

## USE OF FDG-PET/TC SCAN IN THE PLANNING OF RADIATION THERAPY FOR NON-SMALL CELL LUNG CANCER\*

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**Abstract** Radiation therapy represents an important alternative for curative treatment of patients with non-small cell lung cancer. However, an accurate definition of the volume to be irradiated becomes even more important, considering that lungs are highly sensitive to radiation. Most recently, combined FDG-PET/CT scan has been utilized, and the literature reports its significant role in the planning of radiation therapy, since it seems to influence the target-volume delineation in cases of lung cancer. Differences between diagnostic and treatment equipments must be taken into consideration when FDG-PET/CT scan is utilized in the planning of radiation therapy. The present study discusses some of the many technical problems that must be solved when PET is incorporated into the planning of radiation therapy for non-small cell lung cancer.

*Keywords:* Radiotherapy; PET scan; Planning; Lung cancer.

**Resumo** O uso de FDG-PET/TC scan no planejamento da radioterapia em câncer do pulmão não de pequenas células. Radioterapia é uma importante alternativa de tratamento curativo em pacientes com câncer do pulmão não de pequenas células. Entretanto, pulmões são muito sensíveis à radiação e isto aumenta a importância em se delimitar o volume a ser irradiado com precisão. Ultimamente, a tomografia por emissão de pósitron (PET) e a tomografia computadorizada (TC) são feitas de forma combinada, e a literatura sugere que seu impacto no planejamento da radioterapia é significativo. Ao se utilizar exames de PET/TC no planejamento da radioterapia é importante reconhecer e adaptar-se às diferenças entre os equipamentos de diagnóstico e de tratamento. Este texto discute alguns dos problemas técnicos que devem ser resolvidos quando se incorpora PET no planejamento radioterápico.

*Unitermos:* Radioterapia; Tomografia por emissão de pósitron; PET scan; Planejamento; Câncer do pulmão.

### INTRODUCTION

Radiation therapy (RT) is frequently utilized with curative purposes in cases of lung cancer. A probable complication of this treatment is actinic pneumonitis, since the radiation dose required to eradicate cancer (> 50 Gy) is usually higher than the dose tolerated by the lungs (around 20 Gy)<sup>(1)</sup>.

In radiation therapy for non-small cell lung cancer (NSCLC), the target volume

has no longer been the whole mediastinum, but only the areas of tumor involvement<sup>(2)</sup>. As a result, the radiation dose can be increased on the tumor without increasing the toxicity on the normal tissues.

How to know which are the areas affected by a tumor? The definition of the areas of tumor involvement may come from the results of invasive procedures such as mediastinoscopy, although usually it depends on radiological studies, particularly computed tomography (CT).

In the planning of radiation therapy, it may be difficult to accurately define the gross tumor volume (GTV). In some cases, a cancer cannot be differentiated from an equally dense non-tumor like areas on CT, for example, atelectasis or normal regions on the mediastinum. This difficulty can explain the significant interobserver variation in radiotherapy fields delineation in cases of lung cancer<sup>(3)</sup>.

A functional imaging study, like FDG-PET scan that can distinguish a cancer from other equally dense, non-tumor like areas on CT scans, meets the radiotherapist's

need of a biological target to be defined. Recent studies demonstrate that the utilization of combined FDG-PET/CT changes significantly about 50% of the plannings based on CT alone<sup>(4,5)</sup>, and suggest that combined FDG-PET/CT should be routinely utilized in cases of curative radiation therapy for NSCLC<sup>(6)</sup>.

For the last two years, the McGill University Department of Radiation Oncology has been operating in association with the Department of Nuclear Medicine, utilizing a PET/CT equipment adapted for radiation therapy planning. The present study is aimed at discussing aspects connected with the implementation of combined FDG-PET/CT in the planning of radiation therapy, and, particularly, in the definition of GTV in patients with NSCLC.

### PET/CT versus PET alone

FDG-PET scan is used as the acronym for positron emission tomography with <sup>18</sup>F-fluorodeoxyglucose (<sup>18</sup>FDG) as a tracer. The study detects the increased metabolism of glucose that usually is higher in malign-

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nant tumors as compared with normal tissues. As a functional imaging study, FDG-PET is limited as compared with CT to demonstrate anatomic locations. Modern PET equipment are currently available in combination with CT, with the advantage that both studies (PET and CT) require only one visit of the patient to the clinic and are performed one immediately after the other, while the patient lies in the same position on the imaging table. CT is utilized for attenuation correction and better localization of small lymph nodes or non-tumor like soft tissues. Although there is no "significant evidence" justifying the use of combined PET/CT instead of PET alone, like in other radiotherapy technical aspects, it is difficult not accepting the irreversibility of the use of combined PET/CT<sup>(7)</sup>.

