient outcome and for appropriate study recruitment. The ENLIVEN trial has the potential to improve outcomes of a major health problem which does not just affect patients in infancy but goes on to cause life-long disabilities.

An estimated 15 million babies are born preterm worldwide each year, and this number is rising.

Surgical Trials Initiative

Prof Joy Adamson, Mary Kinross Trust & RCS Chair in Surgical Trials and Health Sciences, York with Prof Dion Morton.

The Surgical Trials Initiative was launched in January 2013 and has exceeded all expectations in the last six years. The programme, with six Surgical Trials Centres (STCs) and fourteen Surgical Specialty Leads (SSLs), has been working on developing and delivering high-quality randomised trials across all specialties. The Initiative has grown exponentially under the Directorship of Professor Dion Morton, who completes his term in office in Summer 2019, after 6 extremely productive and successful years. All involved are most fateful to him for his energy, vision and extraordinary accomplishments in post.

Professor Peter Hutchinson has recently been selected from a highly competitive field to succeed Prof Morton as the new Clinical Director of Research. Prof Hutchinson has been serving as the Neurosurgery Surgical Specialty Lead for the past six years and has provided an update on his activities as SSL on page 95 of this report.

The creation of new senior academic posts of RCS Professors at Surgical Trials Centres, will allow for growth in capacity at STCs and build on their successes in delivering complex trials for patient benefit. The first RCS Professor in surgical research was appointed at the University of Leeds in April 2018 with a further five posts appointed to thereafter. The full list of RCS Professors is as follows:

Professor David Jayne – Bowel Cancer UK / RCS Colorectal Research Chair at University of Leeds

Professor Joy Adamson – Mary Kinross and RCS Chair in Surgical Trials and Health Sciences at University of York (Hull York Medical School)

Professor Amar Rangan – Mary Kinross and RCS Chair in Surgical Trials and Health Sciences at University of York (Hull York Medical School)

Professor Thomas Pinkney – George Drexler and RCS Chair in Surgical Trials at University of Birmingham

Professor Michael Douek - Rosetrees and RCS Director of Surgical Interventions Trials Unit

Professor David Beard – Rosetrees and RCS Director of Surgical Interventions Trials Unit.

The following RCS Professorial Chairs will be appointed to in 2019, bringing the total number of RCS Chairs to eight across six RCS Surgical Trials Centres:

- University of Manchester, in partnership with Masonic Charitable Foundation
- University of Bristol, in partnership with Enid Linder Foundation

The programme of STCs, SSLs and specialty-specific / regional research collaboratives continues to provide support for feasibility, pilot and safety studies, which often lead to randomised clinical trials. The support provided by organisations such as the Rosetrees Trust and other trusts, charities and surgical societies, has allowed for this network of researchers to grow exponentially over the last six years.

The joint trials portfolio of the six Surgical Trials Centres has a total of 128 clinical trials, of these 49 are open and recruiting patients, 61 are in follow-up and a further 18 trials have completed follow-up. The STCs also have 40 trials which are currently in 'set-up' and are being developed. A total of over 50,000 patients have been recruited to this joint portfolio for trials in the ten different specialties. On average patients are being recruited from 16 hospitals, with an average of 15 investigators (surgeons, trainees) working on each study.

The Initiative continues to support research and researchers overseas, with further visits to Australasia to support the set-up of the Royal Australasian College of Surgeons (RACS) own surgical trials initiative. RACS and RCS work closely to recruit to the same trials and will continue to work to secure joint-funding to support the development and delivery of new studies.

RCS Surgical Trials Initiative supports three different projects in Low and Middle Income Countries led by teams at the Universities of Birmingham, Leeds and Cambridge. A joint meeting in January 2019, hosted by the College, brought together all the NIHR supported Global Surgery projects to ensure their goals are aligned and best practice is shared. 2019 will also see the start of three global surgery systematic reviews, supported by the Clinical Effectiveness Unit, with teams in Benin, Guatemala and Nigeria/Ghana being supported to carry out their own reviews in cancer and access to surgery in low income settings. The Initiative continues to work in a collaborative fashion, bringing together expertise across specialties and borders, for patient benefit.

RCS Chairs of Surgical Research

Professor David Jayne – Bowel Cancer UK/Royal College of Surgeons of England Colorectal Research Chair.

Prof David Jayne (centre) delivering his inaugural lecture in Leeds with (from L to R) Prof Derek Alderson, Prof Paul Stewart, Deborah Alsina MBE and Prof Dion Morton.

It was a great honour to be awarded the first RCS Chair in Surgical Research in 2018. Funding for the four-year position was made available through the generosity of Bowel Cancer UK (www.bowelcanceruk.org.uk), the largest bowel cancer charity in the UK. In April 2018, I delivered an inaugural lecture to celebrate my appointment - a daunting experience in front of the celebrated guests and the local media.

The purpose of the Chair is to develop and promote bowel cancer research and clinical trials in the UK, which aligns perfectly with my research interests. As Clinical Director of the Leeds RCS Surgical Trials Centre, I am heavily committed to surgical trials research, identifying new CI's and PI's and developing new clinical trials that address some of the most important questions in bowel cancer, with the ultimate aim of improving clinical and patient outcomes. I am also involved in applied basic science with a focus on novel surgical technologies and techniques, again focused on areas of unmet need in colorectal disease. This is supported by NIHR funding for the Surgical Technologies MedTech Co-operative (www.surgicalmic.nihr.ac.uk), a national network of clinicians, academics, patients and public, and industry partners that aims to facilitate the pull-through of new technologies into clinical practice.

Over the past 12-months, I have been working closely with Bowel Cancer UK to help deliver their four key research priority areas: i) prevention, early detection and treatment of bowel cancer, ii) enabling patients to influence the future of bowel cancer research, iii) building bowel cancer research capacity and future leaders, and iv) facilitate collaboration across the bowel cancer research community.

Through the RCS Surgical Trials Centres initiative I have been working closely with colleagues to develop surgical trials investigating new strategies to avoid postoperative complications, enable better patient risk stratification for colorectal surgery, improve surgical outcomes through intraoperative fluorescence-guidance, and explore the use of novel radiosensitisers to downstage rectal cancer. Public and patient involvement has been integral to this process and has been greatly facilitated through Colorectal Research Chair. This is exemplified by the hugely successful PPI workshop jointly hosted by Bowel Cancer UK and the NIHR Surgical MedTech Co-operative in November 2018.

Another exciting new initiative that I have been involved in was the joint Bowel Cancer UK/RCS Edinburgh event in September 2018. The aim was to promote a second Bowel Colorectal Research Chair, hosted by the Edinburgh College. If successful, this will lead to wider UK collaboration, with greater engagement from surgeons of both colleges that will significantly increase surgical trials activity.

In the future, I look forward to building on the common research ambitions shared by The Royal College of Surgeons and Bowel Cancer UK. Bowel Cancer UK are continuing to invest in bowel cancer research, with a portfolio that includes a better understanding of the genetics of bowel cancer in the under 50s, the role of the microbiome in bowel cancer, improved strategies for bowel cancer screening, and a better understanding of people at high risk of bowel cancer. This includes three Bowel Cancer UK/ RCS Research Fellows. I hope to make a major contribution to this exciting platform of research. By working together, and harnessing the collective strengths of RCS and Bowel Cancer UK, I am optimistic that we can make a real difference and improve bowel cancer outcomes in the near future.

Newly appointed Rosetrees/RCS Directors of Surgical Interventions Trials Unit Prof David Beard (middle) and Prof Michael Douek (second from right), meeting with Rosetrees Trust Chief Executive Ann Berger (left), Chairman Richard Ross (second from left) and Head of Research Vineeth Rajkumar (right).

The views of a RCS Surgical Trials Centre, Birmingham Surgical Trials Consortium (BiSTC)

Professor Thomas Pinkney, Clinical Director, BiSTC.

Dr Laura Magill, Operational Director, BiSTC.

With the first phase of the project coming to a close, it is an opportune moment to reflect on the phenomenal success of the RCS Surgical Trials Initiative. Research activity and productivity across the country has advanced significantly both in terms of the number and the quality of surgical trials funded and delivered. The active engagement of surgeons, trainees and allied professionals nationally has generated a culture-shift in clinical surgical research.

For us in Birmingham, a key accomplishment of BiSTC has been the bringing-together of previously disparate researchers and trials units. This has happened both locally, with the three pre-existing trials units in Birmingham coming together under the BiSTC umbrella, and nationally via collaborating with other RCS Surgical Trials Centres (STCs) on specific projects such as Bluebelle (with RCS Bristol STC) and SUNRRISE (with RCS North-West STC). These collaborations improve reach and responsiveness, enhance access to expertise and improve workflow and efficiency.

The core funding from RCS has provided 'pump-priming' capacity to enable us to work with new clinician researchers and take their ideas from concept stage through methodology, systematic review and to subsequent funding application. We have established a 'drop-in' service for clinicians at all stages to discuss their ideas. When taken together with our established investigators, these activities have borne a total in excess of £20M in funding for new surgical trials since BiSTC was established when the Surgical Trials Initiative launched in 2013.

Trainee-centric research has been a major component of our activities in Birmingham for several years. We have been pleased to support and deliver multiple large phase 3 trainee-centric trials through BiSTC, including DREAMS (published in BMJ, 2017) and ROCSS (currently in write-up). More recently, SUNRRISE has been funded by RfPB and ROSSINI-2 – the first surgical MAMS trial – has been funded by HTA which will recruit more than 6,600 patients with the help of trainees nationally.

We have strengthened our links with the NIHR CRN both nationally and regionally to enhance delivery of trials and development of surgical researchers at all levels. This has included i) the creation of joint posts between BiSTC and the CRN to provide infrastructure and personnel to support trainee collaboratives – taking lessons learnt in surgery into multiple other medical specialties and ii) appointment of a peripatetic senior research nurse charged with facilitating engagement of trainees in trials.

The Associate PI scheme has been a more recent development, created in conjunction with the RCS and the NIHR. This aims to engage, recognise and promote junior doctors and allied health professionals involved in clinical trials and to help them develop into the PIs of the future via a standardised and nationally accredited program.

All of these activities and advances leave us confident and optimistic for the future of clinical surgical research in the UK.

"For us in Birmingham, a key accomplishment of BiSTC has been the bringing-together of previously disparate researchers and trials units."

The views of a Surgical Specialty Lead

Professor Peter Hutchinson, Neurosurgery SSL.

Neurosurgical clinical research continues to grow, particularly in relation to multicentre clinical trials and the activity of the British Neurosurgical Trainee Research Collaborative (BNTRC). We hosted a neurosurgical research day at the RCS in 2017, with another scheduled for 2019. Next year we will be publishing a manuscript on the current status of academic neurosurgery in the UK.

The current neurosurgical clinical trial portfolio covers many subspecialties including neurotrauma, neurovascular, neuro-oncology, CSF disorders, functional neurosurgery and spine. Neurosurgery is a relatively small specialty with units working together to apply for, set up, recruit, and publish randomised clinical trials (RCTs) in high impact journals, which are changing neurosurgical practice worldwide. The UK is currently second internationally in terms of the delivery of RCTs. We have developed the Society of British Neurological Surgeons' (SBNS) website to include an interactive map of activity and a directory of academic neurosurgeons. We have worked with the NIHR in terms of a specific intraoperative imaging call and are leading, with the European Association of Neurosurgical societies, a registry of EU clinical trials.

The British neurosurgical trainee research collaborative continues to flourish. Its activities have been highlighted in a recent publication in Acta Neurochir. Original papers have been published on chronic subdural haematoma in the Journal of Neurosurgery and external ventricular drains in the Journal of Neurology, Neurosurgery, and Psychiatry. We have assisted in establishing the Canadian collaborative and have a meeting with the Dutch collaborative in October 2018. We are also promoting mentoring of clinical lecturers via the Academy of Medical Sciences scheme.

Professor Hutchinson in theatre.

In addition to UK activity we have established the NIHR Research Group on Global Neurotrauma (http://neurotrauma.world), which covers a number of themes including establishing a global neurotrauma registry, a systems engineering approach to mapping activity and improving the management and outcome of patients with brain injury in Myanmar, developing and evaluating new technology to improve the investigation and treatment of patients across lower and middle income countries, and expanding research capacity.

Professor Hutchinson presenting on Neurosurgical research.

I would like to thank colleagues on the Research Board at the Royal College of Surgeons and on the Academic Committee of the Society of British Neurological Surgeons, in particular; associate SSLs Angelos Kolias, Ciaran Hill and Aswin Chari; the SBNS research manager, Carole Turner; Martyn Coomer, Murat Akkulak, Professor Dion Morton and Professor Derek Alderson.

Global Surgery

NIHR Unit on Global Surgery: building a platform for high quality global research in surgery

Aneel Bhangu

Prof Ismail Lawani from Benin speaking with Dr Laura Magill, RCS Birmingham Surgical Trials Consortium, in Kigali, Rwanda.

The NIHR Global Health Research Unit on Global Surgery was established in June 2017 through core funding from the National Institute of Health Research (NIHR) Overseas Development Aid funds (from the Department of Health and Social Care) to undertake clinical research to improve care for surgical patients worldwide. The Unit is led by University of Birmingham in partnership with the Universities of Edinburgh and Warwick, along with partners from a number of Low and Middle Income countries (LMICs) across sub-Saharan Africa, Asia including the Indian sub-continent, and Central America.

It is co-directed by Professor Dion Morton, the Barling Professor of Surgery at Birmingham University, and Professor Peter Brocklehurst, Director of Birmingham Clinical Trials Unit.

The Unit has adopted a unique model of research 'Hubs' connected to 'Spokes' to widen the reach of its research impact. In the first phase hubs are being set up in Mexico, Ghana, South Africa, Rwanda and Pakistan. In the next phase at least three more hubs will be set up.

We hold annual LMIC partner-led prioritisation exercises to identify research that is relevant to them, taking into account emerging research priorities and key evidence based initiatives raised by the WHO, and the Lancet commission on Global Surgery. The first prioritised areas are surgical site infection, cancer surgery, and access to care. The second round of prioritisation identified care of the injured patients and reducing morbidity after surgery as the topics for development. The Unit is delivering four multiple randomised trials in parallel and has pump-primed funding of nine further studies.

Want to read more? Visit www.nihrglobalsurgery.org or @NIHR_GSU.

Bill Thomas delivering the RCS Basic Surgical Skills workshop as part of the NIHR Global Surgery Unit prioritisation meeting in Kigali, Rwanda.

From L to R Lord Ribeiro, Mr David Nott, Mr Bob Lane and Prof Chris Lavy at Policy Implementation Committee on Global Surg.

Prof Dion Morton, Co-Director of the NIHR Unit and Director of Clinical Research at the RCS, speaking with delegates in Kigali, Rwanda.

Surgeons and researchers from 25 Low and Middle Income Countries across the globe, gathered for the NIHR Global Surgery Unit's annual prioritisation meeting in Kigali, Rwanda.

Clinical Effectiveness Unit

Professor David Cromwell,
Director of the Clinical Effectiveness Unit

Professor David Cromwell.

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

Visit by delegation of medical staff from Hong Kong University and major China hospitals to the Royal College of Surgeons to hear about how it supports women in surgery and surgical research.

Audit and research

The core activity of the CEU is to conduct national clinical audits and research projects. Many of the national audits are part of the Government's National Clinical Audit and Patient Outcomes Programme (NCAPOP), which is playing an increasingly important role in the Government's strategy to improve the outcome of secondary care.

