Changing paradigms in radioguided surgery and intraoperative imaging: the GOSTT concept

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Published online: 15 October 2011
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Ever since the first descriptions as an aid for sentinel lymph node biopsy in the early 1990s [1, 2], interest in radioguided surgery has been rising sharply and continues to do so with respect to both the number of articles published in the medical literature and the amount of procedures performed. In Europe, lymphoscintigraphic imaging procedures for sentinel lymph node biopsy have markedly increased, by about 17.5%, between the years 2005 and 2008 (source: European Association of Nuclear Medicine), a period during which single photon imaging procedures in general were expected to remain substantially stable or

actually show some decline attributed to competition by the growing number of positron emission tomography (PET) studies.

Several reasons can be envisaged to explain the popularity of radioguided surgery. In particular, prior to the introduction of intraoperative radioguidance, professional skills and dexterity of surgeons had to build on the a priori knowledge of anatomy and while in the operation theatre primarily rely on two senses, sight and palpation. Introducing intraoperative gamma probe counting has forced surgeons to integrate a third sense, hearing, in addition to the prior two. In fact, this “upgrade” proved to be very convenient; the increasing intensity and pitch of the sound as a function of increasing count rates was adopted as a primary guide for the surgeon, in order not to distract him/her from focusing on the surgical field while performing gamma probe exploration, as a solution more superior than observing the numerical display of the count rates [3]. Another important reason for the wide acceptance of the radioguided surgery concept can be attributed to alignment and synergy with current trends of oncological surgery adopting less aggressive and invasive approaches; in this regard, the possibility of identifying with highest accuracy those patients who can be spared unnecessary lymph node dissection (a procedure fraught with a high incidence of morbidity and long-term complications) is certainly a crucial asset that radioguided sentinel node biopsy has brought about in clinical practice, concerning especially early breast cancer and cutaneous melanoma [4, 5]. The success of radioguided sentinel lymph node biopsy in patients with breast cancer or with cutaneous melanoma, where this technique has now become an integral part of the standard of care [6], has driven countless clinical trials aimed at validating the same approach in the management of other solid tumours [7].

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At the same time, applications of radioguided surgery procedures other than sentinel lymph node mapping/biopsy have also grown, most typically for identifying difficult to locate neoplastic lesions to be excised [7]. Intraoperative gamma probe-guided localization of such lesions is based on adequate, and within the surgical context a specific targeting, which is achieved either by direct image-guided intralesional delivery of a radiolabelled agent that does not significantly migrate from the site of interstitial injection (typically, ^{99m}Tc -macroaggregated albumin) or following systemic administration of any given tumour-seeking radiopharmaceutical exhibiting favourable accumulation and retention at the tumour site(s) [7]. Radiopharmaceuticals that meet such accumulation/retention requisites following systemic administration can be labelled with either single photon-emitting radionuclides (such as, e.g. ^{99m}Tc -sestamibi for radioguided surgery of parathyroid adenomas) or with positron emitters, typically [^{18}F]fluorodeoxyglucose (FDG). In the latter case, most frequently the probes for intraoperative radioguidance are designed to specifically detect the high-energy annihilation photons. Alternatively, probes capable of directly detecting the emitted positrons prior to their annihilation are less frequently employed as these approaches are limited by the short penetration range of β^+ mandating direct contact of the probe with the tissue while exploring the surgical field [7].

Yet another current trend of surgery is to adopt minimally invasive approaches for a growing range of procedures, including oncological surgery, as these promise much faster post-surgical recovery of patients. For optimal planning and carrying out of these approaches, accurate pre-surgical characterization of the surgical field and approach is crucial, a prerequisite that is best achieved through diagnostic imaging. In this regard, maximum benefit for the success of minimally invasive surgery derives from integration of anatomical (e.g. CT) and metabolic/functional imaging, typically provided by nuclear medicine procedures. Adding functional imaging to anatomical imaging not only contributes to better characterization of the lesion to be removed, but in several instances enables subsequent intraoperative guidance through the use of gamma probes particularly designed for laparoscopic use. On the other hand, the use of portable, small field of view gamma cameras capable of being employed during surgery for external scintigraphy of the relevant anatomical region further contributes to direct surgical exploration and also allows real-time monitoring of completeness of lesion removal [8–11]. Clearly, preoperative imaging employing hybrid equipment, e.g. single photon emission computed tomography (SPECT)/CT and PET/CT and in the near future PET/MR, maximizes the independent information content, either anatomical or functional information, on

which the surgeon can plan the best surgical approach. These recent developments and expansions of radioguided surgery from the original concept of using a gamma probe as the sole intraoperative guidance to a more complex sequence of procedures involving multimodality preoperative imaging, intraoperative external scintigraphy and intraoperative gamma probe guidance [8, 9, 12, 13] emphasize the peculiarity of radioguided surgery as an intrinsically comprehensive team approach fostering synergistic collaboration among and close coordination of the different specialties involved. Some of the main advantages in terms of incremental value of this novel approach over traditional surgical approaches are to be seen in the application of radioguided surgery for different tumours in different regions of the body.

Finally, the growing interactions between nuclear medicine and surgical specialties have been fostered also by the special momentum both in technology and in clinical research that are opening new avenues and strategies for tailoring surgical approaches to the different disease-specific and patient-specific conditions. In this regard, full integration of radionuclide imaging/detection with such optimized surgical approaches faces new challenges, but also new opportunities. These are represented by the possibility that “mixed reality” surgery (also defined as “augmented reality” surgery) takes advantage of the localizing/detecting capability offered by molecular imaging as typically obtained with nuclear medicine procedures. As of today, such mixed reality environments are mostly based on high-resolution anatomical CT images that allow construction of a 3-D virtual space (or simulator) through which the surgeon navigates with robotic assistance for training purposes [14–19] or for actually performing the surgical procedure [20, 21]. In addition to CT images, anatomical information utilized as an input for novel simulation/planning surgical approaches may include ultrasound imaging [22]. Efforts should therefore be undertaken to include also tomographic radionuclide images (as typically obtained with either PET/CT and/or SPECT/CT) for stereoscopic visualization of a complete medical data set that would include both structural/anatomical information and metabolic/functional information. In these rapidly evolving perspectives, different medical specialties must cooperate to achieve new operational paradigms towards the common goal of improved patient management and overall benefit. In this regard we deem it appropriate to introduce a general term that encompasses this entire domain as “Guided intraOperative Scintigraphic Tumour Targeting” (or GOSTT). This concept includes the whole spectrum of basic and advanced nuclear medicine procedures required for providing a roadmap that would optimize surgery.

In conclusion, we believe that molecular imaging, and in particular radionuclide imaging, is becoming essential for

optimizing and supporting surgical approaches (predominantly in oncology) tailored to the variable patient- and disease-specific conditions encountered. The increasing indications for sentinel lymph node procedures, combined with other emerging techniques of radioguided surgery, call for a concerted effort to improve, standardize and validate GOSTT. Indeed, the common denominator among all these advanced methodologies, including pre- and perioperative imaging and non-imaging procedures, is the aim of improving patient management and outcome and possibly positively impact health economics.

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