



The Royal College of Surgeons of England



*Investing in research to improve patient welfare*

# **Surgical Research Report 2005–2007**

# Contents

- 1 Introduction to Research Report 2005–2007
- 2 In Pictures
- 4 Background and Funding of the Research Fellowship Scheme
- 7 The Audit of the Research Fellowship Scheme
- 8 The Future of Surgical Research in the Age of Modernising Medical Careers
- 9 Joint Fellowship Contributions
- 10 A Journey through South America
- 11 Research Fellows' Reports
- 39 Pump primer Reports
- 43 Preiskel Prize Reports
- 46 Hunterian, Arris & Gale and Arnott Lectures delivered in 2004 and 2005
- 47 Travelling Fellowship Awards
- 48 Fundraising in Focus
- 50 Clinical Effectiveness Unit
- 51 The Centre for Evidence in Transplantation
- 52 The National Collaboration Centre for Acute Care

# Introduction to Research Report 2005–2007

## Professor Anthony Mundy Director of the Research Department



**I mentioned in the previous report that the 10th anniversary of the research fellowships was approaching. We had an excellent day when a large number of our previous fellows showed posters of the work they had done and told us what had happened to them and their research since then. There were well attended workshops on a variety of research topics later on in the day interspersed with plenary presentations by some of our more eminent academic surgeons.**

The research fellowships are the centrepiece of the research department's activity and for this we need support. We have received a substantial boost to our funds from the Dunhill Medical Trust, which is funding five two-year research fellowships into diseases of ageing and surgical treatments for elderly people. We are also delighted to receive new support from several sources including funds towards a three year research fellowship from the Henry Smith's Charity. The Elkin Charitable Foundation, the David and Frederick Barclay Foundation and an estate in the Midlands have all made new funds available. We remain extremely grateful to the many other charitable trust individuals and companies who continue to provide solid support to the research fellowship scheme. We simply could not continue our research activities without both the funds and the encouragement of our funding partners including the Frances and Augustus Newman Foundation, the Enid Linder Foundation, the Freemasons, Cazenove & Co, the Shears Charitable Trust, the Vandervell Foundation, the Kirby Laing Foundation and the Rosetrees Trust.

All our courses continue to receive excellent feedback and large numbers of delegates. 'Clinical Research Methods for Surgeons/ Finding the Evidence', 'Statistical Methods for Surgeons' and 'Developing and Using Clinical Guidelines' have been popular for a number of years now and we plan to continue them.

Our activities depend not just on sponsors and funding but also on my colleagues on the research board and the other numerous surgeons and scientists who give up their time to be assessors for all of the various projects. Thanks in particular go to Martyn Coomer and his team, who coordinate all of the various activities.

Finally, a word about three individuals. Congratulations to Lancashire-born Kathryn D Anderson who has been appointed as the first female president of the American College of Surgeons. Kathryn was surgeon-in-chief at the Children's Hospital, Los Angeles, and has been supervising Wai-Yee Li, one of the College research fellows who is undertaking a two year research exchange.

Sir John Vane, the Worcestershire born pharmacologist, who won the Nobel Prize for his work in unlocking the mysteries of blood clotting and the life-saving aspects of aspirin, died in 2005. Sir John's discoveries led to new treatments for heart and blood vessel disease and to the development and introduction of Ace inhibitors from which tens of thousands of people around the world have since benefited. We remember him for the immense amount of work he undertook during the 18 years when he was senior lecturer in pharmacology at the College when laboratories were on site. It was from here that he moved to the Wellcome Foundation to become their group research and development director.



Mr Ian Donovan, Mr Bernie Ribeiro, Professor Sir John Temple and Mr Hugh Phillips at a College Roadshow hosted by the West Midlands Surgical Society at Russells Hall Hospital, Dudley.

We are all devastated by the death of Mr Hugh Phillips who died in office as president of our College in June 2005. Hugh worked for 30 years as an orthopaedic surgeon at Norfolk and Norwich Hospital where he became an expert on joint replacement having replaced more than 6,000 during his career. He pioneered new types of joint replacement, such as ankle joints and hip resurfacing, which, though commonplace today, were highly innovative in the late 1970s and early 1980s.

Hugh was a much admired and inspirational trainer. He was the principal author of four books about multiple joint replacement, published many papers in learned journals and was respected by colleagues for his sound judgement and the way he made patients' needs a priority. He was a tremendous advocate of the research fellowship Scheme and was constantly enquiring about the diverse range of research work the College supports. His humour, leadership, support and compassion will be much missed by colleagues and staff at the College.



Wai-Yee Li, joint RCS/American College of Surgeons research fellow, Kathryn Anderson (supervisor) and Craig Duncan (President's Advisor) at Miss Li's presentation at the ACS meeting, New Orleans.

# In Pictures

1. Professor John Neoptolemos and Professor Martin Birchall, two Liverpool stalwarts of the research fellowship scheme.
2. Research fellow, Mary Clare Miller (right), with other members of the British Society of Surgery for the Hand at a research away day in Birmingham.
- 3/4. Mr David Jones undertaking a ward round at Beijing Jishuitan Hospital, China.
5. Miss Laura Hancock, Mr Chris Peach and Mr Jonathan Trickett with Chairman Miss Asha Senapati outside Weymouth Pavilion presenting to the Dorset Women's Institute AGM.
6. Dr Ruth Hall, CMO for Wales, talking to the Welsh Board in Swansea.
7. Mr Dermot O'Riordan with members of Colne Yacht Club at a research evening during their Festival of Sail.
8. Freemason research fellow Mr Jonathan Trickett (centre), with Lord Cadogan (left) and Mr Gavin Purser (right) at a presentation to the trustees of the Grand Lodge 250th anniversary fund.
9. Mr Hywel Jones, from the College development office learning about neurosurgical research from Mr Peter Hutchinson and Professor John Pickard at Addenbrooke's Hospital, Cambridge.
10. Martyn Coomer (second left) and former ENT research fellow, Euan Murugasu (centre) with colleagues at the Institute of Bioengineering and Nanotechnology, Singapore.
11. Professor Valerie Lund and Mr Michael Kuo preceding his lecture at the RSM Bicentenary Meeting on Molecular Biology and the Otorhinolaryngologist.
12. Chairman Mr Brian Rees, and fellow members of the Welsh Board.





3



4



8



9



12



13



16



19



20



23



24

- 13. The presidential team outside the new medical school building at Glan Clwyd Hospital, Rhyl, hosted by Mr Richard Morgan, surgical tutor.
- 14. (l-r) Anne Kolbe (President, Royal Australasian College of Surgeons), talking to Miss Sanja Besarovic, Mr Nigel Clay and research fellows Miss Nicola Smith and Miss Nicola Eardley at a reception hosted by the State Governor, Darwin, Australia.
- 15. Mr Andrew Raftery with trainee at the Presidential Roadshow, Russells Hall Hospital, Dudley.
- 16. Miss Mayoni Gooneratne and Mr Nigel Hall talking to Freemasons at a research evening in Surbiton, Surrey.
- 17. Mr Peter Cox (centre) and colleagues meeting Mr Hugh Phillips (second right) and Miss Leela Kapila (right) at West Cornwall Hospital, Penzance.
- 18. Professor Sir Peter Morris and Mr Hugh Phillips learning about the history of hip replacements from Professor Mike Wroblewski at Wrightington Hospital.
- 19. Professor Tony Mundy chairing a question and answer session during the surgical research evening at the College.
- 20. Mr Hugh Phillips with Ms Christine Swabey (chairman of the trust) and Ms Carol Heatley (CEO) at Kingston Hospital, during a presidential visit.
- 21. Mr Phillips and Miss Kapila meeting local MP, Mr Andrew George, and patient representatives at West Cornwall Hospital.
- 22. Mr Henk Giele, Pump Priming winner on the Saving Faces workshop in the Hunterian Museum.
- 23. Mr Gordon Carlson, Professor Martin Birchall and Mr Simon Chaplin at a demonstration of 3D surgery by QinetiQ.
- 24. Mr Ian Loftus, chairman, and host, Mr Bruce Perry at the Freemasons evening in Surbiton.

# Background and Funding of the Research Fellowship Scheme

## Background

Surgical research has played a crucial part in many of the operations that we all take for granted today. It is worth taking a moment to see how far things have progressed. Procedures such as keyhole surgery, hip replacements and coronary artery bypasses would have been unthinkable 40 years ago, yet thousands of these operations take place each week and prolong and improve the lives of millions of people in this country each year. Research is the foundation of good surgical practice and forms an essential source of knowledge for the surgeon, the surgical profession and medicine as a whole.

*Each fellowship costs £45,000 and the College invests £1 million a year to support the scheme.*

The College has played a vital part in the promotion of surgical research throughout its history. From the end of the Second World War until the early 1990s, basic surgical research took place at its Lincoln's Inn Fields headquarters, with significant results. The research from these laboratories was of the highest national and international distinction, and achieved one Nobel laureate and four Fellows of the Royal Society.



Sian Allen, Newman Foundation research fellow, pictured with trustees, Sir Rodney Sweetnam, Mr John Williams and Lord Rathcavan.

However, by the 1990s, major changes in research techniques led to concern about the viability of research taking place away from a university or clinical environment. It was no longer possible to maintain state-of-the-art research in a relatively small institute. A decision was, therefore, made to conduct a major review of the College's research activities and this led to the eventual closure of the College's laboratories and to refocus supporting surgical research in a clinical setting at either a hospital or university.

## The research fellowship scheme

Following this review it was decided that the best vehicle to support and encourage surgical research was to establish a surgical research fellowship scheme. It was hoped that such a scheme would attract young surgeons into an academic surgical career, while contributing to the understanding and treatment of surgical conditions. The scheme was launched in 1993, with the appointment of Professor Sir Peter Morris as chairman of a new research board to implement the scheme.

## Objectives of the scheme

From the outset the following objectives were enshrined into the scheme:

- to contribute to improvements in patient care and recovery;
- to assess new techniques introduced to surgery;
- to look at the causes of surgical conditions and how to treat them and;
- to stimulate a commitment to life-long learning in surgical practice and technique, and understanding of research methodology .

The scheme introduces a solid academic element into the clinical training of surgeons and broadens their knowledge and experience. The overarching aim of the scheme, against which each stage of the assessment process is measured, is to ensure that it has clinical relevance so that future generations of patients will continue to benefit from advances and improvements in surgical knowledge and technique.

Each fellowship endows a full-time research programme lasting from one to three years, which is supervised in a UK department of surgery but occasionally overseas. The fellowships are broad-ranging, from cardiothoracic surgery to surgery of the hand and from transplantation biology to epidemiology. A number of research projects are linked to innovative programmes, which are designed to resolve long-standing clinical problems, while others are self-contained or form part of a larger research programme.

The research fellowship scheme is respected within the surgical community – so much so that it is now being duplicated by other institutions. Over 400 research awards have been made since 1993, at a cost of over £14 million. The College receives far more applications than it can support each year and can fund only one in five of the proposed projects.

*Over 400 research awards, including surgical research fellowships, joint fellowships and RCS/MRC fellowships, have been awarded since 1993, with around 25 currently awarded each year.*



Mr Bernard Cazenove, following his admission as a member of the College's Court of Patrons.

### **The application and assessment process**

Surgeons apply to the College each year with a detailed plan of the research they wish to undertake, supported by the applicant's head of department and proposed research supervisor. All applications are rigorously assessed by a panel of leading experts. These assessors are independent of the candidate's hospital and university, and ensure that the science, surgeon, supervision and facilities are of the highest standard and that the proposed work will be a valid, beneficial and original piece of research, with benefits to patients. Donors can be assured that all fellowships have been thoroughly assessed through an independent peer-review process.

Short-listed candidates are invited to present a poster of their proposed work at the College, where they are interviewed by a panel of leading surgeons before the final awards are made. These interviews

are aimed at ascertaining the applicants' knowledge of the project and their role and aims in undertaking the research. Although regarded as challenging and tough for the applicants, the interviews help the College decide on the very best applications to support. About 25–30 fellowships are awarded in any one year, depending on the funds available. Sadly, the College cannot fund all short-listed candidates, and a proportion of high-calibre projects remains unfunded each year.



Mrs Anna Galeski and daughter, Dame Sue Street, with Nicola Eardley and Nicola Smith, the first recipients of the Stefan Galeski travelling fellowship.



Sophie Noblett, Shears northern research fellow, with her supervisor, Mr Alan Horgan (left), and her fellowship sponsors, Mr Trevor and Mrs Lyn Shears.

### **Other awards**

As well as one-year fellowships, the College has three-year research training fellowships, jointly funded by the Medical Research Council, which have been a huge success. In addition, 67 pump priming awards have been awarded to assist newly appointed consultant surgeons establish themselves in their chosen field of research. The grants are used to purchase equipment and secure technical support to enhance the surgeon's research resources before he or she applies to larger grant giving bodies. The College is also fortunate to offer a limited number of international joint fellowships, lectureships, travel and other awards. The opportunity to travel abroad to develop knowledge and skills in surgery in other countries is something that is hugely beneficial to the clinical practice of those surgeons and trainees who are granted awards such as the Lionel Colledge Memorial Travelling Fellowship, the Ethicon Foundation Awards, the Ronald Raven Barbers' Award, the Stefan Galeski Travelling Fellowship and the Preiskel Prize.

*70% of the costs of the scheme are fundraised from charitable trusts, companies, legacies and individuals.*

### **Monitoring the effectiveness of the scheme**

The College has developed an effective monitoring system for each fellowship and offers training and mentoring sessions to the researchers. Research fellows report to the College at regular intervals, to ensure that their research is progressing satisfactorily and that their work is meeting its objectives.

The College's research board has, through its national and international links, authoritative knowledge of surgical trends and centres of excellence in surgical research and can, therefore, guide funding to high-quality projects that will have a high impact.



## Benefits to donors of supporting the research fellowship scheme

The research fellowship scheme would certainly not have achieved so much were it not for the generous and constant support of our many charitable donors, whose backing has been crucial to the success of this scheme. There is very little statutory funding for surgical research and so the College's own resources are extremely limited because they are called upon to meet the increasing demands put on our education and training programmes. Put simply, the number of research fellowships we award is entirely dependent on external sponsorship.

Our research fellowships are funded through legacies, endowments, charitable trusts, companies and individuals. Our designated research funds are decreasing rapidly and in our work to maintain funding for the fellowship scheme we face an increasingly difficult task. Surgical research is becoming more expensive as new, sophisticated equipment is developed, and salary and support costs rise.

Those who support the research fellowship scheme do so for a number of reasons. Many funders tell us they particularly appreciate the strict assessment process that each fellowship application undergoes. They know that the research will be relevant to patients at the bedside and that only the best projects are supported.

Another benefit to a donor is that most fellowships last for one year only. This enables donors to review the progress of a fellowship at the end of the year before committing to contributing towards another fellowship. The wide range of fellowships available enables donors to select projects that meet their own interests or criteria.

The College organises regular events for donors to meet research fellows. Donors also receive regular feedback on the progress of the research they are supporting.

The College is convinced that its one-year research fellowship has a high impact on patient care through improved knowledge and technique. Securing new funds to initiate a research project is extremely difficult and the College's one-year research fellowship scheme has enabled researchers to collect the initial data and evidence necessary to apply to larger national funding bodies. Many fellows are also inspired to continue their research following a fellowship, thereby strengthening the country's academic base and providing the academic surgeons of the future.

Results from the research fellowships are disseminated widely through publications and presentations at national and international level, a number of which have in no small part contributed to greater understanding of diseases and have enhanced treatments for patients and improved surgical techniques. Even if the research fellow does not continue his or her research following the one year of study, the baton is handed on to another researcher within the academic department in which the research took place, thereby ensuring continuity and progression of the research question.

*Four out of five high-quality applications cannot be supported due to lack of funds.*

## How donors fund the scheme

Charitable donors choose to support the research fellowship scheme in a variety of ways. Some of them support a complete piece of research, often linked to a specific illness or disease area, such as orthopaedics, cancer and paediatric surgery. Others contribute to the scheme in general.

Each research fellowship costs in the region of £45,000, which includes salary, national insurance and other contributions, as well as an additional amount for consumables. Funding for each one can come from either one or several sources. Monies can be directed to a specific surgical, geographical or disease area and the College is delighted to name fellowships eponymously. All support is acknowledged in presentations by the research fellows and progress reports, and presentations are the key methods of reporting back to donors on how their money has been spent.

**We hope that the kind support of our donors will continue. Ultimately, it is patients who will continue to benefit from breakthroughs in surgical care that will improve the quality of their lives and, indeed, save lives from such terrible diseases as cancer, brain tumours and heart disease.**

**For further information on supporting the College's research fellowship scheme please call the development office on 020 7869 6082 or email [development@rcseng.ac.uk](mailto:development@rcseng.ac.uk)**

More information on our programme of surgical research evenings and donors can be found on page 48.



# The Audit of the Research Fellowship Scheme

As the tenth anniversary of the research fellowship scheme approached, the research board of the College decided to evaluate its impact on surgical research and patient care. In order to do this, a questionnaire was sent to 260 research fellows, appointed between 1993 and 2003. There was a response rate of 92%.

## Key results of the audit questionnaire

### Type of research

About three-quarters of respondents conducted purely laboratory-based research. More than half (60.2%) of these laboratory-based projects included cell biology, molecular biology or genetics. Just over a fifth of the respondents conducted patient-based clinical projects, surgical audit or epidemiological research. The remainder of the respondents (5.1%) were involved in other types of projects, such as surgical skills assessment and engineering.

### Impact on surgical research

Almost all of the research fellows had been awarded a higher degree or were working towards it. In just over a quarter of these, this degree was a PhD or equivalent. Two-thirds of fellows had published the results of their fellowship project in peer-reviewed journals. The median number of peer-reviewed publications based on the fellowship project of the fellows was 2 (range 0–21). This number was slightly higher for those who had received their fellowship before 1997 (median 3, range 0–12).

Nearly half of the research fellows received subsequent funding to continue research following the completion of their fellowship. This funding was obtained from numerous organisations including the Medical Research Council and the Wellcome Trust (11.1%), other UK-wide funding bodies (46.3%), local funding bodies (34.3%) and other sources of funding such as 'industry' (8.3%).

The total number of peer-reviewed publications based on work from the fellowship projects was 531.

We found that approximately half of the research fellows wished to pursue a career in academic surgery.

