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ORIGINAL ARTICLE

Clinical impact of ^{18}F-FDG PET-CT in recurrent stage III/IV melanoma: a tertiary centre Specialist Skin Cancer Multidisciplinary Team (SSMDT) experience

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Abstract
Objectives To assess the clinical impact of ^{18}F-fluorodeoxyglucose positron emission tomography-computed tomography (FDG PET-CT) compared with contrast-enhanced computed tomography (CECT) in patients referred via the Specialist Skin Cancer Multidisciplinary Team (SSMDT) with recurrent stage III/IV malignant melanoma (MM).
Methods Forty-five patients were referred for further evaluation with FDG PET-CT. Findings on FDG PET-CT were compared with prior CECT and the clinical impact on subsequent management decisions was determined retrospectively. A major clinical impact was defined as a change in treatment plan resulting from identification of additional sites of disease or by characterisation of indeterminate findings on prior imaging. A minor impact was defined as confirmation of known sites of disease as identified on prior CECT.
Results Fifty-one PET-CT examinations were performed. FDG PET-CT had a major clinical impact in 21 cases (41.2 %), of which 18 examinations were performed in patients with proven or suspected stage IV MM. FDG PET-CT had a minor impact in 23 cases (45.1 %), and there were five false-positive cases (9.8 %) and two false-negative cases (3.9 %).
Conclusion FDG PET-CT is an effective tool in recurrent stage III/IV MM with a significant clinical impact on management decisions in patients who are appropriately referred via the highly specialised forum of the SSMDT.
Key Points
- *FDG PET-CT is an effective tool in recurrent stage III/IV malignant melanoma.*
- *FDG PET-CT has a significant clinical impact on management decisions.*
- *Effective use of FDG PET-CT is via referral from the Specialist Skin Cancer Multidisciplinary Team.*

Keywords Multidetector computed tomography · Fluorodeoxyglucose F18 · Positron-emission tomography and computed tomography · Melanoma · Recurrence

Introduction

Malignant melanoma (MM) is an aggressive form of skin cancer. The degree of disease dissemination at presentation is one of the most important predictors of survival in MM. Patients with loco-regional disease (stage III) have a significant risk of disease recurrence despite comprehensive surgery [1, 2] with 5-year survival rates between 40 % and 78 % [3, 4]. Patients with distant metastatic disease (stage IV) have a worse outlook with a reported median survival of 7–9 months [3], although this is improving with increasing availability of recently developed and successfully trialled novel chemotherapeutic agents [5–7].

Surgery is the cornerstone of management in MM and is offered even in stage IV disease where a complete metastasectomy for oligometastatic disease can confer a survival benefit greater than that provided by conventional systemic therapy

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[8]. However, the pattern of disease spread in MM is unpredictable and does not necessarily occur in a sequential local to regional to distant metastatic pattern [2]. In addition, recurrent disease occurs in a large proportion of individuals following resection (approximately 30 %), with the highest risk in those with late stage disease, where 50–80 % of patients with loco-regional disease and 95 % of those with distant metastatic disease are likely to relapse [2]. Hence, it is of fundamental importance that accurate staging is undertaken in both the primary and recurrent setting, to prognosticate as well as identify sites of disease that may either alter the proposed surgical approach or even preclude surgery altogether and therefore necessitate alternative forms of treatment.

In late stage disease, accurate staging has been achieved using contrast-enhanced computed tomography (CECT) and magnetic resonance imaging (MRI), and more recently ^{18}F-fluorodeoxyglucose positron emission tomography-computed tomography (FDG PET-CT) [9, 10]. FDG PET-CT has emerged as an effective tool for staging MM due to a number of reasons. Melanoma metastases are usually extremely FDG-avid, owing to their high proliferation rate and hexokinase activity, resulting in excellent visualisation on FDG PET imaging [11], and the technique offers total body coverage, which is ideally suited to MM and its unpredictable pattern of disease spread [12, 13]. The addition of the CT component overcomes the inherent limitations of FDG PET in lesion localisation and characterisation, particularly in the context of FDG-negative disease, and results in an overall improved diagnostic accuracy for the detection of distant metastatic disease when compared with FDG PET imaging alone or CECT [13–16]. However, accuracy still remains somewhat limited, specifically in context of sub-centimetre-sized FDG-negative lung metastases and brain metastases [15–18].

