INTERVIEW

For reprint orders, please contact: reprints@futuremedicine.com

Colorectal Cancer

Why I became a cancer surgeon

Graeme Poston* speaks to Roshaine Gunawardana, Managing Commissioning Editor: Graeme Poston (DSc MB BS, MS, FRCS[Eng], FRCS[Ed]) is a consultant hepatobiliary surgeon at the University Hospital Aintree, Liverpool, UK and Professor of Surgery at the University of Liverpool. He enjoys an international reputation in hepatobiliary surgery. To date, he has personally performed over 900 major hepatobiliary resections. His unit at University Hospital Aintree is one of the largest tertiary resectional hepatobiliary practices in the UK, having performed over 2000 liver resections over the last 20 years. He gained his

undergraduate medical training at St Georges Hospital Medical School, London, and postgraduate training at The Hammersmith Hospital and St Mary's Hospital, London and University of Texas Medical Branch, Galveston, TX, USA. He is a past President of the European Society of Surgical Oncology, the Association of Upper Gastrointestinal Surgeons of Great Britain and Ireland, and the British Association of Surgical Oncology. He is Chair of National Health Service England, Hepato Pancreato Biliary Specialized Commissioning, Chair of the NICE Colorectal Cancer Guideline Development Group and Quality Standards Committee, and past Chair of the Cancer Services Committee of the Royal College of Surgeons of England. He is a principal investigator of a number of ongoing national and international clinical trials in hepatobiliary surgery, and co-author of numerous national and international guidelines for the management of hepatobiliary cancers, nine textbooks of surgery, and over 230 papers. Honors and distinctions include a Doctorate of Science honoris causa of King George V University, Lucknow; Ernest Miles Medal of the Royal Marsden Surgical Society; Olaf ac Acrel Medal of the Swedish Surgical Association; Stanford Cade Medal of the Royal College of Surgeons of England; Kilroe Medal of the Christie Hospital, Manchester; N K Misra Medal of the Indian Association of Surgical Oncology; Honorary Fellow of the Association of Surgeons of India and the College of Surgeons of Sri Lanka; Hunterian Professor of the Royal College of Surgeons of England; and numerous international visiting professorships. In what little spare time he has, he enjoys trekking in high places (climbed Kilimanjaro, trekked to Everest and Annapurna Base Camps, and crossed the Lakya La).

First draft submitted: 10 December 2015; Accepted for publication: 14 December 2015; Published online: 5 February 2016

*Department of Surgery, University Hospital Aintree, Liverpool, Merseyside, L9 7AL, UK; Tel.: +44 151 525 5980; graeme.poston@aintree.nhs.uk

KEYWORDS

• colorectal cancer • liver surgery • surgical oncology

Q What would you say specifically influenced you to specialize in cancer research & cancer surgery?

My interest in oncology stemmed from two things. First, I was extremely fortunate as a surgical trainee 30 years ago to work with Professor Leslie Blumgart who at time was at the Hammersmith Hospital in London and one of the pioneers of modern day liver surgery. The second was to work shortly afterward in the laboratories of Dr Jim Thompson and Dr Courtney Townsend at the University of Texas Medical Branch in Galveston, which gave me the opportunity to study peptide hormone regulation of gastrointestinal cancers. These two opportunities, coming close together showed me the opportunity as a surgeon to develop a career in liver cancer surgery, but equally to understand the interaction between cancer biology and cancer surgery, which is the basis of modern day multidisciplinary team working in solid tumor oncology.

Q Can you please tell our readers a little about any research you are currently working on?

My team is working in a number of areas, both clinical and laboratory based. On the clinical front we are extremely interested in the development of bead-delivered intra-arterial regional chemotherapy to treat liver tumors, and metastatic colorectal cancer in particular. ‘Conversion’ therapy for inoperable colorectal cancer liver metastases has been used now for over 20 years. However, such treatments are costly and unpredictable. We are therefore prospectively studying (jointly supported by European Society of Surgical Oncology and the European Organisation for Research and Treatment of Cancer) the outcomes of such treatments in the general population in a Phase IV study across Europe (the CLIMB study) addressing health economics and quality of life in addition to the conventional oncological outcomes of progression-free and overall survival. We are also interested in broadening the concept of ‘conversion’ therapy for inoperable liver tumors from our experience with metastatic colorectal cancer to primary liver tumors, and cholangiocarcinoma in particular. Last, colorectal cancer is a disease of older age and we are extremely interested in improving physical fitness in the elderly to be able to undergo radical cancer surgery with minimized surgical risk. On the laboratory front we are working very closely with our

clinical pharmacologists on the liver’s ability to process cytotoxic chemotherapy, and liver regeneration in general. Furthermore, we are looking at prognostic and predictive molecular markers that influence outcome after liver cancer surgery.

Q As a prolific author in the field of hepatobiliary & colorectal cancer, what would you say is your most significant achievement in your career so far?

I think my most significant achievement so far is to assist the development of multidisciplinary working in the management of patients with stage 4 colorectal cancer. Barely 10 years ago, clinicians (medical oncologists, colorectal surgeons, liver surgeons, thoracic surgeons, interventional radiologists, among others) managed these patients in isolation from each other, none aware of the capabilities of the others, and none aware of when to involve other clinicians in the management decisions necessary to achieve optimal outcomes. 3 years ago, our group pioneered the first dedicated advanced (stage 4) colorectal cancer multidisciplinary team (MDT) in the UK. This weekly MDT involves liver surgeons, medical oncologists, colorectal surgeons, radiation oncologists, thoracic surgeons, interventional radiologists, and imaging and PET radiologists. We discuss over 30 new cases from across our county cancer network each week and our early analysis suggests that by simply getting all the right doctors in the right room at the right time is already leading to significantly better outcomes for all patients found to be in stage 4 colorectal cancer (and not just those with liver-limited disease). As a result, working through the European Society of Surgical Oncology (of which I am immediate past President) we are setting up global preceptorships in MDT working for advanced colorectal cancer.

