

# Additional value of hybrid PET/CT fusion imaging *vs.* conventional CT scan alone in the staging and management of patients with malignant pleural mesothelioma

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## Abstract

**BACKGROUND:** Despite being a relatively rare disease, the incidence of malignant pleural mesothelioma (MPM) is expected to increase over the next two decades due to the long time interval elapsing between exposure to causative factors, mainly asbestos, and disease onset. Early disease stages have been reported to benefit from radical surgery. In more advanced disease stages, a multimodality treatment, including various combinations of chemotherapy, external radiotherapy and surgery,

may provide some favourable results though the prognosis remains poor. In this regard, an accurate pre-treatment staging plays an important role in offering patients a more appropriate therapeutic planning. In some preliminary studies, <sup>18</sup>F-FDG PET has proven to be able to provide useful information for staging purpose, especially for the detection of metastatic spread to lymph nodes and distant sites.

**MATERIAL AND METHODS:** In the present study, we investigated 15 consecutive patients with histologically proven MPM by means of conventional 2-mm thickness whole-body CT scan with and without contrast medium in comparison with whole-body <sup>18</sup>F-FDG PET/CT fusion imaging.

**RESULTS:** <sup>18</sup>F-FDG PET/CT did not provide additional information about the primary tumour (T) compared to CT scan, but identified a higher number of metastatic mediastinal lymph nodes (N) in 6 patients (40% of cases) and unknown metastatic disease to distant sites (M) in 3 patients (20% of cases). On the basis of PET/CT findings, treatment planning was changed in 5 patients (33.3% of cases).

**CONCLUSIONS:** Our data show that <sup>18</sup>F-FDG PET/CT fusion imaging can play a relevant role in the staging and treatment planning of MPM patients.

**Key words:** <sup>18</sup>F-FDG PET/CT fusion imaging, CT scan, malignant pleural mesothelioma, staging, treatment planning

## Introduction

Malignant mesothelioma is an uncommon neoplasia arising in most cases from the pleura (MPM), although less typical origins include the pericardium and peritoneum [1–3]. Asbestos, the most important risk factor for MPM, was largely used until 1980 in Western Europe and considering the relatively long time interval

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elapsing between asbestos exposure and disease onset, the incidence of MPM is likely to increase over the next two decades [4]. Therapeutic approach to MPM is far from satisfactory. The early diagnosis of small primary tumours seems to offer a disease cure by means of radical surgery, while a combination of surgery, external radiotherapy and chemotherapy is employed in advanced stages [1–5]. However, disease response to chemotherapy and external radiotherapy is known to be suboptimal in MPM with the currently applied therapeutic schedules [5]. Experimental treatment approaches including immunotherapy and gene therapy are currently under investigation with preliminary promising results [6]. Despite prolonged survival that has been reported in association with new multimodality therapeutic approaches [5, 6], MPM prognosis remains relatively poor with a median survival ranging between 12 to 18 months from the time of diagnosis [1, 7]. An early diagnosis and an accurate pre-treatment staging are considered the most important steps to cure or improve the quality of life and survival of MPM patients [1, 5, 6, 8].

Conventional computed tomography (CT) scan has been widely considered the gold standard imaging technique for MPM diagnosis and staging. Unilateral pleural effusion, nodular or diffuse pleural thickening and interlobular fissure thickening are common findings at CT scan in MPM patients [2]. However, CT scan is characterised by limited accuracy in differentiating between benign and malignant pleural lesions, particularly when it comes to establishing the nature of diffuse pleural thickening in asbestos-exposed subjects, and in the early detection of metastases to lymph nodes and distant sites [9]. Conversely, some recent studies have shown that metabolic information obtained by  $^{18}\text{F}$ -fluorodeoxyglucose positron emission tomography ( $^{18}\text{F}$ -FDG PET) gave promising contribution to characterise malignant hypermetabolic pleural lesions, to detect metastatic lymph nodes shown on CT scan to be of normal size and to highlight neoplastic spread to distant sites [9, 10]. In addition, some preliminary experiences seem to suggest a prognostic value of  $^{18}\text{F}$ -FDG PET, showing that the patients with the highest hypermetabolism measured by standardized uptake value (SUV) are characterised by the worst prognosis [11]. The limited anatomical details provided by  $^{18}\text{F}$ -FDG PET alone makes it necessary to visually compare PET findings with morphologic information obtained by CT scan. The recent introduction in nuclear medicine practice of hybrid  $^{18}\text{F}$ -FDG PET/CT scanners facilitates the acquisition of both metabolic (PET) and morphologic (CT) information in a single examination. Moreover, fusion PET/CT imaging is provided automatically. This option is particularly useful to precisely localise small tumour foci, such as a metastatic lymph node considered normal by CT according to size criteria [12, 13], thus overcoming the limits related to the repositioning of the patient for individual studies [14]. Furthermore, in the hybrid PET/CT systems, the CT scan is used for attenuation correction, allowing for quantitative analysis of tumour metabolism [11].

