Evolving Surgical Care of Colorectal Cancer into the 21st Century

"It's crucial for better patient outcomes that surgery is not seen as a steady-state treatment, not just a baseline therapy for other approaches and therapies to be compared to but one that can and needs to transform positively onwards"

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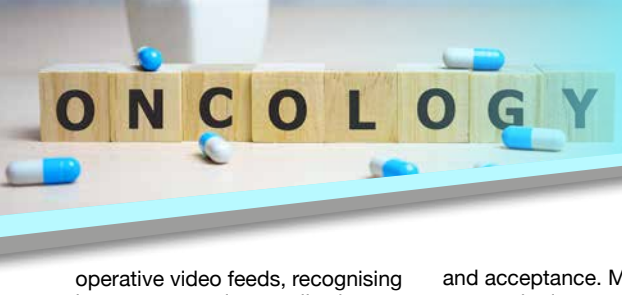
Different to the other commonest solid cancers (i.e. breast, prostate, lung), surgery is the predominant treatment for colorectal cancer, forming all or part of the therapy for the majority of patients with this disease. It remains the only curative modality either as sole treatment in those with localised disease, as majority treatment in those with regional disease or final definitive treatment in those responding to chemo/immunotherapeutics (most especially those with liver metastases but also increasingly those with non-hepatic oligometastatic disease). Furthermore, it has a major role in best palliative therapy to relieve symptoms either by debulking disease in those with peritoneal carcinomatosis or alleviating critical secondary problems such as obstruction or haemorrhage. Indeed along with endoscopic resection of earliest stage cancers at colonoscopy, the majority of colorectal cancer patients are fully cared for completely outside of medical oncology. However surgery is considerably under-recognised in terms of clinical trial and specialty development funding, certainly relative to medical oncology in general and specifically with respect to this disease. For further broad advancement in care of patients with this disease, this clearly needs to be addressed nationally most especially because of the increasing numbers of people being diagnosed (due to both increased incidence especially in younger patients as well as higher rates of detection of earlier stage disease due to population and at risk group screening). To acuminate outcomes in face of this pressure, surgery needs to be better both in terms of even greater efficiency as well as effectiveness everywhere patients undergo operative care.

Surgery is a major undertaking focussed around a single point in time intervention which can often be planned electively (many emergency presentations can too be converted to elective cancer care by managing the acute component separately from the primary cancer resection, e.g. by proximal defunctioning of bowel obstruction etc). However it risks major consequences and complications. While enhanced recovery programmes and prehabilitation exercise optimisation can reduce hospital stay after uncomplicated operations, surgical complications such as anastomotic breakdown undermine greatly the good intentions and expectations of surgery causing considerable misery, risking mortality and consuming high amounts of hospital and community care resources. Anastomotic leak rates have not been significantly affected by specialisation, centralisation or evolution of operative access (from open to minimally invasive) and the continuance of this problem justifies consideration of non-operative or compromised operative care of certain patients, especially the elderly and co-morbid (perhaps the groups who have the most to gain from single modality surgical treatment). New methods to impact this risk and indeed many other surgical complications thankfully are entering practice.

Anastomoses heal best when healthy tissue is opposed without tension. While the potential influence of local microbiomes being better understood through ongoing research efforts, local blood supply is of course a major factor in ensuring successful healing after technically competent anastomotic construction. While, previously, adequacy of perfusion has been judged empirically by subjective assessment intraoperative, near-infrared perfusion assessment is now possible with the addition of a safe fluorescent agent, indocyanine green, with synchronous visualisation using one of the many, widely available near-infrared laproscopes commonly used in key-hole operations. This enables greater appreciation of the presence and dynamics of tissue microperfusion and has been shown in many studies to be associated with significant reductions in anastomotic complication. Additional tissue-responsive fluorphores are also emerging to allow more precise appreciation of anatomy, physiology and pathology within the operative view. The usefulness of computer-assisted video display to provide meaningful additional data to the surgeon is being taken further too with the application of computer vision and artificial intelligence (AI) to the surgical imagery. For near-infrared techniques this can mean specific quantification of blood perfusion among other parameters providing greater sensitivity in appreciation of inter-individual differences at both patient and surgeon level. More broadly, AI methods are beginning to prove capable at automatic step-sequencing of



operative video feeds, recognising instruments and anomalies in anatomy based on appearance and, potentially, revealing insights that prompt reaction during and after surgery on a personalised basis. Furthermore, reformatting of standard preoperative staging imagery such as CT scans can be used to display individual patient anatomical maps to support intraoperative decision making alongside their existing role in delineating disease presence and stage.

