BASO~The Association for Cancer Surgery

Yearbook 2013

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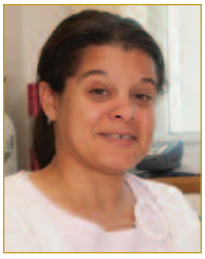

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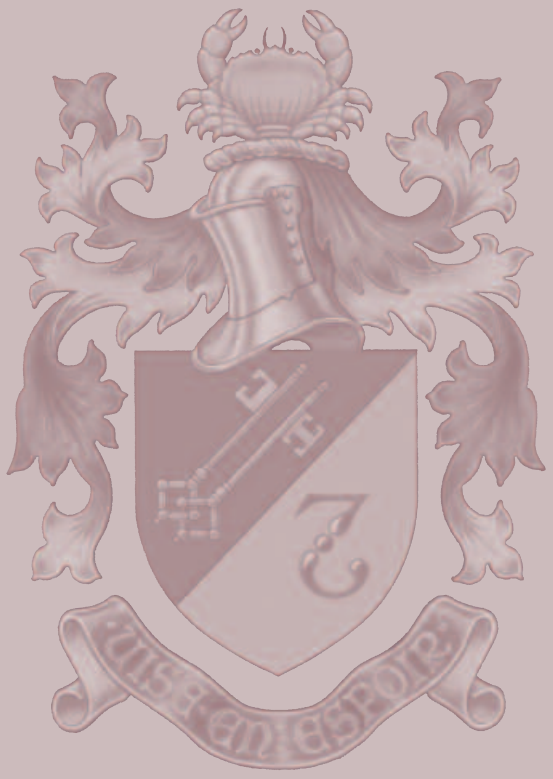
BASO~ACS Membership



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Full Members
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Associate Members
Specialist Registrars, Clinical Assistants and Senior House Officers

Affiliate Members
Clinical Nurse Specialists, Researchers and Allied Health Professionals

Overseas Members
Professionals working in surgical oncology outside the UK. Members from the Republic of Ireland can choose to join as Full, Associate or Affiliate members or as an Overseas member

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Professionals who have retired from practice

Membership benefits include:

- Annual subscription to the European Journal of Surgical Oncology
- Affiliate membership of ESSO
- Reduced delegate rates at the BASO~ACS Scientific Conference

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Download the BASO~ACS membership form at www.baso.org.uk

The Surgical Oncology Trainee Association ("SOTA")

Membership of SOTA is free to trainees from all disciplines having a medical degree and in a dedicated career pathway, or interested in pursuing one, in cancer surgery. Membership includes an online subscription to the European Journal of Cancer Surgery (EJSO), a free SOTA one-day conference, and discounted BASO~ACS conference registration fees.

SOTA Members can apply to join online:
www.baso.org.uk/sota/membership-form.aspx

President's Address

Mr Michael Hallissey
President of BASO~ACS
Consultant in Upper GastroIntestinal, Breast and Complex Pelvic Oncology Surgery and Deputy Medical Director, Queen Elizabeth Medical Centre, Selly Oak Hospital, Birmingham

BASO is now reaching 'maturity' with the Association being 40 years old and with the 40th annual scientific meeting being held this year in November. The Association was formed in 1972 to bring together all those with an interest in the surgical treatment of cancer.

The original group included gynaecological oncologists, head and neck surgeons and sarcoma surgeons to name a few of the groups involved. The aim of the Association was to bring the experience, knowledge and research work of a diverse group together to improve the provision of surgical treatment for cancer at a time when specialisation was rare. The world has changed in this period with the decision to move to site rather than disease specialisation. With the sub-specialisation we have seen across all disciplines, this sharing will be increasingly important to ensure the advances in one aspect of cancer surgery can be shared with all of the others to the benefit of patients.

The development of a vibrant trainees group, SOTA, reflects the desire of the trainees to share in this approach and I am certain this will be a key to the future success of the Association. The first SOTA training day last November gathered General Surgery, ENT, Urology and Plastics trainees together to learn about the basic issues relating to the non-surgical treatments employed in cancer management. With their own President and committee, I hope this venture will go from strength to strength.

The Association continues to have a committee that covers the breath of specialties involved in surgery for cancer and the range of topics discussed at the Scientific meeting continues to cover all aspects of cancer care. The articles in this Yearbook reflect the range of issues that are pertinent to Surgical Oncologists, many of which would be missed in a single specialty meeting.

The talk in November by Professor Dame Val Beral highlighted the impact of the oral contraceptive pill on breast, endometrial and ovarian cancer rates. The enormous reduction in ovarian cancer risk seen shows the unforeseen consequences of our interventions and without an awareness of the impacts on the whole patient we are not able to provide the best of care. Professor Sir John Burn gave a brilliant exposition on Genetics in cancer and the changes seen in the last 10 years. His description of the future in molecular diagnostics outlined how this would be at the bedside within a few years. This ties in with the talk by Parry Guilford who presented data on CDH1 mutation, which is linked to inherited Diffuse Gastric Cancer, and its link to lobular breast cancer that demonstrates that patients do not respect our site specialisation.

I hope the forum that BASO~ACS provides will give you, our members, the chance to gain insights from across the disciplines treating cancer that will continue to enhance the care you provide so effectively.

Mike Hallissey

President, BASO~ACS

Meeting Secretary's Report

Mr Charlie Chan
BASO~ACS Meeting's Secretary
Consultant Surgeon, Cheltenham General Hospital

BASO~ACS Scientific Conference Report 2012

Last November, we held the 39th BASO~ACS Annual Scientific Conference at the Royal College of Surgeons. This was preceded by the inaugural SOTA (Surgical Oncology Trainees Association) meeting on the Sunday afternoon.

The theme for the meeting was "Risk and Uncertainty". This is a topic which vexes patients and their doctors. The patients are regularly concerned about the risk of developing cancer, the underlying risk of their cancer, and the risk of adverse effects of the treatment. Uncertainty about outcome causes significant anxiety for all concerned.

Doctors attempt to assess the prognosis or risk of recurrence, and regularly counterbalance the benefits of treatment against the risk of side-effects. There are many conditions for which there remains uncertainty about which is the best treatment. Indeed, there are also some conditions where it is uncertain whether treatment is even required.

Hence, the meeting opened with a clinical symposium on several conditions, for which there is uncertainty about the correct treatment. This session covered the management of low-grade DCIS in the breast (Professor Sarah Pinder, London), Barrett's oesophagus (Professor Hugh Barr, Gloucester), Anal Intra-epitheilial Neoplasia (AIN) III of the anal margin (Professor John Scholefield, Nottingham), low Gleason grade prostate cancer (Professor Freddie Hamdy, Oxford) and finally melanocytic lesions of unknown malignant potential in the skin (MUMP - Professor John Thompson, Sydney, Australia). This generated much debate afterwards, particularly on the topic of low-grade prostate cancer. Some commentators suggested that this might relate to the age of some of the more senior members within the audience!

Understanding risks

Continuing the theme of uncertainty, Professor David Spiegelhalter, the Winton Professor of the Public Understanding of Risk at Cambridge University, gave a keynote talk on "Understanding risks in cancer". His work has been seminal in improving the public understanding and communication of chance, risk, luck, uncertainty, and probability. Recently, he has been involved in the redrafting of the information for women offered breast screening in the NHS. He has also presented widely on BBC TV and on Radio 4. His lecture exposed many of the pitfalls that lurk for cancer doctors when communicating treatment and risk with their patients. Improving this communication is fundamental to the way in which patients make key decisions about their cancer treatment choices. Highlighting issues such as using a constant denominator and graphic aids, such

Professor John Scholefield, University of Nottingham Queen's Medical Centre, at the 2012 Scientific Conference

as icons (www.iconarray.com) are simple tricks, which transform the understanding and perception of risk by lay people. Martin Burton, the Clinical Lead for the UK Cochrane Collaboration and Consultant ENT Surgeon in Oxford, then went on to discuss how uncertainty affects the way in which patients make treatment choices.

An increasingly common clinical scenario for risk and uncertainty is the question about how to manage patients with a high family risk of cancer. Professor Sir John Burn from Newcastle University gave the Ernest Miles Lecture on "The High Family Risk Colorectal Cancer Patient". This discussed the genetic mutations and microsatellite assessment in families with colorectal cancer, and presented the future in bedside diagnostics with prototypes for a handheld test device for microsatellite assessment for colorectal cancer. Strategies for cancer prevention were also explained.

Adjuvant Treatment

Sir Richard Peto presented the latest Meta-Analysis on the benefits of Adjuvant Treatment of Breast Cancer. He also gave a preview of the data from the ATLAS study on the extension of adjuvant hormone treatment for women with ER positive breast cancer. His colleague in Oxford, Dame Valerie Beral, spoke about the "Causes of Cancer in Women" with particular reference to breast, ovarian, and endometrial carcinoma.

Professor Sir Richard Peto at the 2012 BASO~ACS Annual Scientific Conference

Multi-disciplinary care in cancer is viewed by many as a modern concept. However, this is not as new as many would think. The Sir Stanford Cade Lecture was delivered by one of his successors at the Royal Marsden Hospital, Professor Meirion Thomas. This biographical lecture and review of Sir Stanford Cade's career was a timely reminder of the seminal thinking of one of the key cancer surgeons in the early 20th century.

One of the cancers treated by Sir Stanford Cade was malignant melanoma. Sadly, this is a disease which has shown little improvement in survival over the last few decades. However, new advances in targeted therapies appear to be heralding a new dawn in melanoma treatment. Professor John Thompson from the Melanoma Institute Australia delivered the EJSO lecture on surgery for melanoma. Over the last 2 to 3 decades, Professor Thompson has been one of the advocates of reducing the radicality of melanoma surgery, in favour of understanding its adherent biological nature. This trend has led to less morbid surgery for patients with this increasingly common and virulent condition.

Dame Valerie Beral at the 2012 BASO~ACS Annual Scientific Conference

Improving cancer outcomes is the goal for clinicians at an individual level and also nationally at government level. We were extremely grateful that Professor Sir Michael Richards, from the National Cancer Action Team, was finally able to come and speak at the BASO~ACS Conference. He has been a staunch supporter of surgery as the key plank of effective cancer treatment for most of the common solid tumours. His policies within the UK were contrasted with the European view presented by Professor Peter Naredi, a consultant surgeon in Sweden and the President of ESSO. Professor Naredi also highlighted the holistic way in which surgical oncology training is delivered within Europe. ESSO has numerous initiatives to improve the training of cancer surgery specialists, and there was much that we in Britain might learn from this.

All of us across the world owe an enormous debt to the outstanding contribution to cancer surgery from the NSABP (National Surgical Adjuvant Breast and Bowel

Professor Peter Naredi, President of ESSO, Lecturing at the BASO~ACS Annual Scientific Conference

Professor Sir Mike Richards Lecturing at the BASO~ACS Annual Scientific Conference

Project) in North America. It was with enormous pleasure that we welcomed Professor Norman Wolmark from the NSABP to deliver the BJS lecture on "The Future of Cancer Surgery Trials". Over the last two generations, there has been a fundamental shift in our understanding of cancer and its behaviour. This has been underpinned in a major part by the results of the NSABP trials, which have demonstrated that ultra-radical surgery is no more effective in curing cancer than organ/function preserving surgery. This key shift away from the principles of Halsted has catapulted the importance of our understanding of the molecular processes involved in carcinogenesis and metastasis. Increasingly, surgical trials will focus on less radical surgical treatment, allied to improved molecular prognostic and predictive techniques. Surgeons still have a vital role in improving our understanding with translational trials.

Professor John Thompson (Australia) lecturing on melanoma risk lesions

In the future, we will need to rely on the next generation of cancer surgeons to improve our knowledge and understanding of this complex disease. BASO~ACS has always fostered surgical research amongst its trainees. The Ronald Raven Prize was awarded to Mr Marc Bullock from Southampton, and the BJS Prize to Miss Eleanore Massey for her work at the Paris Breast Centre. The Alan Edwards Poster Prize was awarded this year to a medical student, Miss Kathryn Frewer. It was very reassuring to see continued support from a host of surgical trainees from many different specialties. There was a very noticeable presence from medical students this year who wish to pursue a career in cancer surgery. Allied to this, the successful launch of SOTA and its inaugural meeting bode well for the future of cancer surgery and cooperation between different specialties.

In 2013, we will be celebrating the Ruby Anniversary of the Association. Again we will have a theme underpinning the meeting. We shall be examining "Cancers at the Extremes of Age". There has been much discussion about inequalities of cancer care and opportunities for older patients with cancer. The fundamental issue now is about how we maximise the opportunities for older people, and how we can extend treatment safely to people who are less fit. A forgotten group of cancer patients are the young. They face different challenges, with concerns about their families, fertility, and social stigma. We shall be reviewing many of these topics in November 2013, and I look forward to seeing many of you again at our next Annual Scientific Conference.

Honorary Secretary's Report

Lynda Wyld
Senior Lecturer in Surgical Oncology
Honorary Secretary of BASO~ACS
Department of Surgical Oncology, University of Sheffield,
Sheffield UK

Vise en Espoir - Looking Forward in Hope: the Next 40 Years.

This year BASO~ACS celebrates its 40th anniversary which it hopes to do in style at our Annual Scientific Meeting in November. As always the scientific programme will be wide ranging and include some of the most eminent surgeon scientists practicing today. The hot topic of the day does not appear to have changed much in the 40 years that the association has been in existence: the title of the first BASO Scientific meeting in June 1973, chaired by Ronald Raven, was 'should lymphadenectomy be discarded'. We could easily schedule the same debate today and have a healthy debate about how we manage the nodes in both breast and melanoma surgery . I suspect it will be many more years before this issue is finally resolved by the research that is currently ongoing. Maybe in time for our diamond anniversary!

It is a great pleasure to see that the 2014 Annual Scientific Conference will be co-hosted by our European sister organization the European Society for Surgical Oncology in Liverpool.

The European Society for Surgical Oncology has been developing ever closer links with BASO as it grows in size and develops its activities across Europe. Whilst a younger organization by some 10 years, it is going from strength to strength and its annual meeting is now attended by nearly 1000 surgeons. We hope that next year's meeting will be the most successful ever for both societies. The choice of venue will take us outside of London for the first time in many years. This is partly to reflect the fact that our usual venue, the Royal College of Surgeons, cannot accommodate what is anticipated to be a meeting of 1000 delegates and also to recognize the fact that the incoming President of both BASO and ESSO at the time of the congress will be Professor Audisio of the University of Liverpool and the current ESSO President is Graeme Poston, also of Liverpool. Liverpool was recently European Capital of culture and has undergone huge developments in recent years making the waterfront area of the city a very attractive and compact venue for delegates to explore and enjoy. The congress will be held in the city's new 'state of the art' congress centre which is one of the finest in Europe.

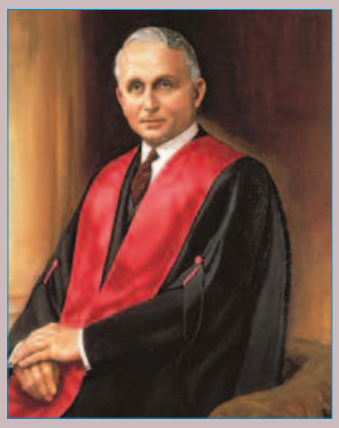
We hope that in addition to attracting a large number of European delegates, UK-based surgeons will continue to be well represented.