One-third of those who reached consultant status had an academic component to their post. This suggests that the scheme fosters the development of a core of surgeons with an interest in, and experience, of surgical research. This is a significant finding given that it has been recognised that there is a dearth of surgeons who affiliate themselves with surgical research. For instance, the Society of Academic and Research Surgeons in the UK only has about 300 practising consultant surgeons in its membership, which is a relatively low number considering the total number of about 6,000 surgical consultants currently working in the UK.

### Impact on patient care

Most of the respondents commented that their ability to apply research evidence in clinical situations has improved and this would be of benefit to the care of patients. Many of the research projects were handed over to other research fellows to continue and a direct impact on surgical care has occurred in several cases, through the development of enhanced or pioneering diagnosis and treatment, as a result of obtaining a research fellowship.

The audit concluded, in the ten years since its introduction, the research fellowship scheme seems to have achieved its aims. Firstly, it has successfully supported many trainee surgeons in the initial phase of their research career. Secondly, it has helped surgical research in general by creating a platform to apply successfully for further funding from national funding bodies and by increasing the pool of surgeons with an academic interest. Lastly, the research fellowship scheme has had an impact on patient care through increased understanding of surgical conditions, development of new treatment and by promoting an evidence-based culture among surgeons.

Results from the questionnaire audit of the research fellowship scheme were accepted for publication by the *Journal of the American College of Surgeons*.

# The Future of Surgical Research in the Age of Modernising Medical Careers

## Professor Anthony Mundy

Many surgeons are attracted by a career in academic surgery when they undertake a year or two of surgical research during their training and decide to devote their careers to academic surgery. Some surgeons lose interest in their research when a national training number (NTN), ie the securing of a post in higher surgical training following basic training, has been obtained. This can be a waste of limited resources which could otherwise be made available to those who truly wish to pursue research. It is accepted however, that even if they do not pursue surgical research in their careers, the experience gained during their time as research fellows helps to propel surgeons in their chosen specialty and has a direct benefit to a surgeon's skills.



Professor Alan Crockard explaining where research fits into MMC.

Modernising Medical Careers (MMC), part of the current NHS reforms in training, aims to improve patient care by delivering modernised and focused career structure for doctors through a major reform of postgraduate medical education. It

aims to develop demonstrably competent doctors who are skilled at communicating and working as effective members of a team. Because training and education are central to the work of doctors and their role in delivering patient care, MMC will also bring about significant changes to career structures, providing qualified staff who are able to meet the needs of patients.

MMC is set to change the way that training is delivered and this is likely to have an impact on the timing of research by interested trainees during their clinical training. It is expected that all trainees will be taught critical appraisal skills so that they can read a scientific paper and evaluate it. It is also expected that at some stage during their training, these skills will be tested by some method of formal assessment. For those wishing to learn more about the scientific basis of surgery or their surgical specialty in particular and more about research methodology, an MSc, part-time or full-time, might be appropriate. For others, a period of time out to develop their intellectual skills and thereby improve their clinical practice may be appropriate in clinical research or technology or medical management even. All the roles of a surgeon, as currently conceived, including those of a communicator, educator and manager, are as important in developing the complete surgeon as the more obvious surgical skills.



(l-r) Mr Richard Canter, deputy director of the RCS education department talking to Mr Chris Russell and Professor William Burr, the postgraduate dean of Yorkshire at an MMC meeting in Barnsley.

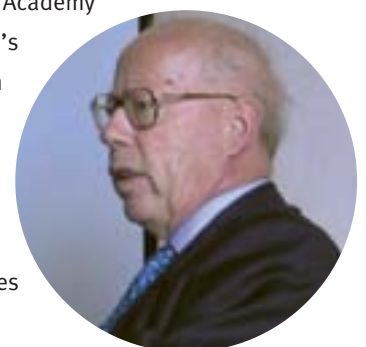
For those who truly wish to do research with a view to an MD or PhD, it is expected that they will take time out from training after their first or second year of clinical training and will then return to their training but hopefully to continue their academic career by means of a clinical scientist post and attachment to the teaching institution where they obtained their higher degree so that a future post as a senior lecturer in that department may allow them to continue their academic interest and career.

In short, I expect that surgical research will continue in the MMC era but at a later phase during training than has recently been the case. It used to be that research was mainly done in the period between registrar and senior registrar training in the pre-Calman era. Since the introduction of Calman training, the timing has gone back to the period after SHO training to add to a surgeon's competencies before obtaining an NTN.

In the future, I think, there will be many drivers to motivate trainees to do research, including a true desire to pursue academic surgery as a career, as surgeons become more experienced in their surgical specialty and competent in some research techniques before making an informed choice about undertaking research. This will ensure that, in the main, those who are committed to a career in academic surgery will be those who will undertake surgical research.

Ultimately, it will be the patients who will continue to benefit from these changes in surgical research.

The College is highly supportive of continuing surgical research as are other bodies, such as the Academy of Medical Sciences. The College's commitment to surgical research fellowships remains as strong as ever, and the research fellowship scheme and the clinical scientists scheme for more advanced academic trainees will continue unchanged.



Mr Gordon Williams, chairman of JCHST, explaining the new curriculum to surgeons in Taunton.

# Joint Fellowship Contributions



Ms Claire Large (Dunhill Medical Trust) outside the College with Mr Paul Cathcart (Dunhill Medical Trust research fellow) and Mr Martyn Coomer.

## The Dunhill Medical Trust

Over the past ten years, the Dunhill Medical Trust (DMT) has been pleased to support a number of surgical research fellowships awarded by The Royal College of Surgeons. The trust

has been particularly keen to promote

opportunities for women as trainee surgeons and the resulting fellowships have proved to be some of the most successful and productive of the Dunhill fellowship programme.

Building on the success of the earlier fellowships, a pilot group of five joint RCS/DMT fellowships were awarded in December 2004. In line with the DMT's priority areas, the focus of these fellowships is research into diseases of ageing and surgical treatments for older people.

The fellowships, which are based in London, Sheffield, Derby and Newcastle upon Tyne, have been awarded to study a range of important issues, including the influence of age on decision making for surgical treatment of urological cancer and understanding the neurophysiological basis of sacral nerve stimulation. The DMT is delighted to have been able to provide this support in partnership with the College and looks forward to the results of this exciting development.

## The Donald Currie research fellowship supported by the *ia* and the RCS

When Donald Currie, the executive committee chairman of *ia*, died suddenly in 2001 a research fund was set up to receive donations given in his memory. Donald had suffered from Crohn's disease and it was decided that the money should be spent on a Crohn's disease project that would be seen as relevant to our members. We decided that our first approach would be to the Royal College of Surgeons because of our links through our president, Professor Norman Williams MS FRCS FMedSci, and our successful research partnerships with the College in the past. As the recipient of the fellowship, Miss Laura Hancock is looking at genetic differences between Crohn's disease and ulcerative colitis in people with inflammatory bowel disease with the aim of being able to use genotyping to decide on the most suitable operation for people with severe colitis.

**Anne Demick, National Secretary**

***ia* (The Ileostomy and Internal Pouch Support Group)**

## The RCS/Healing Foundation research fellowship

The Healing Foundation was established to champion the cause of people living with disfigurement and visible loss of function by

funding research into pioneering surgical and psychological techniques.



The interviewing panel for the joint research fellowship with the Healing Foundation.

Burn injury remains one of the most prevalent causes of serious visible

disfigurement, particularly among children. We share the Royal College of Surgeons' goal of supporting research of the highest quality in this area.

**Brendan Eley, Chief Executive, The Healing Foundation**

## Joint RCS/The National Kidney Research Fund fellowship

The National Kidney Research Fund is delighted to work in partnership with the Royal College of Surgeons this year to support a joint two-year fellowship for clinical research related to kidney disease and the urinary tract. The partnership will maximise the strengths and experiences of organisations, pooling resources and achieving greater efficiency through this joint initiative in a highly topical and relevant study area.

This joint fellowship will ultimately ensure patient benefit by enhancing the knowledge base and developing the research skills of a recently qualified surgeon who will be involved in future clinical research.

**Elaine Davies, Grants Manager**

**The National Kidney Research Fund**



Joint RCS / The National Kidney Research Fund fellowship interviewing panel.

# A Journey through South America

Two years ago, Charlie and I crossed the equator with our bikes, a tent and not a lot of luggage after a cycle ride lasting nine months. We had started 8,135 miles away in Ushuaia, the most southerly town in South America, and had cycled up through the Andes via Argentina, Chile, Bolivia, Peru and Ecuador.

It all began one wet Sunday afternoon in Hampshire when we first dreamed of the trip and scoured the atlas for suitable routes. A desire to visit the southern hemisphere and our love of mountains meant that the Andes was an obvious choice.

We decided immediately to make this an opportunity to raise some money for the Stroke Association, following the recent death of a friend in his early 40s. We were keen that the money was used for a specific purpose and, with my contacts at the Royal College of Surgeons, the idea of funding a research fellowship was quickly developed. Months of fundraising followed; friends, colleagues, neighbours and complete strangers alike were tremendous in their generosity and support, with the result that we raised a total of £23,500.

South America is an extraordinary continent. There is such a diversity of scenery, weather, people and culture that it is impossible not to be constantly amazed. Everything in Patagonia is on a huge scale, with endless skies over towering mountains and mile upon mile of uninhabited land, and yet that is only a small part of Argentina. Chile is a long, thin ribbon of land stretching from the desert to the frozen glaciers of the south. Land-locked Bolivia proudly boasts a navy and the largest salt lake in the world. We were snowed on in Peru despite being in the Tropics, while Ecuador is hot and humid until one reaches the equator which is as dry as a bone.



Bethan overlooking Lago Titicaca.



Charlie with Maria and family in the Bolivian altiplano.

The common trait, however, is the warmth, generosity and hospitality of its people. Invariably, we met kindness, interest and offers of help, regardless of the poverty of the person or their surroundings. We were fed lamb stew in remote farms in Patagonia, given a bucket of strawberries by a passing driver in Chile and invited into homes throughout.

It was truly a fantastic nine months, with difficult days and good ones, but never for one moment predictable. We continue to relive our adventures and those wonderful memories of llamas, condors and a certain black dog that followed us faithfully for days through the Bolivian desert!

Special thanks to Lynn, Sophie and Martyn at the College, for IT wizardry, having faith and making it all happen.

**Bethan Bennett-Lloyd**  
[www.spokesforstrokes.com](http://www.spokesforstrokes.com)

Bethan and Charlie Bennett-Lloyd with the Flores family from Salta, Argentina, at a reunion in the research department.



## Research Fellows' Reports

- 12 Miss Nicola Barnes
- 13 Mr John Beatty
- 14 Mr Andrew Davies
- 15 Mr Joel Dunning
- 16 Mr Richard Edwards
- 17 Mr John Evans
- 18 Mr Paul Gilmore
- 19 Mr Simon Hobbs
- 20 Miss Rachel Kimber
- 21 Mrs Ruth McKee (née Edwards)
- 22 Mr Hammad Malik
- 23 Miss Caroline Moore
- 24 Mr Paul Nix
- 25 Dr Sophie Noblett
- 26 Mr Martin Nuttall
- 27 Miss Joy Odili
- 28 Miss Evelyn Ong
- 29 Mr Marc Pacifico
- 30 Mr Nilay Patel
- 31 Miss Nishat Rahman
- 32 Mr Majid Shabbir
- 33 Miss Nicola Smith
- 34 Mr Oparaku Umez-Eronini
- 35 Mr Chandrakumar Vimalachandran
- 36 Mr Jonathan Waite
- 37 Mr Stuart Winter
- 38 Mr Gregory Wynn

# The role and mechanism action of cyclooxygenase-2 in ductal carcinoma *in situ*

## Miss Nicola Barnes



### Site of Study

The Paterson Institute for Cancer Research, Manchester and Department of Academic Surgery, South Manchester University Hospital

### Supervisor

Professor Nigel Bundred

### Publications

*Clinical Cancer Research* 2005; **11**(6): 2163–2168

*British Journal of Surgery* 2005; **92**(4): 429–434

### Presentations

**27th San Antonio Breast Cancer Symposium**, Texas, December 2004

**4th European Breast Cancer Conference** Hamburg, March 2004



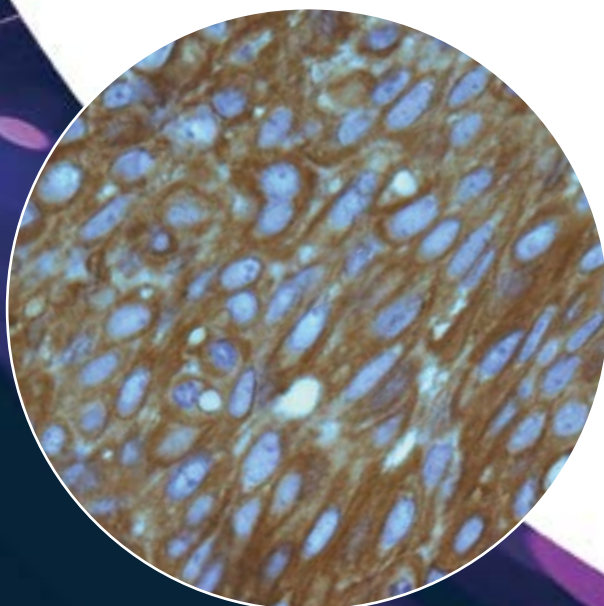
A mammogram showing the white specks of calcification seen in DCIS (arrow).

The first phase of my project looked at predicting recurrence risk in a pre-invasive breast cancer, called ductal carcinoma *in situ* (DCIS); focusing on the cyclooxygenase-2 (COX-2) enzyme. I stained samples of DCIS from patients who, had either recurred or not recurred after surgery, for the presence of a panel of proteins and receptors. Women that recurred had high levels of COX-2 in their tumours and the presence of a growth factor receptor (HER4) predicted women at low risk of recurrence.

*‘Approximately 25% of all screening-detected breast cancers are ductal carcinoma *in situ*.’*

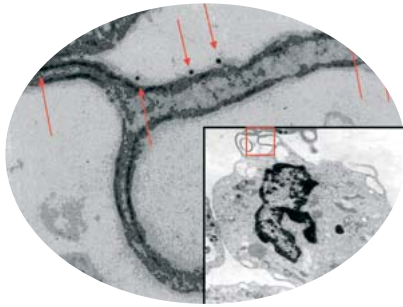
The second phase of my study looked at the effect of blocking the COX-2 enzyme in breast cancer cells. Tumour cells were implanted into mice, which then received treatment with either a drug that inhibited COX-2 (celecoxib) or a control. Tumour size, markers of programmed cell death (apoptosis), proliferation and lymphatic vessel formation were assessed using staining, western blotting and polymerase chain reaction. The experiments were repeated using human DCIS, donated from women undergoing surgery. Tumour cells treated with the COX-2 inhibitor grew significantly less than the controls, a median of 59% less ( $p=0.02$ ), they also showed higher rates of cell death. I was able to identify one of the cellular components, AKT, that was inactivated during treatment. When the experiments were repeated with human DCIS, the same increases in cell death were seen, indicating that the treatment may increase cell death in human tumours. The COX-2 inhibitor also decreased the formation of new lymphatic vessels, and as breast cancers initially spread via the lymphatics, COX-2 inhibitors may be able to reduce tumour spread.

From this project I have identified markers that indicate patients at high and low risk of recurring from DCIS. I have shown that inhibiting COX-2 decreases tumour growth in breast cancer cells by increasing cell death and inhibiting the formation of lymphatic vessels.



A DCIS stained at immunohistochemistry for the COX-2 enzyme (brown).

# To explore the hypothesis that dendritic cell function influences prognosis and therapy in superficial bladder cancer



An electron microscope picture of a dendritic cell in urine. The arrows point to gold labeling of immune receptors used by dendritic cells to present antigen to other immune cells.

Why do live bacteria (BCG), introduced into the bladder, prevent bladder cancer recurrence? Dendritic cells are specialised immune cells that act as gatekeepers to the way our immune system responds to foreign threats such as infection and cancer. It was hypothesised that these cells are present in the blood, urine and tissue of patients with bladder cancer and that their characteristics may reflect patient responses to treatment with BCG.

*‘Bladder cancer is the second most common urological malignancy and live Bacillus Calmette-Guerin (BCG) vaccine the most effective intravesical immunotherapy.’*

Tissue, blood and urine samples from patients with bladder cancer being treated with BCG therapy were collected and analysed using techniques that examine the characteristics and function of individual dendritic cells.

During the research project, dendritic cells were identified in the urine of patients with bladder cancer for the first time. It was established that variability in dendritic cell characteristics and function may reflect changes in immunological activity both in the patients’ circulation and at the site of cancer. Patients who responded to treatment by activating and increasing percentages of dendritic cells seemed to have a better clinical outcome when followed up for recurrent cancer.

By identifying patients who are likely to respond poorly to BCG therapy, alternative treatment strategies can be tried. Favourable characteristics at an immunological level may be manipulated in the future to enhance BCG therapy. It is hoped to build on these techniques to gain further understanding into the complex interaction of the tumour microenvironment and its interaction with dendritic cells.

## Fellowship/Sponsor

Joint RCS/BUF Surgical Research Fellowship

## Mr John Beatty

### Site of Study

Northwick Park and St. Mark’s Hospital, Middlesex

### Further Funding

Ralph Shackman Trust (two years)

### Supervisors

Professor Stella C Knight  
Mr Christopher W Ogden



### Publications

*BJU International* 2004; **94**(9): 1377–1383

### Presentations

**American Urological Association Annual Meeting,**  
San Francisco, May 2004

**British Association of Urological Surgeons Annual Meeting,**  
Manchester, June 2003

### Prize

The Ralph Shackman Trust Grant



A view of superficial bladder cancer through an operating telescope.

# Does metal-on-metal wear debris cause more mutations and more genetic markers of chromosome damage and type IV hypersensitivity than metal-on-plastic wear debris?

## Fellowship/Sponsor

BUPA Surgical Research Fellowship

## Mr Andrew Davies



### Site of Study

Southmead Hospital, Bristol

### Further Funding

Wishbone Trust Pump-priming consumables grant for duration of project

### Supervisor

Dr CP Case

### Publications

*Journal of Bone and Joint Surgery American Volume* 2005; **87-A**: 18-27

*Journal of Bone and Joint Surgery British Volume* 2005; Accepted for publication

### Presentations

**American Academy of Orthopaedic Surgeons**, New Orleans February 2003

**EFORT congress**, Helsinki, June 2003

### Prizes

**Best Poster Hip Section, American Academy of Orthopaedic Surgeons**, New Orleans, February 2003

**Best Paper, International Society for Technology in Arthroplasty**, San Francisco, October 2003

Metal-on-metal joint replacement prostheses have been re-introduced for use in total hip replacements and are being targeted at the youngest patient groups. There is very little information regarding the histological reactions to such implants or the effects of soluble and particulate wear debris products. We studied these aspects by the use of tissues retrieved at revision arthroplasty and exposure of cultured human fibroblasts to synovial fluid from failed implants.