One of the national audits undertaken by the CEU examines the quality of care received by patients with bowel cancer when treated within NHS hospitals. Ms Abigail Vallance took time out from her surgical training to join the audit team and was recently awarded her MD based on the work she did while part of the team. A question examined by Abigail was whether the decision to publish surgeon-specific information on survival after colorectal cancer surgery had an adverse impact on clinical practice. The Bowel Cancer Audit was one of nine surgical specialties that began to publish surgeon-level outcomes in 2013, and the policy had proved controversial, with advocates suggesting it allowed patients to make informed choices, while critics argued that it created the perverse incentive not to operate on the sickest patients.

In her research, Abigail examined how outcomes after surgery had changed between April 2011 and March 2015. She found that the proportion of patients with bowel cancer having surgery did not change after the introduction of surgeon-level reporting, and there was no evidence of surgeons adopting a more risk-averse approach to offering surgery to patients. Among patients that had elective surgery, the introduction of surgeon outcomes coincided with a significant increase in short-term survival after surgery. There was no equivalent improvement in outcomes among patients having emergency surgery for bowel cancer. This suggested that surgical teams had introduced various improvements in the preoperative preparation and planning of perioperative and postoperative care. The results of this work were published by the *BMJ*.

A brief description of other major CEU projects undertaken in 2018 is given at the bottom of this page.

Developing leadership on an expedition to the Amazon

The development and consolidation of leadership skills is considered to be an important part of surgical training. This year, Ms Yasmin Jauhari took a few weeks off from her role as the Clinical Research Fellow on the National Audit of Breast Cancer in Older Patients (NABCOP) to act as the medical officer on the Scientific Exploration Society (SES) expedition to the Amazonas region in Colombia. Yasmin was part of a multi-national expedition team that aimed to conduct environmental studies, and provide community aid to the remote Ticuna community. Part of the aid was the delivery of an ambulance boat.

The medical officers set up and provided some basic community clinics. They also attended to several medical emergencies while there. Yasmin found a visit to the village of San Juan an eye-opening experience in which the health consequences arising from a lack of clean water were starkly evident, with a high prevalence of skin conditions and tropical infections. The returning expedition has since raised funds towards the improvement of the water supply infrastructure in the village.

Ms Yasmin Jauhari.

Teaching

Each year, the CEU runs a course for surgeons and other healthcare professionals on clinical research methods and medical statistics. The course uses a mixture of teaching methods including lectures and interactive seminars to educate participants about how to practise evidence-based surgery. The course is run for the surgical fellows that have been awarded an RCS Research Fellowship and is delivered by CEU methodologists and clinicians.

Major CEU projects in 2018

National Audit of Breast Cancer in Older Patients (www.nabcop.org.uk)

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

National Bowel Cancer Audit (www.nboca.org.uk)

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

CRANE Database (www.crane-database.org.uk)

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

National Oesophago-gastric Cancer Audit (www.nogca.org.uk)

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

National Prostate Cancer Audit (www.npca.org.uk)

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

National Vascular Registry (www.vsqip.org.uk)

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

Selected publications by CEU staff in 2017 and 2018

Vallance AE, Fearnhead NS, Kuryba A *et al.* Effect of public reporting of surgeons' outcomes on patient selection, "gaming," and mortality in colorectal cancer surgery in England: population based cohort study. *BMJ.* 2018; **361**: k1581.

Nossiter J, Sujenthiran A, Charman SC *et al.* Robot-assisted radical prostatectomy vs laparoscopic and open retropubic radical prostatectomy: functional outcomes 18 months after diagnosis from a national cohort study in England. *Br J Cancer.* 2018; **118**: 489–494.

Heikkila K, Mitchell DC, Loftus IM *et al.* Improving 1-Year Outcomes of Infrainguinal Limb Revascularization: Population-Based Cohort Study of 104,000 Patients in England. *Circulation*. 2018; **137:** 1,921–1,933.

Varagunam M, Hardwick R, Riley S *et al.* Changes in volume, clinical practice and outcome after reorganisation of oesophago-gastric cancer care in England: A longitudinal observational study. *Eur J Surg Oncol.* 2018; **44**: 524–531.

Eugene N, Oliver CM, Bassett MG *et al.* Development and internal validation of a novel risk adjustment model for adult patients undergoing emergency laparotomy surgery: the National Emergency Laparotomy Audit risk model. *Br J Anaesth.* 2018; **121**: 739–748.

Fitzsimons KJ, Copley LP, Setakis E *et al.* Early academic achievement in children with isolated clefts: a population-based study in England. *Arch Dis Child.* 2018; **103**: 356–362.

Jemma Boyle talking to a delegation from Li Ka Shing Faculty of Medicine (Hong Kong University) about women in surgery before they attended the 2018 Women Leaders in Global Health Conference.

Each year, the CEU runs a course for surgeons and other healthcare professionals on clinical research methods and medical statistics. The course uses a mixture of teaching methods including lectures and interactive seminars to educate participants about how to practise evidence-based surgery.

Research in the Faculty of Dental Surgery

Professor Stephen Porter,
FDS Research Chair

Professor Stephen Porter.

The Faculty of Dental Surgery continues to invest in the future of research allied to oral health and the careers of talented young researchers. We have continued to offer Research Fellowships and Pump Priming Awards and have been able to extend such opportunities by virtue of collaborative awards with specialist societies allied to dentistry. The spectrum of research questions that have been funded has been diverse, but always related to oral health care problems that are relevant to present day wellbeing (see table). The quality of applications has been remarkably high and the completion for such awards is ever-growing – a reflection perhaps of the demand of young clinicians to gain a foot hold in a research-active career as well as the knowledge that the Faculty is an important potential source of funding.

We have continued to extend the number of Awards by joint funding with specialist Societies allied to oral health. In 2018 there was one jointly funded Pump Priming Grant with the Association of British Academic Oral and Maxillofacial Surgeons (ABAOMS).

The Faculty has a long term commitment to research. In 2019 we will be having a further round of applications that will include the introduction of joint Pump Priming Grants allied to Oral and Dental Radiology as well as a Fellowship that targets Paediatric Dentistry.

Summary of the 2018 Research Awards of the Faculty of Dental Surgery

Applicant	Host Institution	Research Title
2018 FDS-BSOM Pump-Priming Grants		
Maria Tumelty	Glasgow Dental Hospital and School	Can salivary calprotectin be used as a diagnostic biomarker for oral granulomatous disease?
2018 FDS-ABAOMS Pump-Priming Grants		
Bosun Hong	Birmingham Dental Hospital	Patients' preference in anaesthetic modality for surgical removal of mandibular third molar teeth
2018 FDS Pump-Priming Grants		
Robert William Bolt	University of Sheffield	Exploiting salivary extracellular vesicle microRNA biomarker signatures for the early detection of oral and oropharyngeal cancer
Ibraz Siddique	University of Sheffield	Does the presence of cancer-associated fibroblasts at tumour margins confer a worse prognosis for oral cancer patients?
Ishpinder Toor	UCL Eastman Dental Institute	Adhesive bonding with gold alloys
2018 FDS Research Fellowship		
Caroline Elizabeth McCarthy	University of Liverpool	Epigenetic reprogramming in chemoprevention of head and neck cancer: in vitro tissue-engineered model and in vivo validation using the SAVER trial

The Faculty has a long term commitment to research. In 2019 we will be having a further round of applications that will include the introduction of joint Pump Priming Grants allied to Oral and Dental Radiology as well as a Fellowship that targets Paediatric Dentistry.

Such awards have been key to the later academic and research success of many recipients as well as having led to the publication of important, impactful, original research. Such initiatives have thus not only benefited Members and Fellows of the College but also given patients the opportunity to contribute to and influence research as well as be the recipients of the research outcomes.

Deep phenotyping of cleft lip to facilitate a precision surgery approach

Ambika Chadha

FELLOWSHIP/SPONSOR:
FDS Research Fellowship

SUPERVISORS:
Professor David Edwards, Professor Piet Haers and Dr Yanzhong Wang

SITE OF WORK:
Department of Perinatal Imaging and Health, King's College London and South Thames Cleft Service, St Thomas' Hospital, London

PUBLICATIONS:
1. Chadha A *et al.* Advancing Objective Facial Evaluation in Cleft Lip Surgery using Surrogate Marker Statistics, Clinimetrics and Machine Learning – submitted to *JAMA Facial Plast Surg*

2. Chadha A, *et al.* Relative Facial Symmetry Index (rFSI) as a Surgical Outcome in Unilateral Cleft Lip Calculated using Automated Standardisation and Cropping of 3D Photographs – submitted to *Br J Oral Maxillofac Surg*

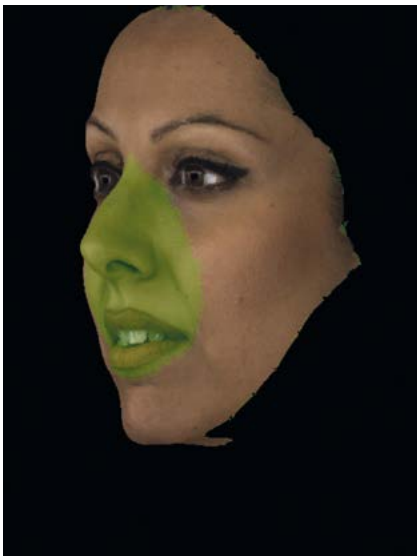
PRESENTATIONS:
1. Chadha A *et al.* The Diagnostic Efficacy Of 3D Photography in Cleft Lip Facial Appraisal – A Systematic Review Using a Hierarchical Model. Presented at: The Conference of the European Association of Cranio-Maxillo-Facial Surgery (EACMFS); Sept 2018; Munich

2. Chadha A *et al.* A Protocol to Deep Phenotype the Unilateral Cleft Lip Deformity. Presented at: The annual Winter Scientific meeting of the British Association of Plastic, Reconstructive and Aesthetic Surgeons (BAPRAS); Nov 2016; London

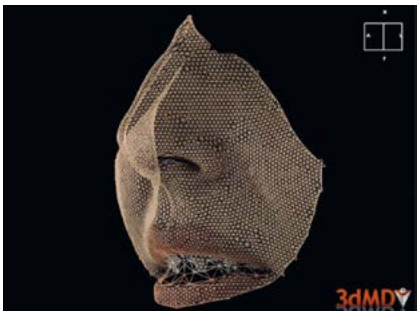
PRIZES:
3D Photography of Cleft Lip: Applying Imaging Biomarkers Pre- and Post-operatively to Facilitate a Precision Medicine Approach was chosen for publication by the RCS Commission on the Future of Surgery. May 2018

FURTHER FUNDING:
British Association of Oral and Maxillofacial Surgeons

Cleft lip is one of the most common congenital conditions of the head and neck and has a significant impact on patients' psychosocial quality of life. Multidisciplinary treatment includes surgeries to repair the primary defect but surgical protocols vary considerably, with a commensurate variation in treatment outcome. These inconsistencies in surgical practice are underpinned by a lack of high-quality evidence, which is challenged, in part, by current systems of cleft lip classification. Traditionally, only a few words are used to describe the cleft lip defect, which neither distinguishes between the subtleties of presentations nor reflects the wide spectrum of this complex deformity. A much more comprehensive approach to cleft lip description (known as 'deep phenotyping') is therefore required to tackle this cleft classification dilemma, in the era of precision treatment.



A three-dimensional photograph superimposed by the nasolabial cropping tool specifically co-designed for this research.



Mesh view of the cropped nasolabial region to be modelled using shape analysis techniques.

Together with a multidisciplinary team of researchers comprising surgeons, image scientists and statisticians, I have mathematically analysed a multicentre cohort of three-dimensional photographs of patients with Unilateral Cleft Lip to generate a numeric indexing system that describes this facial deformity. My research aims to create a 'language' that can describe any and every case of unilateral cleft lip, comprehensively and uniquely, and to observe how cases so described cluster to reveal sub-phenotypes within traditionally established phenotypes. This objective approach to deep phenotyping will enable cases of cleft lip to be classified into more refined groups for follow-up in studies researching surgical protocols. Ultimately, the aim is to be able to offer patients with cleft lip a plan of surgical treatment that is customised to their exact phenotype, based on robust evidence.

Future research plans, upon completion of my PhD, will focus on identifying the deep learning algorithms relating cleft lip presentations to their subphenotypes and to validate these using a second testing sample. An exciting application of this work is the use of validated subphenotypes to direct studies into genetic aetiology.

Modelling the Unilateral Cleft Lip (UCL) defect in three dimensions using shape analysis can potentially distinguish all UCL presentations and accurately reflect the whole spectrum of the condition. It can also identify sub-phenotypes we didn't even know existed.

Exploring the feasibility and acceptability of using Lift the Lip within the routine practice of health visitors in Wales

Mary Wilson

FELLOWSHIP/SPONSOR:
RCS Dental Faculty and British Association for the Study of Community Dentistry

SUPERVISORS:
Anup Karki

SITE OF WORK:
Public Health Wales

PUBLICATIONS:
As a condition of the grant, a paper has been submitted to the Faculty Dental Journal

PRESENTATIONS:
1. British Association for the Study of Community Dentistry Conference, Cavendish Conference Centre, London, November 2018

2. The Bevan Commission Innovators Showcase event, Welsh Assembly Senedd, Cardiff, January 2019

Dental caries is a highly prevalent childhood disease, with a strong social gradient. As well as distress, pain and infection, there can be negative impacts on personal development and social well-being. Attendance to dental services is poorest in deprived groups.

"Lift the Lip" is a simple dental health assessment tool for use with young children and their families by non-dental health professionals, with the aim to facilitate early intervention and contribute to efforts to reduce hospital admissions for severe dental caries. The objective of my project were to explore the feasibility and acceptability of using Lift the Lip within the practice of health visitors in Wales.

Fifteen trained health visitors used Lift the Lip during their visits with children aged 15 months to 3.5 years. After two months, their experiences and attitudes were collected via focus groups and interviews. Transcripts were analysed using the Theoretical Domains Framework.

Health visitors found that Lift the Lip added value to their oral health promotion role during the universal contact visits. They reported that the tool not only supported identifying children with concerns of dental caries, but also was a vehicle to provide enhanced, personalised oral health advice. Barriers to dental attendance were identified, but participants felt that Lift the Lip promoted early dental attendance and facilitated dental access.

Lift the Lip was both feasible and acceptable to participating health visitors. It is a universal approach, to help identify families that require additional early support. Further research is now required to assess if Lift the Lip results in earlier dental intervention.

Dental caries affects 14.5% of 3-year-old children in Wales, rising to 20.2% in the most deprived areas.

Prizes and Travelling Awards

Travelling Awards

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

Rex and Jean Lawrie Fellowship and Stefan and Anna Galeski Fellowship

Each year the families of Rex and Jean Lawrie, and Stefan and Anna Galeski, fund a number of surgeons to undertake various surgical skills workshops and other such activities to help improve surgical skills, and thus surgical care, for people in low and middle income countries throughout the world. Such generosity is deeply appreciated by the RCS, the numerous UK surgeons who receive the fellowships' support and most importantly the surgeons who learn various surgical skills in the host countries.

Emman Combellack teaching in Indonesia.

Emman Combellack teaching in Indonesia.