This year has seen BASO fully financially disengage with the Association for Breast Surgery and for the first time members have been asked to specify whether they wish to remain in one or both Associations. They have also had to pay two separate subscriptions although BASO, by keeping a very disciplined control of its recurring costs, has been able to ensure that its subscriptions remain low. It has been gratifying to see that the membership of the association has remained strong and we have not seen a significant number of surgeons leave BASO to become solely members of

the ABS. We have also seen a major increase in the number of trainee surgeons joining our trainees association, SOTA.

As can be seen from the above, the future of BASO~ACS in its Ruby Anniversary year is looking bright.

However, an anniversary is also a time for reflection on the past achievements of the Association since its creation 40 years ago. It is sobering to reflect that the reason for its formation was to maintain surgical oncology at the forefront of oncological practice, a place which was already being challenged by medical and radiation oncology and which is still a relevant issue today.



Ronald Raven

The original idea for the association was conceived in December 1971 by Ronald Raven and Ian Burn following a meeting of the newly formed section of Oncology of the Royal Society of Medicine. It had been noted that there was no surgical input into this meeting, either amongst the speakers or the audience, which was at odds with the place of surgery as the primary modality (then as now) of cancer treatment. A proposal was sent out to 35 leading cancer surgeons across the UK suggesting the formation of a dedicated society for cancer surgery. Some 18 months later, BASO launched its first scientific meeting, attended by 123 surgeons with an annual subscription of £8.50. Ronald Raven was the first president and the national committee was a who's who of the great and the good of surgery.

Shortly after its formation, the Association selected a motto: VISE EN ESPOIR, Look Forward in Hope, a phrase which holds ever more promise as we see the rapid rate of progress in the treatment for cancer.

Another major achievement of the association over the decades has been the publication of a high quality journal, which has evolved substantially in terms of its impact factor over this time. Shortly after its formation the Association launched its own journal, originally titled Clinical Oncology. This was published for 10 years until it merged with the journal of its sister association (ESSO) the European Journal of Surgical Oncology which has remained the joint publication of both societies ever since.

Looking back through the lists of Past Presidents and Ernest Miles memorial lecturers the names of some of the greatest surgical leaders of the times can be seen, serving as a testimony to the importance of the Association in leading both debate and education in the treatment of cancer. Its role in supporting and encouraging young surgeons to get involved in cancer research is exemplified by the names of the winners of the Raven and Alan Edwards prizes over the years, many of whom have gone on to become the leading surgeons of today.

As we look forward on this 40th anniversary, it is with hope that the next 40 years will continue this great tradition.

Message from the President of the European Society of Surgical Oncology

Professor Graeme Poston
President of the European Society of Surgical Oncology,
Professor of Hepatobiliary Surgery, Aintree Hospital, Liverpool

It is with great pleasure that I announce that in 2014 BASO~ACS and ESSO plan to hold a joint annual scientific meeting to replace their usual stand alone meetings. Liverpool has been chosen as the host venue in recognition of its vibrancy and the top class quality of its conference facilities.

It was voted the European capital of culture in 2008 and has a wealth of cultural, artistic and diverse entertainment opportunities for visitors as well as brand new, state of the art, conference facilities.

The newly opened ACC Conference Centre on the waterfront of the river Mersey is a modern purpose built facility with exceptional auditoria and first class catering, set near the historic Albert Docks, a UNESCO world heritage site. The city also boasts more museums and galleries than any other UK city outside of London, including the Merseyside Maritime Museum, the Beatles Story and the Tate Gallery.

The organizing committee for the congress is a fusion of leading members of both the BASO~ACS and ESSO executive committees with involvement of other key sub-specialty associations to ensure that the congress has something to offer everyone. It is intended that the congress will be arranged into multiple parallel tracks such that a surgical oncologist with a special interest in

breast surgery would be able to spend their time in breast sessions and likewise for colorectal, upper GI etc. In addition world leading experts will deliver plenary lectures of interest to the entire congress.

In keeping with the traditions of the two associations there will also be sessions for the award of the Ronald Raven and Alan Edwards prizes and the Ernest Miles Lecture for BASO. For ESSO, the lifetime achievement award and the Niall O'Higgins award will also be presented.

We hope that this will be the most successful congress yet for both associations and strengthen our links across Europe.

Across the Mersey from the ACC Conference Centre, Liverpool

Surgical Oncology Trainee Association

Message from the SOTA President

Wail Al-Sarakbi

The Surgical Oncology Trainee Association has enjoyed a very successful and eventful year. Our first annual meeting was held on the 18th of November 2012 at the Royal College of Surgeons in London on the eve of the BASO Annual Scientific Conference.

The Conference incorporated an excellent teaching day with lectures from leading figures in cancer surgery. Dr Peter Jenkins gave a talk titled "Radiation Therapy - why and how?" which highlighted the current scientific concepts in Radiation Oncology which was of great relevance to surgical trainees of all specialties. Following that Dr. Jeremy Braybrooke elaborated on the new trends in Cytotoxic Chemotherapy in the UK. The subsequent talk given by Mr David Rew on the medico-legal aspects of cancer surgery generated a great deal of debate and discussion and was found very relevant by all attendees. The last talk, but by no means the least, was delivered by Professor Peter Naredi (President of ESSO) who gave an outstanding presentation of the current status of surgical oncology training in Europe.

The meeting was followed by our first AGM where we agreed on a timetable for the first election of SOTA officers. I am pleased to say that the election campaign generated a healthy competition and resulted in the election of four officers: President, Vice President, Secretary, and Education and Training representative. We had 11 nominations for the above mentioned posts with a remarkable turn out with over 100 members casting their vote online. We elected 5 officers as we had a tie for the Education and Training representative so the consensus opinion was for the two surgeons to share the posts. I hope you will find the short statement of each of our committee member useful and informative. The new committee is starting to make plans for SOTA educational meetings this year.

Our second annual meeting will take place on the eve of the BASO Conference in November and I have been working closely on the programme with Charlie Chan and Lynda Wyld who have shown a great deal of support and guidance over the past year, and I must thank both of them for all their help. The programme and speakers will be finalised and announced shortly once the main BASO meeting has been advertised.

I trust that the new committee will drive our young organization forward and establish strong links with other organizations in the UK and Europe to strengthen our position as the representatives of young cancer surgeons in this country.

Our objectives for the next year are to continue to provide support to our members and consolidate the pivotal role of our organization within BASO and future collaboration with EYSAC (ESSO Young Surgeons and Alumni Club). We hope to continue to organize various educational events and raise the profile of our growing organization.

It has been a challenging and rewarding year, and I would like to take this opportunity to thank all committee members for their enthusiasm and support. I would also like to thank Marcia Woolf, our association administrator, for her hard work providing support to our committee and members.

Finally, I wish to thank BASO for their continuing support for our growing organization.

Wail Al-Sarakbi

President

SOTA Honorary Officers

Wail Al-Sarakbi - President

I qualified in 2001 (St.George's Hospital Medical School) and following my house jobs I completed my BST at the William Harvey Hospital. I undertook a period of full time research in Breast Cancer at St.George's University of London. Currently I am a senior breast trainee in the London Deanery.

I have strong commitment to Cancer Surgery as a specialty of choice for my future career. I was the chair of the Mammary Fold for a period of 12 months and prior to that I was the vice chair for the previous 18 months and was actively involved in its development.

Dara Lundon - Vice President

Dara is a Urology Research Registrar in St Vincent's University Hospital, Dublin. He is currently completing his PhD in University College Dublin investigating treatment strategies for advanced prostate cancer. More recently he has completed a BMedSci and an MSc in Surgery and lectures within the Department of Healthcare Informatics in UCD.

Nicholas Faure Walker - Secretary

Nicholas is currently a CT2 London core surgical trainee in urology and renal transplantation at Guys hospital with an interest in uro-oncology. He did academic foundation training in Bristol on laboratory research into effects of VEGF and clinical research into neoadjuvant chemotherapy for bladder cancer. Nicholas is also involved with a clinical trial and has recently finished some research into pre-operative scanning for radical prostatectomy. As SOTA secretary, he is looking forward to organising our annual conference, enabling trainees' access to all aspects of cancer training as well as providing opportunities to present work. Nicholas is working on establishing links with the European Society of Surgical Oncology and would highly recommend SOTA to any surgical trainee with an interest in cancer.

Carol Norman - Education and Training Representative

Carol Norman is a General Surgery ST4 trainee in the South East Thames Deanery, with a special interest in Breast and Oncoplastic surgery. She graduated from Imperial College in 2005.

She is currently in a busy joint colorectal and breast surgery post at the Princess Royal University Hospital, Bromley.

Brian Kelly - Education and Training Representative

Brian Kelly was elected as one of the Education and Training representatives for SOTA and is currently ST3 in Urology in Birmingham. He has an extensive background in research and education, having completed his M.D by thesis on the field of circulating microRNAs in prostate cancer, as well as a BMedSci and was awarded an MSc in Healthcare Informatics- following presentation of his thesis on Bibliometrics in the Urological Literature. Brian is also Honorary Clinical Tutor in the University of Birmingham, and former Clinical Tutor in Urology in UHG/NUI Galway.

Surgical Training in the Future

James Wheeler
Chairman JCST
Core Surgical Training Committee

There is currently an independent four-country review of the shape of postgraduate medical training in the long term, which has the support of The Medical School's Council, The Confederation of Post Graduate Medical Deans (COPMeD), the GMC and The Academy of Royal Colleges. There are principal themes which include the balance between specialist and generalist training, the breadth and scope of training, the age old problem of service versus training requirements, needs of the health service, needs of patients, and flexibility in training.

The Joint Committee of Surgical Training (JCST) is made up of 10 Specialty Advisory Committees (SACs), including General Surgery and the newly formed Vascular Surgery, and is responsible for the provision of good quality surgical training in the UK. The 10 different surgical specialties have both overlapping and different requirements to provide surgical training for their trainees. Surgical training is likely to change in many ways over the next 20 to 30 years and this will be as a result of different surgical techniques together with changes in the political landscape and health service redesign. It must also be remembered that the population continues to increase in numbers and age, and disease patterns will change.

There will remain difficulties with significant competition ratios between Core surgical training and higher surgical posts. Competition ratios for General Surgery have been constant at approximately at 5:1. It is encouraging that there are an increasing number of surgical trainees being appointed straight from core, and this is likely to be the preferred route in the future. There has been a move for Core surgical posts to be increasingly themed although this still allows the opportunity for trainees to experience two other surgical specialties before embarking on higher surgical training. Although there will always be trainees who do not progress, the competition rates must be set at a sensible level which encourage both competition and opportunities for progression.

Trainees will be part of multi-professional teams and this way of working will need to be reflected throughout their training. It is likely that they will face increasing demands to be flexible with their opportunities for training. With the increased number of female medical students there is already an increased presence of women in surgery and there should now be no real barriers to a surgical career pathway for female trainees. It will however, lead to more surgical trainees pursuing flexible training. This may also include male trainees as surgery is increasingly seen as a career rather than a vocation. There is already a huge provision of a Consultant delivered service and this is likely to increase with public and political demands for Consultant involvement 24 hours a day, 7 days a week. Although this is initially likely to focus on the provision of emergency work, there will be drive for elective work to follow this. However, it is not known how this 40% increase in provision can be afforded in the current economic climate. We tend to focus on the correct balance between service and training for trainees but need to also consider the correct balance for trainers and this must be acknowledged by Trusts with perhaps targets introduced for training provision.

The population continues to age, and there are an increased number of individuals surviving significant health problems and thereby becoming older yet with increased co-morbidity. These patients may be exposed to an increased number of surgical solutions but with the attendant risks of their co-morbidity. In addition, the

public, through the media, will have an increased knowledge and awareness of what is possible surgically, and this will increase their expectations. Public expectations are already high and will only get higher, demanding high quality care. The publication of outcomes by individual Surgeons will be routine and may drive further increased sub-specialization.

Technological advances will continue with an increased range of surgical procedures for various conditions. This will be paralleled by perhaps some surgical conditions being treated non-surgically. There is already a move to more minimally invasive and targeted surgery, with laparoscopic surgery now considered routine within many specialties. Ultimately some surgical conditions will become increasingly rare and treated medically. How many current trainees will have performed an elective gastrectomy for benign peptic ulcer disease? Technological advances will continue to be huge and I am sure surgeons of only 30 years ago would never have envisaged an anterior resection being performed laparoscopically or an aortic aneurysm being stented with radiologists.

Some technologies and therapeutics may become more remote and indeed robotic surgery can already be performed remotely. There will be a greater emphasis on providing technology and hands on learning to support the acquisition of these skills and there is currently a large volume of work being done by the JCST and the Deaneries on simulation based training, which will be placed within the curriculum.

Re-design

There is likely to be service re-design with an increase in centralization of the provision of complex services. Although some surgical interventions may become less invasive, those who carry out the procedures will need to have been trained to a high level of expertise and be able to demonstrate that they are meeting surgical standards.

With these technological advances, there is an inevitable but associated cost and this will be one of many factors that drive a centralization of services. Service re-design will be seen for many complex interventions and has already been observed in upper gastrointestinal cancer and vascular surgery. There will be challenges for some geographical areas but there will be larger centres where complex procedures are performed, surrounded by a network of units that will deliver less complex care. This has implications for the experience of surgical trainees and how their training programmes are designed. Clearly, all surgeons, in both the centres and peripheral units, will still need to be trained to a high level and provide excellent quality care. We may have got too used to using the term "competent" as a measurement of surgical training and should strive towards trainees being expert in the performance of procedures.

There should be an opportunity for all trainees to be trained in the methodology of clinical research although there will remain dedicated academic trainees who pursue a parallel surgical career. However, the craft skills should be the priority for all surgical trainees. Service remains an intricate part of their training and is the most appropriate way to maintain some sort of apprenticeship to learn clinical and technical skills from their trainer.

Not all Surgeons will become specialists and indeed the majority will become expert generalists and it is important that this level of achievement must retain the title, the responsibilities and accountabilities of a Consultant. The profession will need Surgeons who are both competent to deal with common general, elective and emergency, workloads and who are able to identify patients requiring more highly skilled and complex surgery which will be provided in centralized units.

Some surgical specialties have developed the concept of a generalist "curriculum" with specialist training being achieved after CCT. In no way must a generalist be perceived to having skills deficient to those delivering a more specialized service. Surgical trainees will gain a CCT within their specialty, where the trainee is trained in the general elective and emergency workload of the specialty. Further training in sub-specialized areas will take place following CCT as further training may be gained within Fellowships at specialized units or within a mentoring programme as a Consultant within a larger unit. Post CCT training requires organization together with funding and quality assurance.

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BASO~ACS Prizes and Scholarships

Ronald Raven Prize Winner 2012

Identification and characterisation of dysregulated miRNAs during colorectal cancer progression - interplay between tumour stroma and malignant epithelium

Marc D. Bullock, BMBCh MA (Oxon) MRCS (Eng)
MRC Clinical Research Training Fellow and ST6 in General Surgery. Cancer Sciences Division, University of Southampton School of Medicine

Marc is currently an MRC Clinical Research Training Fellow at University Hospital Southampton, conducting pre-doctoral studies in molecular oncology.

Background

Colorectal cancer (CRC) is a key public health issue, and accounts for the second highest cause of cancer related death in Europe.[1] Metastases and disease progression are the principal cause of death and occur in 30% of patients at presentation and subsequently in over 50% of patients after surgery with curative intent.[2] The majority of patients with metastases remain incurable. Without treatment median survival is 8 months, but the addition of chemotherapy and newer targeted therapies may enhance this figure to 12 and 16 months respectively.[3] The emergence of targeted therapies has been made possible through a greater understanding of the molecular characteristics of CRC. Although results of clinical trials have proved disappointing, extending survival by only a few months,[4] these studies offer a proof-of-principle that therapeutic strategies translated from a better understanding of the mechanisms of disease can be applied to CRC. They also highlight the need for a continued effort to unravel the biological mechanisms behind CRC progression.