All these modalities are showing promise in selected centres internationally and indeed nationally and definitive studies are in process to now determine their exact place among current standards of care. As software-based technological innovations, they have the potential to be deployed at scale without major capital investment and so can be capably deployed widely soon after practitioner recommendation and acceptance. Much of these too can be integrated into existing laparoscopic and robotic platforms and, importantly, there are increasingly alternate vendors and visions of differing hardware technology systems entering into the market needing application development work. All these evolving technological capabilities, and others, require appropriate development and research frameworks and all successful outcomes will evolve additional areas for investigation and application. Alongside the traditionally strong surgical research areas of basic science in tumour biology and perioperative care, there is both room and a need for practical and conceptual development of existing and new surgical techniques and technologies for best near-term application into patient care. It's for this purpose that we opened an Academic Centre for Precision Surgery in University College Dublin and a Digital Surgery Unit at the Mater Misericordiae University Hospital that have already been successful in initiating, leading and collaborating in major national and internationally consortium projects for such better surgery.

While the fact that the majority of patients undergoing surgery for colorectal cancer cease to be cancer patients on completion of their surveillance thanks to its high rates of successful cure likely plays a role in its underappreciation as an evolving entity in need of further developmental investment in terms of time, energy and funding. It's crucial for better patient outcomes that surgery is not seen as a steady-state treatment, not just a baseline therapy for other approaches and therapies to be compared to but one that can and needs to transform positively onwards. Alongside the colorectal cancer community itself having a role in facilitating broad ongoing development (and move on now from the recent and rather superficial focus on simply acquiring robotic systems in isolation which has been the main feature of surgical investment at both institutional and national level over the last five years) so too do the major funding bodies and research centres and organisations in Ireland. Correction of the historical deficit in supporting surgical clinical research and networks alongside the already well established pharmaceutical trial groups will give great opportunity to the strong medtech environment that exists throughout the country (both small/medium enterprises as well as multinationals and both incumbent device and smart technologies creatives) in addition to many well distributed, capable surgical units. Through such investment, Ireland will deliver great advantages for its patients, healthcare system and general economy.

News

OncoMark Acquired by Cepheid Inc.

University College Dublin (UCD) has formally announced the acquisition of OncoMark Ltd, a UCD spin-out company, by Cepheid Inc., a US molecular diagnostics company. The transaction was completed in March for an undisclosed sum.

OncoMark was co-founded by Professor William Gallagher and Steve Penney as a spin-out from the UCD School of Biomolecular and Biomedical Science and the UCD Conway Institute, and was based at NovaUCD, the University's Centre for New Ventures and Entrepreneurs.

The company developed a novel test for early-stage Breast Cancer (OncoMasTR) that has the potential to reduce the number of breast cancer patients receiving unnecessary chemotherapy. The test was CE Marked in preparation for launch in EU markets. With the acquisition of OncoMark by Cepheid, the test will now be launched on Cepheid's world-leading GeneXpert Platform in global markets.

The OncoMasTR test is based on a panel of genetic 'drivers' of breast cancer. The original research that resulted in the identification of the panel was led by Professor Adrian Bracken, Smurfit Institute of Genetics, Trinity College Dublin and involved researchers at the UCD Conway Institute, led by Professor William Gallagher. The OncoMasTR technology was subsequently exclusively licenced by both universities to OncoMark.

Subsequent to the sale of OncoMark, a new company, OncoAssure, was established with all former OncoMark staff moving across to OncoAssure to continue the development of biomarkers in other cancers, outside of breast cancer. OncoAssure is headquartered at NovaUCD.

Professor William Gallagher, Professor of Cancer Biology, UCD School of Biomolecular and Biomedical Science, former Chief Scientific Officer (CSO) at OncoMark and currently OncoAssure CSO said,

"I am delighted to see the ongoing translation of OncoMasTR towards the clinic via Cepheid's innovative GeneXpert platform. The underpinning OncoMasTR technology originated from a fantastic collaboration between Professor Adrian Bracken's team based at Trinity College Dublin whose focus on fundamental aspects of cancer cell biology dovetailed very nicely with our interests in translational cancer research at UCD."

Tom Flanagan, UCD Director of Enterprise and Commercialisation, NovaUCD said, "I would like to congratulate OncoMark's founders, senior management team and indeed the entire OncoMark team, following today's announcement that Cepheid Inc. has acquired the UCD spin-out company. OncoMark is an excellent example of the quality of the spin-outs which have emerged from UCD and we have been delighted to support the company to develop and grow over the last number of years."

He added, "I would especially like to commend the entrepreneurial spirit and mindset of OncoMark's founders and management team in immediately establishing a new company, OncoAssure. The company, based at NovaUCD, is focused on developing a new panel of biomarkers for a prostate cancer test and we look forward to working with the team in the years ahead to support them to reach their global ambitions."

Pictured at University College Dublin is Professor William Gallagher, UCD School of Biomolecular and Biomedical Science, co-founder, OncoMark and CSO, OncoAssure. (Mac Innes Photography)

Pictured at NovaUCD is Des O'Leary, former CEO, OncoMark and CEO, OncoAssure (Nick Bradshaw, Fotonic)