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Review

Functional imaging in radiation therapy planning for head and neck cancer

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ARTICLE INFO

Article history:
Received 4 May 2013
Received in revised form 16 October 2013
Accepted 16 October 2013

Keywords:
Radiotherapy planning
Functional imaging
Metabolic imaging
PET/CT

ABSTRACT

Functional imaging and its application to radiotherapy (RT) is a rapidly expanding field with new modalities and techniques constantly developing and evolving. As technologies improve, it will be important to pay attention to their implementation. This review describes the main achievements in the field of head and neck cancer (HNC) with particular remarks on the unsolved problems.

1. Positron Emission Tomography/Computed Tomography (PET/CT) in RT planning

1.1. *Introduction*

PET is a significant advance in cancer imaging with great potential for optimizing RT planning and thereby improving outcomes for head and neck cancer patients. The use of PET-CT in RT planning was reviewed by an international panel. The International Atomic Energy Agency (IAEA) organized two synchronized and overlapping consultants' meetings with experts from different regions of the world in Vienna in July 2006. Nine experts and three IAEA staff evaluated the available data on the use of PET in RT planning, and considered practical methods for integrating it into routine practice. For RT planning, FDG was the most valuable pharmaceutical. There was evidence for utility of PET in head and neck cancers, with promising preliminary data in many other cancers. The best available approach employs integrated PET-CT images, acquired on a dual scanner in the radiotherapy treatment position after administration of tracer according to a standardized protocol, with careful optimization of images within the RT planning system and carefully considered rules for contouring tumour volumes. PET will play an increasing valuable role in RT planning for a wide range of cancers.[1] More recent

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1507-1367/$ – see front matter
http://dx.doi.org/10.1016/j.rpor.2013.10.007

review confirm the value of PET/CT as an adjunct in RT planning for two main reasons: better identification of the disease extent and characterization of the biological behaviour of the disease.[2]

1.2. *Advantages and disadvantages*

Besides the obvious improvement in patient selection for radical treatment due to exclusion of distant metastases and of synchronous primary malignancy,[3,4] there are potential advantages to the use of 18F-FDG-PET/CT in RT planning for HNC: reduction of inter-observer variation in target volume delineation,[5] particularly when an institutional contouring protocol is developed,[6] smaller GTV volumes,[7] and more accurate identification of positive lymph nodes.[8]

The main disadvantages are the limited spatial resolution of PET images, the lower utility for identifying occult nodal metastases,[8] and the false positive readings due to inflammation, infection, radiation effect or physiological uptake.[2] As the spatial resolution of a CT image is below 1 mm, a neat tumour margin is frequently displayed, particularly in contrast-enhanced studies. This is not the case with PET images where the spatial resolution is just below 5 mm. This fact, combined with the background uptake of contrast due to physiologic processes, contribute to the fuzzy appearance of tumour edges. PET/CT does not add value over CT or MRI for T staging[9] and superficial tumour spread in HNC is often missed.[7] Therefore, a limitation of the PET image is its inability to define depth of invasion and relation of tumours to neighbouring structures (Figure 1).

Spatial resolution of PET limits its utility to characterize the micro-regional distribution of tumours phenotype. Preclinical studies have shown discrepancies between imaging with a small-animal PET scanner with a spatial resolution of 2.7 mm and the underlying microscopic reality represented by autoradiography.[10] Such a discrepancy means the macroscopic assessment of tumours with molecular imaging might not necessarily reflect their micro-regional distribution.[11] Many micro-regional tumour areas are likely to coexist within one clinical PET voxel. Negative scan findings cannot, therefore, exclude the presence of microscopic tissue involvement, and precise anatomic location of the signal can be difficult. Despite these inherent weaknesses, PET imaging has proven to generate quantitative tumour maps that accurately reflect the underlying microscopic reality in an animal model with a clinical realistic image contrast.[12] As the set-up tolerance is up to 3 mm for patients with HNC immobilized in thermoplastic masks, caution should also be given to dose prescriptions to a voxel of approximately 4 mm size as its precise location intra- or inter-fraction cannot be assured. Heterogeneous dose prescriptions adapted by voxel may not be possible with current delivery systems due to limited dose distribution spatial resolution and target localization inaccuracies related to set-up and organ motion errors. Furthermore, the microenvironment of treated and untreated tumours changes with time adding uncertainty to voxel oriented dose distributions.[13,14]

Accurate assessment of primary tumour size, extent, and depth of invasion is pertinent to planning the most appropriate local treatment. The most appreciated utility of PET/CT is the detection of an unknown primary in situations where there is a strong clinical suspicion of a primary despite a negative exploration and biopsy. It has been demonstrated that primary tumour detection was significantly higher with PET or PET/CT compared with CT or magnetic resonance imaging (MRI) due to a higher sensitivity.[15]

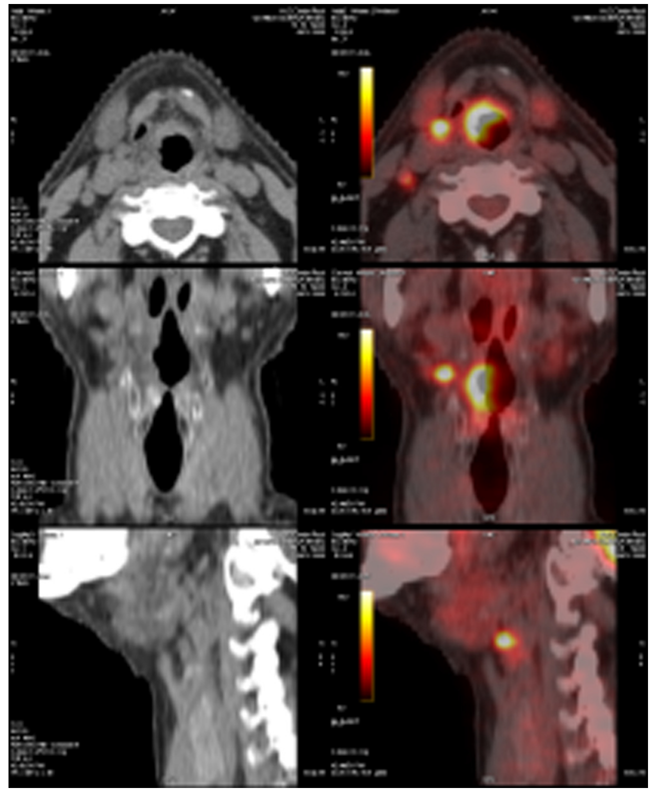

Fig. 1 – 18F-FDG PET/CT on a patient with a supraglottic tumour. Avid tracer uptake helps to identify a positive lymph node located immediately lateral to the primary tumour. Physiologic uptake in the right vocal cords besides the fuzzy appearance of tumour borders due to low spatial resolution of PET image hamper the accurate delineation of tumour contours.

1.3. *The segmentation problem*

Before PET-based GTVs can reliably and reproducibly be incorporated into high-precision RT planning, operator-independent segmentation tools have to be developed and validated.[16,17] Simple visual interpretation of the PET signal is most commonly applied but is highly operator-dependent, as it is susceptible to the window-level settings of the images and to interpretation discrepancies.[5] Visual interpretation has significant inter and intra-observer variations which may be improved when criteria for tissue definition is included during interpretation.[5] Variability of the GTV based on PET images (GTV_{PET}) delineation could be avoided adopting more objective methods, such as iso-contouring based on a fixed standardized uptake value (SUV), or relative thresholds such as a proportion of the maximum SUV