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From interventionist imaging to intraoperative guidance: New perspectives by combining advanced tools and navigation with radio-guided surgery

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ABSTRACT

The integration of medical imaging technologies into diagnostic and therapeutic approaches can provide a preoperative insight into both anatomical (e.g. using computed tomography (CT), magnetic resonance (MR) imaging, or ultrasound (US)), as well as functional aspects (e.g. using single photon emission computed tomography (SPECT), positron emission tomography (PET), lymphoscintigraphy, or optical imaging). Moreover, some imaging modalities are also used in an interventional setting (e.g. CT, US, gamma or optical imaging) where they provide the surgeon with real-time information during the procedure.

Various tools and approaches for image-guided navigation in cancer surgery are becoming feasible today. With the development of new tracers and portable imaging devices, these advances will reinforce the role of interventional molecular imaging.

De la imagen intervencionista a la guía intraoperatoria: nuevas perspectivas combinando herramientas avanzadas y navegación con la cirugía radioguiada

Palabras clave:
Imagen molecular
Cirugía radioguiada
Imagen óptica
Ganglio centinela

RESUMEN

La integración de tecnologías de imagen médica en los enfoques diagnósticos y terapéuticos puede proporcionar una perspectiva preoperatoria tanto en los aspectos anatómicos (tomografía computarizada, resonancia magnética o ecografía) como funcional (tomografía computarizada de emisión de fotón único, tomografía por emisión de positrones, linfogammagrafía o imagen óptica). Además, algunas modalidades de imagen se utilizan también en un entorno intervencionista (tomografía computarizada, ecografía, imágenes gammagráficas o imágenes ópticas), donde proporcionan al cirujano información en tiempo real durante el procedimiento.

En la actualidad, son factibles diversas herramientas y enfoques metodológicos para la navegación guiada por imágenes en la cirugía del cáncer. Con el desarrollo de nuevos trazadores y dispositivos portátiles de imagen, estos avances reforzarán el papel de la imagen molecular intervencionista.

Introduction

The integration of medical imaging technologies into diagnostic and therapeutic approaches can provide preoperative insight

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into both anatomical (e.g. using computed tomography (CT), magnetic resonance (MR) imaging, or ultrasound (US)) and functional (e.g. using single photon emission computed tomography (SPECT), positron emission tomography (PET), lymphoscintigraphy, or optical imaging) patient aspects. Moreover, some imaging modalities are also used in an interventional setting (e.g. CT, US, gamma or optical imaging) where they provide the surgeon with real-time information during the procedure.[1]

Radioguided surgery is defined as any surgical procedure which utilizes a radiation detection device in a real-time fashion within the surgical theatre for the identification of a target-tissue labeled with a radiotracer previously administered and with the purpose of assisting in the successful performance of that surgical procedure.[2]

The introduction of the sentinel node (SN) biopsy in the management of cutaneous melanoma and breast cancer in the final decennium of the past century transformed image guided surgery into an essential tool wherein nuclear medicine acts as one of the leading disciplines. From the beginning this field of research has been characterized by multidisciplinary collaborations between technical and clinical groups.[3,4]

In the recent evolution of radioguided procedures to image guided-intervention, some novel non-nuclear medicine technologies have been added to the conventional portable devices (like gamma probes or gamma cameras) to improve intraoperative detection of target lesions. Today, image guided interventions imply a minimal morbidity in comparison with classical surgical approaches, with the potential of equal or even better staging and regional control.[5]

Hence hybrid approaches provide outcome here; hybrid approaches are a well-accepted means to overcome the limitations of individual technologies and to generate a "best of both worlds" model. Some examples of this paradigm are the fusion of nuclear imaging modalities and radiological modalities (SPECT and PET with CT or MR).