In our institution, referral of patients for evaluation with FDG PET-CT is made via the highly specialised forum of the Specialist Skin Cancer Multidisciplinary Team (SSMDT). It affords all patients with stage IB or higher primary MM and any patient with metastatic disease, at diagnosis or follow-up, access to specialist services and clinical expertise [19]. The multidisciplinary approach is the standard of care for the delivery of optimal oncological patient management throughout the UK [20] and has been shown to be associated with improved survival through benefits gained by specialist review of imaging, improved accuracy of staging and resultant optimisation of surgical management [21].

Several studies have investigated the clinical impact of FDG PET-CT in MM but none in the setting of a multidisciplinary team experience. The majority have shown that FDG PET-CT significantly alters management decisions, but a significant limitation common to many of these studies is the marked heterogeneity of patient cohorts [16, 18, 22–26].

The aim of this study was to assess the clinical impact of FDG PET-CT, compared with CECT of the chest, abdomen and the pelvis, in a homogeneous cohort of patients with recurrent stage III/IV melanoma, who have been discussed and appropriately referred via the SSMDT.

Materials and methods

Inclusion criteria

Formal institutional board review and ethical approval was not required for this retrospective analysis. Between June 2008 and June 2012, 85 consecutive FDG PET-CT examinations in patients with MM were performed. Individual electronic case notes for all patients were reviewed to determine eligibility for entry into the study and to obtain specific demographic, clinical and radiological information. Inclusion criteria were as follows: (1) prior history of treated early stage MM with suspected or proven stage III/IV recurrence; (2) review and referral for FDG PET-CT examination by the SSMDT; (3) staging with CECT of the chest, abdomen and pelvis performed prior to FDG PET-CT examination.

CT protocol

CECT of the chest, abdomen and pelvis was most often performed at our institution on a 64-section CT system (Siemens Sensation; Siemens Healthcare, Erlangen, Germany) (n =36) using a contiguous 5-mm reconstruction following a bolus of 100 ml (75–125 ml) iodinated contrast medium. The remaining CECT examinations were acquired on alternative multidetector CT systems at our institution (n =3) or at one of several regional referring hospitals (n =12) using similar scan parameters.

FDG PET-CT protocol

FDG PET-CT examinations prior to June 2010 were performed on a 16-section Discovery STE PET-CT system (GE Healthcare, Amersham, UK), and from June 2010 on a 64-section Philips Gemini TF64 system (Philips Healthcare, Best, The Netherlands). Total body FDG PET acquisition from the skull vertex to the feet was acquired 60 min following a 400-MBq dose of intravenous fluorine-18 FDG. The low-dose unenhanced CT component was performed according to a standardised protocol with the following settings: 140 kV; 80mAs; tube rotation time 0.5 s per rotation; pitch 6; section thickness 3.75 mm (to match the FDG PET section thickness). Patients maintained normal shallow respiration during the CT acquisition. Images were reconstructed using a standard OSEM algorithm with CT for attenuation correction. Both non-attenuation corrected and attenuation corrected datasets were reconstructed.

Review of imaging investigations

CECT imaging for each patient was retrieved from and reviewed on the institutional picture archiving and communications system (PACS) (IMPAX™; AGFA Healthcare, Mortsel, Belgium), whilst PET-CT imaging was reviewed on a specialised PET-CT workstation (XD3; Mirada-Medical, Oxford, UK). Comparison of prior CECT imaging with PET-CT imaging was performed visually with no additional co-registration software utilised. Imaging was retrospectively reviewed by a consultant radiologist (experienced in PET-CT reporting) and senior radiology registrar, both of whom are members of the SSMDT. Clinical information and CECT imaging were reviewed in conjunction with radiology reports with standard size criteria used to determine lymph node involvement and the presence of new, either solitary or multiple rounded pulmonary nodules of varying size, compatible with pulmonary metastases. The availability of prior CECT imaging overcame several limitations of low-dose unenhanced CT component of the PET-CT examination. Improved anatomical detail allowed more definitive evaluation of lungs, especially in the setting of indeterminate or potentially new pulmonary findings, whilst contrast enhancement provided conspicuity to lesions otherwise invisible on unenhanced CT. Finally, the intervening period between the two examinations provided a means to assess the rate of disease progression, which was of greatest benefit in the interpretation of lesions with minimal FDG uptake. Visual interpretation of the FDG PET-CT examination was qualitative with lesions with FDG uptake above background mediastinal blood pool classed as positive. Any discordances were discussed in order to reach a consensus view.