MicroRNAs: Emerging players in CRC

MicroRNAs (miRNAs) are a class of small highly conserved non-coding RNAs that provide widespread expressional control through translational repression of mRNA. MiRNAs have fundamental roles in regulation of intracellular processes, and emerging data strongly implicates them in the pathogenesis of numerous malignancies.[5] MiRNA expression is dysregulated in all cancers examined to date and increasing evidence confirms many oncogenes and tumour suppressor genes are under miRNA control, potentially promoting all the hallmarks of cancer. In CRC, miRNAs derail a number of cellular signal transduction and cell survival pathways including the Wnt/B-catenin pathway, EGFR pathway, and p53 function, tying miRNA biology to known mutational events in the classical adenoma_carcinoma sequence of malignant transformation.[6] Furthermore, miRNA profiling is able to distinguish tumours of different developmental origins and has potentially powerful applications as a prognostic and diagnostic tool in CRC.[7]

Importance of tumour microenvironment

A further theme in recent years has been the critical role of the cancer microenvironment and the dynamic interactions between cancer and stromal cells in promoting invasion and progression. In the malignant state, the stroma is phenotypically distinctive and termed 'activated stroma' to reflect this. Key cellular components of this stroma are myofibroblasts, a heterogeneous population of cells derived from fibroblast progenitors which provide permissive signals to the malignant epithelium.[8] Recent studies have shown that dyregulated miRNA expression in myofibroblasts provide clinically relevant prognostic information in stage II CRC.[9]

Current research:

The critical aim of the work in our laboratory is to seek the biological consequences of dysregulated miRNAs during CRC progression. Preliminary analysis identified specific epithelial and stromal miRNA expression patterns

during different and clinically relevant stages of CRC.

Stromal and epithelial miRNA candidates were selected for further study based on the magnitude of differential expression between specimens from patients with metastases and from patients who remained metastasis free. The highest scoring miRNAs were subsequently validated by highly sensitive quantitative PCR techniques and examined for functional significance.

The biological consequences of dysregulated miRNAs was assessed using proliferation, survival, apoptosis and migration/invasion assays in cultured CRC cell lines in which individual miRNAs had been stably up-regulated or knocked-down. Stable miRNA over-expression was achieved using plasmid miRNA expression constructs and knockdown achieved using specific anti-sense miRNA inhibitors.

Tumour invasiveness was also assessed using a 3-D organotypic model in which malignant colonic epithelial cells and ex-vivo colonic fibroblasts are juxtaposed in a configuration that recapitulates the morphology of CRC in-vivo. This powerful tool enables synchronous or metachronous over-expression/knockdown of candidate miRNAs in epithelial and stromal cells, facilitating the study of any cross-talk between the two compartments.

This approach identified a number of miRNAs within both stromal and epithelial compartments which may have significant biological relevance in CRC. Potential targets of these candidate miRNAs were identified using in-silico target prediction software and confirmed by Western blotting. Further validation was sought by studying the effects of miRNA candidates in reporter-gene assays, which establish whether direct miRNA/mRNA interactions have occurred.

Personal statement

My research career began with the award of an Academic Clinical Fellowship within the Cancer Sciences Division of the University of Southampton under the joint supervision of Mr Alexander Mirnezami, Professor Graham Packham and Professor John Primrose. This afforded me the flexibility to establish a program of translational research whilst simultaneously combining SPR training in General Surgery with humanitarian-surgical work for the aid agency MSF.

My ambition is to translate novel laboratory findings into tangible improvements in health outcomes for patients with CRC through enhanced molecular staging and prognostication and ultimately by developing targeted therapeutic strategies. I plan to achieve this through continued examination of the pathobiology of stromal and epithelial miRNAs in CRC.

The identification of individual miRNAs and in particular miRNA signatures with utility in the management of colorectal cancer has potentially important implications for molecular diagnostics and therapeutics. Development of specific miRNA profiles with the ability to sub-classify colorectal tumours and enhance prediction of disease recurrence or advanced stage would be of great clinical and commercial value and could dramatically alter the current management of patients. Thus a molecular pathological approach to disease staging, looking for individual and/or communal metastatic markers and profiles, when combined with modern imaging modalities, may provide a more accurate reflection of stage and better inform the multidisciplinary cancer team about the use of chemoradiotherapy. Likewise, analysis of promising individual biomarkers can aid drug discovery programs and ultimately facilitate a shift towards a personalised drug treatment process.

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The Ronald Raven Prize

The Ronald Raven Prize is awarded annually to the best presenting author in the Ronald Raven Prize Session of the BASO~ACS Scientific Conference. Ronald Raven, OBE, was a surgeon to the Royal Marsden Hospital. He had a distinguished career as a surgical oncologist spanning over 30 years and was co-founder of BASO in 1973. The award was first presented in 1973 and with few exceptions has been awarded every year since.
Previous winners of the Ronald Raven Prize were as follows:

1973 - 74	E N Gleave
1974 - 75	C B Wood
1975 - 76	P M Perry
1976 - 77	M J B Chare
1977 - 78	Jointly awarded to M Osborne and P E Preece
1978	S W Hall
1979	J S Simpson
1980	M Burke and W D George
1981	A W Samuel and C Teasdale
1982	Jointly awarded to B Greenway and G T Williams; and J N Fox
1983	M S McCormick and M S Hockey
1984	M W Kissin
1985	J M Morrison
1986	J S O'Neill
1987	Not available for competition
1988	G A Pritchard
1989	Jointly awarded to J H Scholefield and O M Taylor
1990	D A Rew
1991	A Wyman
1992	Miss J Walls
1993	D De Friend
1994	Miss L M Hunt
1995	C Yiangou
1996	S Downey
1997	T J Hugh
1998	L Wyld
1999	B P L Winjnhoven
2000	B M Smith
2001	Miss C J Buskens
2002	P Ryan
2003	G O'Donoghue
2004	E Myers
2005	Miss S Dua
2006	Mr N Alkahmesi
2007	Mr S Somasundaram
2008	Mr D Marsh
2009	Dr G McColl
2010	Mr S Heng
2011	Jointly awarded to Mrs C Schilling and Mr P Farrelly
2012	Mr M Bullock

Ronald Raven Travelling Fellowship 2011

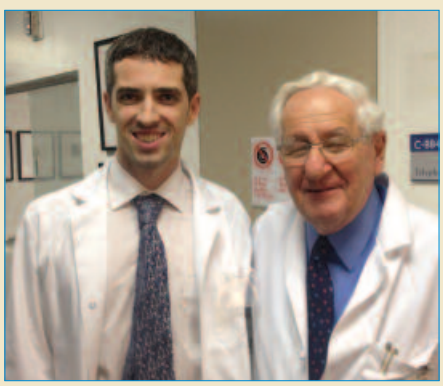
Visit to Memorial Sloan Kettering Cancer Centre, Manhattan, New York City - July/August 2012

Mr Declan Dunne
Senior SpR in Hepatobiliary Surgery, Liverpool

My fellowship supported by BASO has provided me with the opportunity to observe the training and practice of surgical oncology in one of the world's most prestigious cancer centres, Memorial Sloan Kettering Cancer Centre (MSKCC). With its main surgical hospital situated in the Upper East side of Manhattan, my visit and fellowship promised to be impressive and did not disappoint.

MSKCC has a worldwide reputation, both as a hospital providing exemplary care and as a research institution. A quick search of Pub Med identifies nearly 18,000 publications from their institution. The success of both their laboratory and clinical research can largely be attributed to their devotion to data collection. One of the drivers of this passion for data collection was Dr Murray Brennan who was chief of surgery from 1985 till 2006. His passion has developed into institutional culture, and this reservoir of clinical data helps fuel both their clinical research program and their laboratory program. The collection of clinical data for the purposes of research and improving care is now seen within MSKCC as a standard of care.

At MSKCC there is an established multi-disciplinary surgical oncology approach that functions seamlessly. Many of the operations carried out require several surgeons from different specialities. During my time there I saw hepatobiliary operations



Professor Blumgart still teaches after 60 years in the profession

One of the most incredible places I have ever been to. This is the vew from Brooklyn to the financial district in Manhattan.

combined with colorectal procedures, thoracic surgery and intra-operative oncology treatments. These operations are arranged often at only a few days notice, and are a testament to the nature and functioning of the hospital. Outside of the operating room, weekly MDTs help coordinate surgical interventions with the latest chemotherapeutic strategies to provide the best possible care tailored to each patient.

Dr Fong and his wife took my family out for a fantastic evening meal. My daughter insisted on bringing a giant duck she found in the Fongs' home

As there are very few junior doctors working within the surgical units at MSKCC, the oncology fellows provide much of the medical care below the attending (consultant) level. These fellows have completed their surgical residency (five years) and are seeking further training in surgical oncology. The fellowships provide intensive training in all aspects of surgical oncology. A typical working day starts around 6am with rounds.

The working day lasts till 6-7pm, though many of the fellows come back after their evening meal to do further rounds around 9pm. The fellows are on call for their own patients every weekday, though as they often only have 6-8 patients this usually means just the occasional call. They also cover alternate weekends, and staff an on call rota for new admissions.

The reward for this intense workload is an exceptionally well-structured training program. There are multiple departmental oncology meetings throughout the week, which vary between each surgical discipline. These meetings often involve a trainee case presentation, with supporting literature review, and open discussion. These discussions often benefit from the experience and knowledge of leading surgical oncologists such as Dr Murray Brennan and Dr Leslie Blumgart. Within the operating room the fellows are asked to perform all the operations with an attending assisting and training. This is the case for all operations from the most basic to the most complex. The theatre staff expect this, so there is never any concern about late finishes due to operations taking longer as a result of training.

This fellowship has changed the way I think about and approach cancer care, and I hope to take much of what I have learned into my future career as a consultant. I am extremely grateful to Professor Graeme Poston, all the surgeons at MSKCC, and to BASO for providing me with this opportunity and for supporting me in this experience.

Ronald Raven Travelling Fellowship 2013

The Ronald Raven Travelling Fellowship was endowed in 1993 by the Ronald Raven Trustees in Memory of Ronald Raven. It offers support for a senior trainee or recently appointed consultant to gain further experience in surgical oncology in the UK or overseas. It was first awarded in 1994.

Submissions are invited for the BASO~ACS Ronald Raven Travelling Fellowship Award for 2013. The funds for this award are provided by the Ronald Raven Trustees in memory of Ronald Raven, founder of the Association. The award this year is a maximum of £2,000 and can be awarded to one or several individuals as considered appropriate by the BASO~ACS National Committee when considering the merits of the applications.

The fellowship is open to trainees or recently appointed consultants, who have gained the Fellowship of one of the British or Irish Colleges.

Applicants need not be members of BASO ~ The Association for Cancer Surgery, but applications must relate to the aims and objectives of the Association.

Applications should be submitted to Ms Lynda Wyld, Honorary Secretary of BASO~ACS to arrive by no later than **Monday, 30th September, 2013** and should be submitted in the following format:

(i) A personal statement outlining the details of the use to which you wish to put the fellowship and also the benefits you wish to obtain from the visit. Please also include details of any other sponsorships, scholarships or fellowships obtained and whether you are applying for the full scholarship or part of it.

(ii) Curriculum Vitae (brief version - 3 pages maximum)

(iii) A letter of support from an independent referee/ supervisor in the UK as to your suitability for this fellowship.

(iv) A letter of invitation from the Unit/ Institution to be visited, showing that approval has been given for the intended programme.

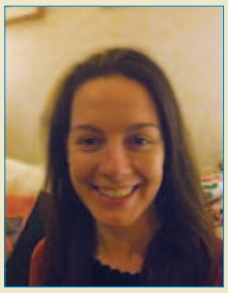
Please send applications as detailed above to: Ms Lynda Wyld, Honorary Secretary, BASO~ACS, at the Royal College of Surgeons of England, 35 - 43 Lincoln's Inn Fields, London, WC2A 3PE.

For further information please contact Marcia Woolf at the above address or by e-mail to: marciawoolf@baso.org.uk

Previous Ronald Raven Travelling Fellowship award holders have included:

2000	Mr S L Parsons
2001	Sri Lanka Tour
2002	Mr A Kumar
2003	Lucknow, India Tour; Mr P Rajeev, Mr A Watson, Mr K Gomez, Mr R Nadeem, Mr A Goyal, Mr A Prabhudesai
2004	Not Awarded
2005	Sri Lanka Tour; Mr B Piramanayagam, Mr C K Khoo, Mr H Ramesh, Mr P Kiruparan, Mr R Nadeem, Mr A Burns,
2006	Mr G Morris-Stiff
2007	Mrs K Hogben
2008	IASO Conference; Mr S Balasubramanian, Mr A Goyal, Mr S Menakuru, Mr H Ramesh, Mr A Subramanian, Mr V Upasani
2009	Ms P Roy
2010	Mr R Jones & Mr I Whitaker
2011	Mr D Dunne
2012	Mr V Yip

British Journal of Surgery Prize



Eleanore Massey
Specialist Registrar
Severn Deanery

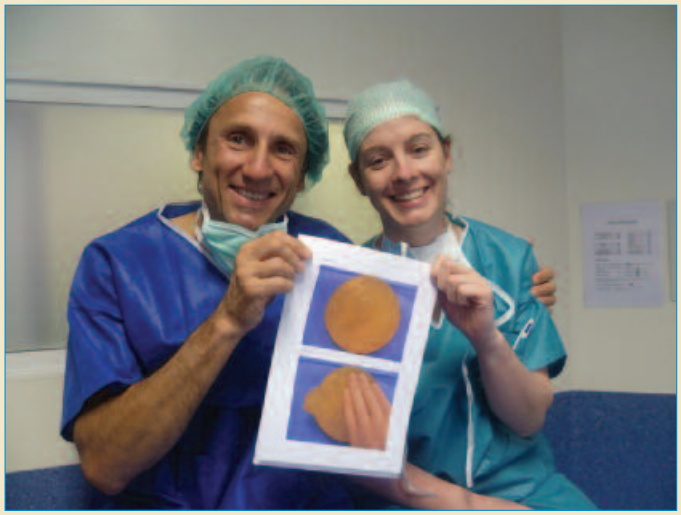
My name is Eleanore Massey. I am a Surgical Registrar in the Seven Deanery with a special interest in Breast Surgery, more precisely, in reconstructive breast surgery. I first heard Krishna Clough speak at the ORBS meeting in 2009. As a result of visiting him at his unit in Paris, I had the wonderful opportunity of returning as his Fellow in 2011, at The Paris Breast Centre, L'Institut du Sein.

And it was an incredible experience: not only did I get to fully appreciate the joys of croissants and macaroons, of Champagne and Camembert, and of how MDTs should really be run (in the evening with canapés and crudités), I also arrived in Paris in the eye of a storm.

The PIP breast implant scandal was just beginning to be a worldwide news event. As it was a French company, Poly Implant Prothèse, and the unit I was working in had used many of the implants, dealing with the fallout very quickly became part of my daily life. Each day, between November 2011 and February 2012, saw new regulations and new anger. Watching the political, media and medical whirlwind unfold was eye-opening.