We compared tissues from cobalt chromium metal-on-metal, cobalt chromium-on-polyethylene and titanium-on-polyethylene prostheses. Cultured cells were exposed to synovial fluids and then processed to reveal the extent of DNA damage incurred by that exposure. We found that there was a marked difference in the tissue reaction with metal-on-metal prostheses compared to metal-on-polyethylene prostheses. In particular there was a peri-vascular infiltration with a single cell type (lymphocytes) that has not been described for metal-on-polyethylene implants. This reaction was associated with early implant failure and may represent a new mode of failure for these prostheses that has not been described before.

In the DNA damage assay we found that cobalt chromium prostheses caused more damage than other alloy types and this appeared to be due to a synergistic effect between cobalt and chromium ions. Both of these studies have generated novel and important data, building on what was known for traditional metal-on-polyethylene implants and highlighting the need for more study and understanding of metal-on-metal implants as these are increasingly used in young patients.

We hope to obtain further funding in the Bristol Implant Research Centre to continue this work, particularly to study the immunological issues surrounding orthopaedic implants. This study is fundamentally concerned with investigating the long-term safety and efficacy of joint replacement implants as these are extremely commonly employed and are being used in younger and younger patients.

*'This study is fundamentally concerned with investigating the long-term safety and efficacy of joint replacement implants.'*

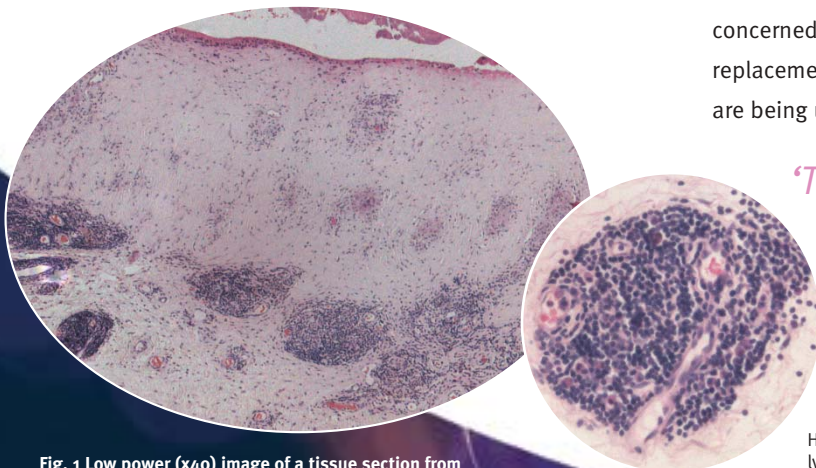


Fig. 1 Low power (x40) image of a tissue section from around a failed metal-on-metal joint replacement to illustrate the layered effect of the tissue reaction.

High power (x200) image of a small area of Fig. 1 to illustrate the lymphocytes making up the peri-vascular collections.



## Mr Joel Dunning

# A multicentre study to develop a set of clinical decision rules for the management of head injury in children



Joel Dunning with head injury patient about to return home.

### Fellowship/Sponsor

The Enid Linder Foundation Surgical Research Fellowship

Our objective was to study the management of all children presenting to 10 hospitals in the northwest of England over a 2<sup>1</sup>/<sub>2</sub>-year period. We sought to assess current clinical practice and derive a novel clinical decision rule to treat these patients better. We instituted a detailed proforma for the assessment of all children attending the Emergency Department. All these children were then followed up and their outcomes determined.

Over a 2<sup>1</sup>/<sub>2</sub>-year period 22,772 children were entered into the study. 281 patients had a positive CT scan, 137 patients had a neurosurgical operation and 15 patients died. The CHALICE rule was derived that has a sensitivity of 98% and a specificity of 87% for the prediction of significant intracranial pathology and requires a 14% CT scan rate. This was shown to be superior to the guidelines used during the study, superior to the new NICE guidelines for head injury management in children and allows all patients assigned as low risk to be discharged without an overnight admission for observation.

*‘We have developed a new clinical guideline that would eliminate the lack of adherence to current guidelines, and better identify those who may require urgent neurosurgery.’*

There are currently no robust guidelines that have been derived or validated in children and this study is thus the world’s largest prospective cohort study into this area and the first to provide robust guidelines, derived in children, for their safe management.

Our rule should significantly reduce the number of children who are admitted overnight to see if they deteriorate and may go on to require urgent neurosurgery, by appropriately recommending a CT scan in high-risk patients and allowing safe discharge for low-risk patients. Furthermore, after a negative CT scan, patients will be safe to go home rather than suffering an anxious night away from their family in hospital just in order to verify that they do not have a serious head injury.

### Site of Study

Manchester Royal Infirmary

### Further Funding

The Child Brain Injury Trust  
The Dickinson Trust

### Supervisors

Professor K Mackway-Jones  
Dr Fiona Lecky



Mr Dunning teaching resuscitation at a College event hosted by the Manchester Literary and Philosophy Society.

### Publications

*Archives of Disease in Childhood* 2004; **89**(8): 763–767  
*Archives of Disease in Childhood* 2004; **89**(7): 653–659

### Presentations

**International Conference in Emergency Medicine**,  
Cairns, June 2004

**Faculty of Accident and Emergency Medicine National Conference**, Leeds, Nov 2004

### Prize

**Professor Rod Little Prize for the best research project in emergency medicine in the UK in 2004**, FAEM Conference, 2004

## Mr Richard Edwards

# Strategies for the prevention of shunt-dependent communicating hydrocephalus

### Fellowship/Sponsor

Mansell Surgical Research Fellowship



#### Site of Study

Frenchay Hospital, Bristol

#### Further Funding

Codman Hydrocephalus Fellowship (one year)

#### Supervisor

Mr Ian K Pople

#### Publications

*Brain Pathology* 2004; **14**: 325–336

*European Journal of Pediatric Surgery* 2003; **13**: S46–47

#### Presentations

American Association of Neurological Surgeons,  
San Diego, April 2003

#### Prizes

Vesalius Award, American Association of Neurological Surgeons, 2003

Prize for Best Presentation, Society of British Neurological Surgeons, Cardiff, 2003

Hydrocephalus is characterised by a build up of cerebrospinal fluid (CSF) within the ventricles (spaces in the centre of the brain) and is usually fatal without treatment. Most patients with hydrocephalus are dependent on CSF shunting to treat their condition. Shunts are valved silicon tubes that divert the excess CSF from the ventricles to another part of the body, where it is absorbed. The choroid plexus, the structure in the ventricles that produces the CSF, frequently grows into the shunt catheters, blocking them. Surgery to revise blocked shunts carries a significant risk.

*‘On average, a baby with hydrocephalus treated with a CSF shunt can expect to undergo surgical revision of the shunt every five years for the rest of their lifetime.’*

A large series of patients with shunted hydrocephalus was studied, some of whom had been previously treated with a ‘keyhole’ technique known as endoscopic choroid plexus coagulation (CPC). It was found that catheter blockage rates were halved in those patients who had undergone previous CPC.

The long-term success of CPC as the sole treatment of post-haemorrhagic hydrocephalus, a condition that affects premature babies, was studied. It was discovered that, although in the short term the hydrocephalus was controlled in 45% of infants, in the long term only 30% remained shunt-independent.

In a separate study, a prospective randomised controlled trial was set up to compare endoscopic treatment with shunting in patients to a normal pressure hydrocephalus, a cause of dementia and walking difficulties in elderly people. Recruitment for this trial is ongoing.

Novel approaches to the treatment of hydrocephalus were also explored. Aquaporin-1, a protein found on the membrane surface of the choroid plexus cells, enables water to pass through the membrane to form the CSF. The amount of this protein on the surface of choroid plexus cells is not reduced in acute hydrocephalus. Drugs targeted at blocking this protein could potentially be used to reduce CSF production and treat hydrocephalus.



Ventriculo-peritoneal shunt insertion by Richard Edwards.

## Mr John Evans

# The role of inflammation on metalloproteinase expression in abdominal aortic aneurysms



Mr Evans in the laboratory in the department of surgery, Leicester Royal Infirmary.

In order to investigate a potential medical treatment for abdominal aortic aneurysms, we targeted two of the major processes involved in aneurysm development. It has previously been shown that the normal aortic wall is broken down under the action of specific enzymes known as matrix metalloproteinases (MMPs) and that this breakdown is accompanied by significant inflammation. In laboratory experiments we used tissue cultures of both human aneurysms and aortas from pigs to look at the effects of specific drugs on these two processes. We used a technique known as gel zymography to show the activity of the main MMPs involved and also measured the degree of inflammation.

We found that, in the laboratory models, a group of drugs known as statins were able to reduce both the activity of MMPs and one of the markers of inflammation, suggesting that these drugs may be able to prevent aneurysm expansion. We also went on to examine the short-term effect of these drugs on aortic aneurysms in patients and found that MMP activity was reduced in the aortic wall.

Aortic aneurysms are a silent killer and it is hoped that in the future they will be detected using a simple screening programme. Those patients who are found to have small aneurysms could potentially be treated with statins rather than having to undergo surgery although the long-term benefits of such treatment have yet to be proven.

*‘Between 5% and 10% of men over the age of 65 have a swelling of the body’s main artery, an abdominal aortic aneurysm. These aneurysms are prone to rupture which is a catastrophic event. Currently, the only treatment available involves surgery and we aimed to find a medical treatment to prevent aneurysm growth and rupture.’*

### Fellowship/Sponsor

Joint RCS/BVF Surgical Research Fellowship

### Site of Study

Leicester Royal Infirmary

### Supervisors

Professor Matthew Thompson  
Professor Janet Powell



### Publications

*British Journal of Surgery* 2002; **89**: 1323

*British Journal of Surgery* 2002; **89**: 529–531

### Presentations

**Vascular Surgical Society Meeting**, Brighton, November 2001

**Society of Academic and Research Surgery Annual Conference**, Leeds, January 2003

### Prize

**Best Scientific Paper, Midlands Vascular Society**, Nottingham, March 2002



Mr Evans undertaking a vascular procedure at Leicester Royal Infirmary.

# Isolation and characterisation of the stem cell phenotype in benign prostatic hyperplasia and prostate cancer

## Mr Paul Gilmore



### Site of Study

Cancer Research-UK Paterson Institute,  
Christie Hospital, Manchester

### Further Funding

The British Urological Foundation  
(one year)

### Supervisor

Mr Noel Clarke

### Publications

*Cytometry Part A* 2003; **54A**: 89–99

### Presentations

European Association of Urology, Vienna, March 2004

Keystone Meeting: From Stem Cells to Therapy,

Colorado, April 2003

### Prize

Lord Lesley Turnberg Prize, Salford Royal Hospitals NHS Trust,

December 2002

*'Prostate cancer is the most common malignancy in men in the UK resulting in approximately 10,200 deaths each year.'*

Aberrant prostate epithelial stem cell have been proposed as the root cause of prostate cancer. Stem cells are believed to reside within the prostate, however, due to a lack of specific markers such cells have been profoundly difficult to isolate. We applied the Hoechst 33342 dye efflux assay to prostate cancers, a technique shown to identify stem cell enriched side populations (sps) by their ability to actively pump out the Hoechst dye.

Isolated SP cells from both benign and malignant prostates were stained for basal, luminal and stem cell markers and viewed with three dimensional microscopy. The SP was shown to consist of small basal cells expressing putative stem-cell markers including p21<sup>Cip1/waf1</sup>, which is believed to control entry into the cell growth cycle. The SP isolated from prostate cancer showed diminished p21<sup>Cip1/waf1</sup> consistent with a loss of cell control leading to uncontrolled cancer cell growth. Single SP cells grown in suspension in Matrigel™ produced ball-like structures, spheroids, consisting of cells of a primitive basal epithelial cells that also formed branching tubules. Taken together, these characteristics show that the SP is highly enriched for stem cells and that there are stem-cell differences between benign and malignant disease. Stem-cell characterisation is ongoing within our group, which is studying the growth characteristics of SP cells to determine whether stem-cell defects are the root cause of prostate cancer and compare the nature of these defects/differences to normal prostate stem cells. The ultimate identification of a cancer stem cell, which may be therapeutically targeted, will increase the capacity for treating the cause of prostate cancer and not just the resultant tumour load.

*Presenting at the 10th anniversary celebrations of the research fellowship scheme not only provided my research with a forum but also gave me an insight into other projects from around the UK. It also gave me the chance to meet and exchange ideas with other junior surgical scientific researchers from around the UK and gain an appreciation of the breadth of ongoing work.*



Paul and supervisor Noel Clarke analysing the results of Hoechst 33342 flow cytometry using benign and malignant prostate epithelial cells.

**Mr Simon Hobbs**

# The effect of exercise on coagulation in patients with intermittent claudication

**Fellowship/Sponsor**

Lea Thomas Surgical Research Fellowship



Intermittent claudication (IC) is exercise-induced pain experienced in the calf muscles of patients with hardening of the arteries supplying their legs. It affects 5% of the middle-aged (55–75 years) UK population and is a common cause of immobility and impairment of quality of life. Although the risk of developing disease severe enough to require amputation is small (1% per year), patients with IC have an annual mortality that is 3–4 times higher than an age and sex-matched non-claudicant population, predominantly due to heart attacks and strokes.

Previous work in our department has shown that subjects with IC have an increased tendency to form blood clots (thrombosis) and we hypothesise that this thrombotic tendency contributes to the high mortality seen in this patient group.

Two treatments that are commonly used to improve walking in IC are supervised exercise and balloon angioplasty. We aimed to assess whether these treatments have any beneficial effect on the thrombotic tendency seen in these patients, in the expectation that if this could be demonstrated then mortality could be reduced.

Preliminary results suggest that balloon angioplasty, but not supervised exercise, significantly reduces this thrombotic tendency, which we believe is due to a reduction in ischaemia-reperfusion injury sustained in the legs during walking.

The implication of these novel data is that despite the attendant costs and risks of balloon angioplasty, this form of treatment may have an increased role in the treatment of IC as it not only increases walking distance but also may have the potential to prevent the serious complications of thrombosis.



Peripheral angiogram demonstration of occlusion of the right common iliac artery supplying the right leg.

## Site of Study

Birmingham Heartlands Hospital, Birmingham

## Further Funding

British Heart Foundation (two years)

## Supervisor

Professor Andrew Bradbury

## Presentations

West Midlands Surgical Society, Dudley, May 2005

Midland Vascular Surgical Society, Shrewsbury, March 2004

## Prize

Registrar Prize winner, West Midland Vascular Surgical Society, Dudley, May 2005

*‘Patients with leg pain due to poor circulation have an increased tendency for clot formation that may explain their high mortality.’*



Subjects participating in a class at the Birmingham Heartlands Hospital.

**Miss Rachel Kimber**

# Pre-clinical assessment of islet isolation from non-heart-beating organ donors

## Fellowship/Sponsor

Enid Linder Foundation Surgical Research Fellowship



The Waters RM3 machine used for pulsatile pancreas perfusion in this study.



## Site of Study

Leicester General Hospital

## Further Funding

Eli Lilly

## Supervisor

Professor Michael Nicholson

## Presentations

Artificial Insulin Delivery, Pancreas and Islet Transplantation Conference, Igls, 2002

Artificial Insulin Delivery, Pancreas and Islet Transplantation Conference, Igls, January 2003

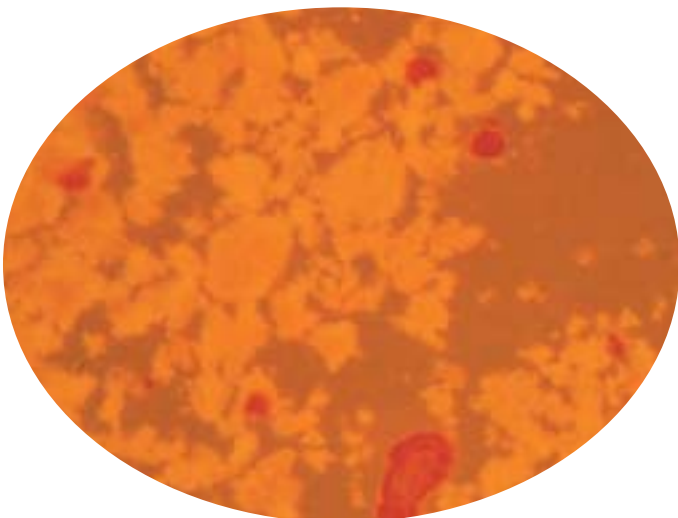
*'More advanced organ preservation techniques are required before non-heart-beating donors can be used for islet transplantation to cure diabetes.'*

Islets are insulin-secreting cells from the pancreas that can be separated from the rest of the pancreas of conventional organ donors (brainstem dead, but heart beating) and transplanted into diabetic patients to cure diabetes. One of the main problems is the shortage of organ donors especially as a diabetic patient often requires islet cells from more than one donor. The aim of this study was to assess the feasibility of using islets from a non-heart-beating donor (a donor who has already suffered a cardiac arrest). This requires advanced organ preservation in order to ameliorate the injury to the islets that occurs after cardiac arrest.

The pancreas was initially subjected to temperature injury similar to that seen with non-heart-beating organ donors. Following this the pancreas was then preserved for four hours using both conventional and two newer organ preservation solutions. In addition, two new techniques were employed to try to reverse the damage to the islets (the two-layer method and pulsatile machine perfusion). The islets obtained were then assessed for quantity and quality.