Analysis of clinical impact

The relevant clinical and radiological information was analysed using both our institutional patient pathway management system (PPM™; Leeds Teaching Hospitals Trust, Leeds, UK) and radiology information system (CRIS™; Healthcare Software Systems, Banbury, UK) in conjunction with a consultant medical oncologist who is also an integral member of the SSMDT. The additional information provided by FDG PET-CT in comparison with prior CECT was used to assess its impact on subsequent management decisions. A major clinical impact was defined as a change in treatment plan, e.g. radical surgery to systemic chemotherapy resulting from identification of additional sites of disease or by characterisation of indeterminate findings on prior CECT imaging. A minor impact was defined as confirmation of known sites of disease as identified on prior CECT. Potentially negative impacts due to false positive and false negative results were also assessed. Confirmation of multifocal metastatic disease was achieved through follow-up imaging. In cases of potential oligometastatic disease on both CT and PET-CT or in cases of discordance between the two imaging modalities, histological confirmation was obtained through percutaneous biopsy or surgical excision.

Results

Fifty-one FDG PET-CT examinations performed in 45 patients fulfilled the inclusion criteria for analysis. Six patients underwent two FDG PET-CT examinations with a median time interval of 8 months (range 3–12 months) between the two studies; all patients had evidence of disease progression on the second FDG PET-CT examination but none of the new sites of disease identified were visible on review of the initial FDG PET-CT examination. The study group included 28 men and 17 women, with a median age of 60 years (range 29–83 years). The original sites of the primary disease, American Joint Committee on Cancer (AJCC) staging at the time of FDG PET-CT and scan indications are listed in Table 1. The median time interval between primary diagnosis and FDG PET-CT examination was 52 months (range 3–217 months); 33 patients (73.3 %) experienced at least one or more previous episodes of local or loco-regional recurrence in this intervening period. The median time interval between CECT and subsequent FDG PET-CT examination was 32 days (interquartile range 20–56 days, range 6–107 days).

FDG PET-CT had a major impact on clinical management in 21 cases (41.2 %), of which 18 examinations were performed in patients with known or suspected AJCC stage IV disease (Table 2). The majority of changes in clinical management resulted from detection of additional sites of disease not previously identified on CECT imaging often resulting in a

Table 1 Primary site of disease, AJCC staging and scan indication

Characteristic	Number of PET-CT examinations
Primary site	
Torso	13
Upper limb	12
Lower limb	10
Head and Neck	9
Ocular	5
Vaginal	2
Disease stage	
Stage III	8
Stage IV	43
Scan indication	
Detection of additional sites of disease	35
Detection of additional sites of disease and lesion characterisation	10
Trial entry	6

Table 2 Details of cases in which ^{18}F-FDG PET-CT had a major impact on clinical management

Stage	Findings on CT	Findings on ^{18}F-FDG PET-CT	Management alteration by PET-CT	
III	Suspicious cervical lymph nodes and 'benign' pulmonary nodule	Cervical nodal metastases and pulmonary metastasis	Surgery	Palliative radiotherapy
III	Solitary site of disease in the supraclavicular fossa	Extensive locoregional soft tissue and nodal disease	Surgery	Chemotherapy
III	Bilateral axillary masses	Nodal, intramuscular, hepatic and bone metastases	Surgery	Chemotherapy
IV	Suspicious pelvic and splenic lesions	Necrotic pelvic lymph node. No focal FDG uptake in the spleen	Chemotherapy	Surgery
IV	Pelvic abnormality	No focal FDG uptake	Surgery	Routine follow-up
IV	Solitary splenic metastasis	Nodal, subcutaneous, solid visceral and small bowel metastases	Surgery	Chemotherapy
IV	Axillary nodal disease and indeterminate pancreatic mass	Axillary nodal disease and pancreatic metastasis	Surgery	Chemotherapy
IV	Solitary adrenal metastasis and chronic middle lobe atelectasis	Adrenal and middle lobe metastases	Surgery	Chemotherapy
IV	Solitary hepatic metastasis	2 hepatic metastases not amenable to surgical resection	Surgery	Chemotherapy
IV	Solitary hepatic metastasis	2 unilobar hepatic metastases	Surgery	Extended hepatic surgery
IV	Iliac pedicle lymph node metastasis	Extensive locoregional nodal disease and femoral bone metastasis	Surgery	Chemotherapy
IV	Lung and mesenteric nodal metastasis. 'Hyperdense' renal cysts	Pulmonary, nodal, gastric, gallbladder, renal and peritoneal metastases	Surgery	Chemotherapy
IV	Suspicious locoregional nodes.	Extensive locoregional nodal, subcutaneous and intramuscular metastases	Chemotherapy	Chemoradiotherapy
IV	Subcutaneous, solid visceral and pulmonary metastases	Additional sites of metastatic disease including bone metastases	Trial chemotherapy	Chemotherapy
IV	Multiple subcutaneous metastases only	Additional sites of subcutaneous disease and bone metastases	Trial chemotherapy	Chemotherapy
IV	Suspicious iliac chain and retroperitoneal lymph nodes	Extensive locoregional nodal disease	Surgery	Chemotherapy
IV	Solitary hepatic metastasis	Numerous hepatic and bone metastases	Surgery	Chemotherapy
IV	Unilobar hepatic metastases	Bilobar hepatic metastases	Surgery	Chemotherapy
IV	Anterior abdominal wall and breast metastases	Several additional soft tissue metastases	Surgery	Extended surgery
IV	Unilobar hepatic metastases	Widespread hepatic metastases and sacral bone metastasis	Surgery	Chemotherapy
IV	Solitary chest wall metastasis	Right axillary subcutaneous and supra-diaphragmatic nodal disease	Surgery	Chemotherapy