As our unit had placed over 700 PIP implants for both cosmetic reasons, and for breast reconstruction after cancer, over a ten-year period, they had been one of the first units to notice, and flag up, an increase in the rupture rate of these implants. As a result, the patients were being contacted and informed of the problem and invited for assessment. It was clear that there was relatively little, known, long-term experience specifically of PIP implants. Hence my consultant was spurred on to collect all the data from his 700+ patients and to use this to help assess the long-term sequelae of PIP breast implants. It became my job to collect and analyse the data from over 800 patient records (all in French!). The resulting series: The Outcomes of 770 PIP Breast Implants is now one of the largest in world, and was presented at the BASO Annual Scientific Conference in November 2012.

The interesting first part of this study was investigating the worldwide use of PIP Breast implants and the international regulations as they were, and as they changed through the crisis. Over 500,000 PIP implants have been used worldwide: predominantly in Europe and Central and South America. Over 45,000 were used in the UK and over 30,000 in France. They were also rebranded as M-implants by a Dutch company and as TiBREEZE implants by a German company. Surgeons who had noticed the high rupture rate were beginning to stop using them in 2009 and in March 2010 AFSSAPS, the



Eleanore Massey with Dr Krishna Clough

French equivalent of the MHRA investigated and closed the company. AFSAAPS initial advice to surgeons was for assessment and surveillance of non-ruptured implants on the basis that there was no evidence that the silicone gel used was dangerous to human health. This advice was freely available in the public arena but it wasn't until the sensational reporting, in October 2011, of the death of a woman, who had PIP implants, from lymphoma, that it became a crisis. Following this, many countries throughout the world assessed the available evidence, conducted further investigations, and issued

recommendations. Of interest, is that despite the same information being available to all governments and Health Authorities, different countries gave differing advice, suggesting that the media, as well as scientific evidence, influenced the political response.

For our series of 770 PIP implants we examined the reasons for implantation, the reasons for explantation, the method and sensitivity of pre-explantation imagining, the explantation implant, and histological, findings. Most implants were placed for reconstruction following surgery for breast cancer: under a third were placed for cosmetic reasons, i.e. augmentation or asymmetry. Most illuminating was that the rate of explantation for non-surgical reasons, i.e. patient choice, increased seven-fold following the media spot light. The conclusions that MRI and USS are sensitive tools for assessing implant integrity supports many previous studies. The rupture rate was significantly higher than published rates for other silicone implants. The rate of cancer events in this series was consistent with known recurrence rates in similar populations and only one patient in the cosmetic group developed a new breast cancer. Thus the conclusion was drawn that, despite the high, early rupture rate, there was no increase in cancer events.

I gained a great deal from working at this unit on this research. Not all of it was related to the surgical outcomes of a faulty prosthesis. I improved not only my spreadsheet, database, and statistical analysis skills, but also my French written comprehension a thousand-fold! I learnt what fear does to normally rational people; how anger can be misdirected at innocent parties; the fragility of regulations and guidelines; how changes in National health policies can be altered by a myriad of different reasons, and that Science and Fact are not necessarily the predominating factors.

The British Journal of Surgery Lecture and Prize

The British Journal of Surgery Society Ltd (BJS) is a registered charity, through which support is provided to surgical bodies, thereby advancing and improving education in surgery, diffusing knowledge on new and improved methods of teaching and practicing surgery in all its branches. The Society provides support for invited lectureships and surgical prizes.

In 2012 the BJS supported a Lecture and a Prize:

* The BJS Lecture, delivered at BASO~ACS' annual Scientific Conference by Dr Norman Wolmark of Allegheny General Hospital, Pittsburgh, USA, was *"The Future of Cancer Surgery Trials".*
* The BJS Prize winner was Miss Eleanore Massey of the Paris Breast Centre, France, for her paper *"The Outcome of 824 Poly Implant Prosthese Breast Implants".*

Previous BJS Lectures have been:

1997 Professor Cornelius Van de Velde
"The Need and Value of Clinical Trials in Surgical Oncology"

1998 Professor Umberto Veronesi
"New Developments in Breast Cancer Treatment"

1999 Professor Yuman Fong
"Gall Bladder Cancer - Treatment Strategies"

2000 Professor R Daniel Beauchamp
"The Role of TGF-Beta in Colorectal Cancer: tumour suppressor or tumour promoter?"

2001 Dr Jon van Heerden
"Surgical treatment of primary hyperparathyroidism"

2002 Professor Peter Goh
"Laparoscopic gastric surgery - development and role in gastric cancer management"

2003 Professor Lars Pahlman (Sweden)
"Rectal Cancer - state of the art staging and surgery"

2004 Mr K B Clough
"Oncoplastic surgery for conservative treatment of breast cancer"

2005 Dr I Amarasinghe, President of the College of Surgeons on Sri Lanka
"Surgical Oncology...a window of opportunity to bridge a chasm"

Previous BJS Lectures continued:

2006 Professor N Vauthey
"Multimodal Therapy of Hepatic Colorectal Metastases: Helpful or Harmful?"

2007 Professor Roger Blamey
"Prognosis of Breast Cancer; the past, present and future"

2008 Dr Paul H Sugarbaker
"Building a Consensus in the Surgical Management of Peritoneal Carcinomatosis"

2009 Dr Tim Rebbeck
"Efficacy of risk reducing oophorectomy-a worldwide review"

2010 Professor Cornelis van de Velde
"The European Vision of Surgical Oncology"

2011 Dr Armando Giuliano
"How SNB has Changed Breast Cancer Management"

Previous winners of the BJS Prize:

2003 Mr M Duxbury

2004 Miss K Boyle

2005 Mr T Vijayaganesh

2006 Dr R Kazi

2007 Mr L Maraqa

2008 Ms Rachael Johnson

2009 Mr Brian Hogan

2010 Ms Rosin Dolan

2011 Mr Samer-ul Haque

The British Journal of Surgery Society Ltd has kindly agreed to support a Lecture and Prize again in 2013. The Prize for 2013 is £600 and the Lecture receives £3000 in sponsorship.

Alan Edwards Prize

Kathryn Frewer
Year 4 MBBCh Medical Student,
Cardiff University School of Medicine

I consider it to be a huge privilege to have been selected to present at the 2012 BASO~ACS conference. Given the exceptional quality of the other contributors it was an unexpected honour to then be awarded the Alan Edwards Prize.

It was whilst taking a one year break from the M.B.,B.Ch. to study for an intercalated B.Sc. in Molecular and Cellular Pathology that I joined the Metastasis and Angiogenesis Research Group (MARG) at Cardiff University to research the role of WISP 2 in colorectal cancer.

Colorectal cancer is the second most common cause of cancer death in Europe and the third most commonly diagnosed cancer in the UK[1]. Patients with colorectal cancer do not die from the primary tumour itself but due to metastasis (most commonly to the liver).

Complex molecular mechanisms are required for colorectal cancer metastasis to the liver. Studies have shown that signalling molecules and signalling pathways involved in adhesion, invasion, motility and growth may be important in the metastatic process[2].

Wnt- induced secreted proteins (WISPs) have been implicated in tumourgenesis and metaplasia in numerous tissues. They are members of the CCN family and downstream components of the wnt signalling pathway[3]. Studies have shown that WISP-2 may act as a protective factor against breast cancer progression by controlling cell adhesion and motility. Disruption or down regulation of WISP-2 signalling in MCF-7 (breast cancer) cells therefore results in a significant increase in cell migration and invasion[4].

Previous research produced by MARG has shown that WISP- 2 may act as a tumour suppressor gene in CRC. Davies and colleagues identified lower levels of WISP-2 expression in CRC tissue compared to normal colorectal tissue. They observed lower levels of WISP- 2 expression in poorly differentiated and more aggressive tumours [3].

In the research I carried out we sought to further understand the role of WISP-2 in colorectal cancer and to specifically investigate how WISP-2 knockout affects Caco2 CRC cell behaviour.

WISP-2 knockout in Caco2 cells was achieved using a ribozyme transgene system. This involved the cloning of a WISP-2 specific ribozyme transgene into a pEF6 plasmid which was then electroporated in Caco2 wild type (WT) cells. In vitro growth, adhesion, invasion and motility assays were then carried out. Caco2 WT and Caco2 pEF6 cells were used as controls. (Caco2 pEF6 cells are Caco2 WT cells transfected with an empty pEF6 plasmid).

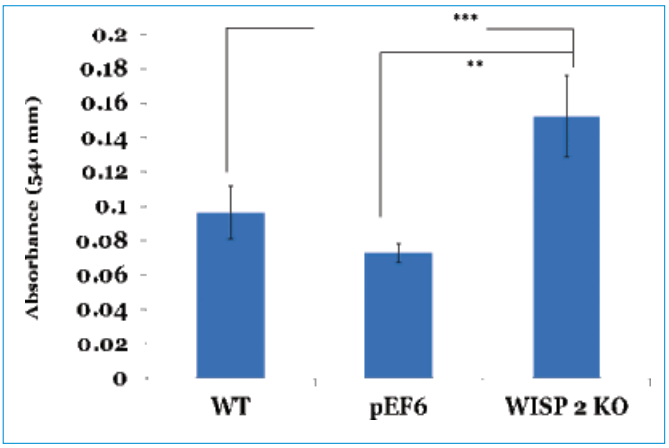


*Figure 1: WISP-2 knockout enhances Caco2 cell motility. Results showed a significant increase in cell motility between Caco2 WT and WISP-2 KO cells (*** p <0.001) and between Caco2 pEF6 and WISP -2 KO cells (** p= 0.01).*

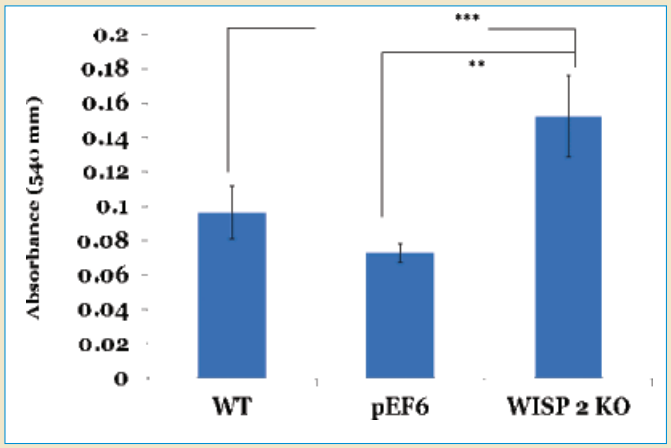


Figure 2: WISP-2 knockout increases Caco2 cell invasiveness

*Results showed a significant increase in cell invasiveness between Caco2 WT and WISP-2 KO cells (p= 0.014) and between Caco2 pEF6 and WISP-2 KO cells (p= 0.016). * = p value < 0.05*

Our results showed that WISP-2 knockout resulted in a significant increase in CRC cell motility (see figure 1). This was observed when Caco2 WT cells were compared to WISP-2 KO cells ($p< 0.001$) and when Caco2 pEF6 cells were compared to WISP-2 KO cells ($p=0.01$). WISP-2 knockout also resulted in a significant increase in Caco2 cell invasion (see figure 2). This was observed when Caco2 WT cells were compared to WISP-2 KO cells ($p=0.014$) and when Caco2 pEF6 were compared to WISP-2 KO cells ($p=0.016$). WISP-2 knockout had no significant effect on CRC cell growth rate or on CRC cell adhesion.

Invasion and motility are important characteristics in CRC metastasis. Our research has shown that loss of WISP-2 expression in CRC cells may lead to increased tumour cell invasion and disease progression. Understanding the mechanisms by which WISP-2 regulates CRC invasion and motility may therefore in the future allow the development of targeted interventions or therapies for the treatment of colorectal cancer metastasis.

I enrolled at Cardiff Medical School at the same time as my twin sister Natasha. We both decided to intercalate (between years three and four of the medical degree), and were fortunate to join MARG together. We were subsequently both awarded first class intercalated BSc honours degrees in Cellular and Molecular Pathology. Whilst I explored the role of WISP-2 in colorectal cancer Natasha researched the effect of MDA-7/IL-24 on lymphangiogensis in breast cancer (and in January 2013 Natasha won the Society of Academic and Research Surgery medical student prize at the Royal Society of Medicine). Having both been awarded intercalated degree bursaries from the Royal College of Surgeons of England we have been able to fully engage in research activities at MARG and contribute to and co author many research articles that have been published in international journals.

Eighteen months ago I was a hard working, motivated, engaged student who was looking towards becoming qualified and practicing medicine. Having tasted the excitement and challenges of research my panoramic view of medicine now has a vista dominated by surgery and clinical research, and this fills me with added expectation and enthusiasm for the future.

I would like to express my enormous thanks to Miss Rachel Hargest (Consultant Colorectal Surgeon, Cardiff) and Professor Wen Jiang (MARG, Cardiff) to whom I owe my success in the field of research. The trust they placed in me to meet their meticulous standards drove me to take full advantage of the opportunities they placed before me.

I would also like to thank my supervisor Dr Andrew Sanders who has supported me throughout my research. He showed patience in teaching me a multitude of scientific skills and helped me develop my ability to analyse scientific data.

I hope to return to MARG soon as my research has opened exciting new lines of enquiry.

Acknowledgements

I would like to thank The Royal College of Surgeons of England for their support in funding my research.

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The Alan Edwards Prize

The Alan Edwards Prize was first awarded in 1978 and is given to the best poster presentation at a BASO Scientific Conference. Alan Edwards was a consultant Surgeon at Whipps Cross Hospital in London and an early member of BASO, who tragically died in a boating accident.

List of previous winners

1978	M Soukop
1979	J Higgs
1984	P J Finan
1985	J R Parry
1986	C Porteous
1987	S R Ebbs and D M Nott
1988	Miss A Samuels
1989	N J Bundred
1990	M Loizidou and L C Barr (jointly)
1991	S C Low
1992	Miss L M Hunt
1993	Dr S Watson
1994	D M Bruce
1995	Miss L L Millar
1996	C R Wilson
1997	J S Chana
1998	S M Dresner
1999	N J Coombes
2000	D Hayne
2001	P J Kneeshaw
2002	D R C Spalding
2003	Dr A Schofield
2004	Mr I Daniel
2005	Mr G Wilson
2006	Mr Tak Loon Khong
2007	Miss Tejal Joshi
2008	Joseph Tang
2009	Ramsey Cutress
2010	Iain Brown
2011	Jagdeep K Singh
2012	Kathryn Frewer

BASO~ACS News Review

Thoracic Surgical Research

Mike Shackcloth
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Thoracic Surgical research in the UK is on the increase. The UK Thoracic Surgery Research Collaborative (UK-TSRC) was formed a couple of years ago in order to provide a platform for multi-centre research across the UK. This initiative under the Chair of Mr Eric Lim, of the Brompton Hospital, has this year produced two multicentre studies.

The first of these is a study investigating the use of PET-CT for staging pulmonary carcinoid tumours. This multi-centre approach has pooled the data on over 200 patients, producing a series over 10 times larger than those previously published. This work has been accepted for presentation at the American Society of Clinical Oncology meeting. The second of these studies was a UK validation of the ThoracoSCORE. It is a multi-centre study that evaluated the ThoracoSCORE risk stratification model in a UK population. Data was submitted on 1536 patients. Only female gender and co-morbidity score were found to be significant predictors of 30-day mortality in this UK cohort. The ThoracoSCORE failed to accurately predict mortality in this population. This study emphasised the continued need to develop an appropriate risk prediction model for the UK. This study was presented at the Society of Cardiothoracic Surgeons annual meeting.