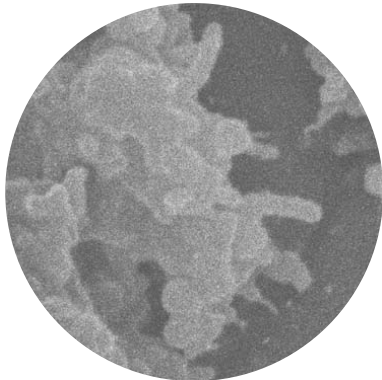
The results showed that the preservation methods studied failed to produce either adequate numbers of islets or islets producing enough insulin for successful transplantation into diabetic patients. However, the project has allowed the development of a test for assessing the quality of a non-heart-beating donor pancreas prior to islet transplantation, and this needs further evaluation

Successful islet transplantation removes the need for insulin therapy in diabetic patients and may reduce the long-term complications of diabetes, such as blindness and kidney failure, by better control of blood glucose levels. Currently organ shortage is a significant problem thus very few patients can receive an islet transplant. If non-heart-beating donors can be used then it would make islet transplantation an option for many more diabetic patients.



Islet cells that have been isolated from a donor pancreas (islets are stained red).

## Bacterial biofilm formation in non-healing wounds



A biofilm formed by bacteria from a chronic venous leg ulcer.

### Mrs Ruth McKee (née Edwards)



#### Site of Study

Wound Healing Research Unit,  
University Hospital of Wales, Cardiff

#### Supervisor

Professor David W Thomas

#### Publications

*Current Opinions in Infectious Diseases* 2004; **17**(2): 91–96  
*The International Journal of Lower Extremity Wounds* 2004;  
**3**(4): 201–208

#### Presentations

**World Union of Wound Healing Societies**, Paris, July 2004  
**Cardiff Institute of Tissue Engineering and Repair, First Annual Conference**, Swansea, September 2004

*‘1–2% of the UK population require treatment for non-healing wounds; infection is a major contributing factor.’*

The problem of non-healing wounds costs the NHS over £1 billion per year, with considerable implications on the quality of life of those affected. All open wounds are colonised with bacteria and low levels of bacteria can actually help stimulate a healing response. However, higher levels of bacteria can delay healing and produce potentially serious infections, including MRSA.

There is growing evidence that in many surgical infections the bacteria live in what is known as a biofilm. Bacterial biofilms are living environments where clusters of bacteria fix to a surface and produce a carbohydrate or ‘slime’ coat to cover themselves. Bacteria within these biofilms are very resistant to many forms of treatment.

This project aimed to investigate whether bacteria in non-healing wounds live in this biofilm state. We demonstrated images of bacteria from chronic wounds growing as biofilms using an electron microscope (see image above). We compared the ability of different types of wound bacteria to take various steps in biofilm formation, such as their ability to stick to different surfaces and their ability to cluster together with other bacteria. We also developed a laboratory model to test the effectiveness of commonly used treatments against wound biofilms to avoid testing on animals or humans (see image below right). We found that flucloxacillin, the antibiotic most commonly used to treat wound infection, has very little effect on bacteria within biofilms. However, iodine, which is often used to clean the skin prior to surgery, and is frequently used in wound dressings, does have a short-term effect on some of the bacteria. This model can be used to develop new treatments against many kinds of biofilms, with implications to improve the management of infections affecting not only wounds but in all other surgical specialities.



Ruth McKee in the laboratory in Cardiff developing a model for biofilm formation.

# Gene expression profiling and candidate gene analysis in loosened aseptic and septic total hip replacements

## Mr Hammad Malik



**Site of Study**

Wrightington Hospital, Lancashire

**Further Funding**

The Wellcome Trust; EFORT (one year)

**Supervisor**

Mr Peter Kay

**Publications**

*Rheumatology* 2004; **43**(Suppl 69): 131

*Journal of Bone and Joint Surgery British Volume* 2005; **87**(Suppl 1): 43

**Presentations**

31st International Conference on Calcified Tissues, Nice, June 2004

British Orthopaedic Research Society Annual Meeting,

Bristol, March 2004

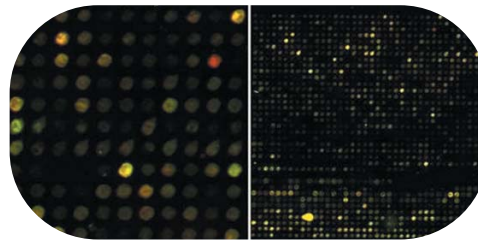
**Prize**

BOA Instructional Course Smith & Nephew Registrar's Research Papers Prize

*'Although mechanical aspects of hip replacement failure are well documented, patient-related factors are poorly understood.'*



X-ray of a failing total hip replacement with gross osteolysis (top right) and demonstrating migration of the implants and osteolytic bone destruction (left).



Scanned microarray chip. Intensity of signal demonstrates the level of gene expression with each locus representing a single gene.

Total hip replacement is one of the most successful procedures in modern medicine. Unfortunately, failure in a certain proportion can be expected. The commonest causes are loosening and infection. Further revision surgery is required to rectify this complication but the results are never as good as the original.

The causes of loosening have not been fully identified. Factors such as the design of implant used and surgical technique can only explain failure some of the time. We believe there may be genetic factors as well, an area that has not been previously researched. Certain molecules have been implicated in previous studies and we have investigated whether natural variation in the genes that code for them is associated with failure. This was achieved by comparing these variations between 100 patients with successful hip replacements that have lasted for more than 10 years and a group of 91 with loosening and group of 70 with infected replacements.

In addition, we have applied the new and powerful technique of microarray gene expression analysis to determine which previously unrecognised gene pathways are involved. The usefulness of this technique lies in the fact that it allows for all the genes that humans possess to be analysed at one time as opposed to previous techniques that only looked at one particular gene in isolation at a time.

We have demonstrated association between a number of candidate genes and failure. The microarray data have suggested a number of new pathological mechanisms that may underlie the process of loosening that have not been considered in the past due to the limitations of earlier techniques.

At present we are applying for further funding to continue and develop this area of research into a major long-term project. The identification of these new pathogenetic mechanisms of total hip replacement failure make new indicators of disease susceptibility and prognosis plus new drug targets distinct possibilities.



# Photodynamic therapy for prostate cancer

## Fellowship/Sponsor

Freemasons Surgical Research Fellowship



Photodynamic therapy uses a photosensitising drug, injected into a vein, to make the whole body sensitive to light. The drug is then activated in the prostate by low-power light from a laser. The activated drug kills tissue around the optical fibre.

The aim of this study was to look at how light is scattered and absorbed in the prostate as this determines the volume of the treatment effect for each light fibre. This information would then be used to help calculate light doses and needle positions for patients having photodynamic therapy as a first treatment for prostate cancer.

Patients having high-dose-rate brachytherapy for prostate cancer participated in the first part of the study. Each patient had needles put into the prostate under general anaesthetic. The needles are then used to deliver a high dose of radiotherapy, using a radioactive wire slid along each needle. Before the patient had the radioactive treatment, we put optical fibres into the needles. One fibre delivered low-power laser light and another fibre detected the light reaching different positions in the prostate. We then calculated the penetration depth of the light at different positions in the prostate.

We found that there was quite a lot of variation in how far the light travelled, which is difficult to predict. It is likely that the number of light fibres needed to treat the whole prostate will be similar to that needed for brachytherapy, eg up to 20. However, this needs to be confirmed by the current study, which is looking at the amount of cell death that occurs when a photosensitiser is given and activated by one light fibre on each side of the prostate. This work, the only study with this drug in the untreated prostate, is ongoing.

*My fellowship has been immensely valuable in seeing what is, and isn't, possible in terms of clinical research, and of the necessary steps to carry out a successful research project. It has also allowed me to work with colleagues from a wide variety of medical and scientific backgrounds, each of whom has a valuable contribution to the project. It has also been a privilege to work with patients who are prepared to take part in research which may be of more benefit to others than to themselves.*

## Miss Caroline Moore

### Site of Study

National Medical Laser Centre and Institute of Urology, University College London

### Supervisors

Mr Mark Emberton  
Professor Stephen Bown

### Further Funding

BUPA Foundation project grant  
St Peters Trust

### Publications

*BJU International*, 2005; Accepted for publication

### Presentations

**The 27th Society Internationale Urologie conference**, Honolulu, October 2004

**International Photodynamic Association**, Munich, June 2005



Caroline Moore with supervisor Mark Emberton undertaking a photodynamic therapy procedure at the Institute of Urology.

Mr Paul Nix

# Markers of radioresistance in laryngeal cancer

## Fellowship/Sponsor

Cazenove Surgical Research Fellowship



### Site of Study

University of Hull

### Supervisors

Professor Nick Stafford, Dr John Greenman and Dr Lynn Cawkwell

### Publications

*Clinical Otolaryngology and Allied Sciences* 2004; **29**: 105–115

*Annals of Oncology* 2004; **15**: 797–801

### Presentations

Royal Society of Medicine Meeting, London, February 2005

Society of Academic Research Surgery Annual Conference, Belfast, January 2004

### Prizes

George Seed Prize for best academic paper by a trainee in the North of England 2004

Garner Prize for best registrar presentation, Yorkshire Otolaryngology Society, 2004

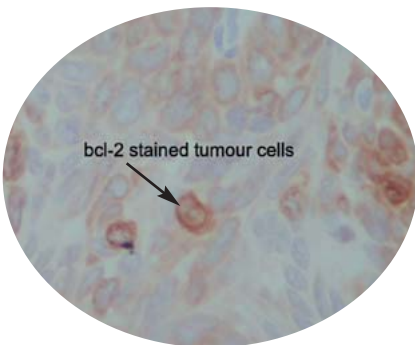
Laryngeal cancer is the commonest type of head and neck malignancy in the UK. It is a potentially curable disease, especially if it is recognised and treated early. Radiotherapy not only provides an effective treatment for early-stage laryngeal cancer but it also preserves the voice box, allowing the patient to speak and swallow following treatment. However, 20% of patients do not respond to radiotherapy treatment and therefore require radical surgery that involves removal of the voice box (laryngectomy). This complex operation is made more difficult for the surgeon due to the previous failed radiotherapy, which results in poor tissue healing.

*‘Up to 20% of patients with early-stage laryngeal cancer fail to respond to initial radiotherapy treatment subsequently requiring salvage surgery, typically involving removal of the voice box.’*

Currently, we cannot predict which laryngeal cancers will respond to radiotherapy. In order to address this question, we have created one of the largest databases of radioresistant laryngeal cancers and used immunohistochemical staining techniques to analyse the samples. By studying biopsy samples from 66 patients with radioresistant cancers compared to a matched group of 66 patients with radiosensitive cancers we were able to predict, using the cellular protein bcl-2, 52% of the radioresistant cancers.

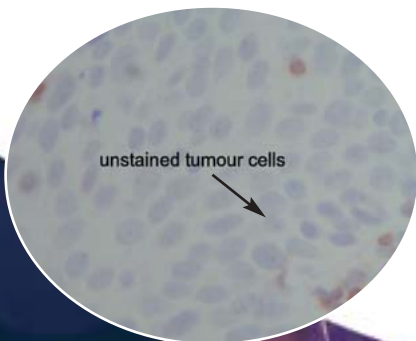
If radiotherapy treatment failure can be predicted using bcl-2, then patients with early-stage laryngeal cancer could be offered conservative laryngeal surgery instead of radiotherapy. This type of surgical treatment, removing only a small part of the voice box, has similar cure rates to radiotherapy and, importantly, also preserves the patient’s ability to speak and swallow following the operation. Patients would benefit from a curative treatment without the unnecessary side effects of radiotherapy.

Further research is ongoing in order to improve the predictive accuracy of any marker of radioresistance.



bcl-2 stained tumour cells

The picture represents a tissue section used to diagnose a patient with laryngeal cancer and contains many tumour cells. All cells have been stained blue to allow identification. The brown stain is the detection of bcl-2 in the tumour cells from a radioresistant laryngeal tumour.



unstained tumour cells

Laryngeal biopsy from a radiosensitive tumour demonstrating no staining of cancer cells for bcl-2.

**Dr Sophie Noblett**

# Fast-track colorectal surgery. The effect of optimising cardiac output by perioperative fluid loading on the systemic inflammatory response, gut perfusion, morbidity and hospital stay

**Fellowship/Sponsor**

*Shears Northern Research Fellowship with support from the Rosetrees Trust*

The purpose of this research was to provide carefully monitored, goal-directed fluid therapy aiming to maximise heart function and assess the effect on outcome following major bowel surgery.

*‘By monitoring how well the heart is working and giving patients extra fluid during surgery, we aim to reduce postoperative complications, shorten recovery rate and length of hospital stay.’*

One hundred and eight patients were randomised into one of two groups. One group received the current standard monitoring and fluid use, the other group received additional fluid based on heart function using a machine called an oesophageal Doppler as a guide. The oesophageal Doppler provided a continuous beat-to-beat ultrasound scan of the blood flow from the heart so hydration state and heart function could be assessed and optimised. All other aspects of patient care were the same for each group.

Patient age, general health and type of operation were similar in each group. The patients in the intervention group had a significantly shorter hospital stay, had a 40% reduction in postoperative complications and were able to tolerate normal diet two days earlier than the control group. Doppler measurement showed that while the heart function was similar in both groups at the start of surgery, the intervention group rapidly improved and maintained a better heart function during their operation compared with the control patients. This allowed the tissues and organs to receive a better blood supply. Chemical markers measured in the blood showed a reduced inflammatory stress response in the intervention patients.

This study complements other work showing the benefits of maintaining good tissue bloodflow and oxygenation. It represents a simple minimally invasive method of accurately monitoring and improving heart function and we have shown important improvements in patient recovery following surgery.

## Site of Study

Freeman Hospital,  
Newcastle Upon Tyne

## Further Funding

Freeman Hospital Special  
Trustees

## Supervisor

Mr Alan Horgan



## Presentations

**American Society of Colon and Rectal Surgeons, Annual Meeting**, Philadelphia, April 2005

**Association of Coloproctology of Great Britain and Ireland Annual Meeting**, Birmingham, June 2004

## Prizes

**North Western Association of Colorectal Surgeons Award Clinical Research Prize, American Society of Colon and Rectal Surgeons Annual Meeting**, Philadelphia, May 2005

**Registrars Prize George Feggetter Medal, North of England Surgical Society Annual Meeting**, Carlisle, May 2005



Sophie Noblett presenting at a College research event.

# Assessment of the feasibility of using routinely collected data to answer clinical questions relating to surgical volume and outcome relationships

## Mr Martin Nuttall



### Site of Study

Clinical Effectiveness Unit, RCS,  
London

### Supervisors

Mr Mark Emberton  
Dr Jan van der Meulen

### Publications

*Journal of Urology* 2004; **172**(6): 2145–2152

*BJU International* 2005; **95**(4): 513–516

### Presentations

**American Urological Association Annual Meeting,**  
San Francisco, May 2004

**American Urological Association Annual Meeting,**  
San Antonio, 2005

*‘Do surgeons/hospitals that do more of a certain procedure get better results than those that do fewer?’*



Martin Nuttall at work in the clinical effectiveness unit in the Royal College of Surgeons.

There have been a number of studies which have suggested that outcomes for surgical procedures are better if they are performed in high-volume hospitals or by high-volume surgeons. Similar results have been found within the field of urological oncology, but in a recent review, we were unable to find any such studies that were performed in the UK, or even within Europe, because all published data regarding surgical volume and outcome relationships are either from the US or Canada.

Volume-based healthcare policies are increasingly being formulated both in the UK and the US, whereby it is recommended that many complex surgical procedures are performed in hospitals, or by surgeons, that perform a large number of such procedures. The aim of this research is, therefore, to investigate surgical volume and outcome relationships in the UK using routinely collected UK data and furthermore to assess the validity of using routinely collected data, such as the hospital episode statistics (HES) database of the Department for Health in England, for this purpose.

First, we identified, by use of the HES database, national figures of surgical activity as well as outcomes for radical urological cancer surgery – cystectomy, nephrectomy and prostatectomy, performed in England within the NHS. Second, we developed a method to account for the presence of co-existing disease in patients identified within routinely collected data such as the HES database. This step was essential in order to assess accurately the surgical volume and outcome relationships, the effect of co-morbid disease on surgical outcomes must be adjusted for as it has previously been suggested that patients with co-morbid disease may have poorer outcomes after surgery. Third, we analysed different methods of measuring outcomes after surgery including the use of hospital readmission, in-hospital death, length of stay and return to operating theatre. Fourth, we incorporated all the above to determine whether a relationship exists between either hospital or surgeon volume and outcomes for radical urological cancer surgery in England using routinely collected UK data. Finally, the results of this research enabled us to assess the validity and reliability of routinely collected data to answer clinical questions.

Following the success of this research project my successor, Paul Cathcart, has been awarded a two-year Joint RCS/Dunhill Medical Trust Research Fellowship to continue this work of assessing extent to which routinely collected data can be used to answer clinically relevant questions.

**Miss Joy Odili**

# **In vivo targeting of melanoma by recombinant antibody fragments (single-chain Fv)**

**Fellowship/Sponsor**

*Freemasons Surgical Research Fellowship*



Patients with melanoma.



Melanoma is potentially curable if it is detected early. However, once it has spread there is no cure. Early detection of melanoma deposits would enable patients to be offered treatments earlier that could prove to be life-saving. Our research aims were, therefore, to develop cancer-specific antibodies for the early detection and treatment of patients with melanoma.

Antibodies were designed through DNA technology to detect melanoma in patients. The antibodies can be made radioactive and injected into patients. X-rays of the patients are then taken at varying time intervals. The antibodies bind to melanoma deposits and these areas became visible on the x-rays. Early results were disappointing. The first antibodies used bound to normal organs as well as to the melanoma, making it difficult to distinguish between healthy and diseased tissue. This resulted in poor quality images. The main objective of this project was to improve the quality of the images by improving the ability of the antibodies to bind to the melanoma. This involved further genetic engineering of the antibodies and testing them in animals.

*‘Our research aims were to develop cancer-specific antibodies for the early detection and treatment of patients with melanoma.’*

We successfully developed antibodies capable of providing superior quality images. Some of these antibodies were also capable of destroying melanoma using the body’s immune system. We hope to reproduce our results in patients. To our knowledge, we are the only UK unit working with antibody fragments and melanoma. There is currently no way of reliably detecting the microscopic spread of melanoma. Antibodies and cancer imaging will provide peace of mind to patients who are disease-free and give hope to those with ongoing disease. This project will continue until we can use our antibodies to detect melanoma in patients and, ultimately, cure them.