### Imaging table and patient positioning

Figure 1 shows two CT images of a same patient: the first one acquired with the patient on a concave imaging table, and the second one, with the patient on a flat table, with the arms up, the typical position during radiotherapy sessions. This is the

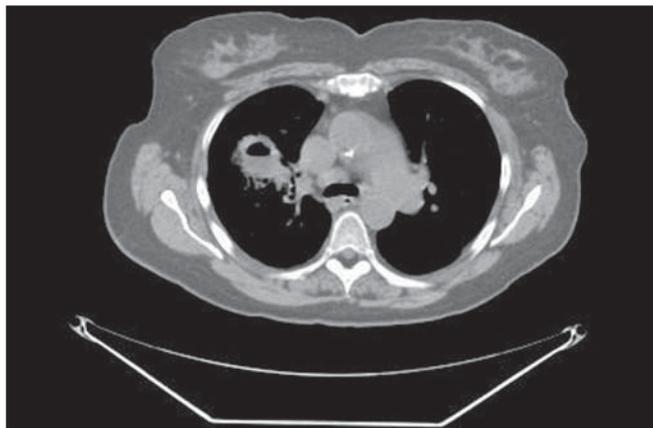
first difficulty to be overcome: standard PET/CT equipment come from the manufacturer with concave imaging tables. On the other hand, RT treatment is delivered by equipment with flat tables, with patients with their arms up in order to allow the use of lateral fields. Therefore, combined PET/CT scan for RT planning purposes should also be performed on a flat imaging table. Besides, the examination room should have the same facilities found in the radiotherapy treatment room (including a laser alignment system for isocenter setup, etc.). This is a paramount condition to allow an appropriate fusion between PET/CT images and simulation CT images utilized in the radiotherapy planning, and that the patient positioning can be adequately reproduced in the different examination and radiotherapy rooms.

### PET may yield false results

There are many studies demonstrating FDG-PET is better than CT alone for lung cancer detection, and so it is useful to define the tumor extent; but PET is not an accurate method<sup>(8,9)</sup>. Figure 2 shows an

example of a false-negative PET. A pulmonary nodule clinically suggestive of malignant neoplasm had not shown any hypermetabolism on PET, but a surgical resection confirmed an adenocarcinoma.

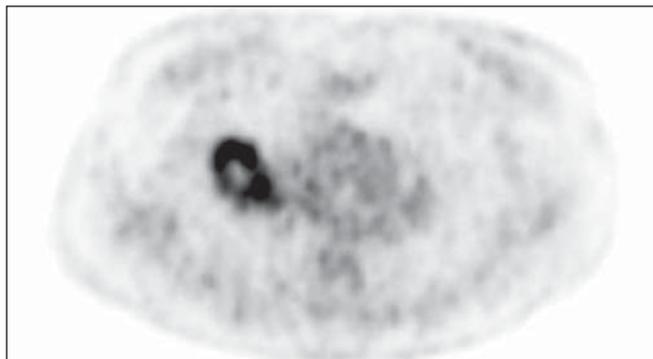
Table 1 demonstrates the comparison between CT and FDG-PET sensitivities and specificities in patients with NSCLC-type lung cancer<sup>(8)</sup>. One can see that FDG-PET is better than CT for cancer detection, but there is still a 10–20% risk of false-negative or false-positive results with FDG-PET. This is a relevant information because patients referred for curative radiotherapy treatment have not been submitted to surgery, and, therefore, there is no histological confirmation of imaging findings, and it is a radiotherapist responsibility to define the target volume (GTV). Figure 1 illustrates such difficulty, with a clinically inoperable smoker patient presenting with hemoptysis, whose CT demonstrated a tumor-like mass in the right lung and mediastinal lymph nodes, besides a 2.0 cm tracheal lymph node. CT showed this lymph node as positive for cancer. Needle biopsy demonstrated that the pulmonary tumor



A

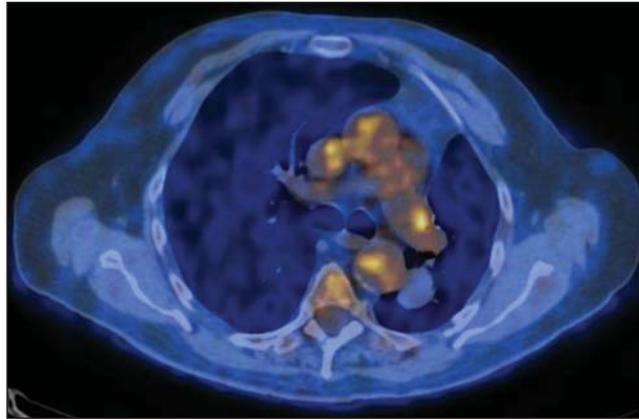


B



C

**Figure 1. A,B:** Computed tomography studies of a same patient on a standard concave imaging table (A) utilized in CT and PET units, and on a flat table (B), typically utilized in CT radiation therapy planning. **C:** Combined PET showing a positive lung tumor with negative pretracheal lymph node.