Recipients 2017

- Ed Fitzgerald – Madagascar
- Yasmin Jauhari – Colombia
- Emman Combellack – Indonesia
- Arun Sujenthiran – Indonesia
- Matt Lechner – Indonesia
- Misha Verkerck – Ethiopia
- Naomi Wright – Mexico and Guatemala
- Rhiannon Harries – Mexico and Guatemala

Recipients 2018

- Muhammed Ahsan Javed – Ghana
- Fran McNicol – Mongolia
- Amy Garner – Egypt
- Robert Staruch – Egypt
- James Glaseby – Rwanda

Recipients 2019

- Rachael Clifford – Sri Lanka
- Veena Surendrakumar – Sri Lanka

Operation hernia report – Muhammad Ahsan Javed

The verse from the Holy Quran, translation of which is 'And whoever saves one - it is as if he had saved mankind entirely' (chapter 5 verse 32), the satisfaction one attains from being able to help the underprivileged, my passion for exploring the world and sense of adventure to work under challenging circumstances are the factors that motivated me to apply for Operation Hernia. I was delighted to hear from Mr Chris Oppong, director of Operation Hernia, that I was going to be part of a team of Operation Hernia visiting Bole District Hospital in Ghana from 4-11 November 2017.

A standard day started at 7:00 am with examining patients already listed and consented for surgery. A significant proportion of the patients were Hep B/C or HIV positive. On average, each day consisted of 10 to 12 hours of operating. The vast majority of cases were inguinoscrotal herniae and hydroceles that were done under local or spinal anaesthesia. The equipment was primitive and the norm was to complete a case using a single vicryl, prolene and a monocryl stitch. We had access to two air-conditioned theatres and although mostly running water and electricity were available, there were occasions where operations had to be completed with the aid of a head light due to electricity disruptions.

The local specialised anaesthetic nurses were highly skilled and particularly efficient at administering spinal anaesthesia. Turnaround time between cases was about 20 minutes. The local scrub practitioners were also very experienced and competent assistants. Our team performed 87 operations including an emergency laparotomy for a young man with peritonitis who had a perforated duodenal ulcer.

I would like to conclude by thanking the Rex and Jean Lawrie family as the award of the Rex and Jean Lawrie Fellowship from RCS enabled me to participate in Operation Hernia. This expedition has helped many underprivileged individuals and has been an enriching experience for me, professionally as well as personally.

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 2017

- Max Almond, Istituto Nazionale dei Tumori, Milan
- Susannah Love, Massachusetts General Hospital, Boston
- Rajeev Mathew, Ayder Comprehensive Specialized Hospital, Ethiopia
- Matthew Ricks, WALANT unit in Calgary
- Sashidhar Yeluri, Bariatric unit in Bruges

Recipients December 2017

- Alistair Mitchell-Innes, Royal Victorian Eye and Ear Hospital, Australia
- Krunal Patel, Toronto Western Hospital
- Rishi Sharma, University of British Columbia
- Sidhartha Sinha, Division of Vascular Surgery, University of Toronto
- Ivor Vanhegan, University of BC, Canada and Midwest Orthopaedics at Rush, Chicago
- Jamie Wilson, Toronto Western Hospital

Muhammed teaching surgical anatomy of inguinal canal to local students in Ghana.

Recipients May 2018

- Gijs van Boxel, University Medical Centre Utrecht, The Netherlands
- Aziz Gulamhusein, Aalborg University Hospital, Denmark
- Muhammad Javed, University of British Columbia, Canada
- Yassar Qureshi, Ngwelezana Hospital, Republic of South Africa
- Andrew Wheelton, Holland Orthopaedic and Arthritic Centre, Canada

Recipients December 2018

- Nikul Amin, The Royal Prince Alfred Hospital, Australia
- Tarek Boutefnouchet Hôpital du Sacré-Coeur de Montréal and Hôpital Jean Talon, Canada
- Jason Fleming, The National Cancer Institute-designated University of Alabama, USA
- Aziz Gulamhusein, Aalborg University Hospital, Denmark
- Christina Kontoghiorghe, University of Cape Town/Groote Schuur Hospital, South Africa
- Antonios Kourliouros, La Pitié Hospital, Paris, France
- Scott McCain, Concord Repatriation Hospital, Australia

Colledge Family Memorial Fellowship Fund

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

Recipients 2017

- Oliver Dale – Royal Adelaide Hospital
- Andrew Hall – Harvard University Medical School and Boston Children's Hospital
- Ashley Hay – Memorial Sloan Kettering Cancer Centre
- Neil Tan – The Queen Elizabeth Hospital, University of Adelaide
- Emily Young – St Paul's Hospital, Vancouver
- Vinay Varadarajan – Vancouver General Hospital and University of British Columbia
- Matthew Ward – Princess Alexandra Hospital, Brisbane

Recipients 2018

- Saif Al-Zahid – University of Malaya
- Stephen Ball – University of Auckland
- George Barrett – Christchurch Hospital
- Sidhartha Nagala – Australia Royal Melbourne Hospital
- Rishi Sharma – British Columbia and Vancouver General Hospital
- Kishan Ubayasiri – Dalhousie University (Canada)
- Navdeep Upile – Royal Brisbane and Women's Hospital and University College of Medicine (Korea)

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'.

2017 Winner

- Candice Downey – Making surgery safer: Will wireless patch detect complications earlier?

2017 Runners up

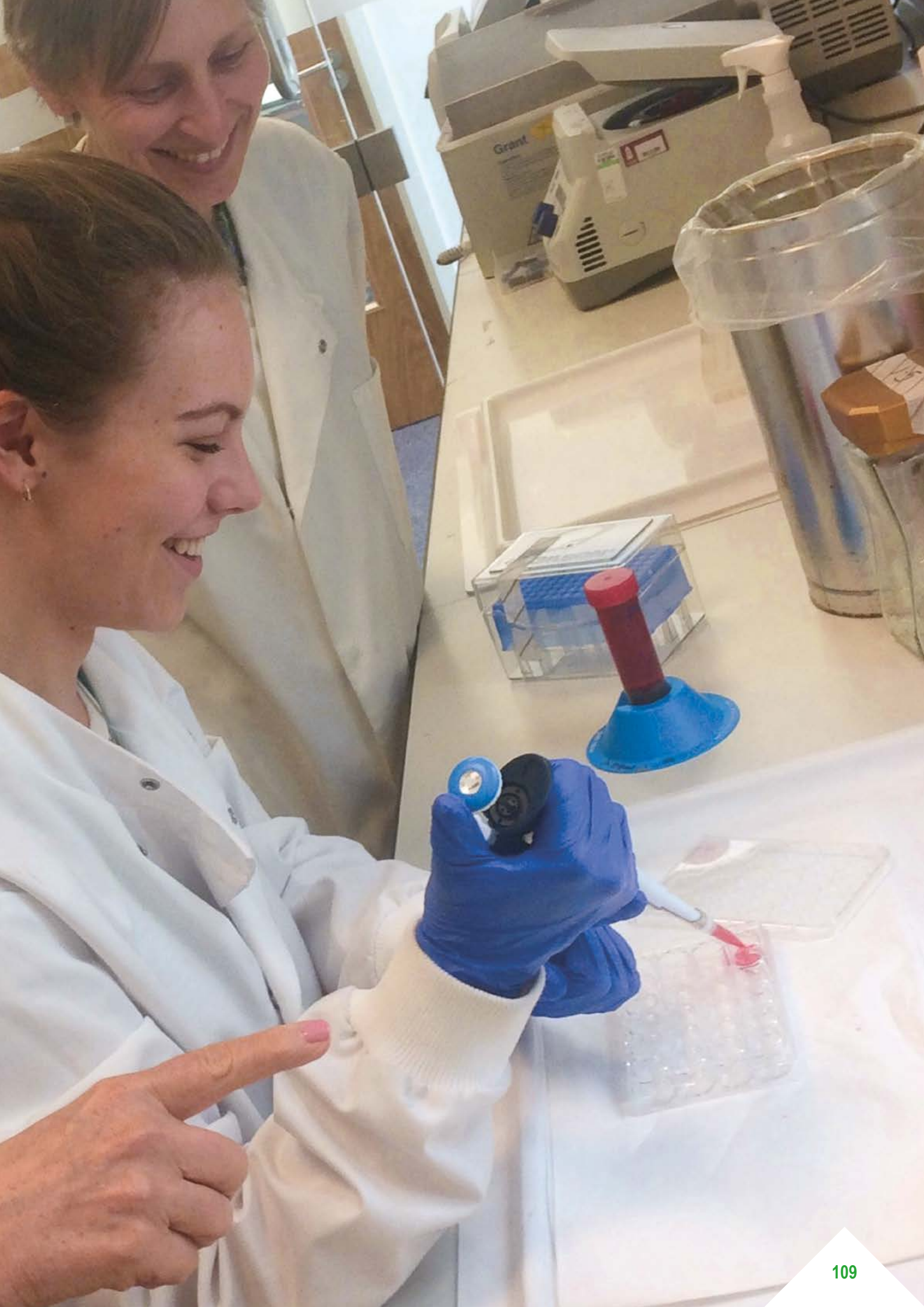
- Ellie Edlmann – Understanding the inflammatory response in chronic subdural haematoma and targeting new drug therapies
- Zita Jessop – 3D Bioprinting Cartilage for Facial Reconstruction

Rosetrees Trust winner Candice Downey & runner up Ellie Edlemann with Mr John Samuels of the Rosetrees Trust.

Higher Degrees for Intercalated Medical Students

Medical students' grants are awarded to medical students wishing to undertake an intercalated Bachelor of Science degree related to surgery. Owing to the variation in the ways students are funded or not funded for such degrees, students require additional support in areas such as bench fees, consumables or subsistence. Each award is worth up to £5,000.

Ahmed Ali
Danny Baker
William Baker
Joseph Battle
Aleksandra Berezowska
Liam Cato
Katherine Emo
Christian Flynn
Benjamin France
Jordan Green
Wais Habib
Patrick Harrison
Rebecca Helliwell
Conor Jones
David Kemball
Mark Kong
Shriya Kumar
Julian Man
Waqqas Patel
Kate Quirke
James Russell
Tanya Ta
Sita Techaboonanake
Jennifer Tempany
Nikhil Thakral
Vidhi Unadkat
Uddhav Vaghela
John Vincent
William Waldock


Grant

The Effects of Cyclic Indentation Mechanical Load and HDAC6 Inhibition on Interleukin-1β Induced Inflammatory Signalling and Cartilage Degradation

Ahmed Ali

MEDICAL SCHOOL:
Barts and The London School of Medicine and Dentistry

LOCATION OF RESEARCH:
School of Engineering and Materials Science, Queen Mary University of London

Ahmed with his supervisor Professor Martin Knight after a presentation of his project.

The award funded a lab-based research project during my intercalated BSc year, which supplied me with the materials required for the experiments (eg culture media, reagents and culture plates). The research investigated one of the inflammatory pathways (IL-1β) that can occur in articular cartilage. It assessed how two factors (mechanical load and a drug called Tubacin) influence the signalling of this pathway and its effects on cartilage on cartilage degradation. This is significant as it is developing our understanding of the basic science that underlies osteoarthritis. In the future, it may allow the development of a novel drug that is disease modifying, slowing down the progression of osteoarthritis in patients, and potentially being able to improve postoperative complications in orthopaedic surgery.

Informed Decision Making in Surgery for Ulcerative Colitis

Daniel Baker

MEDICAL SCHOOL:
Sheffield University

LOCATION OF RESEARCH:
Sheffield Teaching Hospitals

During my Intercalated BSc my researched aimed to elicit patient informational preferences when considering elective surgery for ulcerative colitis. Many patients face the possibility of surgery during their disease course, but the decision to opt for surgery is difficult due to uncertain outcomes and the option for continued medical treatment.

Initial results have highlighted several areas where we may be able to improve patient preoperative information. The majority of the RCS award has been used to pay for travel and accommodation to allow presentation of the research internationally. Results from my BSc have been presented in Dublin, Barcelona and Berlin.

The research has RCS for their generous award which has enabled this research to excel. I look forward to continuing this work further and aspire for a career in academic surgery.

Poster Presentation at ECCO 2017, Barcelona.

Assessment of body composition and physical fitness as markers of postoperative outcome in oesophago-gastric cancer

William Baker

MEDICAL SCHOOL:
University of Southampton

LOCATION OF RESEARCH:
University Hospital Southampton

Oesophago-gastric cancer is a devastating disease possessing a 5-year overall survival less than 15% and treatment limited to neoadjuvant therapy followed by surgery. Modifiable factors, such as body composition and physical fitness, could stratify patients based on their level of risk, which would improve prognostic models and through prehabilitation, allow patients to optimise their preoperative status. This project aimed to investigate changes in muscle and fat during neoadjuvant therapy, in association with physical fitness and the effect these have on postoperative mortality. This is the first study to combine these two physiological parameters in a cancer cohort.

William performing body composition analysis.

I would like to thank the Royal College of Surgeons for their generous support. This year has been an invaluable experience and has allowed me to develop skills in academia and research which I hope to pursue further in a surgical career.

MicroRNAs as Biomarkers of Acute Kidney Injury after Cardiac Surgery

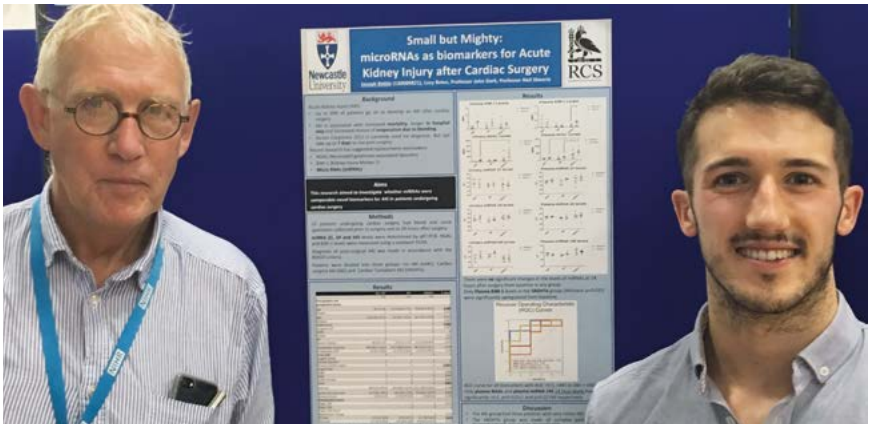
Joseph Battle

MEDICAL SCHOOL:
Newcastle University Medical School

LOCATION OF RESEARCH:
Freeman Hospital and
Institute of Cellular Medicine,
Newcastle University

During my intercalated year I investigated a potentially better and quicker test for acute kidney injury (AKI) after heart surgery. AKI occurs when a patient experiences a rapid reduction in kidney function. AKI is common after heart surgery, affecting three out of ten patients. However, it is hard to spot as the features are inconsistent and there is no single blood test. Previous research has identified a small molecule from the same family as DNA, microRNA.

We found that the levels of microRNA were only slightly increased after surgery. Patients with high levels of microRNA one day after surgery did not go on to develop AKI and microRNA levels were not as effective as the current tests at spotting AKI. Our research showed that microRNAs are worse than the current tests for AKI after heart surgery and that more research is still needed to find a better test.



Professor John Dark and Joe at a poster presentation for his work.