## **Site of Study**

RAFT Institute of Plastic Surgery,  
Mount Vernon Hospital,  
Middlesex

## **Further Funding**

BUPA Foundation (one year)

## **Supervisor**

Dr Jorg Kupsch

## **Publications**

*Hybrid Hybridomics* 2003; **22**(6): 347–355

*Melanoma Research* 2002; **12**(4): 373–379

## **Presentations**

**4th International Conference on the Adjuvant Therapy of Malignant Melanoma**, London, March 2002

**European Association of Plastic Surgery (EURAPS)**,  
Crete, May 2002

## **Prizes**

**2002 Hunterian Professorship, RCSE**

**2002 Schering-Plough Young Investigator’s Award for the Best Presentation, 4th International Conference on the Adjuvant Therapy of Malignant Melanoma**, London



Joy with research fellow Pari-Naz Mohanna after her Hunterian Professorship at the College.

**Miss Evelyn Ong**

## Surgical infants glutamine nutrition trial

### **Fellowship/Sponsor**

Joint RCS/BAPS Surgical Research Fellowship



Drip feeds have dramatically improved survival of newborns with surgical conditions. However, newborns on drip feeds are commonly more susceptible to infections, their gut condition

deteriorates and liver function becomes deranged. These complications increase with duration of use. Previous laboratory work and adult human studies have suggested that glutamine supplementation of drip feeds may reduce complications, particularly in surgical patients. Little is known of its effects in children and this is the first large-scale multi-centre randomised controlled clinical trial looking at surgical newborn patients. We hypothesised that glutamine supplementation in drip feeds in surgical newborns would reduce duration of dependency on drip feeds and would reduce the rate of infection.

### **Site of Study**

Paediatric Surgery Unit, Institute of Child Health and Great Ormond Street Hospital, London

### **Further Funding**

Action Medical Research, British Association of Paediatric Surgeons (three years)

### **Supervisors**

Professor Agostino Pierro  
Dr Simon Eaton

### **Prizes**

British Association of Paediatric Surgeons 53rd International Congress, Dublin, July 2005

British Association for Parenteral and Enteral Nutrition Conference, Telford, November 2005

*‘In the UK, at least 1,000 infants a year are born with surgical conditions and require drip feeding, of which approximately 15% will develop complications related to infection and/or liver dysfunction.’*

We compared two groups of newborns less than three months old; one group received glutamine-supplemented drip feeds and the other received standard feed. We recorded clinical outcomes, liver function tests, immune response to infection and levels of glutamine metabolites.

Preliminary results show glutamine did not impact on length of time on drip feeds or incidence of infection. However, patients on glutamine supplementation had significantly lower levels of chemical mediators of inflammation produced by the immune system in response to infection.

Our clinical outcome results are consistent with a recent trial of glutamine supplementation conducted in 1,433 low birthweight newborns in the US and with the latest results of a Cochrane systematic review. Long-term effects of glutamine supplementation in children has not been examined previously and we hope to study this in future. Although our trial has not shown glutamine supplementation changes clinical outcome in our patients, further analysis of our data suggests children on long-term drip feeds may obtain more benefits. We are, therefore, developing a study of glutamine supplementation in children on long-term home drip feeds.

Alex, the first patient on the trial, and Evelyn Ong.



# Pretargeting of single chain antibody Fv fragments for the radioimmunotherapy of melanoma

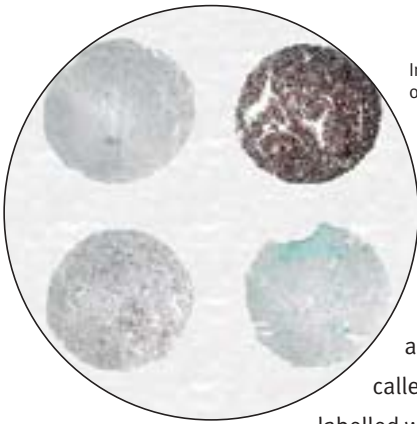


Image of melanoma specimens stained on the tissue microarray.

The main aim of the project was to investigate whether an experimental technique of targeting melanoma cells with anti-melanoma antibodies, so-called 'magic bullets', that were labelled with radioactivity could be improved. The radioactive label would permit detection with special types of scanners, similar to some already in use in hospitals. The eventual hope is that when patients are diagnosed with a melanoma they could have an immediate scan to check if it had spread to any other parts of the body, a service not currently available.

By genetically engineering the antibodies and producing single-chain antibody (Fv) fragments of different conformities, tumour localisation was improved when compared with previous research. This research is very specialised and is only studied in a limited number of centres worldwide. We hope that further development in this area will not only allow us to detect any cancer that has spread but also to destroy it.

*'Statistically, at least 1 in every 50 people will develop a melanoma in their lifetime.'*

Another side of the project involved investigating various biochemical markers to see if their presence in melanoma was in some way related to the disease process and could therefore be used as a tool to predict patient outcome and disease natural history. This was done by using an instrument called a tissue microarray, which enabled over 100 melanoma specimens to be studied simultaneously. Several markers were discovered that related directly to melanoma disease course in patients, some of which had not been shown before. One marker in particular, MCAM, showed very encouraging results. This is a very exciting development as not only will it enable patients to be given a more accurate assessment of their disease but it suggests new targets against which to develop experimental anti-cancer drugs.



## **Mr Marc Pacifico**

### **Site of Study**

RAFT Institute of Plastic Surgery,  
Mount Vernon Hospital, Middlesex

### **Supervisor**

Dr Jörg Kupsch

### **Publications**

*Plastic Reconstructive Surgery* 2005; **115**(2): 367–375

*Melanoma Research* 2004; **14**(1): 39–42

### **Presentations**

**The 7th European Conference of Scientists and Plastic Surgeons,**  
Geneva, September 2003

**The 15th European Immunology Conference,** Rhodes, June 2003



Marc explaining his research project to attendees at the Research Fellows evening.

# The role of the delta-like 4 ligand in human tumour angiogenesis

## Mr Nilay Patel



### Site of Study

John Radcliffe Hospital, Oxford

### Further Funding

British Urological Foundation  
(one year)

### Supervisor

Professor Adrian Harris

### Publications

*Cancer Research* 2005; **65**(17): in press

### Presentations

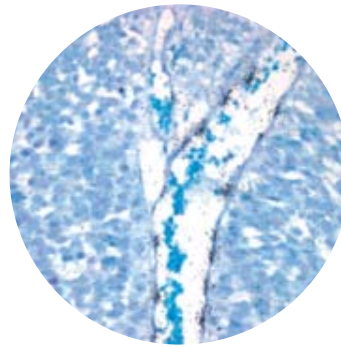
**American Urological Association Annual Meeting,**

San Francisco, May 2004

**British Association of Urological Surgeons Annual Meeting,**

Glasgow, June 2005

*‘Further work is being undertaken in our laboratory in an attempt to take these initial discoveries from bench to bedside.’*



*In situ* hybridisation showing delta-like 4 expression within the vasculature of a bladder cancer. (Left, light field; right, dark field).

Tumour growth and spread is dependent upon the acquisition of an adequate blood supply. A number of molecular pathways have been shown to regulate new blood vessel formation (angiogenesis) and the targeting of these pathways is a potentially novel treatment method for cancer. The Notch pathway is a cell signalling pathway that has recently been shown to play a key role in blood vessel development.

A variety of molecular biological techniques were used to study for the first time the role of delta-like 4, a component of the Notch pathway, in tumour angiogenesis.

The expression of delta-like 4 was studied in bladder and kidney cancers. Delta-like 4 was found to be expressed by the cells that line blood vessels (endothelial cells). Interestingly the expression of delta-like 4 was confined to tumour blood vessels and not vessels within normal tissues.

The biological function of delta-like 4 was studied using endothelial cells cultured in the laboratory. Delta-like 4 was found to be regulated by low levels of oxygen (hypoxia) and vascular growth factors such as VEGF and bFGF. Knocking out delta-like 4, using a technique called RNA interference, inhibited numerous endothelial cell functions including cell growth, migration and network formation. This implies that downregulating delta-like 4 within tumour blood vessels may, by inhibiting tumour angiogenesis, be a potential future cancer therapy for solid tumours.

Much work needs to be done, however, before these findings result in any potential patient benefit. Further work is being undertaken in our laboratory in an attempt to take these initial discoveries from the bench to the bedside.



Scram

Downregulating delta-like 4 using RNA interference (scram = scrambled control, Duplex 1 = delta-like 4 RNA).



Duplex 1



# The cellular basis of bladder sensations



Miss Rahman undertaking a dissection of the urothelium from the underlying detrusor muscle.

## Fellowship/Sponsor

Joint RCS/BUF Surgical Research Fellowship



Bladder dysfunction is extremely common; up to 4 million people in the UK are affected by incontinence. A major cause is a heightened urge to urinate and bladder pain causing a severe reduction in the quality of life. These symptoms

suggest that the bladder is experiencing an inappropriate sensation of fullness. Current treatment by drugs or surgery is often inappropriate, largely because the fundamental reason for this heightened sensation is unknown.

The aim of the project was to investigate how the cells that line the bladder, the urothelium, may initiate sensations of bladder fullness by their contact with urine.

Using preparations of urothelial sheets from human and animal bladders, the movement of charged particles (ions) across this layer was measured and the influence of fluid (mock urinary) composition was quantified.

The research demonstrated, for the first time, the possibility of isolating intact urothelium from the human bladder. It was also possible to demonstrate that the movement of ions across the urothelium is sodium dependant and that sodium transport through specific sodium channels may form the basis of bladder sensation.

This technique provides a powerful tool to define the precise cellular mechanisms involved in bladder sensations and offers the potential to compare the ion transport properties between people with normal and abnormal bladder sensation.

Research into the urothelium is in its infancy and my work has provided invaluable data that have generated much interest and provided a foundation for future work. The answers to our questions will identify potential targets for the modulation of bladder sensation, which should lead to the development of more acceptable treatments for improving symptoms and in the management of incontinence.

## Miss Nishat Rahman

### Site of Study

Institute of Urology and Nephrology, University College London Medical School

### Supervisor

Professor C H Fry

### Publications

*BJU International* 2004; **94**(7): 1174

### Presentations

**British Association of Paediatric Surgeons,**  
Oxford, June 2004

**European Association of Urology,** Vienna, March 2004

### Prize

**European Association of Urology, Best Poster Presentation, basic science section,** Vienna, March 2004

*'Bladder dysfunction is extremely common; up to 4 million people in the UK are affected by incontinence.'*



Miss Rahman in the laboratory processing of specimens.

## Mr Majid Shabbir

# The role of purinergic signalling in urological malignancies

### Fellowship/Sponsor

RCS Surgical Research Fellowship with support from the Rosetrees Trust



### Site of Study

Royal Free and University College  
School of Medicine, London

### Supervisors

Professor Geoffery Burnstock,  
Mr Robert Morgan

### Publications

*Anticancer Research* 2004; **24**(5A): 2853–2859.

*Journal of Urology* 2004; **171**(4 suppl) p260 #983.

### Presentations

**European Association of Urology Meeting**, Vienna, March 2004

**American Urological Association**, San Francisco, May 2004

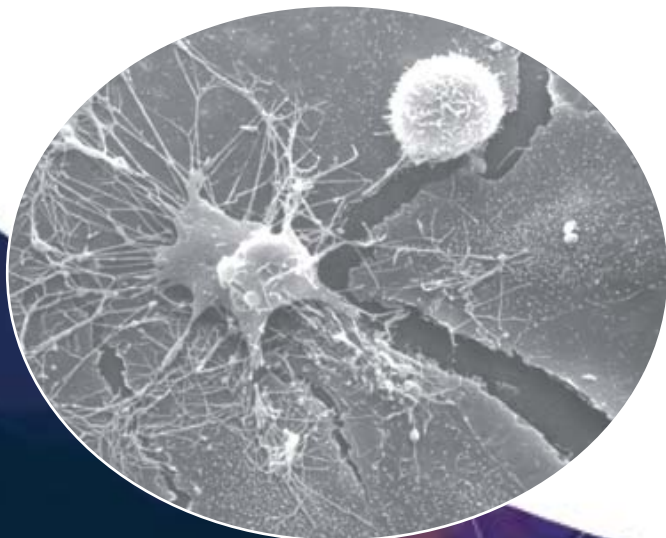
### Prizes

**Best Poster Prize, European Association of Urology Meeting**,

Vienna, March 2004

**International Cardura Award for Urological Research**, 2003

*‘Our experiments showed that purinergic agonists inhibited the growth of both cancers by at least 95%.’*



Electron microscopy images of prostate cancer cells (background) in various stages of cell death (apoptosis-foreground) after treatment with ATP.

The notion of adenosine triphosphate (ATP) as nature’s ‘universal energy store’ was first uncovered in 1941. It wasn’t until 1970 that a wider role for ATP as a neurotransmitter was described. Acting via specific purine receptors, ATP has since been shown to be involved in numerous cell functions including cell growth and cell death. The aim of our research was to investigate the role of this purinergic signalling in urological malignancies. We studied two aggressive cancers, hormone refractory prostate cancer (HRPC) and high-grade bladder cancer.

The treatment for metastatic prostatic cancer, or disease recurrence after surgery or radiotherapy, is hormone ablation therapy. Unfortunately, all patients treated with hormones eventually develop an aggressive hormone-refractory form of the disease, which is difficult to control and is usually fatal within twelve months.

Bladder cancer is the second most common cancer to affect the urinary system. High-grade bladder cancer is an aggressive form of the disease with a greater risk of spreading and recurring despite treatment. Patients with high-grade bladder cancer have a poor outcome, with only 1 in 3 patients still alive 10 years after diagnosis.

Our experiments showed that purinergic agonists inhibited the growth of both cancers by at least 95%. We found that this antineoplastic action was due to activation of either P2X5 and/or P2Y11 receptors in both cancers despite their differing nature, raising the possibility of a common pathway for cancer treatment irrespective of the cancer cell type or origin.

We successfully established animal models of both cancers and were able to confirm that ATP significantly reduced the growth of both tumours without causing any adverse effects to the test animals. We also found that ATP increased the effect of established chemotherapy already in use with both malignancies. Together with the results of a recent trial that showed ATP effectively combats the ‘wasting away’ of patients with advanced cancer, our results raise the potential use of ATP as a treatment for advanced urological malignancies, to combat both the cancer and its effects on the human body.

## Miss Nicola Smith

# Exploiting mechanical stimuli to increase prenatal growth of the hypoplastic lung

### Fellowship/Sponsor

Shortland Legacy Surgical Research Fellowship with support from the Rosetrees Trust



Nicola Smith with the Lady Mayoress of Hereford and Mr Charles Collins at a presentation to Hereford WI.

Congenital diaphragmatic hernia (CDH) is a lethal birth defect affecting 1 in 2,500 births. Despite significant advances in management, mortality persists at around 50%. The major determinant of survival is the degree of associated impaired lung growth (pulmonary hypoplasia). New therapeutic strategies are needed for this lethal

condition. Mechanical stimuli are crucial for normal lung development. Developing airways spontaneously contract and relax in peristaltic waves. The role of airway peristalsis in the regulation of lung growth has not been studied. To evaluate this role, lungs from an experimental model of CDH were maintained in culture. By adding stimulants to the culture system we were able to enhance lung growth and airway peristalsis. We revealed that lung growth is intimately related to airway peristalsis in this culture system; enhancing growth increases peristalsis while directly stimulating peristalsis causes an increase in lung growth. Conversely, by inhibiting one factor a decrease in its counterpart was produced.

Furthermore, during these experiments we noted that, strikingly, over 80% of contractions commence on the right side, leading us to identify a putative lung ‘pacemaker’.

Further characterisation of this activity and the pacemaker area is proceeding within this research group which may reveal new therapeutic targets for lethal pulmonary hypoplasia and, ultimately, improve survival in CDH.

*‘Survival in congenital diaphragmatic hernia is around 50%. Most affected babies die due to inadequate lung development (pulmonary hypoplasia).’*

### Site of Study

University of Liverpool

### Further Funding

Birth Defects Foundation  
(one year)

### Supervisor

Professor Paul Losty

### Publications

*American Journal of Respiratory Cell and Molecular Biology* 2005; **32**(2): 118–127

*Archives of Disease in Childhood* 2005 Apr; **90**(4): 426–428

### Presentations

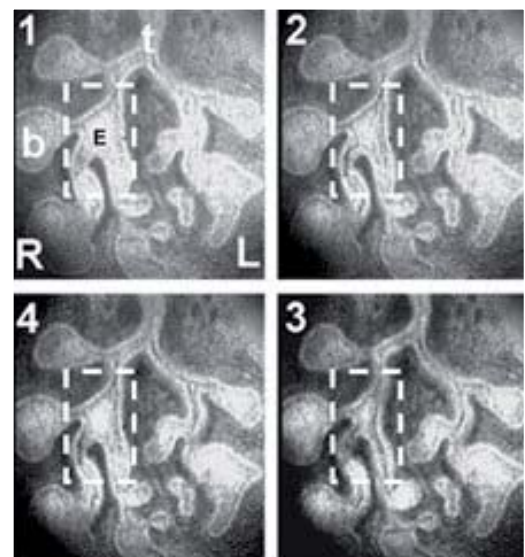
**British Association of Paediatric Surgeons XLX Annual International Congress**, Estoril, July 2003

**16th International Symposium of Pediatric Surgical Research**, Marseille, 2003

### Prizes

**Stefan Galeski Travel Award, Research Fellowship Scheme 10th Anniversary Celebration**, 2003

**President’s Poster Prize for best poster presentation**, Royal College of Surgeons of England, SARS, 2003



Photomicrographs of a lung in culture. The primitive trachea is at the top (t), with right (R) and left (L) lung rudiments marked. Following the panels clockwise from 1–4 the airway within the dashed-box (1–3) contracts before relaxing (panel 4).