In the present study we investigated the clinical usefulness of  $^{18}\text{F}$ -FDG PET/CT fusion imaging in the staging of patients affected by MPM with particular emphasis on the impact on patient management and treatment planning.

## Material and methods

In the period between July 2004 and June 2005, 15 consecutive patients affected by MPM and referred to the Nuclear Medicine Services of Bologna University and Rovigo Hospital, were enrolled in the study.

There were 12 males and 3 females with a median age of 67.1 years (range 44 to 88 years). In 14/15 patients history of exposure to asbestos was recorded. All patients were studied at the initial diagnosis and in all cases final diagnosis of MPM was reached by histopathologic findings.

In all cases both CT scan and  $^{18}\text{F}$ -FDG PET/CT imaging were obtained before any therapy.

The CT scans were performed in different centres, but in all cases the procedure was carried with and without contrast medium and with a 2-mm slice thickness. All CT scans were reviewed at the time of  $^{18}\text{F}$ -FDG PET/CT reporting.

The  $^{18}\text{F}$ -FDG-PET/CT was obtained following standard procedures. Briefly, each patient was injected intravenously with 5.3 MBq/kg  $^{18}\text{F}$ -FDG (median 370 MBq). The bolus of radio-tracer was directly injected through a venous cannula inserted in an antecubital vein and followed by a flush of saline to avoid stagnation. PET/CT images were obtained 60 minutes after tracer administration.  $^{18}\text{F}$ -FDG was produced adopting standard synthesis techniques using an on-site cyclotron [10].

PET/CT scans were carried out using a dedicated PET/CT tomograph (Discovery LS 4-ST scanner, GE Medical System, Waukesha, WI, USA). PET scan emission images were collected for 4 minutes per bed position (for a total of 6 to 7 positions); CT images were used for non-uniform attenuation correction (the parameters of CT acquisition contemporary to the PET study were: 140 kV, 80 mA, 0.8 sec. tube rotation, 5 mm thickness). Patients were asked to fast for at least 6 hours before  $^{18}\text{F}$ -FDG injection. No patient had history of diabetes in the present series.

PET/CT scanning spanned the distance from the skull to the middle part of the thigh. Tumour staging was evaluated according to TNM, UICC, 1997 [15]. The average time elapsed between conventional CT scan and  $^{18}\text{F}$ -FDG PET/CT imaging was 7 days (range, 2–14).

MPM treatment in our centres consists of surgery alone in early disease stages (I, II) whereas a multimodality therapy of surgery followed by radio-chemotherapy is performed in stage III and radio-chemotherapy alone in stage IV.

## Results

Table 1 shows the clinical characteristics, tumour staging, established both with conventional CT scan and  $^{18}\text{F}$ -FDG PET/CT fusion imaging, and treatment planning in our patients' series. It is worth noting that  $^{18}\text{F}$ -FDG PET/CT did not provide additional information about the primary tumour (T) in respect to conventional CT scan in our experience. However,  $^{18}\text{F}$ -FDG PET/CT identified a higher number of metastatic mediastinal lymph nodes (N) in 6 patients (40% of cases) and unknown metastatic disease to distant sites (M) in 3 patients (20% of cases, Figure 1). Of note, on the basis of  $^{18}\text{F}$ -FDG PET/CT scanning results, the treatment planning was changed in 6 patients (33.3% of cases).

The follow-up period ranged from 4 to 16 months, median 7 months. Two patients in stage IV died 5 months and 13 months after treatment, respectively, while 4/5 patients with stage I are disease-free.