**Figure 2.** Example of a false-negative PET. PET-negative nodule in the left lung, beside the aorta (arrow). Surgical resection demonstrated an adenocarcinoma.

**Table 1** Comparison of sensitivity and specificity between CT and FDG-PET in non-small cell lung cancer (NSCLC)<sup>(8)</sup>.

Sensitivity		Specificity	
TC	FDG-PET	TC	FDG-PET
45%	80–90%	85%	85–100%

was an adenocarcinoma. Pretreatment FDG-PET scan was positive for the pulmonary tumor, and negative for the mediastinal lymph nodes. Considering that the tracheal lymph node could not be considered as cancer without a histological study, it was impossible to know whether the mediastinal lymph node should or not be included in the GTV. In this case, a mediastinoscopy demonstrated that, despite increased in size, the lymph node was benign.

**Images acquisition time and motion artifacts**

Tumors and thoracic organs move as a result of respiratory motion<sup>(10)</sup>. With the

currently available FDG-PET/CT equipment, the CT acquisition time is short (measured in seconds), but the PET acquisition time is longer (about 30–45 minutes). So, a tumor visualized on CT reflects only one position during respiratory motion whereas the PET images show the whole area of this movement. Figure 3 illustrates this difference. Considering that radiotherapy sessions take some minutes, maybe the adoption of the volume shown by PET would be more appropriate than the one shown by the simulation CT.

**Tumor extent evaluation by FDG-PET**

Finally, a case where the PET/CT scan was performed with the patient on a flat imaging table, with arms up, with appropriate marking for fusion with simulation CT images, and positive (hyperactive) areas disclosed by PET included in the GTV contour. The radiotherapist has only to define the target volume to be treated. Unfortunately, the size of the hyperactive area de-

tected by PET scan changes significantly, depending on the window selected, as shown on Figure 4.

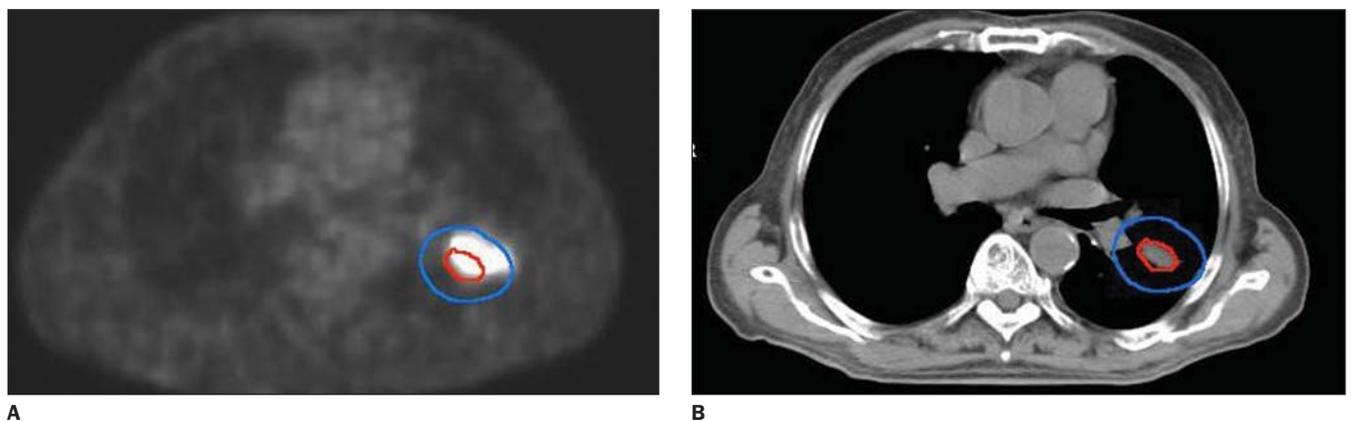
Studies in the literature report different methods utilized to define GTV by means of FDG-PET:

a) Visual method, without any grounding in physics or mathematics, simply based on visual comparison between images by the radiologist. This method was reported in the first studies on the utilization of PET for radiotherapy planning purposes<sup>(11)</sup>.