Quantification and characterisation of silver particles released from coatings used for prosthetic joint bearing surfaces

Aleksandra Agata Berezowska

MEDICAL SCHOOL:
Barts and The London School of Medicine and Dentistry

LOCATION OF RESEARCH:
School of Engineering and Material Science, Queen Mary University London

Despite current efforts, the risk of post-surgical infection following total knee replacements persists, and is a burden not only to the individual, but also the NHS budget. A novel method of prevention involves coating the prosthetic joint with a new nanomaterial containing silver. The aim of my project was to quantify silver particles released from a polished and unpolished versions of the coating and compare them against the recommended safe levels. The generous bursary allowed me to freely use the GFAAS machine in order to optimise the methodology. The experiments demonstrated that sample collection during simulator testing is critical for the results of the experiment, especially with significant numbers of particles being generated, providing thus a good basis for further research. I am very grateful for the financial support that enabled me to gain valuable research skills that, without a doubt, will prove beneficial in the future.

Aleksandra presenting her project during the Intercalated IOB Symposium.

The pleiotropic character of heparin: working towards an understanding of thrombosis in burns trauma

Liam David Cato

MEDICAL SCHOOL:
University of Birmingham

LOCATION OF RESEARCH:
The Birmingham Burns Centre, Queen Elizabeth Hospital, Birmingham

Liam transferring neutrophil cells after he prepared them from burns patient's blood.

I'm very thankful to the RCS and their funding partners for their generous award that funded my research investigating blood clotting in burns patients. This area deserves attention as the drug used to prevent clotting (heparin) is ineffective, and life-threatening selequae are the result.

I measured parameters in the blood of people who had been severely burned (more than 20% of their body surface area) to firstly confirm the presence of the resistance to heparin then, secondly, to find the source of resistance. Results have been interesting thus far and I will continue this work throughout my studies.

The experience in the lab that this grant gave me was exciting and very beneficial. I hope to continue research work in my future career.

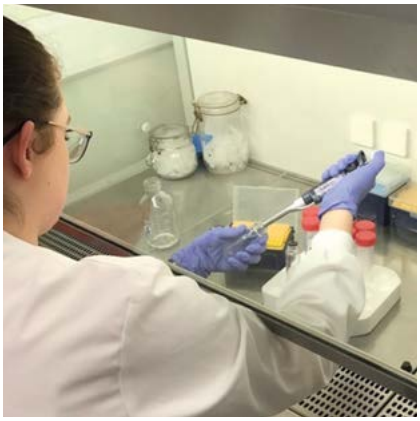
The role of exosomes in mesenchymal-epithelial transition: an investigation into the development of solid tumour metastases

Katherine Emo

MEDICAL SCHOOL:
University of Southampton

LOCATION OF RESEARCH:
Somers Cancer Research Building, Southampton General Hospital

I used the bursary awarded by the Royal College Surgeons to fund an intercalated Master's degree at the University of Southampton. I undertook my research at Southampton Cancer Research UK Centre under the supervision of Professor Mirnezami and Dr Sayan.



Isolating exosomes.

My research focused on a mechanism for secondary tumour formation, in particular the role of exosomes and miRNAs. Exosomes are key communication vehicles between cells, and miRNAs are small molecules which turn genes off. Previous studies have demonstrated that miRNAs can be transported by exosomes and have shown that they both have a vital role in cancer progression and spread (metastasis). I hypothesised that miRNAs transferred in exosomes influence metastasis.

My research found that normal tissues produce high quantities of exosomes and these exosomes contain high levels of miRNA-200. This miRNA-200 can be transferred to cancer cells, inducing metastasis. Initial results are promising and I am currently working towards publication.

Characterisation of laryngeal cancer using positron emission tomography (PET) texture analysis

Christian Flynn

MEDICAL SCHOOL:
Imperial College London

LOCATION OF RESEARCH:
Hammersmith Hospital, London

I am extremely thankful for the RCS grant that enabled me to move to London to study and research at Imperial College London. The grant supported me with accommodation and general costs of living, as well as enabling me to submit my research to international medical academic conferences and journals.

My original research involved applying the novel technique of texture analysis to throat cancer scans to determine whether analysing the scans with software can predict the grade (resemblance to normal tissue) of the cancer. This is usually done with invasive and painful biopsies. These snapshots can only be performed a limited number of times and certain types are not always 100% accurate. We analysed image features of 62 throat cancer scans and created statistical models, with the best model predicting tumour grades to an accuracy of 74.2%. These initial results are promising and warrant further research involving more data.

Preparing 3D PET scan images of laryngeal cancer for texture analysis processing by discriminatively selecting the tumour.

An observational study: does computed tomography imaging of abdominal fat predict emergency laparotomy outcome?

Ben France

MEDICAL SCHOOL:
University of Birmingham

LOCATION OF RESEARCH:
Heartlands Hospital, Heart of England Foundation Trust, Birmingham

This award supported my study of Clinical Sciences at the University of Birmingham. The main aim of my research was to establish whether there is an association between the amount of abdominal fat patients have and their survival at 90 days after surgery. Currently, this is not well understood. We used software that analysed computed tomography (CT) scans from more than 600 patients to measure this.

The main conclusion was that abdominal fat was not associated with increased 90-day mortality in this population. However, this pilot project may now pave the way for a larger study to confirm this finding, thereby shedding light on how fat may or may not affect surgical mortality.

The funding provided by the RCS ultimately enabled me to get the most from my degree. I now have a better understanding of the scientific method, have gained experience of presenting at international conferences and am keen to embark on further surgical research in the future. Thank you RCS!

Ben with supervisors (Prof Fang Gao Smith and Mr Edward Rawstorne) prior to a research presentation.

Is extracorporeal shockwave therapy an efficacious alternative to current management options for intermittent claudication?

Jordan Luke Green

MEDICAL SCHOOL:
Hull York Medical School

LOCATION OF RESEARCH:
Academic Vascular Surgical Unit, Hull Royal Infirmary

Intermittent claudication is a chronic condition affecting 1 in 10 worldwide, often having a dramatic impact on walking ability and quality of life of individuals. Conventional management of claudication is through exercise or surgery, however, a new non-invasive treatment is required to maximise benefits.

Jordan performing shockwave therapy on a trial participant.

This research aimed to evaluate the effectiveness of extracorporeal shockwave therapy for intermittent claudication, a therapy widely known for the treatment of kidney stones. Effectiveness was assessed through a randomised controlled trial that compared shockwave therapy with a placebo for improving the distance individuals can walk, followed for 12 months. The findings of this research demonstrated that shockwave therapy doubled walking distances at 12 months.

These results are promising and have precipitated further recruitment of patients in a second phase of the trial in order to examine this novel treatment further. This research would not have been possible without the generous support of the Royal College of Surgeons.

Can esophageal tumour morphology be used to predict prognosis?

Wais Habib

MEDICAL SCHOOL:
King's College London

LOCATION OF RESEARCH:
Guy's and St Thomas' Hospital

I carried out research on 332 patients who were diagnosed with oesophageal tumours from 2011–2015 and who had surgery to remove their tumour at St Thomas' Hospital. The purpose of this research was to identify whether there was any relationship between the shape and appearance of the tumour and survival.

Wais presenting his work.

We found that certain appearance and shape of tumours have very poor prognosis and patients tend not to do that well with surgery.

Therefore, the implication of this research is to ensure surgeons pay great attention to the different ways tumours can appear on endoscopy as part of initial diagnostic investigations. Also, it can help surgeons decide whether surgery or chemotherapy is appropriate for certain types of tumours.

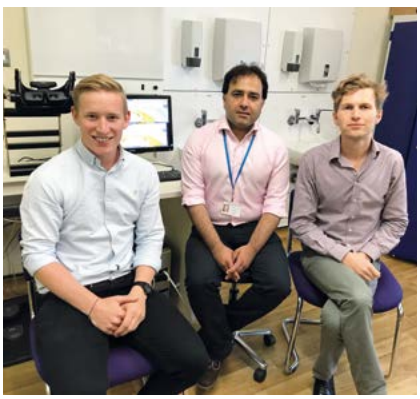
I will be presenting this project at the 16th World Congress of the International Society for Diseases of the Oesophagus in Vienna in September 2018.

Validation of a novel full procedural robotic prostatectomy virtual reality training module

Patrick Harrison

MEDICAL SCHOOL:
King's College London

LOCATION OF RESEARCH:
Sherman Education Centre,
King's College London,
Guy's Hospital, London



Patrick (left) with supervisors Mr Kamran Ahmed (middle) and Mr Nicholas Raison (right) in front of one of the robotic surgery simulators used in the study.

Complicated procedures and reduced training hours make learning the necessary skills harder for trainee surgeons. Simulation is an important adjunct to real-life surgery. The RCS award supported my intercalated BSc at King's College London where I worked as part of a team researching robotic simulation.

We performed a prospective study to validate a novel, full procedural, robotic prostatectomy virtual reality training module. We recruited surgeons and medical students to complete the module and analysed their performance and opinions. We then randomised 26 medical students to receive a 5-hour training programme using either the procedural prostatectomy module or basic virtual reality exercises. We then assessed the performance of students using the da Vinci™ robot on a fresh frozen cadaver. I am extremely grateful for the RCS's support that enabled me to travel to present this research internationally.

Exploring vascular smooth muscle cell function/dysfunction through progression of abdominal aortic aneurysm

Rebecca Helliwell

MEDICAL SCHOOL:
University of Leeds

LOCATION OF RESEARCH:
Leeds Institute of Cardiovascular and Metabolic Medicine

Abdominal aortic aneurysm (AAA) is often a silent disease with potentially fatal consequences. Little is known regarding the cellular changes that occur during early aneurysm development, as it is difficult to acquire early aneurysm tissue. This laboratory group developed a novel porcine bioreactor model to improve understanding of this elusive disease. This project allowed me to explore the functional behaviour of vascular smooth muscle cells through the progression of AAA, thus highlighting potential therapeutic targets of this deadly disease.

Working as part of an established laboratory team this year allowed me to learn a multitude of laboratory skills, which I would have not been able to develop on the standard medical curriculum.

I would like to thank RCS for supporting me in this project allowing me to gain insight into laboratory research.

Rebecca working in the laboratory with support from her supervisors Dr Karen Porter (left) and Dr Karen Hemmings (right).

DNA Methylation in Rectal Cancer: Validation of a Genome-Wide Analysis

Conor Jones

MEDICAL SCHOOL:
Peninsula College of Medicine and Dentistry

LOCATION OF RESEARCH:
University of Exeter Medical School and the Royal Devon and Exeter Hospital, Devon

Conor using the PyroMark® Q24 Vacuum Workstation to bind amplified DNA to streptavidin beads.

The generous support of the RCS allowed me to complete an MSc by Research at the University of Exeter.

Preliminary genome-wide analysis of matched rectal tumour and adjacent mucosa identified 176 differentially methylated probes (DMPs) associated with rectal cancer (p=<1E-07). In order to validate these findings, I designed, optimised and applied bisulphite pyrosequencing assays for nine highly significant DMPs. Additional replication was performed in a larger cohort and correlations were drawn with clinicopathological tumour features. The luminometric methylation assay was used to compare global methylation levels of rectal tumour and adjacent tissue.

The completion of this degree has given me insight into, and appreciation for, the importance of translational research in the care of surgical patients. In addition, I believe that I have developed valuable skills that will remain fruitful throughout my career in academic surgery.

An evaluation of the use of surgical headlights in Sierra Leone

David Kemball

MEDICAL SCHOOL:
The University of Leeds
Medical School

LOCATION OF RESEARCH:
Masanga Hospital, Masanga Village,
Tonkolili District, Sierra Leone

The award allowed me to conduct a research project into the use of low-cost surgical headlights to improve surgical lighting in a low income setting in Sierra Leone.

The burden of surgical disease is high across lower and middle-income countries (LMICs) and it is often unmet due to infrastructure and safety challenges. Recent research into lighting in LMICs has found that it is often inadequate and poses a barrier to patient safety, one that is not easily fixed given financial constraints. Our study found that low-cost surgical headlights provide a safe and effective way of overcoming these challenges and improving surgical care in low resource settings.

My thanks to the RCS for funding this research project, we hope to publish and disseminate our results internationally as part of the continuing drive to improve surgical care in low-resource settings.

David leading a focus group discussion on the shortcomings of existing surgical lighting.

The impact of Necrotising Enterocolitis on brain development in preterm infants

Mark Kong

MEDICAL SCHOOL:
Southampton University Medical School

LOCATION OF RESEARCH:
Clinical Neurosciences, Clinical and Experimental Sciences, University of Southampton

The Royal College of Surgeons of England very kindly supported the research conducted throughout my intercalated master's degree. This enabled my contribution to a case-control study, investigating how the white matter structures of the brain were altered in preterm infants with a bowel disease named necrotising enterocolitis. The aim was exploratory, using MRI techniques to assess brain white matter and to describe whether this was further accompanied by neurodevelopmental impairment.

My work involved using post-processing techniques to analyse MRI data, which provided a number of invaluable skills. The preliminary results are promising and have allowed me to present at national and international conferences.

With the generous support from the RCS, I have been awarded a First Class Honours that has provided a great research experience that I will take with me into the future.

The MRI machine after an infant brain scanning session, University Hospital Southampton.

Replicating measurements of total haemoglobin mass within a single day: a feasibility study in healthy volunteers

Shriya Balendra Kumar

MEDICAL SCHOOL:
University of Southampton School of Medicine

LOCATION OF RESEARCH:
Critical Care Research, University Hospital Southampton, Southampton, Hampshire

Anaemia, resulting from chronic illness and blood loss during surgery, is a significant problem in patients undergoing surgery. The RCS grant allowed me to carry out research that may lead to a more bespoke approach to managing and diagnosing anaemia in patients.

We used the innovative optimised carbon monoxide rebreathing technique (developed initially for sports and exercise research) to measure the total circulating mass of haemoglobin in the blood of healthy volunteers. We sought to demonstrate the feasibility of using this technique, in order to make patient-specific studies possible for the near future. Using this research, we hope to develop a simple, point-of-care tool, which can measure haemoglobin more accurately than the methods used currently.

I am extremely grateful to the RCS for their generous award which supported my Master's of Medical Sciences research project this year.

Shriya with supervisor James Plumb (Senior Fellow in Anaesthesia and Critical Care).

Investigating the factors associated with the development, progress and outcome of Dupuytren's disease treatment: a systematic review

Julian Man

MEDICAL SCHOOL:
Imperial College London

LOCATION OF RESEARCH:
Charing Cross Hospital, London

This award helped finance my project on Dupuytren's disease (DD). DD is a common hand condition characterised by the formation of nodules and restricted finger movement. A variety of treatment options are available. In order to appraise these treatment options, factors associated with treatment outcome must be better understood. My project was a systematic review identifying which factors may be associated with the development, progress and outcome for DD and recurrence after treatment.

Julian presenting findings to his peers.

The results of the review show that factors such as little finger involvement and the presence of knuckle pads were associated with DD, whereas the majority of studies found no significant associated between the disease and family history, diabetes and epilepsy. This review challenges previously held notions that factors such as family history are associated with DD. Further work into the generalisability of these results to the UK population should be conducted.