The BASO prize for the best paper on the science and practice of cancer surgery was introduced to the Society of Cardiothoracic Surgeons meeting in 2012. This was awarded to Annabel Sharkey for her presentation on 'Analysis of potential quality outcome measures for lung cancer surgery across a cancer network'. She found significant differences between MDTs in the number of patients undergoing systematic lymph node dissection at resection, and the number of those undergoing video assisted thoracoscopic resection as opposed to resection via thoracotomy. However, there were no significant differences in procedure performed, preoperative mortality risk, post-operative length of stay or mortality.

The 2013 BASO prize was won by Mr Matthew Smith with his presentation 'Is plasma fibrinogen a novel independent prognostic factor in patients undergoing surgery for Non-Small Cell Lung Cancer (NSCLC)?' He investigated the relationship between preoperative plasma fibrinogen level and clinicopathological factors, pathological TNM stage and survival in patients with non-small cell lung cancer. He found that fibrinogen level was associated with tumour size and grade. Although survival data was immature, fibrinogen ≥4 g/dl may prove to be a novel independent prognostic factor following surgical resection of NSCLC.

The PulMiCC (Pulmonary Metastasectomy in Colorectal Cancer) trial continues to recruit patients. PulMiCC is a randomised controlled trial funded by Cancer Research UK which aims to determine the feasibility of recruitment into a randomised study comparing active monitoring to active monitoring with pulmonary metastasectomy. Patients with a history of resected colorectal cancer who are found to have pulmonary metastases are first registered for evaluation (stage 1) and, if subsequently eligible for the trial, they are invited to be randomly allocated to 'active monitoring' or 'active monitoring with pulmonary metastasectomy' (stage 2). The clinical outcomes are overall survival, relapse-free survival, lung function and patient-reported quality of life. Currently there have been 123 patients enrolled into Stage 1 and 36 patients randomised into Stage 2.

After the success of the MARS (Mesothelioma and Radical Surgery) trial (1) funding has been secured for the MARS2 trial. The MARS trial was a multicentre

randomised trial to investigate the effects of extra-pleural pneumonectomy (EPP) on survival and quality of life in patients with malignant pleural mesothelioma. The MARS trial involved 12 UK hospitals. Patients who had pathologically confirmed mesothelioma and were deemed fit enough to undergo tri-modal therapy were included. In a pre-randomisation registration phase, all patients underwent induction platinum-based chemotherapy followed by clinical review. After further consent, patients were randomly assigned (1:1) to EPP followed by postoperative hemithorax irradiation or to no EPP. The hazard ratio [HR] for overall survival between the EPP and no EPP groups was 1·90 (95% CI 0·92—3·93; exact p=0·082), and after adjustment for sex, histological subtype, stage, and age at randomisation the HR was 2·75 (1·21—6·26; p=0·016). Median survival was 14·4 months (5·3—18·7) for the EPP group and 19·5 months (13·4 to time not yet reached) for the no EPP group. Of the 49 randomly assigned patients who consented to quality of life assessment (EPP n=23; no EPP n=26), 12 patients in the EPP group and 19 in the no EPP group completed the quality of life questionnaires. Although median quality of life scores were lower in the EPP group than the no EPP group, no significant differences between groups were reported in the quality of life analyses. There were ten serious adverse events reported in the EPP group and two in the no EPP group. The trial concluded that in view of the high morbidity associated with EPP in this trial and in other non-randomised studies a larger study is not feasible. These data, although limited, suggest that radical surgery in the form of EPP within trimodal therapy offers no benefit and possibly harms patients. Due to the results of the MARS trial and the mortality and high morbidity of EPP, the lung sparing operation of radical decortication has gained popularity, and for many is the operation of choice for mesothelioma. The MARS2 trial is a randomised trial that aims to investigate radical decortication and chemotherapy versus chemotherapy alone for patients with mesothelioma.

With the increase in quality and quantity of thoracic surgical papers at this year's Society of Cardiothoracic Surgeons of GB and Ireland annual meeting as further evidence of the healthy state of thoracic surgical research in this country the future looks bright. With continued enthusiasm and the hard work of Thoracic Surgeons this country can continue to produce the evidence and scientific basis to provide the best possible care and treatments of patients with Thoracic malignancies.

Update on Hepatopancreatobiliary Surgery

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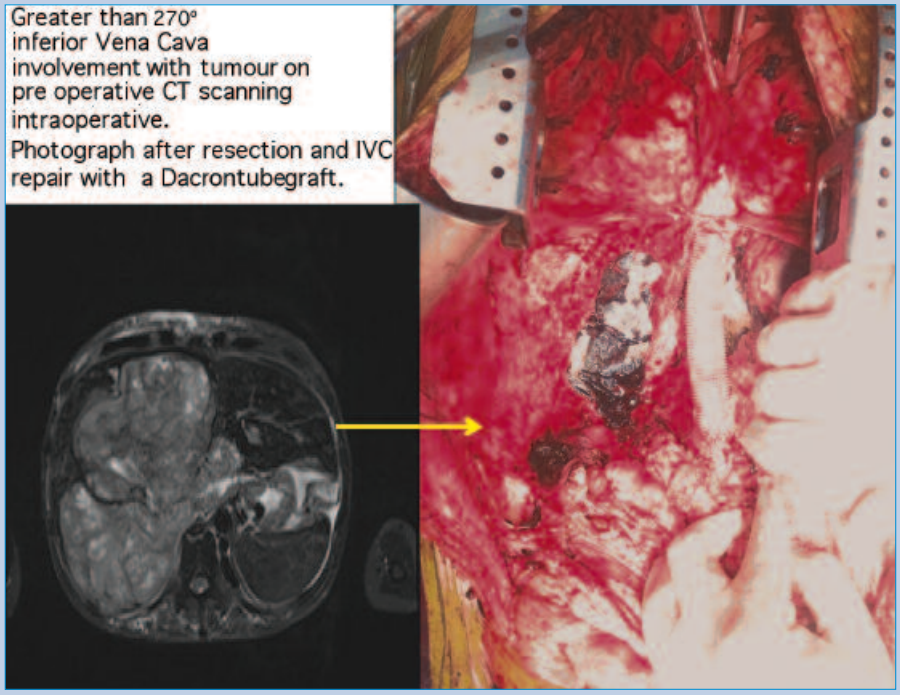
The last few years have seen various developments in hepatobiliary surgery as a whole. New guidelines have been published; more surgical oncology trials are being presented that could potentially change clinical practise; pre-operative assessment and enhanced recovery following major hepatobiliary surgery; as well as new surgical techniques. As a surgical specialty, we are making tremendous strides.

Recently, the new NICE guidelines on the management of colorectal cancer have been published. The key point of these guidelines is dealing with the uncertainty about which patients should be referred for consideration of resection of colorectal cancer liver metastases. The guidance on referral for all patients with liver-limited disease who are fit for surgery, that they should be referred to specialist liver surgery multidisciplinary teams for decisions on further imaging and operability. This practice will substantially increase the chance of such patients being offered potentially curative surgery. Nevertheless, there is still a discrepancy on referral practices depending on geographical location. This is a barrier that needs to be overcome, and the successful treatment of colorectal liver metastases depends highly on good multidisciplinary working among the different healthcare teams.

New trials are currently being published that have had an impact on the management of hepatobiliary cancers. Published data have observed that biological agents, such as cetuximab, may be beneficial as part of a down-staging programme in patients with colorectal liver metastases. The addition of cetuximab to current established chemotherapy regimens in patients with KRAS wild-type colorectal cancer has been shown to increase the response rates and the number of patients being down-staged, leading to more patients being offered potentially curative resection. In addition, NICE has recently published guidelines on the use of biological agents in the treatment of metastatic colorectal cancer.

Advances have also been made with respect to delivery of chemotherapy. Direct segmental administration of chemotherapy-eluting beads represents a novel drug delivery method that allows for the locoregional delivery of chemotherapy, such as irinotecan, to colorectal liver metastases. This method has shown impressive response rates and tumour destruction, and could potentially be an appropriate method of delivery for integration into future therapeutic regimens. However, results on long-term outcomes are still awaited.

Recently, more data on pre-operative assessment and enhanced recovery following hepatobiliary surgery have consistently shown a shift in practice with regards to emphasis on optimising patients prior to surgery and discharging patients as soon as appropriate. In most hepatobiliary practices, more elderly patients are being considered for major surgery. Hence, accurate assessment of operative risk is crucial. Some units have adopted preoperative cardiopulmonary exercise testing in high-risk patients undergoing hepatic resection and early results are promising. This assessment may be adopted more widely in times to come. Published literature has shown good evidence in implementing an enhanced recovery pathway following hepatobiliary surgery. At present, there is more funding and emphasis being invested into patient education on pre- and post-operative care, mobilisation and early introduction of oral intake that has led to a significant decrease in length of hospital stay compared to historical practices. This has been a "hallmark" of how far this specialty has progressed.



There are also new surgical techniques being developed. Two recent strategies that have emerged are: a) the "liver-first" or reverse strategy; and b) in situ liver transection with portal vein ligation as a form of two-staged liver resection. The "liver-first" approach may be beneficial to a selected group of patients with synchronous rectal tumour and liver metastases. The rationale behind this approach is that it allows control of the liver metastases first, optimising the chance of potentially curative liver resection, which influences long-term survival in these patients (Pawlik and Schulick, 2008). The liver resection may occur after chemo-radiotherapy for a rectal primary tumour or more often is frequently preceded by a period of neo-adjuvant chemotherapy which allows down-staging of the disease. With respect to the in situ liver transection with portal vein ligation, this is a new two-step technique for obtaining adequate but short-term parenchymal hypertrophy in patients requiring extended hepatic resection with limited functional reserve. This has been shown to be an alternative to portal vein embolization and recent data has shown early promising results. However, the patient selection criteria and long-term outcomes remain to be determined.

Briefly, this year saw the publication of the Francis Report with regards to practices at a particular Trust, and various recommendations have been suggested. Although we as a specialty are making steady progress, accountability and auditing our practices in our hepatobiliary unit is something that we neglect at our own peril. We are all here for improving patient outcomes, and we owe it to them to audit our practices, to enable us to keep improving the service we deliver.

Lastly, although we have and are currently overcoming many barriers, there are always new barriers and challenges ahead of us. The future for hepatobiliary surgery is not only bright, but interesting times lie ahead.

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Hot Topics in Breast Surgery

Non-Sentinel Node Predictive Nomograms in the Post ACOSOG Z0011 Era

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Undoubtedly one of the most controversial issues in breast surgery in recent years has been our management of the axilla.

There has been gradual but complete acceptance that full axillary dissection is not needed in every case, and may be replaced instead by techniques to identify if the axilla is involved. These techniques are varied and include pre-operative ultrasound and core biopsy, a range of sentinel node technique and even non invasive imaging with MRI scanning. The involved axilla would then be surgically cleared in most cases.

Controversy was heightened in 2010 by the publication of the ACOSOG ZOO11 trial[1] which called into question the need for further axillary surgery in some patients. It is probably too early to adopt this strategy without further, broader based research and longer-term follow up. In the meantime our management of the SLNB positive axilla may be aided by predictive models which have been developed to identify patients with low a risk of residual disease. These models tend perform best at the units in which they have been developed, but have also been validated in other centres with varying results. The main reasons for the inconsistent performance of predictive models may be the variability of histopathological methods used to assess the sentinel node metastases as well as differences in the case mixes between the centres.

The variable performance of the predictive models was addressed in two recent papers[2,3]. Sentinel node biopsy cases from five European centres formed a series of 1000 patients in these studies. The first paper assessed the performance and clinical utility of eight different nomograms. Histopathological methods and the case mixes varied between the units.

Accordingly, both the performance and the clinical utility of the eight nomograms varied greatly from unit to unit.

The second paper utilized the same patient series to examine the performance of the existing nomograms in predicting patients with high risk of residual disease. All of the nomograms performed relatively poorly in the high-risk setting. The results of these studies emphasised the importance of local validation of any nomogram. Furthermore, they displayed the need for a predictive tool that would accurately predict high-risk patients.

The original patient series of 1000 SNB patients was used to construct a novel predictive tool that was validated internally in 500 additional patients and externally in 1068 patients from eight other centres[4,5]. This novel predictive tool was able to accurately predict also a high risk of residual axillary disease. The model incorporated centre-specific prevalence of NSN metastases as a variable into the predictive equation thus facilitating calibration of the model into each centre.

The value of all NSN nomograms may be questioned in the “ACOSOG Z0011 era”. However, the Z0011 results are not generalizable to all patients including those undergoing mastectomy or having a high risk of NSN metastases. Therefore, predictive models still have value in clinical practice. A free application has been generated and can be downloaded on your smart phone or iPad when searching for "predictive tools for breast cancer"

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Hot Topics in Breast Surgery

Acellular Dermal Matrix (ADM) for Breast Reconstruction

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Implant reconstruction is an attractive option for patients who opt for a shorter recovery time and no donor site morbidity. It is the commonest type of post-mastectomy reconstruction undertaken in the UK and accounts for approximately 37% of all immediate reconstructions[1].

In the United States, in recent years there has been an increase in immediate breast reconstruction and this is largely due to increased use of implant reconstruction[2]. Traditionally, implant reconstruction was undertaken in 2 stages: an expander implant to expand the skin and soft-tissues followed by a second operation to exchange the expander with a permanent implant. With the introduction of anatomical implant expanders[3], it was anticipated that their use will avoid the need for 2 operations (other than for the removal of the implant port) and provide better definition of the inferior pole but this remains to be proven in a randomized controlled trial[4]. In order to avoid subcutaneous placement of the implant inferiorly, some surgeons choose to position the implant completely sub-muscularly (deep to pectoralis major) or recruit serratus anterior to cover the implant laterally. This requires more operative dissection and is believed to cause more pain. Although the latter remains to be proven, it is also a challenge to achieve good lower pole definition and a ptotic shape, with this approach.

The introduction of acellular dermal matrix (ADM) presents a paradigm shift in immediate implant breast reconstruction. ADMs are biological devices, are sterile (terminally sterile or containing preservative), acellular, surgical meshes derived from human, porcine or bovine tissue, most commonly, dermal. The dermis is stripped of all cellular components leaving a structurally intact and biochemically inert extracellular matrix, rich in collagen. Following implantation, it is believed ADMs provide a scaffold allowing in-growth and regeneration of tissue, add structural support and additional soft tissue cover. ADMs are used for lower pole cover when undertaking submuscular implant reconstruction. The perceived advantages are improved lower pole definition, improved cosmetic outcome, reduced post-operative pain and reduced operative time. All of these outcomes, remain to be proven in large prospective trials[5]. A recent systematic review and meta-analysis by Ho et al.[6] of complications following implant based reconstruction, with and without ADM, found an increase complication rate when ADMs were used. However, all these trials were retrospective without standardized protocols. In the UK, the POBRAD Trial[7] was setup to prospectively evaluate the outcome and complications of ADM (Surgimend PRS® - TEI Bioscience Inc. Boston, USA) implant reconstruction, within a standardized protocol. Initial outcomes of this trial are awaited later this year.

Current indications for ADMs

The British Association of Breast Surgery (ABS) and British Association of Plastic, Reconstructive and Aesthetic Surgeons (BAPRAS), published their recommendations of current indications for ADMs, for breast implant reconstruction[8]. Clinical indications include immediate and delayed post-mastectomy reconstruction (both for cancer and risk-reducing), implant revision surgery and bilateral reconstruction, particularly in those with small to moderate size breasts and a normal body mass index (BMI). Also, ADM immediate implant reconstruction can be considered for patients who are unwilling or unfit to undergo autologous reconstuction.