change from potentially radical surgery to systemic chemotherapy (Figs. 1 and 2). Frequently encountered sites of additional disease on FDG PET-CT which were 'occult' on CECT imaging included subcutaneous and intra-muscular metastases ($n=8$), sub-centimetre nodal disease ($n=9$), intra-abdominal metastases including solid visceral ($n=8$), gastrointestinal tract ($n=2$) and peritoneal deposits ($n=3$) and bone metastases ($n=6$).

In two cases of presumed oligometastatic stage IV MM, FDG PET-CT identified additional sites of disease still amenable to surgical management and resulted in a major impact by altering and widening the field of surgical resection. A notable case of major clinical impact occurred in a patient who, while being assessed for a radical lymph node dissection, was diagnosed with stage IV MM on CECT imaging through the identification of presumed multiple splenic metastases; FDG PET-CT, however, successfully characterised these lesions as benign via the absence of focal FDG activity within the spleen and these remained stable on follow-up imaging over an 18-month period (Fig. 3). In six cases, FDG PET-CT was used to determine whether patients were eligible for entry into a chemotherapeutic clinical trial for inoperable stage IV MM. In two cases, a major impact resulted from the detection of FDG-avid bone metastases that were not visible on CECT imaging, resulting in exclusion from the trial.

FDG PET-CT had a minor impact in 23 cases (45.1 %) where findings on prior CECT imaging were confirmed; although no change in clinical management was effected, confidence in the planned treatment was increased. There were five false-positive cases (9.8 %) and two false-negative