Outcome measures reported in clinical trials evaluating the management of Lymph Node involvement in Melanoma: A systematic review

Waqqas Mohamed Patel

MEDICAL SCHOOL:
Imperial College London School of Medicine

LOCATION OF RESEARCH:
Department of Plastic Surgery, St Mary's Hospital, Imperial College

NHS Trust, Nuffield Department of Rheumatology and Musculoskeletal Sciences, University of Oxford

Department of Dermatology, Churchill Hospital, University of Oxford

With the continual evolution of healthcare, appropriate selection of outcome measures is critical for results of future trials to directly influence patient care. The management of melanoma with spread to lymph nodes remains controversial, with clinical trials traditionally focusing on clinical rather than patient-reported outcome measures (PROMs), possibly neglecting important patient-relevant issues.

During my intercalation, I performed a systematic review, generously supported by the Royal College of Surgeons to identify outcome measures in clinical trials of melanoma with lymph node involvement. The award funded training in literature and database searching, successful submission and acceptance to present at an international conference and supported a multi-centre collaborative project between Imperial College London and the University of Oxford.

I would like to thank the Royal College of Surgeons, and the supervision team led by Professor Jain for their support and guidance throughout.

Waqqas practising the oral presentation.

The development and validation of an assessment tool for training in Percutaneous Nephrolithotomy (PCNL)

Kate Quirke

MEDICAL SCHOOL:
King's College London

LOCATION OF RESEARCH:
MRC for Transplantation, King's College London and Guy's Hospital, London

Kate in discussion regarding the PCNL Assessment Score with a PCNL expert from Turkey at the European Association of Urology Conference in Copenhagen.

The aim of the project was to develop a tool for trainee urologists to use when learning how to conduct a percutaneous nephrolithotomy (kidney stone removal via a tube placed into the kidney through the skin). In order to ensure the tool was applicable to hospitals across the world it was essential to discuss the tool with surgeons from various countries and hospitals. The RCS award has provided me with the opportunity to travel to different parts of the United Kingdom, Europe and to attend the European Association of Urology Conference (Copenhagen) to speak to 20 experts in this operation and develop a final percutaneous nephrolithotomy assessment score.

Assessment of prostatic ductal adenocarcinoma on multi-parametric MRI

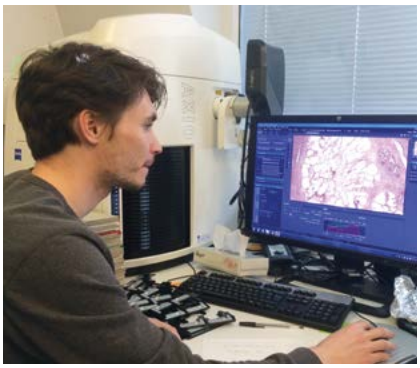
James Russell

MEDICAL SCHOOL:
King's College London

LOCATION OF RESEARCH:
Guy's Hospital, London

My research focused on an aggressive form of prostate cancer called ductal adenocarcinoma. The aim of my project was to determine whether there are any differences between ductal adenocarcinomas and conventional forms of prostate cancer on MRI. I also wanted to assess the diagnostic accuracy of MRI for these tumours. The generous funds provided by the RCS meant I could use a scanner to analyse prostate specimens with ductal adenocarcinomas and compare these with the MRI scans.

My results demonstrated that ductal adenocarcinomas are often underestimated on MRI and that there are very few features that distinguish them from conventional prostate cancers. Through comparing the scans with the prostate specimens, I showed that these tumours can sometimes go undetected using this imaging modality. The data from my project can provide surgeons with further insight into the clinical presentation of this disease and therefore aid decision making with regard to treatment.



Using the AxioScan slide scanner to take high resolution images of ductal adenocarcinoma specimens that were then analysed and compared with MRI images.

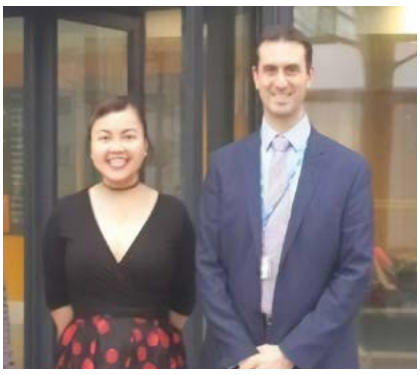
Outcome measures for Chronic Rhinosinusitis: How do we best evaluate current and future treatment options in Chronic Rhinosinusitis using quantitative and qualitative methods?

Ngan Hong Ta (Tanya Ta)

MEDICAL SCHOOL:
Norwich Medical School

LOCATION OF RESEARCH:
James Paget University Hospital, Great Yarmouth Norfolk

The generous grant from the RCS has enabled me to complete my Master's in Clinical Research in Otorhinolaryngology at Norwich Medical School. We conducted the first ever mixed-method study assessing redundancy of proposed objective outcome measures for a Chronic Rhinosinusitis trial (the MACRO trial) using a combined approach of considering both statistical findings and participants' perspectives. The results of the study helped to minimise patient burden and research waste. I have also completed an extensive systematic review on the relationship between objective outcome measures and patient-rated outcome measures in sinonasal disorders. Our review results will assist clinicians in choosing the most appropriate objective tools to reduce redundancy in future studies and routine clinical practice. Spending a year in full-time clinical research has been the most rewarding experience in my medical training so far. I am grateful for my supervisor Professor Carl Philpott for his tireless support and the invaluable financial support from the RCS.



Tanya with her supervisor Professor Carl Philpott.

Systematic review of postoperative mortality following colorectal resection for cancer in low- and middle-income countries

Sita Techaboonanake

MEDICAL SCHOOL:
University of Birmingham

LOCATION OF RESEARCH:
National Health Institute for Health Research Unit on Global Surgery, Birmingham

The award has granted me the opportunity to conduct research into the mortality following colorectal cancer surgery of patients in low- and middle-income countries (LMICs).

Sita with her supervisors; from left to right Mr James Glasbey, Mr Aneel Bhangu and Mr Dmitri Nepogodiev.

There were 14 million new cases of colorectal cancer in 2012, around half of which occurred in LMICs. Previous studies have suggested poorer outcomes for emergency surgeries in LMICs compared to high-income countries but no specific study of colorectal cancer surgery in LMICs exists. Our systematic review has identified low death rate following colorectal cancer surgeries in middle-income countries. The lack of data from low-income countries also highlights the need for high-quality, multicentre studies to identify real-world outcomes and targets for improvement in the future. We will present the results at the European Society of Coloproctology conference this year and plan on publishing this work. I am grateful to the RCS for this grant, without which this project would not be possible.

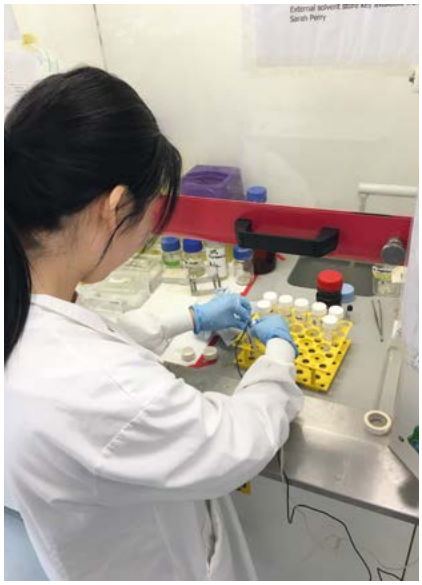
Novel gold electrode for real-time, early detection of anastomotic leakage following colorectal surgery

Jennifer Tempany

MEDICAL SCHOOL:
University of Leeds Medical School

LOCATION OF RESEARCH:
St James's University Hospital Leeds

I used the award to support proof of concept laboratory experiments in the first evaluations of a prototype for a novel probe to detect changes associated with anastomotic leak after colorectal resection. The probe detects changes in pH and ammonia levels, and so we spent some time calibrating the probe with known concentrations of ammonia in the lab, developing the laboratory protocol and documenting the probes sensitivity. Following this, we collected stoma effluent from postoperative patients in the hospital, and documented the amount of effluent the probe could detect. The data will be used to improve the design of the probe, to make it more sensitive to changes associated with an anastomotic leak.



Jennifer detecting changed in pH and ammonia levels in stoma effluent from postoperative patients.

Using statistical process control charts to monitor Anastomotic Leak

Nikhil Thakral

MEDICAL SCHOOL:
University of Exeter

LOCATION OF RESEARCH:
Royal Devon and Exeter Hospital

My project involved using measuring Anastomotic Leak rates at Royal Devon and Exeter Hospital in Colorectal operations. This was carried out using the methodology 'statistical process control charts', which allow outcomes to be plotted over time. We were able to retrospectively map periods where there had been a statistically significant change in the leak rate and outcomes will now be mapped prospectively. The award was very helpful in terms of day-to-day expenses as well as attending the Association of Surgeons in Great Britain and Ireland International Congress in Glasgow, 3–5 May 2017.

A systematic review and meta-analysis of predictors for short-term mortality in peripheral vascular disease related major lower limb amputations

Vidhi Vijaykumar Unadkat

MEDICAL SCHOOL:
Cardiff University

LOCATION OF RESEARCH:
Royal Gwent Hospital,
Newport, Wales

My intercalated project combined available research to understand why the death rate associated with major lower limb amputations is high and what can be done to reduce this. My supervisors and I are in the process of writing up our research for publication in a peer-reviewed medical journal. Most of the award will go to fund open access fees, which will allow researchers, clinicians and patients to read the article without having to pay.

A small proportion of the award will be used to attend The Vascular Society's annual scientific meeting, where I will present the research to healthcare professionals who care for patients undergoing amputations.

I am grateful to the Royal College of Surgeons for this award. I would also like to thank my supervisors Mr Christopher P Twine and Mr Graeme K Ambler for their support and guidance.

Vidhi working on her project in the library.

Biomechanically optimised mechanical stimulation for resolution of Lymphoedema

Uddhav Vaghela

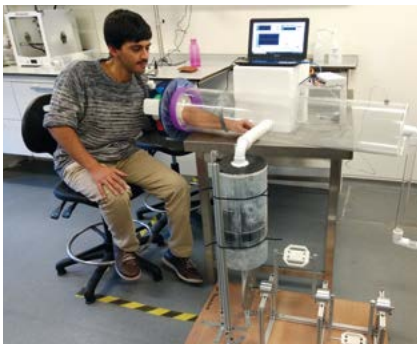
MEDICAL SCHOOL:
Imperial College London

LOCATION OF RESEARCH:
Bioengineering Department, Royal School of Mines, London

Our research hypothesis posited that vacuum would expand the collecting lymphatic vessels to increase the effective fluid volume cleared during vessel wall contraction and positive external pressures. Thus, using the award, we designed a novel mechanical stimulation device, which generated sinusoidally alternating supra- and sub-atmospheric pressures around the upper-limb.

The operating characteristics were predetermined by a computational MATLAB model. Real-time pressure readings were outputted to a computer interface to guide the frequency and magnitude of the applied treatment pressures.

During a 30-minute regimen, the assembly was tested on healthy volunteers (n=5), and their change in arm volume pre- and post-treatment was measured using 3D scanning techniques.



A representation of the device in use.

Statistically significant reductions in arm volumes were observed (p<0.01), which could be correlated to bolstered lymphatic circulation.

Overall, the award permitted the complementary theoretical and experimental arms of this project to converge and yield encouraging, positive device performance results, notably, despite involving healthy volunteers with previously unperturbed fluid homeostasis.

RISUS (Rugby Injury Surveillance in Ulster Schools) study

John Vincent

MEDICAL SCHOOL:
Queen's University Belfast

LOCATION OF RESEARCH:
Musgrave Park Hospital, Belfast and data collection was carried out in 26 of the rugby playing grammar schools in Northern Ireland

For the research component of my intercalated degree, I assisted in the RISUS Study. The aim of this study is to collect data regarding the number and nature of injuries that occurred in under-15 schools rugby in Northern Ireland in the 2016–17 season. This enabled me to examine trends in injury data to identify the areas of rugby where the most injuries occur. Injury prevention initiatives can then be introduced to ensure that rugby remains a safe and enjoyable sport for all. My main role in the study was data collection. The generous grant from the RCS covered all of my transport fees as I travelled between the 26 schools. The grant also greatly contributed towards tuition fees and living costs for the year. Without the grant, my year would have been impossible and I am very grateful.

John undertaking his research.

Augmented intraoperative surgical vision for the assessment of GI cancer resection margins

William Waldrock

MEDICAL SCHOOL:
Imperial College London

LOCATION OF RESEARCH:
St Mary's Hospital, London

William preparing to use MATLAB to run the DRS spectra script.

The project uses diffuse reflectance spectroscopy (DRS) light technology, which detects the type of tissue being scanned due to the unique absorbance and scatter of light exposed to the tissue.

Gastrointestinal (GI) cancer is a fatal condition of over 50s, causing changes in bowel habit, with a 5-year survival rate of less than 40% after metastasis. The earlier the surgeon identifies and removes the cancer, the higher the survival probability for the patient.

Colonoscopy misses up to 22% of pre-cancerous lesions, demonstrating the need for DRS to utilise unique light signatures for the identification of tissues.

The money was greatly appreciated for supplying funds for additional equipment for the DRS machine accessories and to support me as a student living in London. I am very grateful to the RCS for supplying the funds to support my role in such a worthwhile project.

Elective Prize Reports

The Elective Prize in surgery is awarded to clinical students at a UK medical school wishing to pursue a career in surgery and planning to undertake their elective attachment in surgery in the developing world. Each award is worth up to £500.

This award is possible thanks to the kind donations from the Preiskel and PKK families.

Timothy Campbell
Benjamin Clayphan
Henry de Berker
Wisha Gul
Sieu Jeak Ha
Angus Hall
Laura Hamilton
Hafizul Haq
Ali Omar Hashmi
Gwyneth Jansen
Felix A Jozsa
Nida Kalyal
Farhaan A Khan
Jack Kingdon
Roshni Mansfield
Claire Perrott
James Wadkin

Cleft lip and palate surgery at the Charles Pinto plastic surgery department, India

SK PRIZE:

Timothy Campbell

MEDICAL SCHOOL:
Manchester University

LOCATION OF ELECTIVE:
Charles Pinto cleft lip and palate centre, Jubilee Mission Hospital, Thrissur, Kerala, India

This summer I spent my elective period at the Charles Pinto cleft lip and palate centre in India. I hope to pursue this field as a future career, and the much higher rates of cleft lip and palate in India meant I had exposure to a greater number of patients. I learnt a huge amount, especially under the guidance of Dr Adenwalla who at 88 years old is still operating and heading up the department. He had been taught by Sir Harold Gillies – the founding father of plastic surgery, and it was a pleasure to listen to his stories.

Pre op cleft lip and palate.

During op.

Comparing and contrasting the care pathways for acute appendicitis in Tanzania and the UK

ELECTIVE PRIZE:

Benjamin Clayphan

MEDICAL SCHOOL:
University of Birmingham

LOCATION OF ELECTIVE:
Kilimanjaro Christian Medical Centre, Moshi, Tanzania

My objective for the four-week period was to compare how cases of acute appendicitis were managed compared with in the UK. While I did accomplish this, what was most interesting was to see the variety of different cases that the general surgeons manage there; from certain neurosurgical cases to amputations, I was very inspired by their work ethic and breadth of knowledge and skill. I was lucky enough to work beside these impressive surgeons in theatre daily and learnt a lot from them that I can implement into my own practice once I qualify.

Ben assisting Dr Marianne with a thyroid operation.