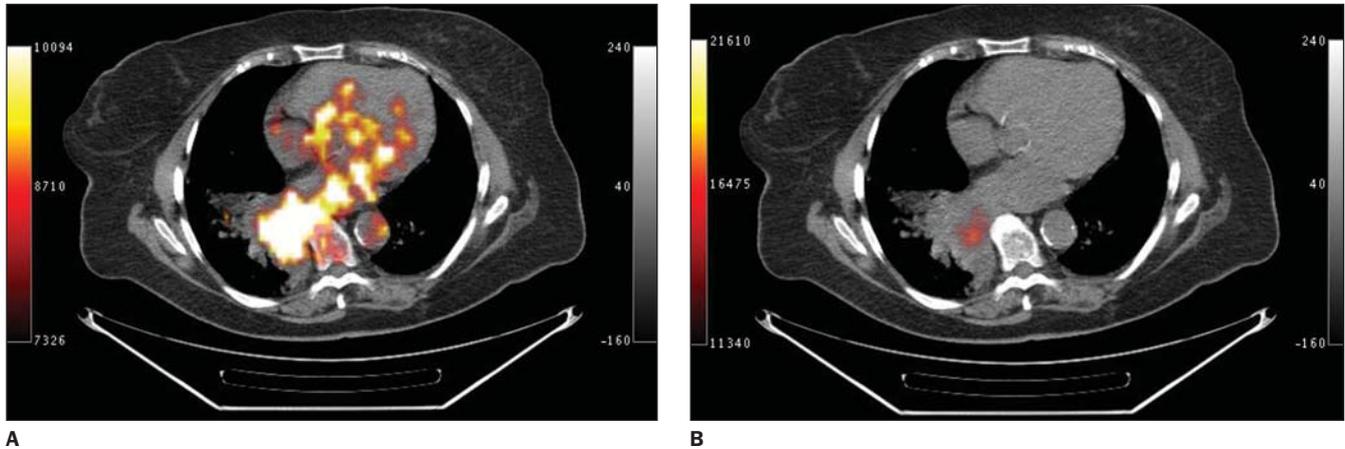
b) A percentage of the highest hypermetabolic value (the threshold) defines the tumor margins. Based on simulations, a threshold of 40% has been adopted<sup>(12,13)</sup>. This contour may be automatically calculated by a relatively simple software. Unfortunately, one cannot guarantee that areas with a threshold lower than 40% are free from active cancerous cells; this is usual in necrotic areas, for example.

c) A certain standard uptake value (SUV) will define the tumor volume; for example, a SUV higher than 2.5 that is considered by the majority of nuclear medicine specialists as an activity probably positive for NSCLC<sup>(9)</sup>. Also by this method, a software can automatically calculate the tumor volume, but one cannot guarantee that areas with SUV < 2.5 are free from cancerous cells.

A definition on which would be the best method to define GTV by means of FDG-PET is still to be known. What should be done? Considering the absence of a consensual guidance about this matter, the recommendation is that all of the factors must



**Figure 3.** PET/CT simulations on a same patient, both performed on a flat table, in the same positioning, and with the isocenter appropriately marked with laser. Because of respiratory motion and PET acquisition time (30-45 minutes), the image of the same tumor appears larger than on CT.



**Figure 4.** Patient with right lung adenocarcinoma. PET/CT fusion of the same study seen on two different windows, showing a significant alteration on the PET image.

be taken into consideration in a GTV delimitation, and the clinical common sense should be adopted for each case individually<sup>(14)</sup>. Recently, the Radiation Therapy Oncology Group (RTOG) initiated the study RTOG-0515 called “A comparative study of gross tumor volume definition with or without PET fusion for patients with NSCLC”. This study is aimed at determining the impact of PET/CT fusion on the GTV delimitation as compared with CT. Considering the limitations of PET in the definition of tumor margins, this protocol establishes that “the tumor volume (primary tumor and lymph nodes) contour should be based only on the CT images from PET/CT studies”.

## CONCLUSION

There is no imaging method with 100% sensitivity and specificity for lung cancer. Therefore, besides clinical information, the radiotherapist depends on the imaging methods available to define and delineate tumor margins, and CT remains as the method most frequently utilized for treatment purposes. FDG-PET/CT has shown higher sensitivity and specificity in the determination of lung cancer extent. For some experts, FDG-PET is essential in the planning of radiation therapy in patients with NSCLC; for others, the FDG-PET/CT value as a clinical tool has been overesti-

mated<sup>(7)</sup>. Although the role of FDG-PET/CT in the optimization of radiotherapy is controversial<sup>(8,9)</sup>, it seems there is no doubt that this is an extremely useful imaging method for evaluating tumors extent, and, also, delimiting GTV in patients with NSCLC. Presently it is still to be established if FDG-PET-based radiotherapy planning will improve treatment outcomes and/or quality of life of patients affected by NSCLC.

Positron emission tomography (PET) performed with <sup>18</sup>F-fluorodeoxyglucose (FDG) represents a significant first step towards the application of this technique in oncology. Other tracers have been studied, representing promising alternatives for cancer diagnosis and staging, as well as in the planning of radiation therapy.

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