Image-guided surgery

By Kalli Spencer

Nuclear medicine studies such as PSMA PET scans can guide prostate cancer staging prior to surgery but are also used after surgery to search for disease recurrence or evidence of disease spread. These studies involve intravenous injection of radioactive tracers which are then tracked using specialised cameras to detect the cancer which lights up in various colours. It may be useful to pick up disease not seen on conventional CT scans or MRI. For those patients with intermediate and high-risk disease the surgeon may also do a lymph node (gland) dissection at the time of prostate removal (prostatectomy). Enlarged lymph nodes are difficult to detect with conventional imaging if they are less than five millimetres in diameter which makes surgical dissection challenging. This blog will look at some of the novel techniques under investigation which guides surgeons during robotic assisted laparoscopic prostatectomy.

Image guided surgery which allows for localisation of the cancer intra-operatively, includes radionuclide-guided surgery (RGS), fluorescence guided surgery (FGS) and multimodal guided surgery which includes both FGS and RGS.

RGS involves intravenous injection of PSMA-targeted ligand labelled with a radionuclide tracer before the operation. A probe is used to detect gamma photons to identify the original cancerous tissue, any residual cancer tissue and positive lymph nodes. Gamma photons can almost infinitely penetrate human tissues and are highly sensitive. Indium chloride (111In) is the radionuclide originally used and emits gamma photons. In one study, lymph node metastases were injected with 111In-PSMA at 24 hours prior to surgery and all the positive lesions detected on pre-operative PET/CT were found intraoperatively, and this was confirmed on the pathology report[1]. In another study PET positive metastases were identified in 30 out of 31 patients; in addition, another 5 positive samples were detected in 3 patients[2]. The suboptimal nuclear properties, the high cost and the limited availability of 111In have greatly restricted its routine use. Another tracer was therefore developed, 99mTc. Compared with 111In, 99mTc is cheap and easily available in most nuclear medicine disciplines, and it possesses lower radiation energy and shorter half-life that expose patients and doctors to less radiation. For the index case all the suspected lesions detected on single-photon emission computed tomography/computed tomography (SPECT/CT) exhibited high 99mTc-PSMA uptake and were removed during surgery[3]. A subsequent trial showed that all lesions shown by PSMA-PET were resected and other metastases as small as 3 mm were detected in two patients. In addition, there were still 13 patients with no biochemical recurrence after follow-up for 13.8 months, and 20 patients did not need further treatment after a median follow-up of 12.2 months[4]. In a prospective study for patients who developed disease recurrence after their initial procedure, 99mTc-PSMA RGS guided dissection was compared to a standard non image guided dissection of lymph nodes[5]. Out of 42 patients, 29 patients were treated with the conventional surgical approach, while 13 patients were treated with 99mTc-PSMA-RGS. The final pathological results showed all the visible lesions on the preoperative PSMA-PET images were pathologically confirmed to be resected in the patients undergoing 99mTc-PSMA-RGS. There was also significant declines in PSA. Whilst the results seem promising further follow long term follow up is required.

FGS is a technique that uses a fluorescence signal to highlight tumours, which assists with real time dissection of the cancer. This precision also avoids damage to surrounding structures such as the rectum, the urethra and sphincter (which when damaged result in incontinence) and nerves (which when damaged can result in sexual dysfunction). Indocyanine green is an agent used in radical prostatectomies to prevent nerve damage. However, non-targeted fluorescent agents only produce limited signal differences between cancerous tissues and surrounding normal tissue background and the boundaries may be difficult to delineate. PSMA-targeted fluorescent agents have received

increasing attention and have been created by coupling different near-infrared fluorophores (NIFs) with small molecular ligands. Most of the existing studies focused on NIFs (wavelength, 700–900 nm), because haemoglobin in red blood cells, water, and other biological molecules produce low levels of autofluorescence within this wavelength range with a bright star lighting up on a dark background. A disadvantage of FGS is the signal can't be seen more than 1cm deep into the tissue.

Multimodal imaging-guided surgery has integrated the sensitive location of RGS with the high spatial resolution and accurate delineation potential of FGS based on fluorescent agents or photosensitisers. This technology can be integrated into surgical robots. Kularatne et al developed a novel PSMA-targeted fluorescent tracer named OTL78, which combined a high affinity PSMA-ligand with a near-infrared dye that specifically binds to the PSMA-positive tumours using sub-nanomolar concentrations to visualize small tumours[6]. It was cleared rapidly from PSMA-negative tissues allowing FGS to be performed within 1–2 h after injection, and the fluorescence signal lasted for over 48 h resulting in enhanced tumour visualization and negative surgical margins. In the future photosensitisers will be combined with photodynamic therapy (specialised light) to target and treat non-resectable tumour remnants[7].

For now FGS and multimodal imaging-guided surgery are still in the preclinical stages of development. Further studies are required to determine whether they have more advantages than traditional surgical techniques, especially in terms of overall survival and prognosis.

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Kalli is an internationally renowned Urological Surgeon, specialising in oncology and robotic surgery. He trained and worked in South Africa, before relocating to Australia where he has worked at Macquarie University Hospital and Westmead Hospital. His passion for what he does extends beyond the operating room, through publichealth advocacy, education and community awareness of men's health, cancer and sexuality.

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