Developing a referral pathway for encephalocoele in Addis Ababa, Ethiopia

PREISKEL PRIZE:

Henry de Berker

MEDICAL SCHOOL:
University of Oxford

LOCATION OF ELECTIVE:
Yekatit-12 Hospital; Black Lion Hospital; St Paul's Hospital; Zewditu Hospital, Addis Ababa, Ethiopia

Henry with the plastics residents at Yekatit-12.

I journeyed to Addis Ababa Ethiopia with the intention of assessing the quality of neurosurgical care available to patients with neural tube defects (namely encephalocoele) in the capital. I conducted this research alongside a placement in plastics and reconstructive surgery at Yekatit-12 Hospital, working under Dr Mekonen Eshete. Currently, referrals depend on the complex myriad of personal and professional relationships that between consultants and trainees; were a challenge to navigate, but I believe that my report will be useful to visiting charities and the plastics department at Yekatit-12.

A general surgery elective in the National Hospital of Sri Lanka

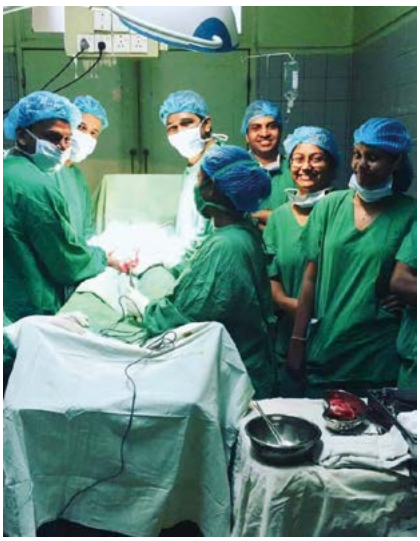
ELECTIVE PRIZE:

Wisha Gul

MEDICAL SCHOOL:
Lancaster Medical School

LOCATION OF ELECTIVE:
National Hospital of Sri Lanka, Colombo, Sri Lanka

I conducted my elective placement in general surgery in Sri Lanka's largest national hospital. Working in a high-volume, resource-limited setting proved to be an invaluable experience. By working alongside local medical students, I was able to partake in one of the best teaching sessions. This was facilitated by patients being extremely welcoming, to being clerked and examined by medical students. In theatre, the surgeons were true generalists; performing a medley of vascular, plastics and general surgical procedures, thus providing ample opportunities to scrub in. My elective placement in Sri Lanka has allowed me to experience a unique blend of high-quality medicine in a resource-limited environment and has ultimately heightened my enthusiasm for the speciality.



Wisha assisting the surgeon with a right hemi-colectomy and anastomosis procedure, with other medical students observing.

Paediatric orthopaedic surgery in Nepal

PPK PRIZE:

Sieu Jeak, Ha (Jakey)

MEDICAL SCHOOL:
Warwick Medical School

LOCATION OF ELECTIVE:
Hospital and Rehabilitation Centre for Disabled Children (HRCD), Nepal

I completed my elective at HRDC Nepal, a low-resource, non-profit hospital that addresses physical disability of underprivileged children. I was given the opportunity to work in different areas: outpatient department, operation theatre, physiotherapy, and prosthetic and orthotics department. These rotations enabled me to develop invaluable skills in all aspects of managing an orthopaedic condition, from clinical assessment, surgical techniques to rehabilitation exercises. I also learnt about orthotic shoes and prosthetic legs (its role and how to make them), which is a topic not covered in medical school. My experience in HRDC inspired me further to pursue a career in surgery.

Jakey in scrubs. Background of scrubbing area.

A general surgical elective in Fiji: investigating diabetes and surgical site infection

PREISKEL PRIZE:

Angus Hall

MEDICAL SCHOOL:
University of Birmingham

LOCATION OF ELECTIVE:
Labasa Hospital, Labasa, Fiji

My elective working in the surgical department of Labasa Hospital was brilliant. The surgeons at the hospital cover all surgical specialties and as a result, I was able to assist and observe a huge variety of surgeries, improving my basic surgical skills and learning some new ones. I also carried out some research into surgical site infection within the hospital, which I hope will prove useful to the department. Experiencing healthcare in a different cultural setting with limited resources, and seeing how the surgeons adapted to these limitations, was an invaluable experience that I will take with me through my career.

Angus interpreting a CT scan with Dr Mugi.

Angus outside the Hospital.

The Darlow Fellowship to Hong Kong

DARLOW FELLOWSHIP:

Laura Hamilton

MEDICAL SCHOOL:
King's College Hospital, London

LOCATION OF ELECTIVE:
The Prince of Wales Hospital, Hong Kong

I have a keen interest in minimally invasive surgery and new arthroscopic techniques, and my senior hand colleagues informed me that Hong Kong was at the cutting edge in hand surgery. Led by possibly the world leader in hand arthroscopy, Professor PC Ho responded with enthusiasm to my email and invited me to spend two weeks observing his practice at The Prince of Wales Hospital. This trip was generously funded by The Darlow Fellowship, which supports surgeons who wish to travel abroad to improve their knowledge. I saw exciting new techniques to allow major hand procedures to be performed under local anaesthetic, which I hope can be implemented in my current practice at King's College Hospital. I also saw progressive arthroscopic techniques to allow percutaneous scaphoid fracture bone grafting, as well as treatment of arthritis with debridement and arthroscopic assisted fusion. While in Hong Kong I was given the honour of presenting my MSc on finger fractures at the International Young Hand Surgeons Lecture, as well as attending the Hong Kong Society for Surgery of The Hand 30th Annual Congress, where I met delegates from Spain, Japan, Korea, Belgium and Russia.

International delegates watching Professor PC Ho performing keyhole wrist surgery using a 1.9mm arthroscope.

A surgical elective in plastics and reconstructive surgery with a focus on burns in Vietnam

PREISKEL PRIZE:

Hafizul Zaheer Haq

MEDICAL SCHOOL:
University of Leeds

LOCATION OF ELECTIVE:
Cho Ray Hospital, Ho Chi Minh City (Saigon), Vietnam

Hafizul (left) helping prepare before gauze is applied.

I had the incredible opportunity to spend my surgical elective in the plastics and burns department at Cho Ray Hospital. Cho Ray serves the massive Ho Chi Minh province. Despite a language barrier, I was welcomed into the brilliant plastics team. There, I assisted in numerous operations, becoming particularly familiar with skin-grafts, given how common partial-thickness and full-thickness burns are. I also recognised the challenges that the surgeons had to overcome due to their significantly limited resources. Meeting such an amazing team and inspirational patients has left a profound impact on me that I hope continues into my career.

Hafizul (left) welcomed as part of Dr. Phuc's (centre) team for the day.

Drivers and barriers to the routine use of the WHO surgical safety checklist in a limited resource setting – A quality improvement project in Pakistan

PPK PRIZE:

Ali Omar Hashmi

MEDICAL SCHOOL:
University of Manchester

LOCATION OF ELECTIVE:
Liaquat National Hospital (LNH), Karachi, Pakistan

Ali visiting a patient with achondroplasia in Nawabshah, a small city approximately 321 kilometres north east of Karachi. Patients typically travel long distances to receive treatment and follow up in Pakistan.

In Karachi, at LNH, I audited the use of the WHO surgical safety checklist. Surgical safety is key to reducing perioperative morbidity and mortality. The checklist was introduced in 2008 but was unheard of in this department, although some aspects were used during operations. I observed approximately thirty operations and assisted in eighteen, improving on my suturing ability. I prepared a presentation for the surgical team informing them on the use of time out (pre-anaesthesia, pre-incision and postoperatively) to minimise risk. This experience has further fuelled my desire to pursue a career in surgery.

Plastic surgery in Nepal

SK PRIZE:

Gwyneth Jansen

MEDICAL SCHOOL:
Barts and the London School of Medicine and Dentistry, Queen Mary University of London

LOCATION OF ELECTIVE:
Kirtipur Hospital, Kathmandu, Nepal & Lalgadh Leprosy Hospital, Lalgadh, Nepal

My elective was an eye-opening experience into resource-limited healthcare. Kirtipur Hospital was a specialised urban centre with interesting complex cases, for example, extensive hand traumas that required intricate surgeries to preserve and restore function. The varied caseload plus excellent teaching gave me a better understanding of surgical decision making. Lalgadh Leprosy hospital showcased surgical care in a rural setting more limited by resources and expertise. I saw how surgery fit into the holistic care of patients with leprosy and the value of community programs to prevent surgical readmissions. Overall, my experiences have made me more determined to become a surgeon.

The team at Kirtipur Hospital with me near the back.

Trauma and Neurosurgery in Argentina

PREISKEL PRIZE:

Felix Jozsa

MEDICAL SCHOOL:
King's College London

LOCATION OF ELECTIVE:
Hospital Centro de Salud Zenon J Santillan, San Miguel de Tucuman, Argentina

My elective in the city of Tucuman in northwest Argentina was based in trauma and neurosurgery. It was a fantastic opportunity to be involved in managing a range of emergencies from firearm injuries to scorpion bites. I was also able to see a variety of elective neurosurgical cases. These were often late presenting due to limited access to healthcare in some rural communities, posing challenges for the team to optimally treat these patients. Working as part of the team at Centro de Salud was an inspiring experience from which I learnt a huge amount, and living in Argentina is fantastic!

Felix assisting in neurosurgery.

Neurosurgery elective in a unit serving 33 million people in Pakistan

PREISKEL PRIZE:

Nida Thamenah Kalyal

MEDICAL SCHOOL:
GKT School of Medical Education at King's College London

LOCATION OF ELECTIVE:
Pakistan Institute of Medical Sciences, Islamabad, Pakistan

Nida (centre) with house officers after a 30-hour call.

I arranged an elective in neurosurgery as this is what I hope to specialise in and this experience has only increased my enthusiasm for it. Being based in a busy neurosurgical unit helped me to develop my confidence in clinical skills, including intubation and suturing when managing trauma patients. Assisting in both elective and emergency surgeries allowed me to greatly improve my surgical skills. I left the unit inspired by both the doctors who work with limited resources and high patient volume, as well as the patients, who despite facing difficult diagnoses, had a very positive outlook on life.

Nida with local children during a visit to the villages.

Surgery in the developing world – A Cambodian affair

PREISKEL PRIZE:

Farhaan Khan

MEDICAL SCHOOL:
University of Cambridge

LOCATION OF ELECTIVE:
The Children's Surgical Centre, Phnom Penh, Cambodia

Farhaan (middle) assisting in surgical theatres.

Visiting an non-governmental organisation (NGO) centre providing rehabilitation surgery to poor, disabled Cambodians was an awe-inspiring experience. There, I shadowed several surgical teams: T&O, Plastics, ENT and Ophthalmology. I observed strange pathologies rare to the UK, scrubbed into surgery as an active member of the team, saw pre-op and post-op workup of patients and witnessed the innovative ways that outcomes would be met in a limited resource setting. A key focus at CSC is training and education of local surgeons, which I contributed to by delivering oral presentations and generating posters. The lessons learned, and memories made will surely remain unforgettable.

The physiotherapy area where post-op patients would undergo rehabilitation.

Surgical Elective in South Africa

PREISKEL PRIZE:

Jack Kingdon

MEDICAL SCHOOL:
King's College London

LOCATION OF ELECTIVE:
Tygerberg Hospital and Groote Schuur Hospital, Cape Town, South Africa

In January I travelled to Cape Town for a 10 week placement to experience surgery and perioperative care. My elective consisted of two parts, trauma surgery at Tygerberg Hospital followed by orthopaedic surgery at Groote Schuur Hospital.

It was a unique opportunity to experience acute surgical and trauma presentations, and their management, in a volume and nature not seen in the UK. I assisted in more than 15 knee replacements, experience and exposure that is difficult to come by as a medical student in the UK (image 1).

A surgical theatre in Cape Town, with Jack assisting in a total knee replacement.

I also volunteered with 'SHAWCO', an organisation who provide primary-care services to townships otherwise without access to healthcare (image 2).

An evening SHAWCO clinic in a township on the outskirts of Cape Town.

I could not recommend Cape Town highly enough to any future medical students interested in surgery and trauma medicine, it was an experience of a lifetime!

OxPLORE (Oxford Paediatrics Linking Oncology Research with Electives), Bhutan

PPK PRIZE:

Roshni Mansfield

MEDICAL SCHOOL:
University of Oxford Medical School

LOCATION OF ELECTIVE:
Thimphu, Bhutan

I was attached to paediatrics and paediatric surgery while in Thimphu, Bhutan. I attended jam-packed surgical clinics, where I saw a wide range of common paediatric surgical conditions and scrubbed in for several operations, including VP shunt placement and hernia repairs.

I taught anatomy to students at the school of traditional medicine and helped to obtain funding for the transfer of textbooks from Oxford to the future medical school in Thimphu. My research collaboration (gathering data on the management and outcomes of paediatric solid tumours) with Dr Karma Sherub is now underway.

I would fully recommend this elective to others!

Roshni (left) with Dr Karma Sherub and a fellow medical student in theatre at the end of a long day.

General Surgery in Zanzibar

ELECTIVE PRIZE:

Claire Perrott

MEDICAL SCHOOL:
University of Southampton

LOCATION OF ELECTIVE:
Mnazi Mmoja Government Hospital, Stone Town, Zanzibar, Tanzania

My elective in general surgery was my first insight into surgical care provision in the developing world and it was a truly eye-opening experience. Working alongside the surgeons increased my understanding of the challenges faced when diagnosing using only clinical presentation and when medical supplies are very sparse. It was fascinating to learn

Claire (second from the left) outside the hospital with fellow medical students.

Claire in theatre with the local team carrying out a laparotomy.

how local culture had an impact on the community's health, where patients would often use herbal remedies before presenting to the hospital, resulting in more advanced pathologies. This was an inspiring experience and I hope to use the skills I have gained in surgical volunteering projects in the future.

Orthopaedic surgical elective exploring the epidemiology of fractures in Labasa Hospital, Fiji

ELECTIVE PRIZE:

James Wadkin

MEDICAL SCHOOL:
University of Birmingham

SITE OR LOCATION OF ELECTIVE:
Labasa Hospital, Labasa, Fiji

Head of Surgery Dr Maloni Bulanauca (centre), with James (on his right) and elective students from the UK.

I spent my elective period with the surgical team in Labasa Hospital in Fiji. I assisted in theatre and in the ward management of surgical patients alongside completing a research project exploring the epidemiology of fractures seen in the hospital. This opportunity enabled me to compare surgical practice in the developing world to that of the UK while also enhancing my clinical skills and learning from the skills of local doctors practising in a different healthcare setting. Completing my research project allowed me to contribute to the local healthcare system alongside learning about local cultural beliefs and attitudes to health.

James performing an ultrasound scan on a patient in the hospital.

RCS Senior Clinical Fellowship Scheme

The Senior Clinical Fellowship Scheme allows trainees approaching the end of their specialist surgical training to undertake a practical Fellowship lasting between 6-18 months to focus on expert training in a surgical sub-specialty. This scheme is jointly approved by the RCS and appropriate Surgical Specialty Associations and Fellows often undertake research and audit activities in addition to receiving a high quality training experience.

Whilst most of the approved Fellowship programmes are in the UK, there is one in Ireland and two in India.

The table below list the successful candidates for 2017-18.