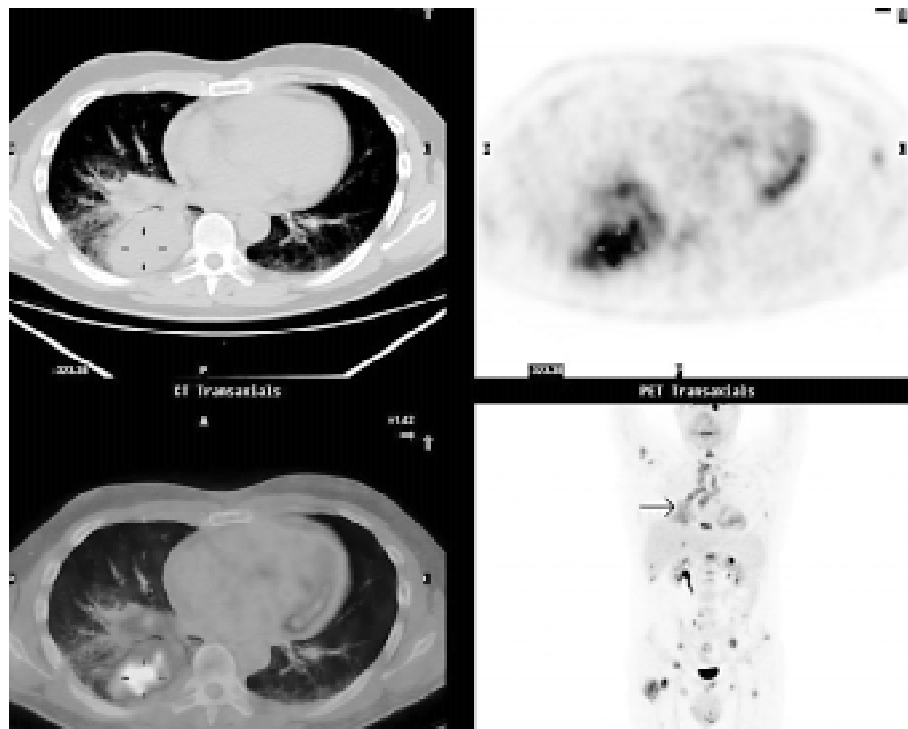
## Discussion

Malignant pleural mesothelioma is a relatively rare disease but its incidence is expected to increase in the next two decades as

**Table 1. Clinical characteristics, imaging findings and therapeutic approach in a group of 15 patients affected by malignant pleural mesothelioma (MPM). Staging accordingly to the UICC, TNM classification of malignant tumours, 1997 [15]**

Patient	Gender/Age (years)	CT	CT	PET/CT	PET/CT	Treatment planning*
		TNM	Stage	TNM	Stage	
1	M/88	T1N1M0	III	T1N1M0	III	Unchanged: surgery followed by RCT
2	M/55	T3N1M0	III	T3N1M0	III	Unchanged: surgery followed by RCT
3	M/67	T1N2M0	III	T1N2M0	III	Unchanged: surgery followed by RCT
4	M/44	T2N1M0	III	T2N3M1 (M = bone + liver)	IV	Changed: RCT alone
5	M/82	T1N0M0	Ia	T1N0M0	Ia	Unchanged: surgery alone
6	M/63	T1N0M0	Ia	T1N0M0	Ia	Unchanged: surgery alone
7	M/59	T1N0M0	Ia	T1N2M0	III	Changed: surgery followed by RCT
8	M/74	T1N0M0	Ia	T1N0M0	Ia	Unchanged: surgery alone
9	M/64	T1N1M0	III	T1N3M0	IV	Changed: RCT alone
10	M/66	T1N0M0	Ia	T1N0M0	Ia	Unchanged: surgery alone
11	F/63	T1N0M0	Ia	T1N1M0	III	Changed: Surgery followed by RCT
12	F/80	T1N2M0	III	T1N2M1 (M = bone)	IV	Unchanged: RCT alone
13	M/74	T1N0M0	Ia	T1N0M0	Ia	Unchanged: Surgery alone
14	M/71	T2N1M0	III	T2N3M0	IV	Unchanged: RCT alone
15	F/57	T1N0M0	Ia	T1N1M1 (M = bone + liver)	IV	Changed: RCT alone

\*Therapy planning modification on the basis of  $^{18}\text{F}$ -FDG PET/CT fusion imaging against conventional; CT scan alone; RCT — radio-chemotherapy