Based on this modality, it is possible today to generate real 3D roadmaps for localization of SNs or tracer avid lesions enabling surgeons to use specific anatomical landmarks to retrieve the detected target lesions during operation. This approach has been reinforced with the synergy of preoperative SPECT/CT and PET/CT with intraoperative portable imaging technologies. Dedicated intraoperative portable gamma cameras have increasingly been incorporated in radioguided surgery in the last decade. Real-time imaging with an intraoperative gamma camera provides a larger field of view than a gamma probe can cover, as well as visual assistance in localization and verification of resection of the targeted tissue. Its position can be adjusted to also show SNs near the radiotracer injection site or to distinguish between two radiolabeled tissues, which may easily be overlooked by using a conventional handheld gamma probe. Another important advance in the use of SPECT/CT and PET/CT for the surgical act, is their transference to the operating room using mixed reality protocols. The concept of mixed reality concerns the merging of real and virtual elements to produce new environments for adequate surgical navigation.[6–8]

To obtain additional information, optical imaging can be used in parallel or in combination with nuclear imaging. The addition of optical imaging to the radioactive signature can provide an improvement into intraoperative visualization, as fluorescence or optical signals can be used to accurately delineate a superficial lesion in real-time. Optical imaging via the use of blue dye is often used to complement nuclear medicine-based radioguided surgery, and optical imaging based on fluorescence imaging can enhance intraoperative visualization. Hybrid (combined radioactive and fluorescent) agents has been designed for this and other purposes.[9–11]

Another approach combining optical and nuclear imaging is Cerenkov luminescence imaging (CLI). Utilizing light emission provoked by β-particles crossing through a dielectric medium such as tissue, CLI enables detection of positron emission tomography (PET) tracers with optical cameras, and can be used intraoperatively to guide cancer surgery.[12]

So, luminescence and radioactivity have the potential to complement each other as interventional molecular imaging methods, acting in a synergistic way.

The complementary features of both modalities ensure that neither can replace the other, and a hybrid approach that combines the two could therefore result in additional information during the intervention.

In a more extensive way, intraoperative molecular imaging requires some innovations; a fluorescent agent that can be administered into the patient and selectively accumulates in the tumour tissues and a camera system that can detect it. Several fluorescent agents exist to highlight tumours and target them by a diversity of mechanisms (receptor-mediated binding, permeability, etc.). The expertise generated in SN biopsy and other radioguided procedures provides the technological basis for many other valuable indications such as tumor specific imaging, new modalities and even multimodal applications of optical approaches in preclinical research (e.g. use of disease models using tumour cell lines genetically transfected with fluorescence proteins and/or bioluminescence enzymes).

As will be reviewed in this paper, various tools and approaches for image guided navigation in cancer surgery are turning feasible today. With the development of new tracers and portable imaging devices these advances will reinforce the role of interventional molecular imaging. This paper summarizes the topics presented at the second Interventional Molecular Imaging Symposium, held in Barcelona on 23 and 24 February 2017. The different lectures/subsections involved and their interaction are depicted in Fig. 1.

New technologies in radioguided surgery

From the past to the present: imaging of melanoma patients scheduled to undergo sentinel node biopsy

Identifying SNs requires a concerted effort from nuclear medicine physician and surgeon. Preceding the operation, the nuclear medicine physician can identify the nodal region to explore and determine the number of SNs with their exact anatomical location. This is of crucial importance for the surgeon as drainage may occur to multiple regions and 12% of the SNs in melanoma patients are found outside a recognised nodal basin.

Dynamic lymphoscintigraphy visualises the vessel that collects lymph from the melanoma and the lymph gland to which it drains directly. This vessel distinguishes the SN from second-tier nodes that are depicted later. Early and late static imaging follows dynamic imaging. The addition of single photon emission tomography combined with computed radiographic tomography (SPECT/CT) depicts the SNs in their anatomical habitat (Fig. 2). This further improvement can visualise sentinel nodes that may go unnoticed with conventional scintigraphy.[13]

SPECT/CT also enables the surgeon to prepare better for the procedure. The nuclear medicine physician marks the location of the SNs on the skin.

Two recent studies of new developments are presented showing a new option for imaging in frail patients and limitations of further imaging in SN-positive patients.

Once their location is pinpointed, focussed ultrasound examination of the SNs can be performed. This may reveal non-palpable metastases larger than a few millimetres and enables fine needle biopsy for confirmation. Patients with ultrasound-detected metas-