Certificates awarded in July 2017

Fellow	Fellowship	Supervisor	Date of Fellowship
Arion Kapinas	Nottingham Advanced Spinal Surgery Fellowship – Nottingham University Hospitals NHS Trust	Mr Khalid Salem	November 2013 – May 2016
Sam Ford	Birmingham Sarcoma Fellowship MARSU – University Hospital Birmingham Foundation Trust	Mr David Gourevitch	October 2014 – January 2016
Philip Holland	South Tees Fellowship in Shoulder and Elbow Surgery – South Tees Hospitals NHS Foundation Trust	Professor Amar Rangan	August 2015 – August 2016
Joseph Hardwicke	Coventry Microsurgery and Major Trauma Fellowship – University Hospitals Coventry and Warwickshire NHS Trust	Miss Joanna Skillman	May 2016 – February 2017
Ayman Sorial	Harrogate Hip Fellowship – Harrogate District Foundation Trust	Mr Jon Conroy	August 2015 – August 2016
Jeffrey Lim	Swansea Advanced Pelvic Oncology Fellowship – ABMU (Abertawe Bro Morgannwg University) Healthboard	Mr Martyn Evans	October 2016 – March 2017

Certificates awarded in October 2017

Andrew Kinshuck	North Thames Laryngology Fellowship – Charing Cross Hospital, London	Mr Guri Sandhu	May 2016 – April 2017
Divyank Bansal	Clinical Fellowship in Laryngology – Deenanath Mangeshkar Hospital, Pune, India	Dr Sachin Gandhi	July 2016 – June 2017
Rohan Bidaye	Clinical Fellowship in Laryngology – Deenanath Mangeshkar Hospital, Pune, India	Dr Sachin Gandhi	July 2016 – June 2017
Marcin Czyz	Nottingham Advanced Spinal Surgery Fellowship – Nottingham University Hospitals NHS Trust	Mr Khalid Salem	October 2014 – August 2016
Rohin Mittal	Advanced Laparoscopic Colorectal Fellowship – Colchester General Hospital and ICENI Centre	Mr Tan Arulampalam	March 2015 – July 2016
Rohin Mittal	Advanced Laparoscopic Colorectal Fellowship – Colchester General Hospital and ICENI Centre	Mr Tan Arulampalam	March 2015 – July 2016
Hazem Hassouna	Sports Hip and Knee, Lower Limb Arthroplasty Senior Orthopaedic Fellowship – Ashford and St Peter's NHS Foundation Trust	Mr Paul Trikha	January – July 2015

Fellow	Fellowship	Supervisor	Date of Fellowship
Adam Williams	Oxford Pituitary and Anterior Skullbase Senior Clinical Fellowship – Oxford University Hospitals NHS Trust	Mr Simon Cudlip	August 2016 – August 2017
Andrew Tarnaris	Oxford Fellow of Functional Neurosurgery – Oxford University Hospitals NHS Trust	Mr Alexander Green	February 2016 – January 2017
Ricardo Aveledo	Fellowship in Shoulder and Elbow Surgery – South Tees Hospitals NHS Foundation Trust	Professor Amar Rangan	August 2016 – August 2017
George Mirmilstein	Hertfordshire and South Bedfordshire Urological Cancer Centre – The Lister Urological Robotic Fellow	Mr James Adshead	August 2016 – August 2017
Deb Roy	Salford Royal Neurosurgery Spine Fellowship – Salford Royal Foundation Trust	Mr Kuriakose Joshi George	October 2016 – July 2017
Jonathan Shapey	King's College Hospital Neurosurgical Endoscopic Pituitary and Skull Base Fellowship – King's College Hospital NHS Foundation Trust, London	Mr Sinan Barazi	August 2016 – August 2017
Konstantinos Barkas	King's College Hospital Neurosurgical Endoscopic Pituitary and Skull Base Fellowship – King's College Hospital NHS Foundation Trust, London	Mr Sinan Barazi	August 2015 – August 2016
Ali Alavi	Anterior Skull Base Endoscopic Fellowship – Leeds Teaching Hospitals	Mr Nicholas Phillips	August 2016 – August 2017

Certificates awarded in January 2018

Brian Parsons	The Guy's Bladder Cancer Fellowship Programme – Guy's and St Thomas' NHS Foundation Trust	Mr Muhammad Shamim Khan	September 2016 – August 2017
Chris Mann	Laparoscopic Colorectal Fellowship – St James's University Hospital, Leeds	Professor Peter Sagar	February – August 2017
Angelo Pichierri	Surgical Neuro-oncology Fellowship – North Bristol NHS Trust	Mr Venkat Iyer	August 2016 – August 2017
Evangelos Tsialogiannis	Sports Hip and Knee, Lower Limb Arthroplasty Senior Orthopaedic Fellowship – Ashford and St Peter's NHS Foundation Trust	Mr Paul Trikha	September 2016 – July 2017
Waleed Al-Khyatt	Chichester St Richard's Bariatric Fellowship – Western Sussex Hospitals NHS Foundation Trust	Mr Will Hawkins	October 2016 – October 2017
Andrew Harris	Newcastle Female and Functional Urology Fellowship – Freeman Hospital, Newcastle	Mr Christopher Harding	September 2016 – September 2017
Muhammad Mansha	Nottingham Advanced Spinal Surgery Fellowship, Nottingham University Hospitals NHS Trust	Mr Khalid Salem	August 2016 – August 2017
Aarti Kalyanaraman	The Peterborough Laparoscopic Colorectal Fellowship Programme – North West Anglia NHS Foundation Trust	Mr Rohit Makhija	October 2016 – September 2017
Oluwafikayo Fayeye	Neuro-oncological Surgery Fellowship – Leeds Teaching Hospitals NHS Trust	Mr Simon Thomson	September 2016 – August 2017

Certificates awarded in April 2018

Catherine Rennie	Rhinology Fellowship – Charing Cross Hospital and RNTNEH	Mr Hesham Saleh	November 2016 – November 2017
Julian Cahill	Wessex Neuro-oncology Fellowship – University Hospital Southampton NHS Foundation Trust	Mr Paul Grundy	January – December 2017
Dimitrios Pournaras	Post-CCT Fellowship in Bariatric and Benign UGI Surgery – Musgrove Park Hospital	Mr Richard Welbourn	October 2016 – October 2017
Ian Anderson	King's Neurovascular Fellowship – King's College Hospital NHS Foundation Trust	Mr Christos Tolias	February 2017 – January 2018
Kenneth Muscat	Advanced Head and Neck Surgical Oncology Fellowship – Guy's and St Thomas' Hospital NHS Foundation Trust	Mr Ricard Simo	July 2016 – June 2017
Prem Thomas Jacob	Beaumont Hospital Renal and Pancreas Transplantation Fellowship – Beaumont Hospital, Dublin	Ms Dilly Little	July 2015 – July 2016

The neurovascular structure-adjacent frozen section examination (NeuroSAFE) approach to nerve sparing in robot-assisted laparoscopic radical prostatectomy in a British setting – a prospective observational comparative study

Dr George Mirmilstein

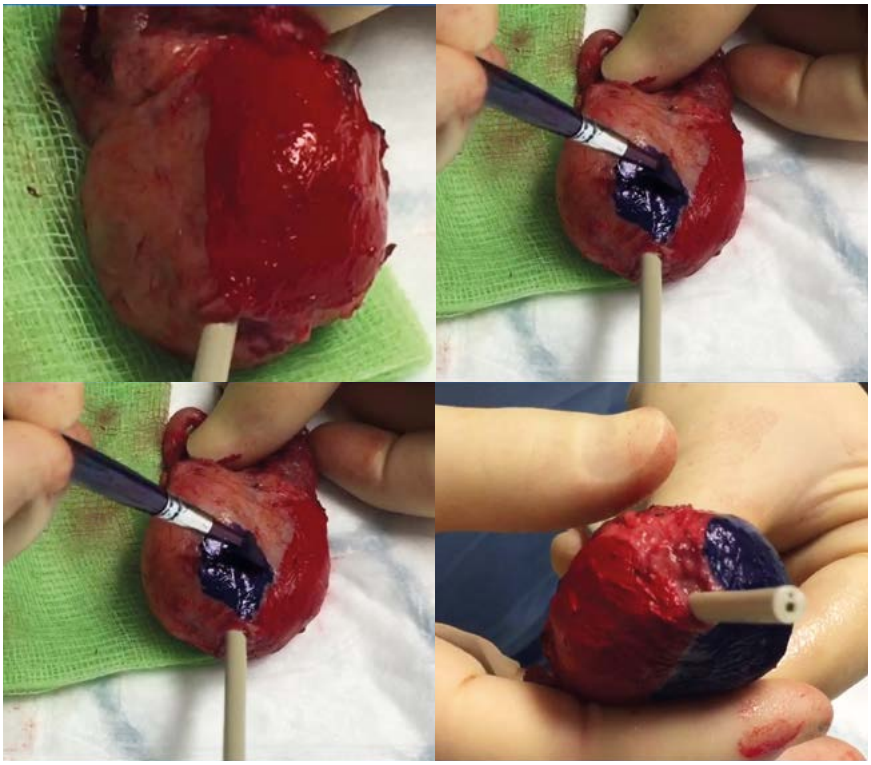
SUPERVISOR:
Mr Jim Adshead,
Lead Robotic Surgeon

SITE OF WORK:
Hertfordshire and Bedfordshire Urological Cancer Centre at the Lister Hospital, Stevenage, Hertfordshire, UK

PUBLICATIONS:
Mirmilstein G, Rai BP, Gbolahan O *et al.* The neurovascular structure-adjacent frozen-section examination (NeuroSAFE) approach to nerve sparing in robot-assisted laparoscopic radical prostatectomy in a British setting – a prospective observational comparative study. *BJU Int* 2018; **121**: 854–862

PRESENTATIONS:
External validation of the neurovascular structure-adjacent frozen section examination (NeuroSAFE) approach to nerve sparing in robot-assisted laparoscopic radical prostatectomy in a British setting – a prospective observational comparative study. Presented at: BAUS Annual Scientific Meeting; 2017; Glasgow

Radical prostatectomy for the management of localised prostate cancer carries a significant risk of erectile dysfunction. This is risk is reduced when a nerve sparing technique is utilised. Despite improved understanding and technical advancements, nerve sparing prostatectomy has often been compromised in an attempt to ensure a negative surgical margin. Current strategies including imaging, preoperative DRE and biopsy information are poor in predicting neurovascular bundle cancer involvement. Intraoperative frozen section analysis of the excised prostate specimen during a radical prostatectomy has the potential to address these issues. The Martini-Klinik in Hamburg, Germany developed the intraoperative neurovascular structure-adjacent frozen section examination (NeuroSAFE) technique, which was adopted at the Lister Hospital, Stevenage in 2012. We found a significant improvement in outcomes of our nerve sparing prostatectomies including being able to offer nerve spares for higher risk patients, reduce positive surgical margin rates and improve potency at 12 months.



Painting prostate after removal in preparation for frozen section.

A comparison of the minimum data sets for primary shoulder arthroplasty between national shoulder arthroplasty registries. Is international harmonization feasible?

Ricardo Aveledo

SUPERVISOR:
Professor Amar Rangan

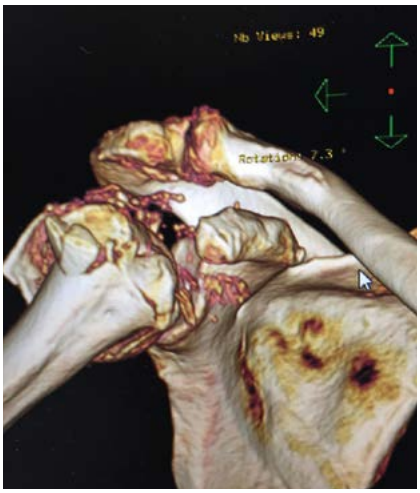
SITE OF WORK:
James Cook University Hospital, South Tees Hospitals NHS Foundation Trust

PRESENTATIONS:
A Comparison of the Minimum Data Sets for Primary Shoulder Arthroplasty Between National Shoulder Arthroplasty Registries. Is International Harmonisation Feasible? Presented at: 27th Congress of the European Society for Surgery of the Shoulder and the Elbow; September 2017; Berlin

PRIZES:
Awarded 'Special Mention', 18th EFORT (European Federation of National Associations of Orthopaedics and Traumatology) Congress 2017, Vienna, Austria

Ricardo Aveledo and colleagues just after accomplishing a shoulder replacement surgery.

The use of shoulder arthroplasty is rising in tandem with an ageing population, and its association with arthritis, rotator cuff tears and fragility fractures. Joint registries have been implemented to monitor the performance of implants used for arthroplasty, the effectiveness of different types of surgical techniques, the incidence of complications, and to analyse risk factors. The aims of this study were to identify the common components of the minimum data set of current national shoulder arthroplasty registries in the world that could be pooled for analysis. There were nine national shoulder arthroplasty registries reporting a total of 97,388 primary shoulder replacements up to November 2016. This research concluded that as numbers within individual registries are relatively small, international collaboration would harness the global strength of knowledge and experience in shoulder replacement. Several similarities were identified between the current national registries that could become unified with only minor changes by a few registries, highlighting the potential feasibility of MDS harmonisation.



A 3D Computed Tomography Scan that shows a complex proximal humeral fracture that required shoulder replacement.

Celebrating 25 years of the RCS Research Fellowship Scheme

2018 marked the 25th anniversary of the RCS Research Fellowship Scheme and since its inception in 1993, more than 750 fellowships have been awarded worth more than £40 million.

The milestone was celebrated in November with a dinner attended by a small number of current and past research fellows, surgeons who have helped to advance the scheme through donations, assessment and support, and several generous benefactors who have remained loyal to the scheme throughout its history.

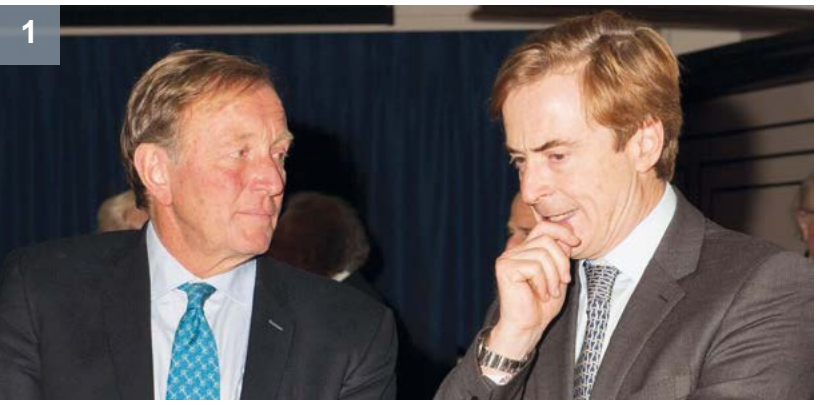
A series of short talks gave a glimpse into what has been achieved so far.

The research fellows spoke of the advances they have made in areas such as transplantation, cancer treatment, military surgery and 3D bioprinting of human cartilage.

RCS President, Professor Derek Alderson, said: 'Research is the area of activity that we as a college prize more than anything else in order to improve outcomes for our patients, and it will always be so.'

Surgeon Commander, Catherine Powell, described her research fellowship as a springboard that changed the course of her career. She said: 'I cannot thank you enough for introducing me to the world of research and the doors that it opens.'