Operative technique

Following mastectomy, the pectoralis muscle is mobilized from the chest wall and lower insertion, disconnected, inferiorly. The ADM size is selected and the device is then prepared according to the manufacturers' instructions. It is secured inferiorly to the inframammary fold, and superiorly to the freed infro-lateral edge of pectoralis major. This creates a submuscular pocket for the implant and the ADM acts as a hammock or sling, supporting the inferior pole of the silicon implant. When using fixed implants, it is important to ensure the skin flaps are not under excessive tension. When using an anatomical expander, full expansion can be delayed to avoid excessive tension. A large bore drain is usually used to drain seroma fluid and the drain is kept in-situ for 1-2 weeks. Antibiotic prophylaxis is usually administered in view of the recognized risk of infection.

ADMs and radiotherapy

Chest wall radiotherapy is offered to patients who are heavily node positive (> 3 nodes)[9] as it improves local control and overall survival. As well as adversely affecting the skin and subcutaneous tissue, radiotherapy also significantly increases the complication rate seen with implant based reconstruction[10]. However, since the recommendation for radiotherapy is made after surgery and reconstruction is increasingly undertaken immediately, many patients undergo implant reconstruction and then receive radiotherapy, or opt for implant reconstruction despite the recommendation of chest wall radiotherapy. There is some evidence that ADMs may reduce the capsular contraction rate with radiotherapy[10] but the published series are small and follow-up is short, particularly in studies using ADM.

There are a number of unanswered questions relating to the clinical application of ADMs for breast reconstruction. The cosmetic outcome compared to autologous reconstruction, in the longer term is not known. The true complication rate and incidence of further surgery (including delayed autologous recontruction) is also unknown. Most importantly, in view of the cost of ADMs, cost-effectiveness is important in comparison to other reconstructive options. However, in general terms, ADMs provide soft tissue cover without requiring additional muscle mobilization and without donor-site morbidity. Training in the technique, experience with managing complications and auditing results are important in order to ensure complications are kept to a minimum level. Further, adequately powered trials are required to provide more data and clarity, and to facilitate choice of the optimal reconstructive option for patients.

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Hot Topics in Breast Surgery

Sentinel Node Biopsy Using a Magnetic Tracer: The SentiMAG Multicentre Trial

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Sentinel lymph node biopsy (SLNB) is now the standard technique used to stage the axilla in breast cancer patients, with a clinically and radiologically negative axilla. The gold-standard for sentinel node biopsy is the 'combined technique', using both blue dye and radioisotope injection[1, 2].

However, the combined technique has significant drawbacks. The use of radioisotope exposes patients and healthcare workers to radiation, is heavily controlled by legislation, and provides poor pre-operative spatial resolution on lymphoscintigraphy. Intra-operative blue dye injection can obscure the surgical field and frequently leaves a skin residue (tattoo stain), which can take months to fade and is occasionally permanent. There is also up to a 0.4% risk of anaphylaxis[3], as a result of which some centres in the UK have stopped using blue dye. The magnetic technique[4-6], is a novel non-invasive method for identifying the sentinel node using a magnetic tracer (Sienna+, Endomagnetics Ltd, UK) and a hand-held magnetometer (Sentimag, Endomagnetics, UK). Sienna+ is a blackish-brown sterile aqueous suspension of superparamagnetic carboxydextran-coated iron oxide particles, and is intended for use with the Sentimag device. The particle size of Sienna+ is equivalent to that of Tc99m-nanocolloid (60nm). The iron oxide particles are typically deposited within lymph node sinuses and not in metastatic deposits[7]. (Figures 1a and 1b)

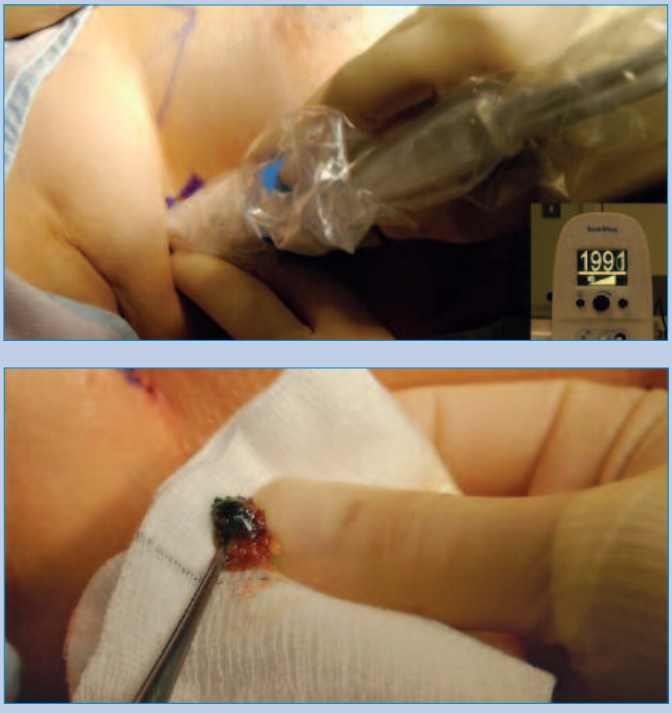

Figure 1: Sentinel node biopsy undertaken with both the combined technique and the magnetic tracer.

a) (upper figure) the magnetometor identified a node with a high count in the right axilla

b) (lower figure) the node is blue and black.

The SentiMAG Multicentre Trial[8] is an international phase II paired equivalence trial. It is an NIHR-adopted trial, running at 7 sites (6 in the UK and 1 in the Netherlands). It is evaluating the new magnetic technique for sentinel node biopsy (SLNB) against the standard (radioisotope +/- patent blue dye). The magnetic technique provides both a colour change (brown / black) and a hand-held probe for node localization. The trial compares identification rate of sentinel nodes with the new magnetic technique against that of the standard technique. It has accrued the 160 patients required for the primary analysis, and results are awaited later this year. The trial has been extended to recruit 350 patients in order to evaluate sentinel node identification rates between trial sites, with both techniques.

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Update on the Surgical Management of Colorectal Cancer

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The last year has seen tremendous advances in the evidence base for the surgical management of the full range of colorectal cancer, from small, early lesions, through to advanced, multi-compartmental recurrence. The quality of evidence surrounding these areas has also improved, with data from randomized trials, population level registries and formalized consensus processes emerging.

Bowel cancer screening

With the advent of the National Bowel Cancer Screening Program based on faecal occult blood testing, the detection rate and incidence of early colorectal cancer is predicted to rise. The program currently offers screening every two years to all men and women aged 60 to 69. People over 70 can request a screening kit by calling the program (0800 707 6060). Those with positive faecal occult blood tests are typically sent for colonoscopy to rule out malignancy and identify polyps.

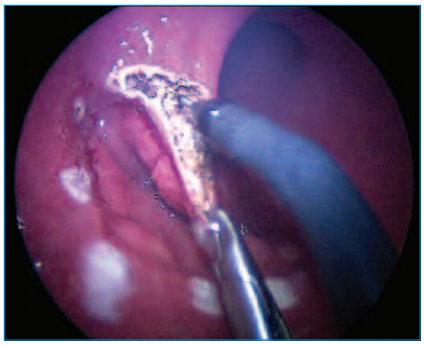
The first meeting of the international BeyondTME Collaborative. Total participation included 75 consultants from 11 countries over 4 continents.

Since colonoscopy is time-consuming and carries an associated morbidity rate, there is interest in exploring alterative screening strategies for symptomatic patients. The recently published SIGGAR randomised controlled trial showed that computed tomographic colonography provided similar sensitivity to colonoscopy and thus may provide a less invasive alternative. The detection rates for colorectal cancer or large polyps in this symptomatic group were 11% for both procedures. However, further research is needed to identify patients who should be referred for whole colonic imaging following screening, and the best modality to provide that imaging.

Management of early rectal cancer

The management of early rectal cancer has continued to evolve. Imaging and technological advances have allowed for organ sparing local resections to become established. In the rectum, transanal endoscopic microsurgery (TEM) affords a low morbidity option to patients with small, accessible tumours. In the colon, endoscopic mucosal resection/dissections techniques have evolved rapidly to allow for similar benefits in previously inaccessible locations. Both techniques require super-specialised training and a multidisciplinary approach to care. The benefits of organ sparing surgery include an avoidance of post-operative complications (including anastomotic leak) and improved functional outcome.

Salvage total mesorectal excision (TME) is the expected care pathway following either adverse histology or recurrence following failure of local excision of rectal cancer. However, recurrence following local excision is non-operable in 20% of cases, and in 50% of operable cases, a multivisceral resection is required for these initially small (T0-T2) lesions. This suggests that the selection criteria for patients likely to benefit from local excision have not yet been optimised. It is likely that patients with T0-T1 tumours may benefit, although further stratification of T1 cancer by depth of invasion is warranted. Those with poor tumour differentiation, extramural vascular invasion or higher T-stage are at high risk of recurrence and so may benefit from radical resection. There is interest in the ability of magnetic resonance imaging to identify these patients pre-operatively. The Cancer Research UK funded randomised controlled TREC trial (Transanal Endoscopic Microsurgery and Radiotherapy in Early Rectal cancer) is close to completing the feasibility stage. It is randomising between radical TME versus short course radiotherapy followed by delayed local excision (TEM) for T1-2N0M0 cancer. Progression into a full phase III study will provide further valuable outcome data to improve selection.

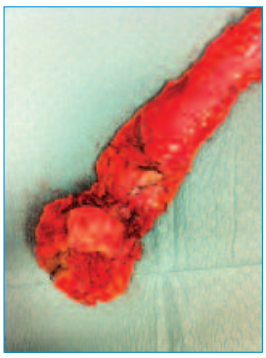


Example of transanal endoscopic microsurgery (TEM) for an early rectal cancer.

Ensuring negative lymph node status is important to prevent under-staging. The use of laparoscopic posterior mesorectal clearance has been explored, but is not yet in routine use. Additionally, laparoscopic fluoroscopic techniques may be able to identify positive lymph nodes, although this technology in the pelvis may prove difficult to produce and research to validate its specificity is needed.

Minimally invasive surgery

As the National Training Program in Laparoscopic Colorectal Surgery continues, the rate of patients undergoing laparoscopic resections is steadily rising. With 40% of patients undergoing a laparoscopic resection in 2012, this shows the achievements that have been made from the 5% rate in 2005/2006. Further technological advances include the use of single incision and robotic surgery. The first reports of totally transanal mesorectal excision are also emerging. However, these techniques are potentially costly and the realisation of improvement in patient related outcome measures is awaited before their widespread acceptance.



Abdominoperineal resection specimen following radical excision of an advanced rectal cancer, including removal of the sphincter complex and coccyx.

Low rectal cancer

The National Cancer Action Team funded Low Rectal Cancer National Development Programme (LOREC) program is an MDT based quality improvement program, which is establishing extra-levator abdominoperineal resection as the standard of care for patients with low rectal cancer where anastomosis is not possible. The program expects to reduce the 30% margin positive rate currently associated with this type to surgery to at least 15%, and provide much needed data on quality of life outcomes and the optimum method for perineal defect closure.

Advanced colon cancer

Progress in the management of advanced colorectal cancer has been equally as exciting. The Cancer Research UK funded Foxtrot group have been investigating the feasibility of preoperative chemotherapy for advanced, operable colon cancer. Publishing their pilot, the impressive improvements in negative resection margin (4% versus 20%) and tumour regression (31% versus 2%) will surely translate into greater long-term survival during the phase III trial, and will establish a standard of care globally. The study will also test the addition of an EGFR-targeted monoclonal antibody to pre-operative chemotherapy for patients with wild-type KRAS tumours, in a modern trial design that should influence the design of future trials by surgical oncologists.

Pelvic exenteration for advanced rectal cancer

Finally, the management of primary rectal cancer beyond TME planes and recurrent rectal cancer takes a big step towards standardisation with completion of a consensus statement by the BeyondTME group. These patients, who require multivisceral, exenterative type surgery, are subject to wide variation in practice and outcome.

This global, multidisciplinary group took part in a formal Delphi process, including two dedicated international

meetings, to produce much needed guidelines of care, which can be applied globally. This type of surgery is only performed in a handful of centres in the UK, but ensuring equal patient access to these services, irrespective of that patient's geographical location, is a priority. Abdominosacral resection, multivisceral pelvic resection, cystoprostatectomy and pelvic reconstruction are all specialised surgical techniques utilised by these super-specialised multidisciplinary teams.

Genetic stratification of colorectal cancer

Huge strides continue to be taken in understanding the molecular classification of colorectal cancer, with the identification that they represent a heterogenous group of genetic pathways. KRAS mutation, BRAF mutation, CpG island methylator phenotype status and microsatellite instability status are all biomarker contributors to the personalised medicine pathways that patients with colorectal cancers are now tested for, and which stratify pre-operative and adjuvant treatments. These are contributing to a modern and bright future for the specialty. The vision of personalised pre-operative therapy to significantly downstage tumours and prevent metastatic disease, combined with minimally invasive techniques to reduce morbidity, pain and length of stay, are becoming a modern reality.

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Hot Topics in Sarcoma and Melanoma Surgery

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While this article is entitled "Hot topics in Sarcoma and Melanoma Surgery" the reality is that the major recent clinical advances in both of these tumour types is in adjuvant and systemic treatments rather than specific changes in surgical strategies. This update will review the current important changes in practice and areas of investigation.

Sarcoma

For Soft Tissue Sarcoma, the major surgical developments centre around two large retrospective case controlled series from Paris[1] and Milan[2] of radical versus conservative surgery for Retroperitoneal Sarcomas published in Journal of Clinical Oncology. Both papers concluded that local recurrence was less when a liberal approach to en bloc resection of surrounding organs was undertaken when compared with resections that preserved organs and resected only the tumour itself. The accompanying editorial by Peter Pisters from MD Anderson[3] drew attention to the methodological weaknesses of these retrospective analyses but nevertheless viewed the data as important and hypothesis generating. Comparisons of outcomes within a number of large North American retrospective series in which conservative surgery was employed with European Series in which a more radical approach with en bloc visceral resection was undertaken also appears to suggest that intra-operative relapse is lessened by the more radical surgical approach.

EORTC trial

The data in favour of en bloc radical surgery was viewed as sufficiently powerful that this surgical approach was incorporated as the standard surgical treatment for a major EORTC trial that opened for recruitment in Spring 2012 that compares surgery alone to preoperative radiotherapy surgery in Retroperitoneal Sarcoma. The benefits of radiotherapy in reducing local recurrence in extremity sarcomas have been known for many years. This however does not impact on survival. For tumours arising in the retroperitoneum the major cause of death is relapse within the abdomen and accordingly any treatment that could decrease the rate of relapse within the abdomen should translate into an effect on survival. However, for retroperitoneal sarcomas when tumours are very large and abut crucial radiosensitive anatomical structures, administering preoperative radiotherapy is more complex than in a limb. The data from a number of small retrospective series about the therapeutic benefits of preoperative radiotherapy have been inconclusive with some studies suggesting a benefit[4] and others suggesting a detrimental effect[5]. An attempted American randomised trial of preoperative radiotherapy prior to surgery was abandoned because it failed to recruit

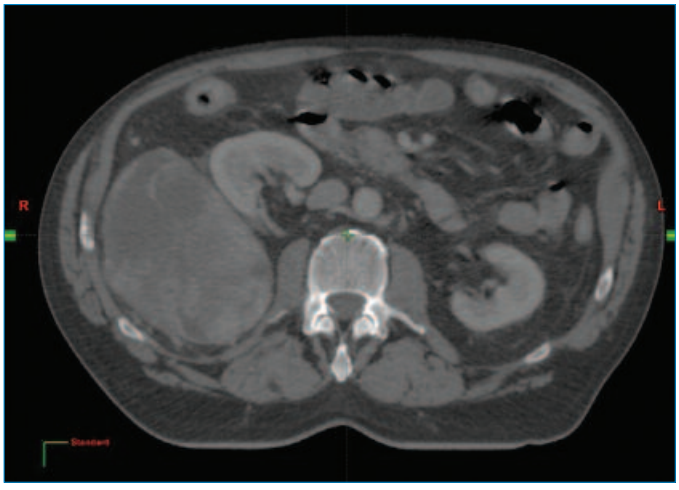

Figure 1 Panel A: A retro-peritoneal liposarcoma arising in the right perinephric fat. This was resected with an en bloc resection of the right colon and right kidney.

