Target volume definition with $^{18}$F-FDG PETCT in radiotherapy treatment planning

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Introduction

External beam radiotherapy has a key role in the management of many cancer patients. The aim is to deliver a dose of radiation to a well-defined target volume that will kill the tumour cells while sparing surrounding normal tissue. The first and critical step in radiotherapy planning (RTP) is the delineation of the gross tumour volume (GTV) by the radiation oncologist. A margin is added to the GTV to account for microscopic disease, creating the clinical target volume (CTV). The planning target volume (PTV) is obtained by adding further margins accounting for internal organ motion and setup variability (figure 1).

Advances such as intensity modulated radiotherapy (IMRT) and stereotactic radiotherapy, which shape the radiation beam more precisely to the target, mean that accurate target definition is even more important to ensure geographic miss does not occur.

Radiation oncologists use imaging techniques, along with knowledge of the physiology of the disease, to define the GTV. CT images are generally used because they provide electron density information, required in radiation dose calculations, as well as anatomical information. However, \(^{18}\)F-FDG PET has shown to have better sensitivity and specificity than CT in a variety of tumour sites and this has led to huge interest in using PET in the RTP process.

Different tracers can be used for PET imaging, with the most common being \(^{18}\)F-fluorodeoxyglucose (\(^{18}\)F-FDG), a glucose analogue. The first papers investigating the use of \(^{18}\)F-FDG PETCT in RTP were published in the late 1990s and since then an ever-expanding body of published work in both nuclear medicine and radiotherapy journals has developed.

The main area of interest has been in non-small-cell lung cancer (NSCLC) patients, because loco-regional failure remains a significant problem for these patients undergoing radical radiotherapy. It is anticipated that the use of PET, which has both greater specificity and sensitivity than CT, would allow targets to be more accurately defined, thereby allowing greater radiation doses to be delivered. There has also been a significant amount of work published on head and neck cancer, lymphoma and oesophageal cancer.

In considering whether PETCT is useful for delineating the GTV, CT images are generally used because they provide electron density information, required in radiation dose calculations, as well as anatomical information. However, \(^{18}\)F-FDG PETCT in radiotherapy treatment planning is limited to a relatively small number of centres. However, with increasing interest in this area the International Atomic Energy Authority (IAEA) has provided guidance. This attempts to standardise procedures, which is vitally important in the introduction of PET into the RTP process. However, outstanding issues with the use of PET for delineation of target volumes remain.

Issues in the use of PETCT images in delineation of target volumes

Acquisition and timing of the scans

When PETCT scans are used directly in RTP for delineating target volumes, they must be acquired with the patient in the treatment position on a flat couch top and immobilised as they will be for radiotherapy (figure 3). The PETCT scanner must also be subject to the same quality control and procedures performed in CT planning. It has been established that RTP scans can be acquired using PET-CT scanners, and a number of centres are now performing these scans.

However, there is no clear consensus on how best to incorporate PETCT scans into the RTP process. For example, is a dedicated RTP PETCT scan required or can a PET scan be acquired which is used for both planning and staging? A recent study has shown the importance of the scan being acquired in the treatment position with the acquisition of a dedicated planning PETCT scan being justified if only a diagnostic PETCT scan is available.

Patients who are having radical radiotherapy may also have induction chemotherapy before their treatment and planning scan. This may lead to issues with interpretation of the PET scan as the RTP scan may need to be performed soon after the chemotherapy is completed.

Delineation of the volume

A major challenge in using \(^{18}\)F-FDG PET for delineating the GTV is the lower spatial resolution of PET compared with CT. This means the edges of the tumour are blurred, making it difficult to decide where to draw the outline. A variety of approaches, including visual assessment and automatic segmentation techniques, have been used.

Visual assessment is simple and analogous to the technique used to outline GTVs on CT images. However, the apparent tumour edge will be influenced by how the images are displayed and, without the careful use of predefined protocols, introduction of this technique may lead to very variable results.

Thresholding methods, either adaptive or fixed, have been very popular, partly because they are straightforward to implement. Most of the work on determining appropriate thresholds has been performed on phantoms, although recent studies have used pathological samples. The variability in threshold values reported for lung tumours of different volumes (20-55%) indicates that no standard value is applicable for all patients.

Automated methods cannot distinguish between uptake in a tumour and that due to other processes, such as infection. If such methods were to be used in RTP it would be as an aid to the radiation oncologist in the outlining process.

The small number of studies providing inter-comparisons of the different techniques, or comparing them with a gold standard such as pathological samples, mean that there is no consensus on the best one to use. The IAEA guidelines do, however, state that automated methods which employ a single crude factor such as a particular standardised uptake value (SUV) are too simplistic and not recommended.

In Belfast, have shown that the well known inter-observer variation, seen when different radiation oncologists delineate the GTV on CT images, is reduced when PETCT images are used.

Significant experience in using PETCT in radiotherapy planning is limited to a relatively small number of centres.
Delineation of GTVs using PET will require close collaboration between nuclear medicine physicians or radiologists experienced in PETCT with the radiation oncologists doing the out-lining."

**Dealing with respiratory motion**

Tumours may undergo physiological movement and this is particularly problematic in NSCLC where respiratory motion of up to a few centimetres is possible. CT acquisitions provide a snapshot at a random point in the respiratory cycle. However, PET takes a few minutes to acquire one field of view, so it produces images that are averaged over the respiratory cycle. Therefore, PET images are blurred with an apparent increase in tumour size and decrease in intensity. This may mean that the PET derived GTV may be larger than the CT derived GTV (figure 4).

If GTVs are being defined using PET images it is important to consider the effect of respiratory motion. Alternatively, respiration may be compensated for by acquiring gated images where a trigger based on a signal related to the tumour position is used to instruct the scanner when to start acquiring. The data between triggers is acquired into a number of bins, so the result is a series of images at different points over the respiratory cycle.

**How should PET-defined GTVs be expanded to PTVs?**

The GTV defined using CT images is assumed to represent a static situation with a margin added to account for motion in the expansion to the PTV. However, as discussed above, PET images already include motion. Therefore, it has been proposed that the margins added to non-gated PET defined GTVs do not need to account for motion and could be tighter.

**Conclusions and future directions**

The use of 18F-FDG PET for GTV delineation is still the subject of on-going research and development and, despite a large body of published work, unresolved issues still remain, in particular the best means of defining the tumour edge on PET images. In addition, there are very few studies in which patients have been treated using PET derived GTVs and a lack of high quality evidence specifically supporting the use of PET in RTP. Clinical trials are required to determine the benefit on outcome when PETCT is used in RTP.

Other developments will be very important to the use of PETCT in RTP. Most of the work to date has used 18F-FDG, but tracers that can visualise biological pathways with particular significance for tumour response to treatment, eg hypoxia, cell proliferation and angiogenesis, have been developed in recent years. These will be vital for the idea of ‘dose painting’ where different radiation doses would be delivered to different tumour regions based on uptake of these tracers.

The use of PETCT in RTP to delineate GTVs is a multi-disciplinary area that requires collaboration between many different staff groups in nuclear medicine and radiotherapy. There is still a lot of work to be done before this becomes a routine procedure and many exciting developments are likely in the future.

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**References**


**FIGURE 1**

Target volume definitions according to ICRU50.

**FIGURE 2**

Illustration of the GTVCT (red) and GTVPET (blue) for a NSCLC patient with atelectasis.
FIGURE 3
PETCT scanner and patient set-up for RTP scanning.

FIGURE 4
PETCT images showing the GTV_{PET} (green) is larger than the GTV_{CT} (blue) due to respiratory motion.