# To evaluate the use of polyHIPE as a possible substitute in the tissue engineering of urological tissue for reconstructive surgery

## Mr Oparaku Umez-Eronini



### Site of Study

School of Surgical and Reproductive Science, University of Newcastle

### Supervisor

Dr A Collins

### Publications

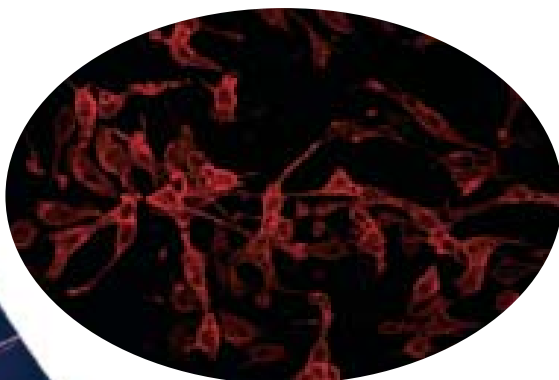
*European Cells and Material Journal* 2002; **4**(Suppl. 2): 77–78

*European Urology Supplements* 2003; **2**(1): 121

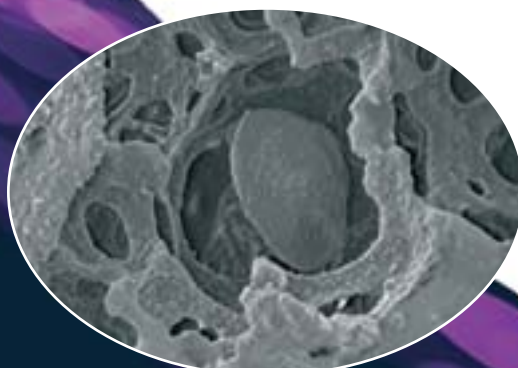
### Presentations

**European Urological Association Meeting**, Madrid, March 2003

**Canadian Urological Association Meeting**, Montreal, June 2003



Laser microscope image of bladder lining cells (urothelium) stained with an antibody to confirm the cell type.



Rounded cell present in a pore within the structure of porous polyHIPE scaffold.

Bladder reconstructive surgery is performed to treat urinary incontinence and prevent kidney failure. Current surgical treatment involves using segments of bowel to act as patches or folded to create a new bladder resulting in significant complications, including mucous production, formation of bladder stones, metabolic disturbances, growth retardation and probably an increased long-term risk of malignancy.

*‘Annually 2,000 operations in reconstructive surgery are carried out using bowel segments due to a lack of suitable bladder substitute.’*

Tissue engineering techniques could provide an abundant source of tissue for use in this setting and involve growth of the cells in the laboratory (*in vitro*) to provide adequate numbers. The cells then have to be combined and scaffolds are needed to help produce organised development. The scaffolds have to be porous to allow infiltration of the cells as well as diffusion of the nutrients to the cells. PolyHIPE is a new technique that produces a very porous microstructure, making it potentially an ideal material.

The aim of the work carried out was to determine the bio-compatibility of polyHIPE derived scaffolds and develop an animal model using polyHIPE to investigate the effects of polymer characteristics on bladder cultures.

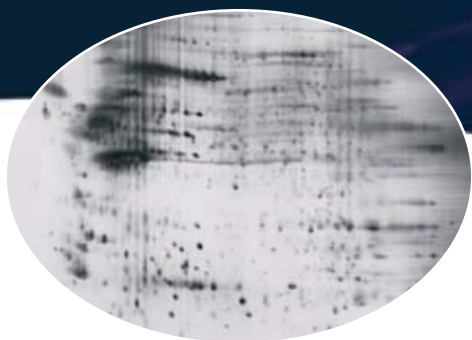
Primary urothelial (lining) and stromal (muscle) cultures were established from human bladder samples obtained during open urological procedures and used for *in vitro* and animal models.

We demonstrated growth of both cell types on the polyHIPE polymers in the *in vitro* setting with cells surviving for up to three months on the scaffold. Implants produced also proliferated in mice animal models with the production of organised muscle tissue after six weeks.

Early results indicate polyHIPE supports the growth proliferation of bladder cells for prolonged periods both *in vitro* and *in vivo*.

**Mr Chandrakumar Vimalachandran**

# Protein expression in the pancreatic cancer microenvironment



Protein map following extraction and separation of proteins from cells of interest. Silver staining is used to stain and visualise individual proteins (black spots).

## **Fellowship/Sponsor**

*Lillian May Coleman Surgical Research Fellowship*

Pancreatic cancer is a leading cause of cancer-related death, accounting for over 6,000 deaths in the UK. Surgical resection offers the only hope of cure. However, the disease often presents at an advanced and inoperable stage and this course of treatment is only possible in approximately 10% of patients. Improved methods of detecting the disease at an earlier stage or improved methods of treating the cancer, which is relatively resistant to chemotherapy and radiotherapy, are desperately needed.

Proteins are functional molecules and analysis of protein expression (proteomics) is thus believed to have advantages over more traditional gene-based studies. The laboratory I worked in has previously employed proteomics in pancreatic cancer research and has identified a number of proteins that are over-expressed in pancreatic cancer cells.

My research project has extended these studies further by analysing the relationship between pancreatic cancer cells and their surrounding host cells, which can account for over 70% of the tumour volume. I aimed to determine differences in the protein expression between these host cells and pancreatic cancer cells. It is believed that cancer cells communicate with such host cells and I explored this hypothesis by determining the protein expression in those host cells lying immediately next to cancer cells.

*‘Improved methods of detecting the disease at an earlier stage or of treating pancreatic cancer are desperately needed.’*

Cancer cells and host cells both adjacent to and distant from cancer cells were dissected from each other using microscopic dissection. Proteins were then extracted from these cells and separated to give a map of protein spots. Maps of tumour cells and host cells were compared to determine protein differences. Using this technique, I have identified and validated a number of proteins, some of which appear to be specific to host cells immediately adjacent to the cancer cells. Research into the role of these proteins will be undertaken shortly.

## **Site of Study**

Royal Liverpool University Hospital

## **Supervisor**

Dr Eithne Costello-Goldring



## **Publications**

*Cancer Research* 2005; **65**(8): 3218–3225

*Expert Review in Proteomics* 2004; **1**: 493–501

## **Presentations**

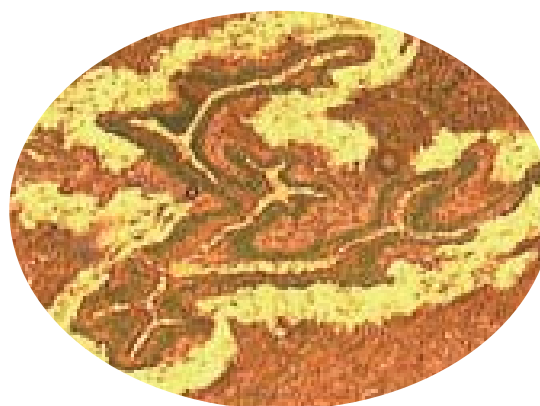
**Society of Academic and Research Surgery Annual Conference**, Newcastle, January 2005

**American Pancreatic Association**, Chicago, November 2004

## **Prizes**

**President’s Poster Prize, Society of Academic & Research Surgery**, Newcastle, January 2005

**Poster Prize, British Association of Cancer Research**, Manchester, June 2004



Microscopic section showing microdissection of surrounding host cells from pancreatic cancer cells.

**Mr Jonathan Waite**

# Tibial translation and cruciate reconstruction

## **Fellowship/Sponsor**

*Joint RCS/Nuffield Orthopaedic Centre Fellowship*



## **Site of Study**

Nuffield Orthopaedic Centre

## **Supervisor**

Professor David Murray

## **Publications**

*Knee Surgery, Sports Traumatology, Arthroscopy* 2005; in press

## **Presentations**

**European Federation of Sports Traumatology Conference,**  
Monaco, 2003

**11th Combined Orthopaedic Associations Meeting,**  
Sydney, 2004

Sports that involve twisting and turning frequently result in knee injuries. The most common significant knee injury that occurs as a consequence of these sports is rupture of the anterior cruciate ligament (ACL). Patients with an ACL-deficient knee are frequently unable to function at previous levels without symptoms of the knee 'giving way'. Surgical reconstruction of the ligament is often necessary to allow patients to return to their chosen sport.

Although much work has been done to study the abnormal knee movements that occur as a result of this injury, few studies have been able to reproduce the levels of activity during which symptoms occur.

Our aim was to accurately calculate three-dimensional knee movements that occur during high-level activities in patients with ACL-deficient knees, prior to the knee 'giving way'. The gait laboratory at the Nuffield Orthopaedic Centre in Oxford contains infrared video cameras that track reflective marker balls placed on the skin. It has enough space to allow running and side-stepping during analysis.

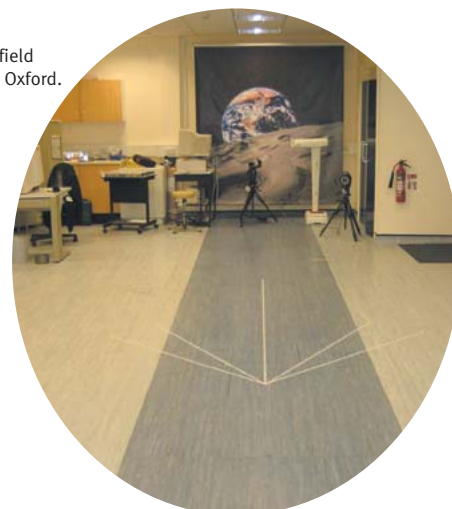
In this study we established that although the quadriceps and hamstring muscles are able to provide knee stability in some planes they are less effective at preventing abnormal rotation at the knee joint. Minimising this potential for abnormal rotation may be the key to preventing the symptoms of 'giving way'.

Surgical reconstruction of knee ligaments is a continually advancing field, and better understanding of knee kinematics is vital to appreciate what needs to be restored during these procedures.



Marker ball set-up for analysis.

Gait Laboratory, Nuffield Orthopaedic Centre, Oxford.



# Transcriptional response to hypoxia and anaemia in head and neck carcinoma

Head and neck cancer represents the fifth most common cancer in men and eighth most common in women worldwide and despite improvements in the treatment the five-year survival rate remains at around 50%.

Hypoxia is found in many tumour types and results in cell death if it is severe or prolonged. However, cancer cells can adapt to this hostile environment allowing them to survive and proliferate. It is, in part, this ability to adapt to a hostile environment that defines their malignant potential and characterises a more aggressive phenotype.

The aim of the study has been to identify novel hypoxia regulated genes, using *in vivo* samples and gene microarray analysis and to validate the findings using immunohistochemistry on a large cohort of samples with defined clinical outcome.

*‘Our findings to date have identified several new genes involved in hypoxia and related to disease progression.’*

Our findings to date have identified several new genes involved in hypoxia and related to disease progression. One gene, PDK-1, which is involved in lactate metabolism, I have shown to be regulated by hypoxia and involved in promoting tumour cell survival under hypoxia. Further to this, I have identified HIF-1 alpha to be a marker of an aggressive phenotype and identified a novel role for HIF-2 alpha in disease progression and tumour aggressiveness.

The study is part of the ongoing research programme run by Professor AL Harris. This period of study has allowed me to publish a review article with two further papers in press.

## Mr Stuart Winter



### Site of Study

John Radcliffe Hospital, Oxford

### Further Funding

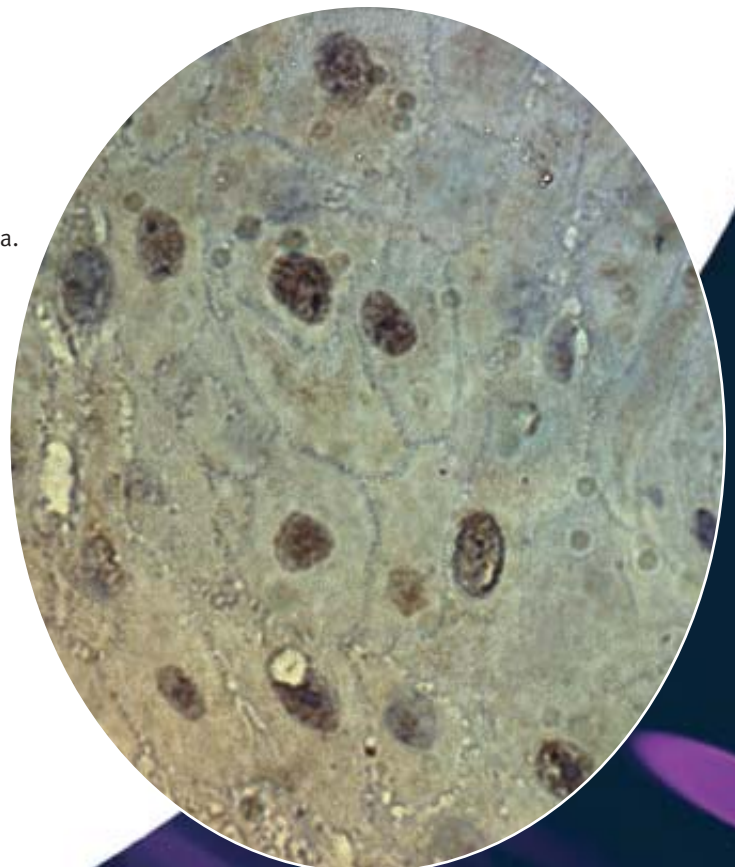
University of Oxford (one year)

### Supervisor

Professor Adrian Harris

### Publication

*Clinical Otolaryngology and Allied Sciences* 2005; **30**:99–104



The affect of High HIF-1 alpha versus low HIF-1 alpha on patient survival with HNSCC.

**Mr Gregory Wynn**

# The role of ATP in mechanosensory transduction in the rat colorectum

## **Fellowship/Sponsor**

*Buckston Browne Surgical Research Fellowship*

## **Site of Study**

Autonomic Neuroscience Institute,  
Royal Free Campus

## **Supervisor**

Professor Geoffery Burnstock

## **Publications**

*American Journal of Physiology. Gastrointestinal and Liver Physiology* 2004; **287**: G647–657

*Gastroenterology* 2003; **125**: 1398–1409

## **Presentations**

**International Union of Physiological Sciences (IUPS) Congress,**  
San Diego, 2005

**33rd Annual Meeting of the American Society for  
Neurochemistry,** Palm Beach, 2002

*‘Patients with chronic abdominal pain, such as those with irritable bowel syndrome, often face a future that provides no real prospect of an effective cure.’*



Undertaking bowel surgery.



Adenosine triphosphate (ATP) a molecule known to provide living cells with their energy source, also acts outside the cell to signal various important functions. In particular, ATP has been shown to stimulate nerves. We also know that when cells are stretched or damaged, they release ATP in large quantities. We wanted to find out if ATP was released when the gut was distended and if so, whether this contributed to painful sensations, especially after inflammation. This might shed light on why patients with functional disorders such as irritable bowel syndrome suffer chronic abdominal pain.

We made nerve recordings from an isolated piece of large bowel from the rat whilst applying ATP and related compounds. The resulting nerve activity was compared at rest and during distension. A pathological model of colitis was also studied. The nerve responses were greater in the presence of ATP. Individual nerve-fibre recordings showed that the same neurons were activated by painful distension and ATP. Furthermore, ATP allowed pain-sensing nerves to be activated at lower pressures.

Other scientists have already shown an important role for ATP in the transmission of pain from other tissues, but this is the first study to demonstrate a link between ATP and how chronic pain may develop from the gut.

Patients with chronic abdominal pain, such as those with irritable bowel syndrome, often face a future that provides no real prospect of an effective cure. The eventual goal of this study is to reveal the underlying mechanism of chronic abdominal pain from the gut and, therefore, provide the means for identifying an effective treatment.

*In the future all procedures and treatments that we carry out on patients will be subject to providing an evidence base for that course of action. If we cannot analyse evidence effectively and, therefore, distinguish between good evidence and poor evidence then we will not be able to reassure our patients that we are giving them the best care. The best way to learn this skill is to undertake a period of research and acquire the knowledge for yourself.*



## Pump-primer Reports

40 Professor St John Crean

41 Mr Paul Johnson

42 Mr Giles J Toogood

# A cultural and molecular analysis of bacteria associated with oral cancer

## Professor St John Crean Professor/Honorary Consultant Surgeon

### Site of Study

Department of Oral Microbiology, University of Wales School of Medicine Dental Institute

### Further Funding

University of Wales College of Medicine and Dentistry, Research Award (three years)

### Publications

*Oral Oncology* 2005; 1(1): 77

*Journal of Dental Research* 2004; 83(Special Issue B): 6

### Presentations

International Association of Dental Research, Hawaii, 2004

British Society of Dental Research Dundee 2005

### Prizes

Scientific Research Award, British Association of Oral and Maxillofacial Surgeons, Birmingham, 2001

Basic Science Award, 10th International Congress on Oral cancer, Crete 2005



Interest in the relationship between bacteria and cancer development increased following the classification by the World Health Organization of *Helicobacter pylori* as a class 1 carcinogen. Despite this, the association of bacteria with oral cavity carcinogenesis has not yet been studied. The primary objective of this research was to identify whether bacteria are present deep within oral squamous cell carcinomas.

For this study 1cm<sup>3</sup> portions of resected oral cancers and control tissues were aseptically collected and divided into deep and superficial specimens. Great efforts were made to eliminate surface decontamination. The specimens were initially cultured and sub-cultured to allow microbial growth. Analysis of the sequenced bacterial DNA against computer based GenBank nucleotide database permitted identification of bacteria. The remaining specimens had their DNA extracted using an extraction kit. The DNA was amplified and cloned and the sequences of genetic material were analysed using the same GenBank database.

Twenty deep tissue specimens, 19 corresponding superficial tissues and 12 control tissues were studied. We have shown a significant number of different taxa from the superficial ( $n=78$ ), deep ( $n=54$ ) and control tissues ( $n=39$ ), of which 11 were previously unknown. Additional molecular analysis from 10 deep tissue tumours revealed 46 different phylotypes compared with 34 from control tissues.

For the first time a study has confirmed, by a combination of cultural and molecular methods, a diversity of viable bacteria to be present deep within oral squamous cell cancer tissue. But the question is what are they doing there? The ability for bacteria to interact with host cells and influence cell division, proliferation and apoptosis does raise the exciting possibility of a role for these organisms in the carcinogene process.

The next stage of the project is designed to look at the interaction of each bacteria at a molecular level, with cultures of human cell tissue lines, to establish if any interactions could initiate changes associated with carcinogenesis.

It is hoped that the information may open novel, preventative, therapeutic, diagnostic and predictive information on this lethal disease. Current survival for all stages of oral cancer is a little over 50%, reaching as low as 8% for the more advanced stages. This project will hopefully make inroads into the mechanics of the disease and have a significant benefit on future management approaches.



Professor Crean combines clinical research and teaching.