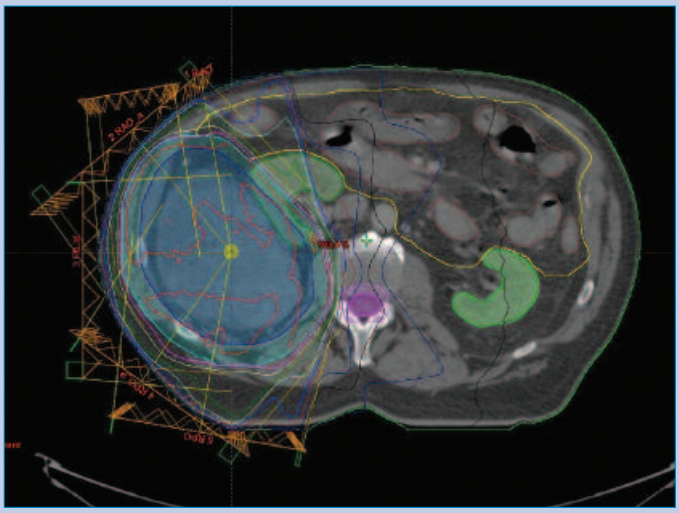

Figure 1 Panel B : A radiotherapy planning CT scan demonstrating the preoperative radiotherapy fields defined by Intensity Modulated Radiotherapy (IMRT) as part of the STRASS clinical trial. (The patient was randomised to receive preoperative radiotherapy).

sufficient patients The STRASS trial (A phase III randomized STudy of preoperative RAdiotherapy plus Surgery versus surgery alone for patients with Retroperitoneal Sarcoma) is an EORTC sponsored study that will be recruiting from high volume European centres and aims to randomize 256 patients with primary retroperitoneal sarcomas with the primary endpoint being abdominal local recurrence free survival and a number of secondary endpoints relating to acute and chronic toxicities. Modern radiotherapy techniques will allow the administration of high dose RT to retroperitoneal sarcomas while minimising toxicities to adjacent uninvolved viscera (Figure 1 previous page). Presently, the study is ahead of its recruitment schedule with over 40 patients randomised from centres in Paris, Milan and London with certain other centres still to open.

Vortex Study

The other major randomised study in the field of soft tissue sarcoma that is underway in the UK is the VORTEX clinical trial that is looking at the volume of radiotherapy administered post-operatively to sarcomas comparing the traditional high volume treatment field encompassing the whole compartment bearing the sarcoma with a more biologically appropriate small volume that irradiated only the tumour bed itself. The primary endpoints in this trial are limb toxicity and local recurrence.

Melanoma

By far the most important developments in the field of melanoma relate to the development of targeted and immunological therapies that have demonstrated a survival benefit in melanoma. Melanoma is a particularly chemo. resistant tumour type. Standard chemotherapy has very low response rates in the order of 7-12% and has no benefit in the adjuvant setting and is used only in a palliative context. Despite the advances in cytotoxic chemotherapy that have been seen in other tumour types, the standard cytotoxic chemotherapy that is used in melanoma (dacarbazine) has been unchanged for the last 30 years!

However in 2010 two back-to-back papers in the New England Medical Journal reported the results of randomized trials of two new biological agents that demonstrated for the first time statistically significant differences in progression free and overall survival in patients with stage IV metastatic melanoma[6,7]. The first agent, vemurafenib, is a potent inhibitor of mutated BRAF, an intra-cellular signaling protein in the RAS- RAF signaling pathway. B-RAF is mutated in 40-60% of cutaneous melanoma and in 90% of cases this is because of a single amino acid substitution at codon 600 resulting in constitutive signaling of the B-RAF protein which leads to increased cellular proliferation. In terms of overall survival the patients with mutated BRAF receiving vemurafenib had a 84% overall survival at 6 months compared with 64% for patients receiving dacarbazine[6]. Moreover if patients have a mutated BRAF gene the likelihood of a response is over 90%. While it is certainly the case that the duration of response to vemurafenib is short, this is proof of principle that targeted therapies in melanoma can be effective in a notoriously chemo resistant cancer.

The second agent, ipilimumab, works by a completely different immunological mechanism. It is a monoclonal antibody that blocks cytotoxic T-lymphocyte-associated antigen 4 (CTLA-4) and is a negative regulator of T cells and augments T-cell activation and proliferation. Accordingly it is potentially active against all patients with metastatic melanoma and not just patients harbouring specific mutations. Once again a durable and highly significant increase in survival is seen, in the order of 10% in patients receiving ipilimumab in addition to dacarbazine when compared to dacarbazine alone[7]. This effect was only seen after three months of treatment confirming a likely immunological mechanism.

Not surprisingly, the demonstration of an effect of new agents in the metastatic setting has lead to great interest in the possibility of a benefit in adjuvant setting. To date

over twenty previous randomised studies of cytotoxic and immunological therapies have never conclusively shown a survival benefit as an adjuvant treatment. However, with demonstration of a survival benefit of these new agents in the metastatic setting, new adjuvant trials are opening for high risk stage II melanoma patients and Stage III patients who have undergone definitive surgery. Other targeted therapies are also in use in melanoma, specifically imatinib mesylate (Glivec®) in acral lentignous and mucosal melanomas harbouring a mutation in the c-kit gene .

A randomised study analysing the role of adjuvant radiotherapy in operated stage III melanoma was reported in Lancet Oncology in 2012[8]. While the headline conclusion of the trial was that there was a significant reduction of the number of in-field recurrences with the use of adjuvant radiotherapy but with no effect on overall survival, concerns have been raised with this study, in particular the high rates of local relapse in the control arm, the lack of any long term toxicity data of radiotherapy and surgery together and finally the absence of any data on overall local control (as opposed to data on first in field local recurrence). Hence it is unlikely that the use of adjuvant radiotherapy in patients with stage III melanoma will be recommended other than in certain exceptional circumstances.

As can be seen from the above, the rate of progress in both sarcoma and melanoma is gratifying and should give hope for the future to all those affected by these cancers.

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Staying Safe: Complaints, Policies, Appraisal and Revalidation for Cancer Surgeons

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2013 is the year in which GMC-directed Revalidation comes of age for UK registered medical practitioners. By the time that you read this article, some of you will already have been through the formal process, and many others will be approaching the challenge of documentation with varying degrees of anxiety and irritation.

The revalidation process is but one element of a tidal wave of bureaucracy and oversight which threatens to engulf busy, responsible and conscientious surgeons. It represents but one end of a spectrum of the administrative detail to which individual practitioners must submit, which also includes detailed job planning and employer led Annual Appraisal.

The clear purpose of the process of Appraisal and Revalidation is to ensure that the interests of a range of parties to the clinical transaction between doctor and patient are better protected than in the past. Of course it is about the safe treatment and the best interests of patients at a vulnerable time in their lives, but it is also about the interests and the reassurance of the employers, the regulators and those charged with the administration of health care on behalf of parliament.

Full and informed engagement with the processes of Appraisal and Revalidation are thus critical to the self-interest and self protection of all clinicians, and particularly to surgeons, who are under intense scrutiny and who are personally very vulnerable when things are perceived to go wrong. The high profile cases which secure adverse coverage in the national media are the tip of the iceberg of the personal misery, distress and embarrassment arising from complaints, professional investigations and referral to the GMC, to which surgeons in oncological practice are far from immune.

It is thus worth considering the functions of each component of official oversight of surgical practice, each of which demands time and effort on the part of each and every individual to address.

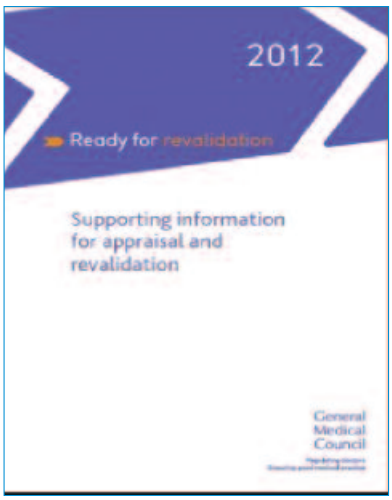
Annual Job Planning is a process which is usually conducted at Trust Divisional and Clinical Director level. It is the process by which the employer is assured that the practitioner is working in a structured and accountable fashion on a session by session basis, such that resources, effort and time can be efficiently allocated.

Annual Appraisal is the process by which the employer, usually an NHS Trust, is able to review the work and output of the individual, and to identify and rectify any problems and issues at an early stage. Professional careers are not constants, and they are not cast in stone from an early date. Personal practice, health, attitudes, domestic circumstances and professional relationships all change with time, and have a bearing on conduct and outcomes in the daily workplace. Age and experience are no guarantor of wisdom in matters professional, and the more senior surgeons who respond inappropriately to the unwanted challenges and frustrations of the modern workplace are as vulnerable as (if not more than) younger and inexperienced colleagues.

Revalidation shares many of the processes of Appraisal within your Trust, but there are key differences and fundamental implications for your personal licence to practice, which is gifted to you by the GMC as the

professional licensing body in the UK. While the Responsible (or Reporting) Officer (RO) is usually the Trust's Medical Director or Appointee, it is critical to understand that for the purposes of Revalidation, the RO is responsible to the GMC and not specifically to the Trust. An individual may be certain that, in any future GMC investigation into his or her practice, the appraisal and revalidation folders WILL be held as evidence. It is thus critical that you complete all requisite documentation for revalidation, including requests for reflective writing.

There is another theme to this brief essay on professional awareness and self-protection for cancer surgeons, which we might address under the subheading of "complaints and concerns". Complaints vary in their content from the minor to the very distressing and very damaging, and in their impact to psychological destabilisation and the termination of careers. They cover the whole spectrum of issues from environmental circumstances over which individual surgeons have no control, to matters of personality, behaviour, attitude and adverse clinical outcome. While many complaints are both valid and intentionally constructive, some complainants can be virulent and wholly unreasonable in their actions against individual surgeons.



While there exists an official and formal escalator for complaints from local departmental level and up through a Trust or Service, the reality is that complaints, like meteorites, can come from any direction and enter the system at any level, including directly through the GMC's on-line complainants reporting system. In general terms, the complaints handling system has been centralized in every Trust, and there is a formal process which is set out in every case. Complaints can often be highly distressing for the recipients and the temptation to fire off an angry or ill-considered response must be resisted. Individuals will invariably be judged by the third party complaints investigators by the manner of their response, as much as by the nature of the original complaint. A cool, forensic, structured and apologetic, insightful and reflective tone will be necessary.

Many surgeons are unaware of the range of protections which are available to them when things go wrong. Each Trust has a mandatory set of policies for employee protection in adverse circumstances which are rarely read or understood by the employees themselves, and are often now so complex as to be honoured in the breach when things go wrong. Individuals may (and often should) turn to their Professional Indemnity organizations for advice, or to the BMA where the issues relate to employment and employer relations. They may also look to the Royal College of Surgeons of England, whose accommodation we share, and to its Confidential Support and Advice Service.

In terms of the reporting of concerns, teamwork is of the essence for surgeons in terms of their outpatient work, administrative work, inpatient and theatre work, and their higher management functions. For clinical effectiveness, all cancer surgeons now work in multidisciplinary teams, where they can provide leadership but where their practice is also under daily scrutiny. Harmonious MDTs can be a source of professional strength and mutual support.

Where disharmony reigns within an MDT, the risks to individual surgeons, to teams and Trusts can be considerable, and the fallout reaches the national media. The early identification and discussion of concerns about problems in local practice can be a particular challenge, and I commend the pamphlet "Acting on Concerns", published by the Royal College of Surgeons in early 2013, for the clarity of its guidance. Anticipatory clinical governance is now the buzz phrase.

The processes of Enhanced Appraisal and Revalidation, Complaints and Concerns impose new demands upon all surgeons. We urge full, constructive and anticipatory engagement to pre-empt future problems in individual professional practice, and effective preparatory use of the many resources that have been made available by the various professional bodies.

The Management of Borderline Pathologies

The overarching theme of the BASO~ACS Conference in 2012 was how to deal with uncertainties in decision making, both from the perspective of how we deal with lesions of uncertain malignant potential, such as LCIS and Barratt's oesophagus but also terms of the more general concept of how we deal with these uncertainties.

Keynote speakers from the Conference have kindly written articles for the Yearbook.

Barrett's Oesophagus

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The major interest in Barrett's Oesophagus relates to its identification as a risk factor for the development of oesophageal adenocarcinoma. It is an endoscopic diagnosis confirmed by histopathological analysis. It is "an oesophagus in which any portion of the normal squamous lining has been replaced by a metaplastic columnar epithelium which is visible macroscopically". In order to make a positive diagnosis of "Barrett's oesophagus", a segment of columnar metaplasia of any length must be visible endoscopically above the oesophago-gastric junction and confirmed or corroborated histologically.

The exact prevalence of Barrett's oesophagus is unclear, but conservative estimates of prevalence are between 1 million and 4 million. There is some evidence that the incidence of Barrett's oesophagus is increasing by around 2% per year. The condition predominantly affects white men with the chief risk factor for development being chronic gastro-oesophageal reflux disease (GORD). Between 8% and 30% of all adults are affected by GORD and 5% to 12% of these may subsequently develop Barrett's oesophagus. Evidence suggests that symptom frequency and symptom chronicity are better predictors of the presence of Barrett's oesophagus than symptom severity at any given time. There is also evidence that smoking, high alcohol intake, high BMI and centripetal obesity are linked to Barrett's and an increased risk of progression to cancer.

The progression of Barrett's oesophagus to adenocarcinoma is the subject of much research. There is a clear genetic predisposition identified for reflux disease to progress to Barrett's oesophagus as an adaptive response to increased cell loss as a result of chronic inflammation. The is a clear genetic predisposition recently identified for reflux disease to progress to Barrett's oesophagus in certain patients. The metaplasia appears to originate from stem cells located in the oesophageal gland squamous ducts which undergo point mutations in tumour suppressor genes (TSG), typically p16 and p53, in response to chronic reflux.

Several of these molecular changes have been defined (mostly those necessary for the development of Barrett's oesophagus and early changes in the pathogenesis of dysplasia) but most of the key steps that enable cells to become cancerous remain unclear. It appears that mutations in genes responsible for DNA repair, chemical processing and the inflammatory response may all have a role.