Q You are a representative of AUGIS (Association of Upper Gastrointestinal Surgeons of Great Britain & Ireland), & a past President. Can you explain a little about your role within AUGIS?

Association of Upper Gastrointestinal Surgeons of Great Britain and Ireland (AUGIS) was founded nearly 20 years ago in 1996 and represents UK and Irish surgeons whose major clinical interest is in foregut (esophagus, stomach, liver, bile ducts and pancreas) surgery. One of its major achievements during my presidency (2010–2012) was to produce service specifications that defined cancer surgery services for

both esophagogastric cancer and hepatopancreatobiliary cancers. We defined annual minimum center and surgeon operation volumes and populations necessary (2–3 million) to support such viable centers in England. These recommendations from AUGIS were rapidly adopted by the then English Department of Health and have now been incorporated into the Specialized Commissioning Service Specifications of National Health Service England (which I also currently chair). The AUGIS recommendations are freely available at the AUGIS website (www.augis.org).

Q You have been involved with many different national & international clinical trials, in some cases as principal/co-principal investigator. What changes would you like to see in the way clinical trials are conducted?

The biggest challenge to any clinical trial remains adequate funding. This is particularly the case for investigator-led studies where the competition for such funding is extremely hard. The second problem is the conduct of clinical trials in cancer surgery. The outcomes of such studies are often not apparent until at least 10 years after the study has closed, and such studies are frequent victims of quality assurance issues in the conduct of the operative procedures (not all surgeons do certain operations in exactly the same way). Therefore, I would encourage more surgeons to address questions in surgical oncology practice by conducting population-based Phase IV studies within the general population. Such studies are feasible, and what is more, reflect the reality of day-to-day practice (rather than the ‘ideal’ conditions found within the rarified atmosphere of prospective Phase III trials).

Q What are the challenges in the treatment & overall management of liver metastases originated from colorectal cancer?

The first challenge is defining those patients who are suitable for surgical resection with either curative or improved survival intent. Presently, about 20% of patients with liver-limited disease (LLD) can benefit from surgery (either resection or tumor ablation) at the time the metastases are detected. Furthermore, 30–40% of the remaining LLD patients can ‘convert’ to resectability if they achieve a good response to systemic therapy. However, there is not a global consensus that defines such resectability among the liver surgery

community, and even less among the colorectal surgeon and medical oncologist ‘gatekeepers’ who refer these patients to the liver surgeons.

The second challenge is persuading the medical oncology community to consider that the primary objective of first-line systemic chemotherapy in treating patients with unresectable LLD is disease response and not progression-free survival. Very few patients with unresectable LLD convert to resectability following second or later lines of systemic therapies.

Q What is the most challenging case of colorectal cancer you have ever seen?

I have a patient who currently remains disease free (and has been for the last 3 years) who originally presented in 2002 with stage 4 colorectal cancer, originating in his colon with multiple bilobar liver metastases. He underwent resection of his primary tumor followed by systemic chemotherapy before he underwent his first liver resection. He subsequently recurred in his liver on five occasions, and following systemic therapy on each occasion, came to further liver resection or ablation, including resection of an involved preaortic lymph node in 2009. He clearly has ‘good’ biology, but this case demonstrates that there are patients in whom, after continued aggressive treatment, the disease ‘burns itself out’.

Q You are involved in medico-legal work: what would you say is the biggest hurdle for experts working in this area at the moment?

The biggest medico-legal problem remains delays in diagnosis at the outset, and whether or not such delays translate over to stage progression during this time. The two major issues of ‘causation’ (the damage done) relate to progression to stage 3, and therefore the need for adjuvant chemotherapy after surgery, and progression to stage 4 and so possibly incurable disease. In reality, because of the relatively slow growth rate of the majority of colorectal cancers (often present for >5 years before onset of symptoms, liver metastases occurring up to 2 years before becoming radiologically evident), it is often difficult for claimants who can establish ‘liability’ (blame) against the treating clinician, to be subsequently successful in convincing the court that they can establish causation (that on the balance of probability, the outcome would have been any different), and so the claim fails.

Q Do you have any closing remarks for the readers of colorectal cancer?

Stage 4 colorectal cancer remains a clinical challenge. However, in 2016, with advances in both systemic therapies and greater utilization of surgical interventions, nearly 40% of these patients are alive 5 years after diagnosis, with 20% of those coming to surgery being alive, disease-free 20 years later. This is a tremendous advance over the 30 years that I have been interested and involved in the management of these patients. In the mid 1980s, barely 5% of patients with LLD were considered for surgery, and median survival for the rest was barely 6 months. This is a greater than 1000% improvement during this time in the number of patients surviving 5 years after being diagnosed in stage 4; we have not seen such an improvement in outcomes in

any other area of gastrointestinal cancer at any previous time.

Disclaimer

The opinions expressed in this interview are those of the interviewee and do not necessarily reflect the views of Future Medicine.

Financial & competing interests disclosure

G Poston has served on the pharmaceutical advisory boards for Merck Serono, BTG and Ipsen, and has been on the pharmaceutical speaker panels for Merck Serono and SirTex. G Poston has no other relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript apart from those disclosed.

No writing assistance was utilized in the production of this manuscript.