Professor Alderson told the donors and supporters in attendance: 'Without your support, the scheme would not be flourishing in the way it currently does.' 'I hope that in 25 years' time people are meeting here once again and I hope that we continue to progress and to develop surgery and that research will remain the jewel in this college's crown.'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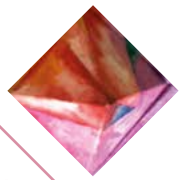
1. Prof Neil Mortensen & Mr Julian Soper
2. Mr John Smith & Mr Dan Tindall
3. Mr Michael Whitehouse & Prof Ashley Blom
4. Prof Tim Rockall, Prof Mark Emberton, Mr Christian Brown & Prof Caroline Moore
5. Prof Rory Rickard, Surg Cdr Catherine Powell & Major Robert Staruch
6. Prof Peter Hutchinson & Miss Ellie Edlmann
7. Current and past presidents
8. Mr Andrew Reed and Miss Leela Kapila
9. Miss Yasmin Jauhari, Mr Robin Street, Mr Richard Street, Dame Sue Street and Miss Amy Garner
10. Mr Paul Copsey, Mr Richard Ross and Lt Col Linda Orr
11. Mr Andrew Schache
12. Mr Piers Boshier

Hunterian, Arris & Gale, Arnott and Lionel Colledge Memorial Lectures 2017/18

Hunterian	Mr Adel Helmy, Addenbrooke's Hospital, Cambridge *Neuroinflammation in Traumatic Brain Injury* SBNS, Oxford, 29 March 2017
Hunterian	Professor Anan Shetty, Spire Alexandra Hospital, Kent *Cost effective cell and matrix based, minimally invasive, single stage, chondroregenrative technique developed with validated vertical translation methodology* Royal College of Surgeons, London, 28 April 2017
Hunterian	Miss Anita Balakrishnan, Addenbrooke's Hospital, Cambridge *Micro-managing the gut: A new role for microRNAs in intestinal adaption* ASGBI meeting, Glasgow, 4 May 2017
Arris and Gale	Professor Munther Aldoori, Royal College of Surgeons, London *The Significance of Pharyngeal Veins During Carotid Endarterectomy: Description of an Anatomical Triangle* Yorkshire Vascular Forum, Leeds, 19 June 2017
Hunterian	Mr Jonothan Earnshaw, Gloucestershire Royal Hospital *Aortic aneurysm screenings: from evidence, through implementation to optimization* NHS AAA Screening Programme, Birmingham, 27 June 2017
The Lionel Colledge Memorial Lecture	Professor Trevor McGill, Boston Children's Hospital, Boston *Paediatric ENT: a Transatlantic View* ENT UK, London, 8 September 2017
Arris and Gale	Mr Peter Rhys Evans, The Royal Marsden Hospital, London *Aural Exostoses (Surfer's Ear) Provide Vital Fossil Evidence of an Aquatic Phase in Man's Early Evolution* ENT UK, London, 8 September 2017
Hunterian	Mr Matthew Costa, University of Warwick and University of Oxford *Multicentre clinical trials: what's the point?* BOA 2017, Birmingham, 19 September 2017
Arnott	Professor Peter Anderson, Women's and Children's Hospital, Adelaide *Cranial Sutures – just joints of bones?* SBNS, Liverpool, 21 September 2017
Hunterian	Mr Amit Roshan, Cambridge University Hospitals NHS Trust *Deciphering keratinocyte behaviour real time in human skin: Implications for wound healing and skin cancer* BAPRAS winter scientific meeting, London, 29 November 2017
Hunterian	Mr Ranjeet Jeevan, Clinical Effectiveness Unit, RCS *Reconstructive utilisation and outcomes following mastectomy surgery in women with breast cancer treated in England* BAPRAS winter scientific meeting, London, 1 December 2017



Hunterian	Mr Bijan Modarai, St Thomas' Hospital, London *Novel diagnostic and therapeutic strategies for critical limb ischaemia* SARS 2018, Nottingham, 10 January 2018
Hunterian	Mr Christopher Johnston, University of Edinburgh *TGM – a novel helminth parasite-derived immunomodulatory molecule that ameliorates allograft rejection* ASGBI, Liverpool, 10 May 2018
Hunterian	Mr Adam Frampton, *microRNAs as biomarkers for detecting and stratifying Pancreatic Cancer* ASGBI, Liverpool, 10 May 2018
Hunterian	Mr Mustafa Zakkar, *NF-kB classical pathway activation by acute high shear stress and vascular inflammation: Implication for vein graft failure* SCTS, Glasgow, 20 March 2018
The Lionel Colledge Memorial Lecture	Professor Anil D'Cruz from Tata Memorial in Bombay *How to conceive, execute and deliver on clinical trials* BACO, Manchester, Wednesday 4 July 2018

Professor Munther Aldoori receiving his Arris & Gale medal from Mr Ian Eardley.

Fundraising in Focus

Make a donation or leave a legacy to surgical research

Our surgical research programme relies on voluntary income that has been gifted through donations, legacies and grants.

Surgical research is vital to allow new techniques and technologies to be developed, evaluated and implemented into clinical practice as quickly and safely as possible.

Help us to expand the horizons of surgery. We need your support to continue funding innovative ideas and new treatments for better patient outcomes. With every small success, you pave the way for the next breakthrough.

If you would like to make a donation or discuss a legacy, please contact the RCS's Development Office on 0207 869 6086, or by email at fundraising@rcseng.ac.uk.

Grants are not restricted to research fellowships and we would be 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.

Martyn Coomer, Head of the Research Department, taking inspiration from thought provoking works by Christabel MacGreevy.

Funding Partnerships:

- Addenbrooke's Charitable Trust
- Association of Breast Surgery
- Association of Coloproctology of Great Britain and Ireland
- Association of Upper Gastrointestinal Surgeons of Great Britain and Ireland
- Ballinger Charitable Trust
- Bowel Disease Research Foundation
- Bowel Cancer UK
- Breast Cancer Now
- British Association of Paediatric Surgeons
- British Association of Plastic, Reconstructive and Aesthetic Surgeons
- British Association of Surgical Oncology
- British Association of Urological Surgeons
- British Orthopaedic Association
- British Society of Endovascular Therapy
- British Society of Surgery of the Hand
- Cancer Research UK
- Circulation Foundation
- Colledge Family Fund
- Crohn's and Colitis UK
- Dinwoodie Charitable Company
- Dunhill Medical Trust
- EIDO Healthcare
- Edwin George Robinson Charitable Trust
- Enid Linder Foundation
- ENT UK
- Frances and Augustus Newman Foundation
- Freemasons Fund for Surgical Research
- George Drexler Foundation
- Golden Bottle Trust
- Heartburn Cancer UK
- Henry Lumley Charitable Trust
- Mary Kinross Charitable Trust
- McKinsey
- National Joint Registry
- Orthopaedic Research UK
- Pancreatic Cancer UK
- Pancreatic Cancer Research Fund
- Philip King Charitable Settlement
- Prostate Cancer UK
- Reuben Foundation
- Rosetrees Trust

- Sahlgrenska Hospital, Gothenburg
- Saven Research and Development Programme
- Shears Foundation
- Society for Cardiothoracic Surgery in Great Britain and Ireland
- Vascular Surgical Society of Great Britain and Ireland
- Virginia Mason Hospital, Seattle
- Wellington Hospital
- Welton Foundation
- Wyndham Charitable Trust

Endowments, restricted and legacy funds:

- Anderson Reid Fund
- Annie Julia Speight Legacy
- Barlow Research Fellowship
- Bernhard Baron Fund
- Black Legacy
- Blond McIndoe Fund
- Buckston Browne Gift
- Burghard Bequest
- Carol Rummey Legacy
- Cicely Fay Simpson Legacy
- Dennis F Clark Legacy
- Doris K King Legacy
- Dr Shapurji H Modi Memorial ENT Research Fund
- Edward Lumley Fund
- Eleanor M Heslop Legacy
- Ethicon Foundation Fund
- Fletcher Legacy
- Gwendoline Shrimpton Legacy
- Harold Bridges Bequest
- Harry S Morton Fund
- John L Williams Legacy
- Laming Evans Research Fund
- Lea Thomas Fund
- Lillian May Coleman Legacy
- Miss D M H H Cothay Legacy
- Osman Hill Collection and Research
- Parks Visitorship
- Patricia Constance Curry Legacy
- Philip and Lydia Cutner Legacies
- PKK and SK Families
- Preiskel Prize Fund
- Renee Recheal Liebesny Legacy
- Rex and Jean Lawrie
- Shirley M Kanaar Legacy
- Sir Arthur Sims Fund
- Sorab (Soli) Jamshed Lam Legacy
- Starritt Legacy
- Stefan and Anna Galeski
- Tudor Edwards Fellowship
- Vandervell Research Fund
- The Worshipful Company of Barbers
- The Worshipful Company of Cutlers

Dame Sue Street and Richard Street of the Galeski family with Yasmin Jauhari, who they supported on expedition up the Amazon to deliver a hospital boat.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Picture Gallery

1. Research Fellows Miss Zita Jessop & Miss Jemma Bhoday being quizzed at the Bbraun annual business conference
2. Prof Alderson & Prof Morton experiencing 3D technology at Bbraun HQ in Tuttlingen, Germany
3. Mr Bjorn Saven with some of the surgeons he has supported over the past year
4. Prof Andy Carr & Prof Sir Peter Morris at presidential visit to Oxford
5. From L to R Mr Nigel Mercer, Mr Nick Ross & Sir Michael Rawlins members of the oversight committee for surgical trials
6. Mr David Nott demonstrating on an anatomical model at his Foundation's open evening
7. Lord Ribeiro, staunch supporter, at House of Lords
8. Buckston Browne dinner 2018
9. Prof Sir Peter Morris & Prof Derek Alderson at presidential visit to Oxford
10. Mrs Lyn Shears being admitted to the Court of Patrons
11. Dr Richard Reznick about to receive his honorary fellowship in Liverpool
12. Dr Luis Hernandez Miguelena and Mr Bill Thomas in Kigali, Rwanda
13. Mr Aneel Bhangu, Mr Dmitri Nepogodiev and Prof Dion Morton outside the Skills Centre in Kigali, Rwanda
14. Prof Takeshi Sano from Cancer Institute Hospital Tokyo receiving his honorary fellowship with Mrs Sano at Fishmonger's Hall, London
15. Prof Bijan Modarai receiving his Hunterian Professorship medal at SARS 2018

Royal College of Surgeons
ADVANCING SURGICAL CARE

The lives of tens of thousands of people throughout the UK are saved and transformed daily by surgery. Almost five million surgical patients are admitted to hospital every year in England alone for procedures ranging from straightforward gallbladder removal and joint replacements, to complex transplants and emergency trauma repair.

The Royal College of Surgeons of England safeguards the experience, treatment and outcomes of the UK's surgical patients through the ongoing state-of-the-art training of our surgeons and pioneering research.

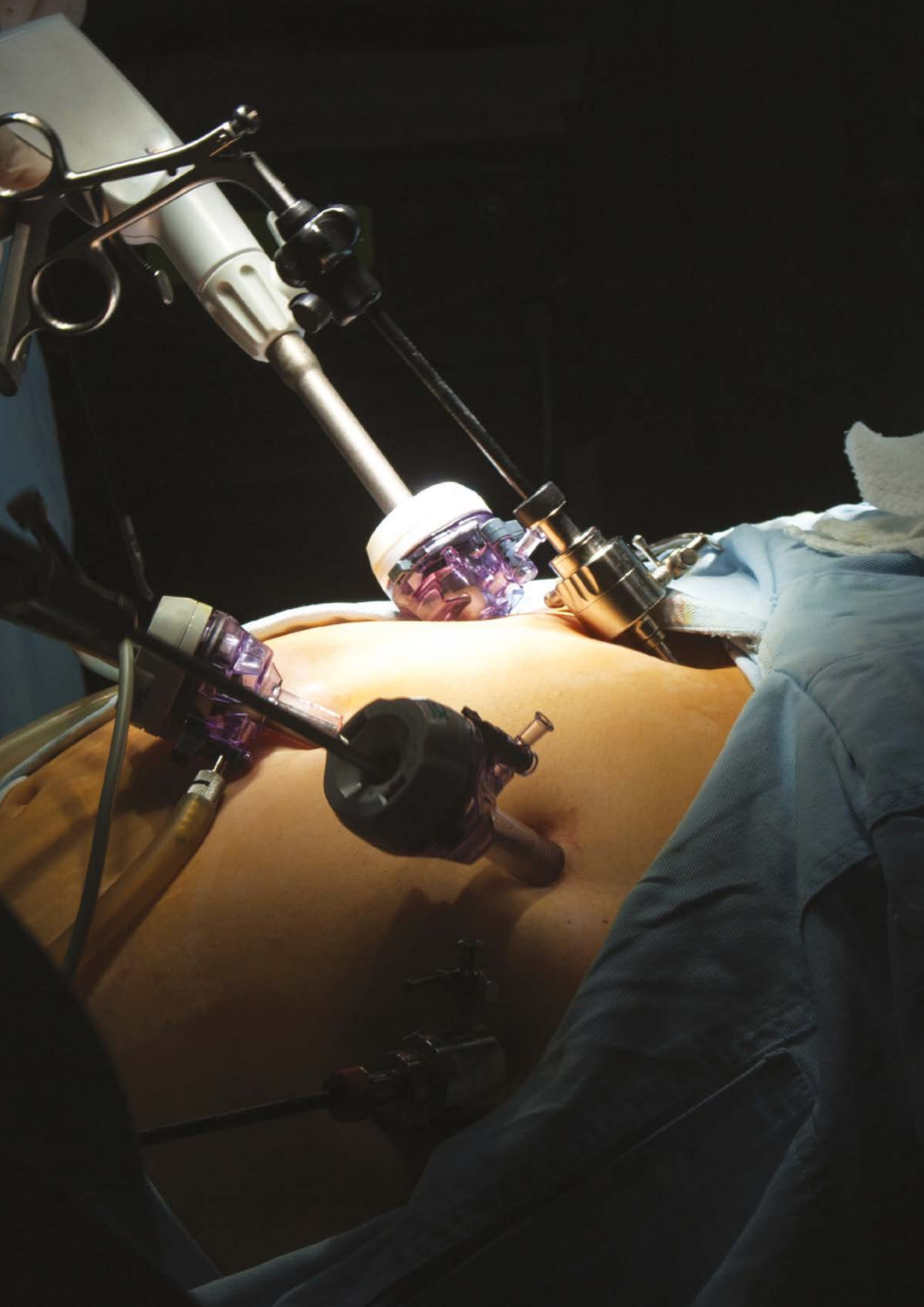
Research at the RCS relies almost exclusively on legacies, gifts and donations. We need your help if this work is to continue and flourish. Making a will is a significant personal responsibility and the people and causes you remember in your will are a positive recognition of all that is important to you.

We understand that the welfare and concern for your family and friends comes first. Just as a will brings security to those closest to you, a legacy to surgical research at the Royal College of Surgeons will play a crucial role in maintaining and improving the surgical care for patients.

Please contact us to find out how leaving a gift to the RCS in your will would advance our work.

t 020 7869 6086 e fundraising@rcseng.ac.uk
w www.rcseng.ac.uk/fundraising #surgerysaveslives

Registered charity no 212808



The Butterfly Effect. © Stephen J Brooks 2018
Watercolour, pastel and pencil on formed paper.

From a series of paintings based on the uncertainty of order and the predictability of the chaotic state and how they both look different through a change of direction and view.

For information on donating
visit **www.rcseng.ac.uk/donate**
email **fundraising@rcseng.ac.uk**
or call **020 7869 6086**

To contact the research department
email **research@rcseng.ac.uk**
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