# A study of the cellular derivation of pancreatic islets during embryonic development



**Mr Paul Johnson**  
Reader in Paediatric Surgery,  
University of Oxford, and Director  
of Oxford Islet Transplant Programme

## Site of Study

Nuffield Department of Surgery

## Further Funding

Allison Foundation; Medical Research Foundation;  
Diabetes Research and Wellness Foundation  
(five years)

## Publications

*Organogenesis*, 2004; **1**(2): 45–51

*Pediatric Surgery International* 2005; **21**(3): 138–142

## Presentations

**British Association of Paediatric Surgeons, 51st Annual International Congress**, Dublin, 2005

**International Pancreas and Islet Transplant Association**, Geneva, 2004

## Prizes

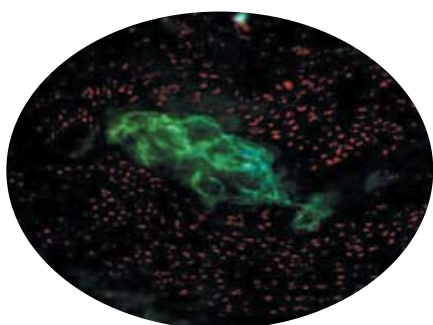
**Novartis Prize**, International Symposium of Paediatric Surgical Research 2004

**Peter Paul Rickham Prize**, British Association of Paediatric Surgeons 2005

Insulin-dependent diabetes mellitus affects millions of children and adults worldwide and is associated with significant complications. Indeed, it is the commonest cause of blindness in the western world and one of the commonest causes of kidney failure. Pancreatic islet transplantation is a minimally invasive procedure that has the potential to reverse diabetes and its complications, and has achieved considerable clinical success over the past few years with leading centres achieving insulin-independence rates of up to 85% one year post-transplantation. However, the worldwide shortage of human donor pancreases and the relative inefficiency of the islet isolation process are both factors that are significantly hindering the widespread application of this treatment. Even if these factors are improved, the number of potential diabetic recipients will always outweigh the number of suitable donor pancreases. An alternative source of islets is therefore required. Islets derived from stem cells offer an exciting alternative. However, the islet stem cell remains elusive. Ongoing studies of normal pancreas and islet development are, therefore, essential.

*‘Stem cell therapy offers a potential cure for diabetes in children.’*

Standard teaching is that all cells within the definitive islet are derived from the embryonic epithelium and that embryonic mesenchyme contributes signals rather than cells to this process. However, very few studies have actually fate mapped the pancreatic mesenchyme in any detail. Using an established chick–quail chimaera model of pancreatic development, our group has followed the fate of the mesenchymal cells and confirmed for the first time that these cells can indeed form islets. The application of these findings is that mesenchyme is more readily available and accessible than embryonic epithelium and therefore may provide a potential source for new islets that can subsequently be used for transplantation. Our ongoing work is investigating whether this finding is unique to this developmental model and also trying to determine the molecular mechanisms responsible for this mesenchyme-to-epithelial transition.



Mesenchymally-derived islet.



Mr Johnson undertaking a microdissection of a developing pancreatic bud.

## The effect of cyclooxygenase-2 inhibition on colorectal cancer liver metastases



**Site of Study**  
St James's University Hospital

**Further Funding**  
Merck Sharpe & Dohme Ltd

### Publications

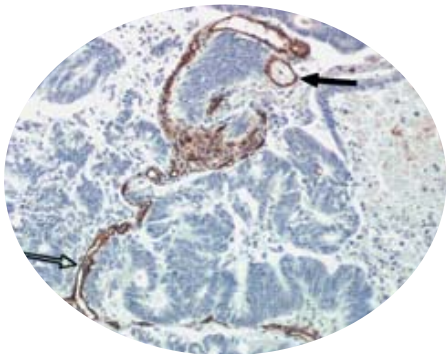
*Gastroenterology* 2003; **125**: 716–729

*Clinical and Experimental Metastases* 2000; **18**: 21–27

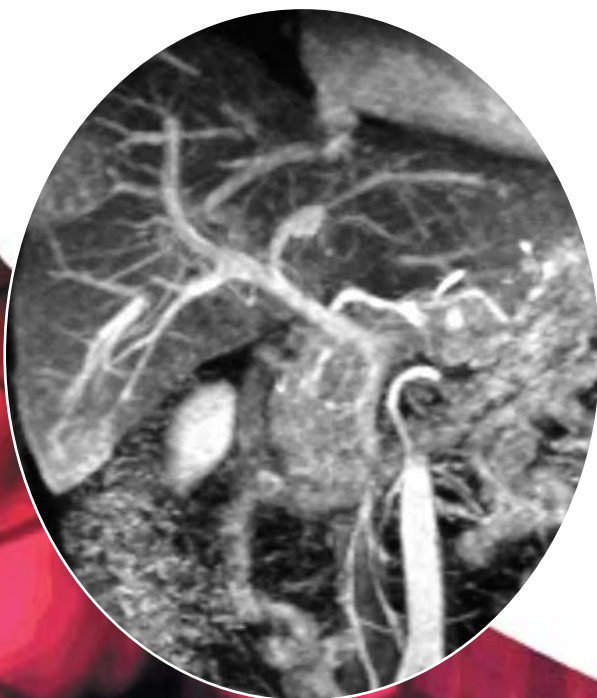
### Presentations

**Association of Surgeons of Great Britain and Ireland,**  
Manchester, May 2003

**International Hepatico Pancreatico Biliary Association,**  
Brisbane, May 2000



Detection of microvessel endothelial cells within a colorectal cancer liver metastasis using CD31 immunohistochemistry.



MRI scan showing colorectal deposit in segment 7 of liver.

In the UK, large bowel cancer (colorectal cancer) is common. Each year around 31,000 people develop colorectal cancer. In addition, every year around 14,000 patients develop secondary deposits in the liver. A small percentage of patients with liver metastases may benefit from surgery. However, for the majority there is little chance of cure.

There is increasing evidence to suggest that anti-inflammatory drugs, such as aspirin, may have anti-cancer properties. This may be due to inhibition of an enzyme called cyclooxygenase-2 (COX-2) which is not present in normal tissue although it is found in a number of cancers. In a preliminary study we demonstrated that COX-2 is expressed in 100% of liver metastases from colon cancer.

Recently, a number of drugs that specifically target COX-2 have become available. They are mainly used for treating inflammatory conditions, such as arthritis. We tested one of these drugs, called rofecoxib, to see whether it had any anti-cancer effects in patients with colorectal cancer liver metastases.

We conducted a clinical trial of rofecoxib in patients with liver metastases. We selected patients scheduled for liver surgery as we needed to obtain tumour tissue. Patients received either rofecoxib or a placebo tablet every day for at least two weeks before their surgery. Once the liver tumours were removed, they were analysed and compared. The major finding was that treatment with rofecoxib appeared to reduce the amount of microvessel density in liver metastases. Furthermore, there was an increase in tumour cell death and reduction in tumour cell proliferation. Tumours depend on angiogenesis to enable them to grow. This finding indicates that drugs such as rofecoxib may have a role in the treatment of colorectal cancer.

Future work will look at the effect of longer term treatment in patients who are unsuitable for liver surgery. This research may eventually lead to the development of new, more effective drug treatments for patients with this common cancer.

This work was carried out by one of my research fellows, Mr Steve W Fenwick, and co-supervised by Professor Mark A Hull. The Pump Priming Award enabled us to proceed with this successful piece of research. We also received support from Merck Sharp & Dohme Ltd (through the International Medical School Grants Programme).

## Preiskel Prize Reports

- 44 Jack Broadhurst  
Adam Culverwell and Charles Tapping  
Rashmi Mathew
- 45 Erlick AC Pereira  
Gurminder Carter Singh  
Ankur Thapar and David Golden

## Jack Broadhurst

### A comparison between the complexity and volume of the surgical workload compared with the opportunities for training for a BST or HST in the UK

**Site of Study:** Kisiizi Hospital, Uganda

I went to Uganda to work in the department of surgery in Kisiizi Hospital. Kisiizi Hospital is a non-governmental organisation hospital with 200 beds in a rural situation in south-west Uganda. Around 800 major cases and 1,000 minor cases are dealt with each year. The type of surgery is 'general' in its broadest respects. The hospital has a large catchment area and attracts cases from as far afield as Kampala on account of the reputation and care provided at the hospital.



Jack assisting with surgery on a boy who had fallen out of a tree onto his scythe.

The aim of my trip was to participate in the delivery of healthcare in the developing world setting and to experience first-hand conditions not normally seen outside specialist units in the UK, as well as diseases in a far more advanced condition than those seen in developed healthcare systems. I also aimed to investigate the complexity and volume of the surgical workload undertaken at the hospital and to compare it with opportunities for surgical training in the UK.

## Adam Culverwell and Charles Tapping

### The burden of congenital deformity in Wewak General Hospital

**Site of Study:** Papua New Guinea

Our elective was based in Wewak General Hospital, the main hospital and referral centre for the East Sepik province. The under-funded hospital has 14 wards and approximately 250 beds divided over surgical, medical, tuberculosis, paediatric and obstetric and gynaecology wards.

We were attached to the surgical unit, which comprised two wards with a consultant surgeon and a registrar. The clinical work was varied, comprising ward work, surgery, community outreach work and research. The surgical conditions that we saw were mostly trauma cases. Other conditions included tropical ulcers (mycobacterium ulcerans) requiring skin grafts, abscesses in need of draining, appendicectomies and gangrenous amputations.



Adam in the operating theatre.



Charles examining an x-ray in the operating theatre.

Although the registrar was nearby to help out if needed, the responsibility was inspiring. We learned quickly and our skills and self-confidence improved enormously. Immunisation trips and outreach work aided our research into childhood deformity, its social and cultural aspects, and the burden it has in a developing country.

## Rashmi Mathew

### The outcome and cost-effectiveness of cataract surgery performed in eye camps and government hospitals in India

**Site of Study:** St Stephen's Hospital and Eye Camps, Delhi, India

There are an estimated 9 million blind people in India and 81% of this blindness is due to cataract, a treatable cause. The government of India has employed eye camps to tackle this cataract backlog. Eye camps are mobile surgical operating units, that reach out to the rural regions and establish temporary operating services. There is little published information on the outcome of cataract surgery in eye camps; however, a study in South India showed that although these camps provide cheap cataract surgery, the outcomes of surgery have been significantly worse.

The aim of my study was to evaluate the outcome of cataract surgery performed in an eye camp in Delhi, North India and compare it to that performed within the hospital itself. Unfortunately, two days before flying out to India the British

foreign office warned against going there, due to potential eruption of war between India and Pakistan, so I carried out my elective in the prestigious Wilmer Eye Institute at the Johns Hopkins University Hospital, USA.



Rashmi assisting in a blepharoplasty.

There I observed in all the sub-specialties of ophthalmology and had the opportunity to witness first-hand the impact this magnificent specialty has on people's lives. Although I was unable to carry out my elective project, I found my alternative elective to be a real 'eye-opener' and came away knowing that ophthalmology was definitely the specialty for me.

## Erlick AC Pereira

### Burns management in a resource-limited developing country

**Site of Study:** United Bulawayo Hospital, Zimbabwe

I spent my elective in the general surgery department of a government hospital in Zimbabwe. I wanted to see the diverse pathology of diseases in a developing country and improve my diagnostic and practical skills in an environment with great clinical need. United Bulawayo Hospital has 600 beds, covering most surgical specialties. Over 50 patients were seen in each ward round and clinic, with typical cases including abscesses, burns, trauma, gangrene, cancers and peritonitis.

Alongside work in Bulawayo, I made several charitably funded 'flying surgeon' visits to rural hospitals. Zimbabwe has many scattered hospitals in remote areas without surgeons.

Erlick (far right) with the local surgeons on a veranda outside theatres.



My elective gave me an unforgettable insight into the practical realities of surgical practice in the developing world: advanced presentation of disease, HIV, limited resources and a phenomenal breadth of clinical practice and different cultures. Research during the elective focused upon resource limitations including a review of burns management, a rationale for conservatively managing acute appendicitis and a description of fishing line as suture material.

## Gurminder Carter Singh

### Plastic and reconstructive surgery – microvascular free-tissue transfer

**Site of Study:** Chang Gung Memorial Hospital, Linkou, Taiwan

My elective experience at the Chang Gung Memorial Hospital in Taiwan under the supervision of Professor Fu Chan Wei provided me with a wealth of experience in plastic and reconstructive surgery. I hoped to develop an understanding of the basic plastic surgical principles used globally to restore normal function and appearance following a broad range of pathological and traumatic processes. I also had a desire to develop clinical and basic science research skills that will aid me in my future training in the NHS.

Most of my time in Taiwan was in the operating rooms and I spent some time in the research laboratories. I also actively partook in both grand round teaching sessions and outpatient clinics.

The Chang Gung Memorial Hospital is the world leader in microvascular surgery and attracts countless international trainees. I feel I contributed in the operating rooms and indeed in the post-operative rehabilitation of patients in a multidisciplinary setting in a purpose-built centre.



Gurminder measuring the temperature of a reconstructed leg using a laser thermometer.

## Ankur Thapar and David Golden

### Trauma in South Africa

**Site of Study:** Johannesburg General Hospital, Republic of South Africa

David and I chose to work in the Johannesburg General Hospital trauma unit from September to November 2003. This is a teaching unit with clear protocols and sees a wide mix of blunt, penetrating and facial trauma. The adjacent University of Witwatersrand offered classroom teaching in topics such as ballistics and assessing facial injuries etc – things which we had never learned at medical school. We were also allowed to sit as observers on the in-house ATLS course. We had the opportunity to take part in two to three resuscitations per shift and assist in theatre with emergency laparotomy, thoracotomy and limb revascularisation (a steep learning curve!)

Ankur and David waiting for casualties outside the trauma unit.



Ankur performing delicate suturing of the ear.

We gained a lot of confidence in assessing patients within a structured ATLS framework and in practical procedures such as suturing, intubation and diagnostic peritoneal lavage. We also had the unforgettable experience of going on the road with rapid response cars and being the first on the scene to treat casualties. There are also opportunities to work in the trauma ITU.

# Hunterian, Arris & Gale, Arnott Lectures

## Delivered in 2004 and 2005

- Hunterian **Professor Peter Brennan**, BAOMS, RCSEng, London, 1 June 2004  
*The role of nitric oxide synthase enzymes in the expression of the transcription factors HIF-1 and NF-KB in oral cancer*
- Hunterian **Mr Stephen Billing**, RSM, London, 18 June 2004  
*The potential for induction of transplantation tolerance by donor-specific bone marrow cells*
- Hunterian **Mr Andrew Ballaro**, BAUS, Harrogate, 24 June 2004  
*The elusive electromyogram in the overactive bladder; a spark of understanding*
- Hunterian **Mr Kevin Turner**, BAUS, Harrogate, 24 June 2004  
*Hypoxia inducible factors in human kidney tumours*
- Hunterian **Mr Paris Tekkis**, ACPGBI, Birmingham, 29 June 2004  
*Risk-adjustment and evaluation of surgical performance in colorectal surgery*
- Arnott **Mr David George Stainsby**, BOA, Manchester, 15 September 2004  
*The anatomy, the structure, and the mechanics of the human foot and the importance of lateral swing movement at the transverse tarsal joints*
- Hunterian **Mr Robert Grimer**, BOA, Manchester, 16 September 2004  
*Successful surgery for sarcomas*
- Hunterian **Mr Giles Cunnick**, BASO – Association for Cancer Surgery, RCSEng, London, 22 November 2004  
*Lymphangiogenesis and human breast cancer*
- Hunterian **Miss Alison Halliday**, VSGBI, Harrogate, 25 November 2004  
*Asymptomatic carotid surgery trial (ASCT) – early carotid endarterectomy can decrease stroke risk in patients with neurological asymptomatic carotid artery stenosis*
- Hunterian **Adriaan Grobbelaar**, BAPS (Plastics), RCSEng, London, 1 December 2004  
*A new surgical solution in surgical treatment of facial paralysis*
- Arris & Gale **Miss Aina Greig**, BAPS (Plastics), RCSEng, London, 2 December 2004  
*Purinergic receptors could provide novel therapeutic targets for non-melanoma skin cancers and their precursors*
- 2005**
- Hunterian **Mr Nikunj Patel**, SBNS, Edinburgh, 21 April 2005  
*Neurotrophic factor therapy for the treatment of Parkinson's disease and its potential applications for other disease*
- Hunterian **Mr James Brown**, BAOMS, Newcastle 10 June 2005  
*The prognostic implications of the presence and pattern of tumour invasion of the mandible in oral cancer treated by primary surgery*
- Hunterian **Mr Edward Kiely**, BAPS (Paediatrics), Dublin, 15 July 2005  
*A technique for excision of abdominal and pelvic neuroblastomas*
- Hunterian **Mr Glynne Andrew**, BOA, Birmingham, 21 September 2005  
*“Can't take the pressure” – particles, hydrostatic pressure and orthopaedic implant loosening*
- Hunterian **Mr Fares Haddad**, BOA, Birmingham, 22 September 2005  
*Evaluation and management of the perprosthetic fracture epidemic*
- Hunterian **Mr Andrew Williams**, BOA, Birmingham, 22 September 2005  
*How the knee really moves in health and disease – the application of weight-bearing “dynamic MRI”*



# Travelling Fellowship Awards



Members of the Ethicon Travelling Fellowship Committee.

The College is pleased to be able to offer a variety of fellowships 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 fellowships is that the surgeon who benefits can translate the experience and know-how gained during the overseas fellowship to his/her own knowledge base to benefit future patients in this country. The committees that decide the recipients of the travelling fellowships always include leading surgeons.

Here is a selection of the fellowships offered:

## Ethicon Foundation Fund Travel Award

The Ethicon Foundation Fund was established by the generosity of Ethicon Limited. The Fund promotes international goodwill in surgery by providing financial assistance to fellows who are travelling abroad for research or training purposes. 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.

Mr Fraser Sutherland, a specialist registrar in cardiothoracic surgery from Glasgow, visited the Division of Cardiothoracic Surgery, East Carolina University, North Carolina, USA, in October 2004, to learn advanced techniques in robot-assisted keyhole mitral valve surgery. The potential benefits of keyhole cardiac surgery resemble those observed in other keyhole surgeries such as arthroscopy or laparoscopic surgery, where the absence of a major incision is found to promote more rapid recovery and return to normal daily activity.

The use of robots in cardiac surgery has been pioneered in the US, at the East Carolina University, and clinical trials have been taking place there. This centre was, therefore, the ideal place to undertake the Ethicon fellowship. Mr Sutherland learned many new techniques during his time in the US and found the experience thoroughly rewarding from a professional point of view and, ultimately, for patient care. He hopes that his experience will assist in his quest to bring the advantages of robot-assisted keyhole surgery to patients with valvular heart disease in the UK.