The most important marker for subsequent degeneration to cancer is dysplasia. This is defined as "an unequivocal neoplastic alteration of epithelium which has the potential to progress to invasive malignancy but remains confined within the basement membrane of the epithelium within which it arose." It is classified as either low grade (LGD), or high grade (HGD) based on its histological appearances. HGD has a higher malignant potential than LGD and malignant transformation classically occurs through a stepwise progression. There is considerable over-diagnosis of LGD in non-specialist hospitals and the true significance of the diagnosis has probably been underestimated by most reported series. Agreement between pathologists for LGD has been shown to be poor to moderate (Kappa =0.2-0.6) and only minimally improved by education. The recent 'Barrett's

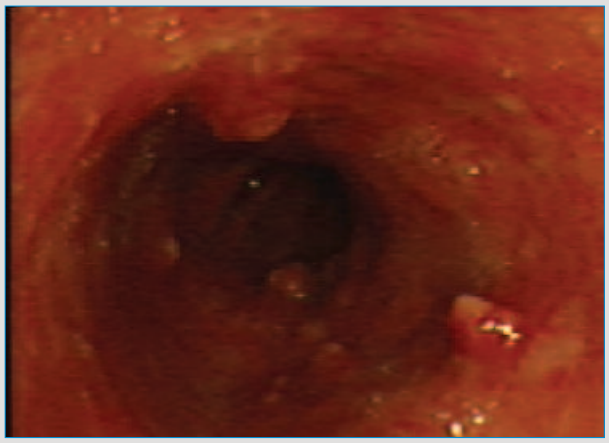

Figure 1. Endoscopic appearance of high grade dysplasia in Barrett's Oesophagus

Dysplasia and Cancer Taskforce' (BAD CAT) has stressed that accurate assessment of dysplasia and early invasive cancer is best following an endoscopic resection. It is particularly important to accurately stage early (T1) tumours. Intramucosal cancers (T1a lesions confined to the mucosa) have a very low incidence of lymphatic invasion (<5%) whereas, invasion into the submucosa is associated with lymphatic spread in 20-45% of cases. This data is becoming increasingly important as surgical oesophagectomy and lymphadenectomy provide the only chance of cure for patients with lymphatic spread, whereas endoscopic therapy is potentially curative in those without lymphatic invasion.

Risk of cancer, surveillance, and treatment.

A recent population based case control study of 11,028 patients followed for a median of 5.2 years indicated an annual risk of malignant progression of just 0.12%, and a relative risk of 11.3 for developing adenocarcinoma compared to the general population. However, only 7.6% of the total oesophageal adenocarcinomas diagnosed nationwide over the study period had a previous diagnosis of Barrett's oesophagus. It is essential to appreciate that whilst patients with Barrett's oesophagus have an increased relative risk of developing adenocarcinoma, the majority will die from other causes. A study from the UK has demonstrated an increase in overall mortality and oesophageal cancer mortality in Barrett's patients compared with an age- and sex-matched population without Barrett's. There were more cancer deaths from other cancers (18%) than from oesophageal cancer (10%) and by far the greatest cause of mortality was cardiorespiratory disease. Patients with Barrett's oesophagus are typically endoscopically surveyed (Figure 1) to monitor for dysplastic and malignant change. The level of surveillance depends predominantly on the presence and degree of dysplasia identified, but also to a lesser extent on patient age, comorbidity and preference. Current recommendations of two yearly endoscopy with protocol biopsy are being tested within a randomized control trial; the Barrett's Oesophagus Surveillance Study (BOSS).

The natural history of HGD is also unclear although this diagnosis is known to confer a significant risk of progression to adenocarcinoma. It is important to consider what proportion of HGD patients who undergo oesophagectomy have an occult cancer detected in the resected specimen. Reported rates vary widely (0-73%) but the average appears to be around 40%. This emphasizes the importance of using strict biopsy protocols in patients with Barrett's oesophagus.

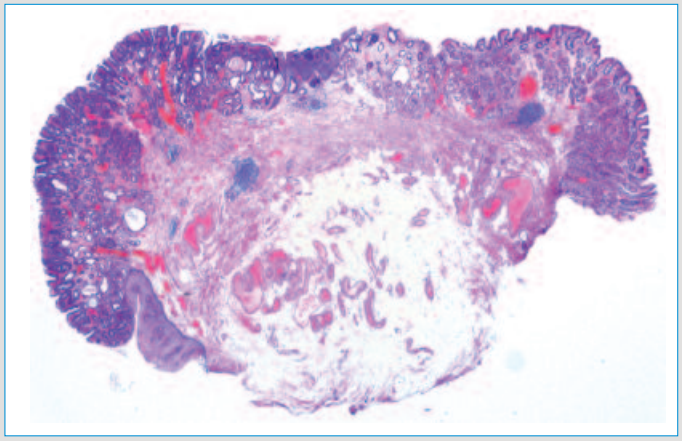

Figure 2. Endoscopic resection of focal HGD with clear margins

Given that intramucosal cancers (T1a) may be managed by endoscopic therapy, it may be more pertinent to ask the prevalence of submucosal invasive cancer at oesophagectomy for HGD. There are two main forms of endoscopic therapy available to treat HGD and intramucosal tumours - endoscopic resection (figure 2) and endoscopic ablation. These techniques aim to destroy the lining of the oesophagus and promote regenerative re-growth of normal squamous mucosa. In order for this to occur, (as opposed to columnar re-growth) some of the superficial squamous lined ducts must survive the process. Techniques for mucosal ablation include photodynamic therapy, thermal ablation, radiofrequency ablation and argon plasma coagulation. Endotherapy is indicated in selected patients with HGD, intramucosal cancer (T1a) and early submucosal cancers (T1b). It offers an attractive alternative to radical surgery in terms of reduced mortality and morbidity, with excellent short and medium term results, but long-term efficacy remains unclear.

Endoscopic ablation techniques aim to destroy the lining of the oesophagus and promote regenerative growth of normal squamous mucosa. Techniques for mucosal ablation include argon-beam plasma photocoagulation (APC), multipolar electrocautery (MPEC), laser therapy and cryotherapy; chemical methods, such as photodynamic therapy (PDT); and radio-frequency (RFA) ablation. A large randomised trial of RFA by demonstrated successful resolution of dysplastic Barrett's oesophagus following treatment with RFA Complete eradication of LGD was seen in 90.5% (ablation group) compared to 22.7% (control group) (P<0.001). Complete eradication of HGD occurred in 81.0% (ablation group) versus 19.0% (control group) (P<0.001). RFA also decreased the likelihood of disease progression (3.6% vs. 16.3%, P=0.03) and cancer (1.2% vs. 9.3%, P=0.045).

Intense interest and study of Barrett's Oesophagus is leading to the possibility of breaking the cycle of poor survival in patients with oesophageal cancer.

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Low Grade DCIS and Pleomorphic LCIS

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At the biological and genomic level increases have been made in our understanding of the range of clonal lesions that are potential precursors of invasive breast cancer. These include flat epithelial neoplasia, atypical ductal hyperplasia (ADH) and ductal carcinoma in situ (DCIS) and lobular in situ neoplasia (the latter term incorporating atypical ductal hyperplasia and lobular carcinoma in situ (LCIS). However, the clinical behaviour of some of the less common forms of these lesions remains unclear, predominantly because large series with long-term follow up data are scarce.

At one end of the spectrum low grade DCIS must be distinguished histologically from ADH. Both ADH and low grade DCIS are formed from regular, evenly-spaced, cells but low grade DCIS is more extensive, both with regard to the degree of involvement of the membrane-bound spaces (complete) and the overall number of spaces bearing the atypical proliferation (more than two) (Figure 1). Intermediate and high grade DCIS show more cytological atypia and do not have extent/size criteria for diagnosis. However, whilst DCIS is now well recognized to be heterogeneous biologically and genetically, as well as radiologically, clinical and histologically, the risk factors for progression to invasive disease are relatively poorly understood. It is, however, evident that the cytonuclear grade of DCIS is of prognostic significance; low grade DCIS is both less likely to recur locally after excision (hazard ratio about 0.5 compared to high grade disease in UK DCIS I[1] and to take a longer period of time to progress to invasive cancer. However, the natural history of untreated low grade DCIS can only be estimated from series of patients with missed disease (mostly symptomatic presentation) or who have refused therapeutic surgery and amount to less than 50 women in the published literature. Overall, less than 50% of these have developed invasive disease, which continues to present up to 42 years after the original biopsy. A more recent series includes women with oestrogen receptor positive DCIS (not only low grade lesions) who elected to have hormone therapy with ongoing surveillance rather than surgery. Whilst 6 (43%) remain on surveillance (at median 32 months), 8 had subsequent surgery and 5 had invasive disease. Significantly this was all stage 1 at detection[2], and it must also be noted that low grade DCIS does not progress to high grade DCIS (which shows very different genetics and biology) but typically to low grade invasive cancer rather than to an aggressive invasive lesion. It is also the case that there is no evidence for any survival advantage to the patient with the detection of low grade DCIS[3].

It is thus widely believed that low grade DCIS represents a breast lesion that is potentially over-treated and The Low Risk DCIS Trial (LORIS) (Principle Investigator, Adele Francis) of active monitoring of low grade DCIS (confirmed on central pathology review) vs standard surgical excision which is to commence soon will provide invaluable data on the clinical behaviour and management of this disease. Widespread support of this clinical trial is essential, however, as only about 10% of

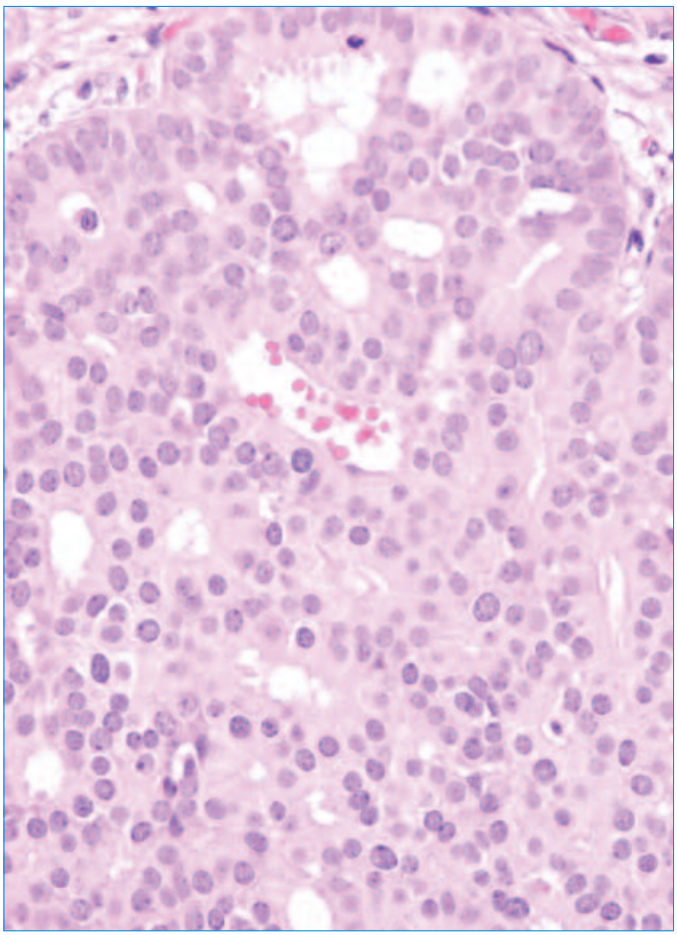

Figure 1: Low grade ductal carcinoma in situ.

screen-detected DCIS in the UK is of low and 29% intermediate grade (Sloane project data, unpublished). High grade DCIS, which makes up the majority of screen-detected DCIS in the UK, is regarded as a quite different entity for which therapeutic excision with widely tumour-free margins and radiotherapy remains the treatment of choice.

Lobular carcinoma in situ (LCIS) has for a long time been regarded as a bilateral risk factor for the development of invasive breast cancer (10x increased risk) with atypical lobular hyperplasia (ALH) conferring a 4x increased risk. However, the risk associated with lobular in situ neoplasia of this classical form is increased in the ipsilateral, compared to the contralateral, breast with disease being 3x more common. Some groups have therefore reverted to suggesting local surgical treatment for LCIS may be warranted; this has not been widely applied for this process that is predominantly identified as an incidental finding in histological samples.

However, pleomorphic LCIS (PLCIS) is a morphologically different lesion. The cells are large and pleomorphic, as the name suggests, unlike the small to moderate sized, regular cells of the classical form (Figure 2). There is often central comedo-type necrosis in PLCIS and this lesion is often (80-100% in the small series to date) screen-detected with radiologically suspicious calcification akin to those seen high grade DCIS. However, biologically PLCIS shows the features of other lobular lesions, both in situ and invasive; there is typically a loss of the cell-cell adhesion molecule, E-cadherin, immunohistochemically. PLCIS also more frequently shows HER2 over-expression and amplification (with immunohistochemistry and in situ hybridization respectively) and typically has a higher proliferation index (e.g. with Ki67) and lower oestrogen and progesterone receptor positivity.

Although there is limited clinical data regarding the behaviour of PLCIS, both the molecular and the morphological features suggest that this is likely to be a more aggressive entity than classical LCIS. For this reason, more authorities suggest that PLCIS should be treated as akin to DCIS. Indeed, it is undoubtedly the case that pathologists have previously classified this lesion as high grade DCIS and it has thus been managed as such historically. In a needle core biopsy specimen, pathologists will report this lesion as B5a, in situ disease (unlike classical LCIS and ALH, which are reported as B3, uncertain malignant potential). Although, yet again there is little robust data, it has been reported that in 30% of such cases invasion is identified histologically in the therapeutic surgical specimen[4].

Given the limited information on clinical outcome of patients diagnosed with PLCIS, making recommendations regarding management is problematic. The largest series to date is of 26 patients who have undergone segmental mastectomy with a range of treatment given[5]. Thus no guidelines exist regarding the optimum margin width of uninvolved tissue that should be obtained in surgical specimens (although most authorities would recommend the same wide margin with complete surgical excision as for high grade DCIS). There is, however, almost no data on the benefit of subsequent radiotherapy after wide local excision and it is impossible to determine its role in the management of patients with PLCIS at present. It is clear that long-term clinical follow up studies are urgently needed to explore the behaviour and optimum management of PLCIS; in this respect, submission of cases to the Sloane Project (www.sloaneproject.co.uk), which continues to collect data on the lobular lesions as well as ADH and the rarer forms of precursors, is strongly encouraged.

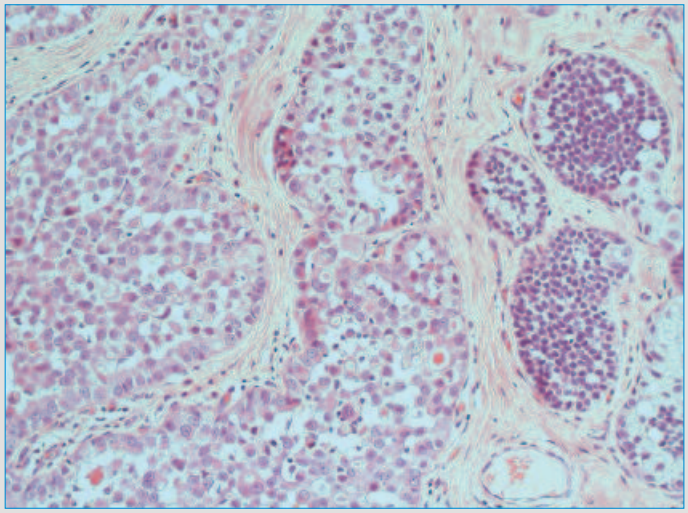

Figure 2: Pleomorphic LCIS (left) with classical LCIS also present (right); the two processes may co-exist.

In summary, although our understanding of the biology of the precursors of invasive breast cancer is an area of increased interest and research, the clinical behaviour of the less common sub-types remains poorly understood. This causes difficulties in making evidence-based recommendations regarding optimal clinical management. It is essential that Breast Units participate whenever possible in large national data collections in order to collate data on these uncommon potential precursors of invasive breast cancer to inform future guidelines.

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