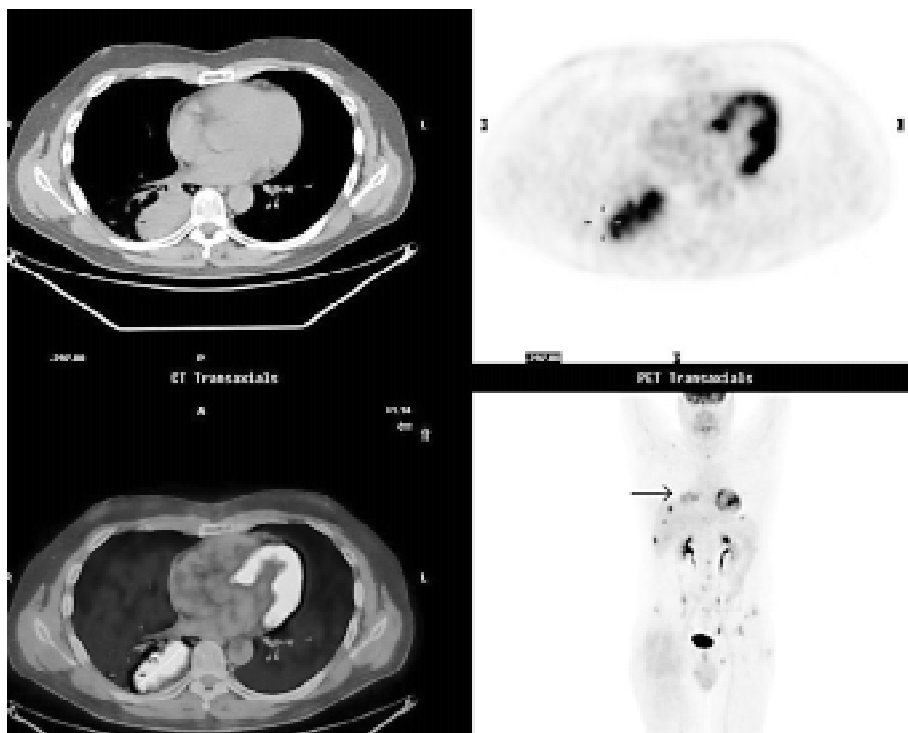


**Figure 1A.**  $^{18}\text{F}$ -FDG PET/CT fusion imaging in a 44 years old male patient (n. 4, Table 1) affected by malignant pleural mesothelioma, showing multiple areas of pathologic radio-tracer accumulation in the base of the right lung (primary tumour), numerous metastatic foci in lymph nodes, liver and bone. Of note, the conventional CT scan revealed only the primary tumour and an ipsilateral enlarged mediastinal lymph node. Upper left image — trans-axial CT scan; upper right image — trans-axial PET scan; lower left image — PET/CT fusion image; lower right image — 3-D image. Arrow indicates the primary tumour.

a consequence of the long time interval typically elapsing between exposure to causative agents, such as asbestos, and disease onset [4]. Different treatment options have been attempted in MPM patients combining surgery (in early stages), to external radio-

therapy and chemotherapy in advanced stages (III, IV) with discordant results [1–8].

Conventional CT scan has been considered the gold standard imaging technique for diagnosis and staging purposes in



**Figure 1B.**  $^{18}\text{F}$ -DG PET/CT fusion imaging of the same patient of Figure 1A after radio-chemotherapy treatment, showing a good response in lymph nodes, a moderate reduction of radio-tracer uptake in the primary tumour and bone, while a disease progression in the liver. Upper left image = trans-axial CT scan; upper right image = trans-axial PET scan; lower left image = PET/CT fusion image; lower right image = 3-D image. Arrow indicates the primary tumour.

MPM. However, our data, in agreement with some studies published recently [9–14] suggest that the  $^{18}\text{F}$ -FDG PET/CT fusion imaging is valuable in providing additional information especially about metastatic lymph nodes and tumour spread to distant site. This has resulted in modification of the treatment planning in one third of patients. Interestingly,  $^{18}\text{F}$ -FDG PET/CT was able to diagnose small metastatic foci in lymph nodes considered normal by CT criteria in 6 of our patients (40% of cases). Moreover, the fusion imaging of PET and CT allows to precisely localise the metastatic lymph nodes in the mediastinum (ipsilateral to the primary tumour, subcarinal, contralateral) with an important impact on surgical or radio-chemotherapy treatment planning. In this respect, the present data show that the PET/CT fusion imaging is superior to PET imaging alone for the purpose of an accurate localisation of metastatic deposits.

The relatively short follow-up period in our patients' series did not allow us to draw a definitive conclusion regarding the impact of  $^{18}\text{F}$ -FDG PET/CT on long-term survival of patients affected by MPM. However it is important to emphasise that treatment planning was changed in 33.3% of cases and that after a median follow-up of 7 months 13 out of 15 patients are still alive and 4 of them are disease-free. Further studies of larger patients' populations followed-up for a prolonged period are necessary to completely elucidate the clinical role of  $^{18}\text{F}$ -FDG PET/CT fusion imaging in the management of MPM patients.

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