## The Royal College of Surgeons Foundation Inc New York Travel Award

The trustees of The Royal College of Surgeons Foundation Inc, based in the United States, fund travelling fellowships to enable young surgeons and dental surgeons to visit the US to observe surgical procedures first-hand.

Mr Sanjeev Bassi, a consultant neurosurgeon at King's College Hospital, London, visited the Montefiore Hospital, New York, in October 2003. Mr Bassi is interested in a career in paediatric Neurosurgery and his fellowship at the Montefiore Hospital was intended to gain thorough experience of paediatric and craniofacial neurosurgery. Mr Bassi spent time with the internationally acclaimed paediatric neurosurgeon, Professor J Goodrich. Mr Bassi's fellowship consisted of day-to-day management of patients admitted to the paediatric neurosurgery departments and shadowing Professor Goodrich to master new techniques. The highlight of his fellowship was observing the separation of nine month-old conjoined twins, joined end to end at the head. This operation attracted a large amount of media attention. The whole experience of the fellowship has been extremely worthwhile for Mr Bassi. He has adopted some new surgical technical manoeuvres and has made several contacts at the hospital with whom he can liaise in the future on the rare and difficult surgical cases he will be managing in the UK.

## The Lionel Colledge Memorial Travelling Fellowship

The Lionel Colledge Memorial Travelling Fellowship was established by Miss Cecilia Colledge in 1979 in memory of her father, the distinguished surgeon Lionel Colledge, to promote and advance the study and knowledge of surgery, in particular head and neck surgery, for the benefit of patients. Miss Colledge remains a trustee of the fund and takes an active interest in its activities.

In 2004 Mr Mark Simmons, a specialist registrar in ENT surgery, spent time at the Oregon Health & Science University, Portland, Oregon. Mr Simmons gained first-hand observation of many operative procedures under one roof, in a renowned centre of excellence in facial plastic and reconstructive surgery. He learned skills in sinus surgery reconstructive work for trauma and skin tumours, as well as sinus surgery and image-guided surgery. His intention in visiting the US was to develop skills to perform new procedures on his return to the UK. He feels the experience gained through this fellowship exceeded his expectations.

# Fundraising in Focus

As mentioned earlier in this report, the College has, over the years, benefited greatly from the constant generosity of our funding partners in meeting the costs of the research fellowship scheme. Charitable trusts, companies and individuals recognise the importance of research to improve surgical care for patients, whether it is the development of effective joint replacements or a new treatment for prostate cancer. It is clear from many of the articles and reports contained within this report that advances in the understanding and treatment of a host of illnesses could not have progressed as quickly were it not for charitable donations. A large part of the success of the research fellowship scheme is the result of the loyalty and encouragement of our donors. The College, surgeons and patients have every reason to be grateful to them.

The College continues to organise events to highlight the work of our research fellows. Between sixty and eighty supporters attended three research evenings at the College during the last two years. These events have proved to be effective in communicating to our donors and others the results of some of the research they are funding. Current research fellows make short presentations on their research and guests have the opportunity to take part in a question and answer session, and meet the research fellows and other surgeons at a reception afterwards, hosted by the president.

Rowan Pritchard-Jones, Joint BAPS/RCS research fellow, presenting at the College research evening.



A special research evening to mark the 10th anniversary of the research fellowship scheme was held in November 2003. Presentations by the following former and current research fellows were made:

*The leukocyte and chemokine infiltrate in colorectal cancer*

**Mr Charles Bailey** – Joint Royal College of Surgeons and Foyle Foundation Research Fellow

*Photodynamic therapy for prostate cancer*

**Miss Caroline Moore** – Freemasons Research Fellow

*The cause of stroke – getting to the heart of plaque rupture*

**Mr Ian Loftus** – A former recipient of the Lea Thomas Research Fellowship



Research presentation evening to the Freemasons, Chelmsford.

*Neurosurgery and intracerebral haemorrhage*

**Miss Helen Fernandes** – A former recipient of the Louis Alexander Research Fellowship

In addition, the director of research, Professor Tony Mundy, reviewed the results of the audit of the research fellowship scheme during the evening (see page 7).

Another research evening took place in May 2004 and guests listened to presentations by the following research fellows:

*Retroviral gene therapy for pancreatic cancer*

**Miss Nicola Eardley** – Dunhill Medical Trust Research Fellow

*Clotting and peripheral arterial disease*

**Mr Simon Hobbs** – Lea Thomas Research Fellow

*'Biofilms' and wound healing*

**Miss Ruth McKee (née Edwards)** – Bernard Sunley Research Fellow with support from the Rosetrees Trust

*Understanding head and neck cancer genes*

**Mr Stuart Winter** – Freemasons Research Fellow

Our late president, Mr Hugh Phillips, chaired the research evening in February 2005, when 70 guests attended and listened to the following presentations:

*Fast track colorectal surgery – improving patient outcome*

**Miss Sophie Noblett** – Shears Northern Research Fellow with support from the Rosetrees Trust

*Reducing neurological complications after coronary artery surgery*

**Mr Reza Motallebzadeh** – Freemasons Research Fellow

*Plexin B1 and prostate cancer*

**Miss Tharani Nitkunan** – Royal College of Surgeons Research Fellow

*Preventing the spread of skin cancer*

**Mr Rowan Pritchard-Jones** – Royal College of Surgeons and British Association of Plastic Surgeons Research Fellow

**The College would like to acknowledge all those charitable trusts, companies, College Fellows and individuals who have supported surgical research at the College including:**

**Foundations, charitable trusts, individuals and corporate donations**

Andrew Anderson Charitable Trust  
 Ballinger Charitable Trust  
 Britannic Assurance plc  
 BUPA  
 Cazenove Charitable Trust  
 David & Frederick Barclay Foundation  
 Donald Forrester Charitable Trust  
 Dunhill Medical Trust  
 Elkin Charitable Foundation Number 1  
 Enid Linder Foundation  
 Ethicon Ltd  
 Family Rich Charities Trust  
 Fellows Fellowship Fund  
 Fitton Trust  
 Frances & Augustus Newman Foundation  
 Grand Lodge of Freemasons 250th Anniversary Fund  
 Henry Smith Charity  
 Inman Charity  
 Kirby Laing Foundation  
 Mr R E W Lumley  
 Mrs Bella Hopewell  
 Rosetrees Charitable Trust  
 Shears Charitable Trust  
 Sir Jules Thorn Charitable Trust  
 Sir Samuel Scott of Yews Charitable Trust  
 Susan Komen Foundation  
 The Caravan Club (Suffolk Centre)  
 The Family of the late Mr Stefan Galeski FRCS  
 The Preiskel family  
 Thomas Sivewright Catto Charitable Settlement  
 Vandervell Foundation  
 Wyndham Charitable Trust

**Joint fellowships**

British Association of Endocrine Surgeons  
 British Association of Paediatric Surgeons  
 British Association of Plastic Surgeons  
 British Urological Foundation  
 British Vascular Foundation  
 Cancer Research UK  
 CORE  
 Society of Academic and Research Surgeons  
 The American College of Surgeons  
 The Arthritis Research Campaign  
 The Botnar family  
 The British Society for Surgery of the Hand  
 The Healing Foundation  
 ia – The Ileostomy and Internal Pouch Support Group  
 The Medical Research Council  
 The National Kidney Research Fund  
 The Royal Australasian College of Surgeons  
 The Stroke Association

**Endowments and legacy funds**

Anderson Reid Fund  
 Bernhard Baron Fund  
 Buckstone Browne Gift  
 Burghard Bequest  
 Burton Legacy  
 Campbell Legacy  
 Children with Cancer Research Fund  
 Collett Legacy  
 Cutner Bequest  
 Darlow Research Fellowship  
 Denker Legacy for Research in the UK  
 Edward Lumley Fund  
 Fellows' Fellowship Fund  
 Fletcher Legacy  
 Green Legacy  
 Gyatt Legacy  
 Harold Bridges Bequest  
 Harry Morton Fund  
 Heslop Legacy  
 Hiller Legacy  
 Joers Legacy  
 Kannaar Legacy  
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Research fellow Mr Ged Lambe undertaking a consultation over dinner.



Professor John Dark (centre right) with Lord Barnard (centre left) at a Freemason's research evening in Durham.

The College is also grateful to its many members and fellows who donate regularly to the fellowship scheme.

Further information on how to donate tax-efficiently, via gift aid, and all enquiries regarding fundraising can be obtained from the development office on telephone **020 7869 6082** or email **development@rcseng.ac.uk**

# Clinical Effectiveness Unit

**Jan van der Meulen** Director

The national clinical audit programme of the clinical effectiveness unit (CEU) investigates the practice and outcome of surgical services in the UK. The questions of the audit projects that we carry out depend on the state of knowledge in a particular surgical area and on whether benchmarks can be specified, as is shown schematically in the diagram below.

A general characteristic of all our projects is that they can be seen as epidemiological studies of the quality of surgical care. In addition to these audit activities, we also carry out studies on clinical and cost effectiveness of surgical interventions.

The CEU is an academic collaboration between the College and the London School of Hygiene and Tropical Medicine (LSHTM). Its remit is to become a national centre of expertise in methods, organisation and logistics of large-scale studies of the quality of surgical care. To achieve this, we foster collaborative links with professional organisations, bodies within the NHS, the Department of Health and the Healthcare Commission.

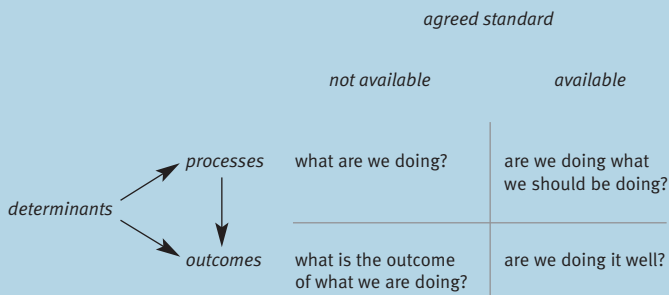


(l-r) Lynn Copley, Nick Black, Jan van der Meulen and John Browne in a project team meeting for phase II of the PROMS project.

An important new component of our programme of work is the exploration of the usefulness of existing routine databases for clinical audit, such as the hospital episode statistics system that holds information about every admission in an NHS hospital in England. Another recent development is the use of web-based interactive systems for data entry and feedback. Such systems allow local units to enter their data directly into a central database located in the College.

A list of the projects that the CEU is currently undertaking can be found on the College's website. The CEU's portfolio is gradually expanding. Since April 2004 we have been responsible for the analysis of the data collected in the National Joint Registry, the database of all hip and knee replacements in England and Wales. In August 2004 the Centre for Evidence in Transplantation was established, led by Sir Peter Morris. You can read about the centre on page 51. In April 2005 we were commissioned by the NHS cleft development board to host the CRANE register of congenital craniofacial abnormalities. At the same time, a team of CEU staff members and other staff members of the health services research unit of the school was awarded a contract by the Department of Health to pilot the routine use of patient-reported outcome measures in the newly established treatment centres.

## Philosophy behind the CEU audit programme



The projects that are part of our programme of work are expected to produce findings that are of importance to the quality of specific surgical services. More importantly, they will also provide the opportunity to strengthen and develop audit and research methods with a special focus on those issues that are encountered within the area of surgery. Most of the CEU's projects are therefore multidisciplinary collaborations in which surgeons and other healthcare professionals work with CEU staff members who have a background in epidemiology, statistics, outcome assessment and data management.

## Clinical Effectiveness Unit *continued*

Developing and using clinical guidelines course run by Dr Arash Rashidian (standing) of the CEU.



The national prospective tonsillectomy audit is a good illustration of the collaborative work that the CEU is currently undertaking. In the Spring of 2003 the ENT community in England and Northern Ireland was invited to participate in a national audit of complications that occurred after tonsillectomy. This audit was funded by the departments of health of England and Northern Ireland, and carried out in close collaboration with the British Association of Otorhinolaryngologists – Head and Neck Surgeons (BAO–HNS).

Between July 2003 and September 2004, post-operative complications were investigated in more than 40,000 tonsillectomies. An interim analysis was carried out after 13,000 patients had been included (*Lancet* 2004; **364**: 697–702).

On the basis of these interim results, the National Institute of Clinical Excellence (NICE) and the BAO–HNS issued guidance and advised that ‘hot’ surgical techniques (variations of ‘electrosurgery’ where heat is generated by an electric current to stop the bleeding) should be used with caution. The final analysis of the audit data demonstrated that there was a clear shift towards the use of surgical techniques with a lower risk of haemorrhage after NICE/BAO–HNS had issued guidance.

## The Centre for Evidence in Transplantation

**Professor Sir Peter Morris** Director

The Centre for Evidence in Transplantation (CET) was established within the clinical effectiveness unit (CEU) at the College in late 2004. It is under the direction of Sir Peter Morris AC FRS FRCS and has two research associates on the staff, Dr Liset Pengel PhD and Miss Leticia Barcena TLV. It is linked with the London School of Hygiene and Tropical Medicine, as is the whole of the CEU. Within the CEU and the adjoining National Collaborative Centre for Acute Care it can call on the expertise of many medical statisticians, systematic reviewers and information technologists. The vision for the centre is for it to become, to some extent, a virtual reality centre that transplant units around the country can call on for assistance in evaluating evidence for current practice in organ and tissue transplantation. In the second part of 2005, the first research fellows will join the centre, jointly supervised by the CET and the host unit on specific projects of interest to both the host transplant unit and the CET.



Leticia Barcena (left) and Liset Pengel in the Centre.

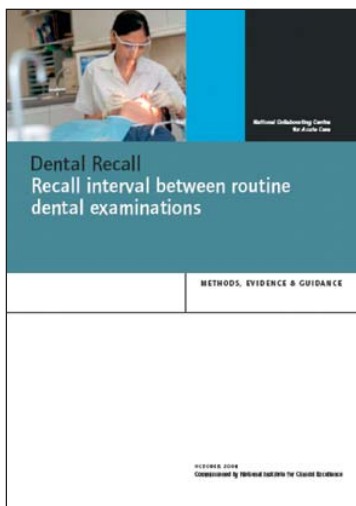
Two projects are currently in progress. The first is an analysis of randomised trials in organ transplantation performed in 2004 with an assessment of the quality of the trials. Although randomised trials are regarded as level 1 evidence, this depends on the quality of the trials, which is quite variable. This will appear as a regular feature within the journal *Transplantation*. The second project is a study of the impact of the source of support for randomised trials on the quality of trials and the interpretation of the outcome for the years 2002 and 2003.

# The National Collaborating Centre for Acute Care: It's all adding up...

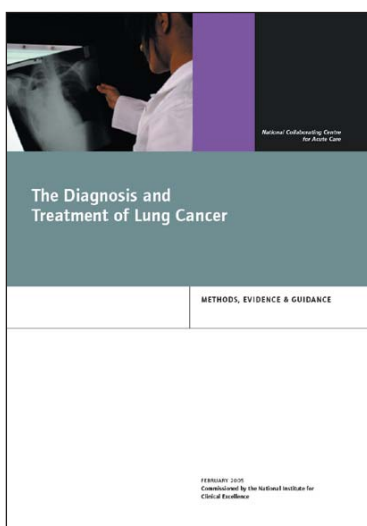
## Dr Jacqueline Rainsbury Director

April 2005 marked the start of our fifth year as a National Collaborating Centre and we are extremely proud of our accomplishments since our inception.

The past 12 months have been busy and during that time we have published two guidelines, one conjointly with the Scottish Intercollegiate Guidelines Network (SIGN). The first of these publications was the dental recall guideline which was launched in October 2004. Welcomed by the chief dental officer, Ramen Bedi, this guideline marked the successful collaboration of our centre with staff from the Cochrane Oral Health Group and the International Centre for Evidence-based Periodontal Health.



The second publication, in February 2005, was that of the lung cancer guideline. Accolades from cancer tsar Mike Richards attest to the time and dedication put in by centre staff and the lung cancer guideline development group for this project. This guideline was especially challenging since it was our first formal collaboration with another guidelines organisation.



The centre continued to have a strong team of staff members, including two with ties to the London School of Hygiene and Tropical Medicine and to the clinical effectiveness unit at the College. It is worth noting that turnover at our centre has been low over the past five years with the majority of staff members having a minimum tenure of 2.5 years.

Our achievements at the centre could not have been accomplished without the wonderful support of the NCC-AC management board and our host organisation, The Royal College of Surgeons of England. We meet with the former on a quarterly basis but all board members have generously given their time and attention to matters outside of the formal meetings. Current board members include:

- Dr Douglas Justins**, chairman – Royal College of Anaesthetists
- Dr John Sparrow** – Royal College of Ophthalmologists
- Professor Fraser MacDonald** – Faculty of Dental Surgery
- Mr John Black** – The Royal College of Surgeons of England
- Mrs Elizabeth Brain** – Royal College of General Practitioner's Patient Partnership Group

Observers on the board include:

- Dr Jan van der Meulen/Dr John Browne** – Clinical Effectiveness Unit
- Dr Jacqueline Rainsbury** – National Collaborating Centre for Acute Care
- Professor Peter Littlejohns** – National Institute for Clinical Excellence
- Mr Craig Duncan** – The Royal College of Surgeons of England

The board chairman maintains this post for one year and is then succeeded by a board member from one of the other royal colleges. Dr Douglas Justins acted as chairman for 2004 to 2005, and was succeeded by Mr John Black from April 2005.

We have another challenging and busy year ahead as we near completion of the nutrition support guideline's first draft and commence working on a guideline for the prevention of venous thromboembolism and another on the management of faecal incontinence in adults. Also, as I write this, our funding body NICE is undergoing substantial change, which includes merging with the Health Development Agency and thus expanding its agenda to encompass public health issues. This reorganisation will take some time and our centre is currently uncertain of what it will mean in practical and financial terms for us.

However, I strongly believe that the equation of a talented team of staff, a supportive board and a co-operative hosting organisation will continue to add up to many more achievements in the next year.



The Royal College of Surgeons of England

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The saving of life, the relief of pain and improved quality of life are ways in which The Royal College of Surgeons is helping millions of people each year. Advancements in surgical science are improving the lives of many people through new techniques, training and research.

The College invests in highly focused pioneering research into cancer, heart disease, nerve damage, and diseases in children and the elderly. However, as a registered charity it is not part of the NHS and relies substantially on legacies and donations to continue its activities.

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You may have benefited personally from surgery or know someone who has. If you would like to help our operation be a success through a gift or legacy, please contact the College for more information at the following address:

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