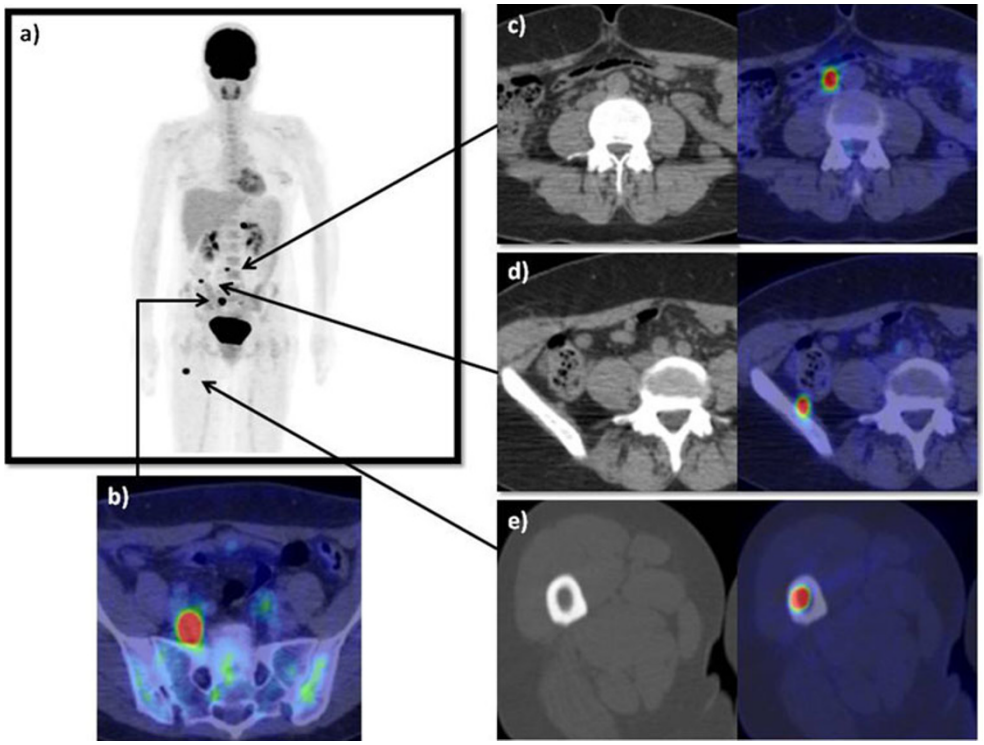

Fig. 1 A 37-year-old woman, diagnosed with MM 8 years previously and a prior right groin recurrence 2 years later, was found to have a solitary right 1.5-cm iliac pedicle lymph node on a surveillance CT. A subsequent FDG PET-CT revealed several sites of markedly FDG-avid disease on the PET maximum intensity projection (**a**) and corresponding axial unenhanced CT and fused PET-CT images including the known enlarged right iliac pedicle lymph node (**b**), a 5-mm aorto-caval lymph node (**c**), a 4-mm retroperitoneal nodule overlying the right iliacus muscle (**d**) and a solitary right femoral bone metastasis inconspicuous on CT (**e**). This resulted in a change from potential radical surgery to chemotherapy—a major clinical impact

cases (3.9 %) (Table 3). False-positive cases included two instances in which FDG-avid lung nodules were incorrectly labelled as metastatic melanoma deposits; in these cases diagnoses of primary lung sarcoma and lung adenocarcinoma were made following surgical resection. Although these lesions were not melanoma metastases, they were malignant in aetiology and PET-CT was beneficial in these cases through the exclusion of distant metastatic disease prior to thoracic surgery. Other false-positive cases included an endobronchial FDG-avid focus histologically proven to be impacted inflammatory mucoid debris secondary to a proximal obstructing FDG-avid endobronchial melanoma metastasis, FDG-avid cervical lymphadenopathy with reactive histological changes only and an FDG-avid soft-tissue lesion, compatible with benign post-surgical change. False-negative cases included a solitary 15-mm FDG-negative lung metastasis and an FDG-negative sub-centimetre liver metastasis, incorrectly labelled as benign, which on subsequent follow-up imaging had grown in size in addition to the development of several new hepatic metastases compatible with progressive disease.

Sub-group analysis of different time intervals between FDG PET-CT and preceding CECT imaging revealed that 32 FDG PET-CT examinations were performed less than 6 weeks following CECT with a major impact on clinical management in 12 cases (37.5 %) and a minor impact in 13 cases (40.6 %). Thirty-eight FDG PET-CT examinations were performed less than 8 weeks following CECT with major impact in 16 cases (42.1 %) and minor impact in 15 cases (39.4 %). The numbers of false-positive and false-negative cases were unchanged.

Discussion

This study shows that in patients with recurrent stage III/IV MM, FDG PET-CT has a significant clinical impact when compared with CECT of the chest, abdomen and the pelvis, with an alteration in treatment strategy made in 21 cases (41.2 %). Several studies have investigated the clinical impact of FDG PET-CT on management decisions, but there is a wide range of figures (12–57.8 %) quoted in the literature [16, 18, 22–26]. This is due to varied study methodologies; in particular, the presence or absence of comparative baseline imaging prior to FDG PET-CT examination and heterogeneous patient cohorts undergoing FDG PET-CT examination, i.e. inclusion of patients with all AJCC stages of MM with both primary and recurrent disease, which makes it difficult to draw definitive conclusions for the use of FDG PET-CT in specific patient groups.

Our reported change in management of 41.2 % is at the higher end of the quoted literature but there are several factors underpinning this. Firstly, all FDG PET-CT examinations were performed in patients with recurrent stage III/IV disease and many of these patients had already experienced previous episodes of local or loco-regional recurrence prior to FDG PET-CT, which would be expected to increase the likelihood of further disease recurrence. White et al. [1], in a study of 2,505 patients with stage III disease treated with radical lymph node dissection, observed that most patients experienced some form of recurrence within 2 years of surgery, with a 10-year recurrence-free survival of only 20 %, and that distant disease

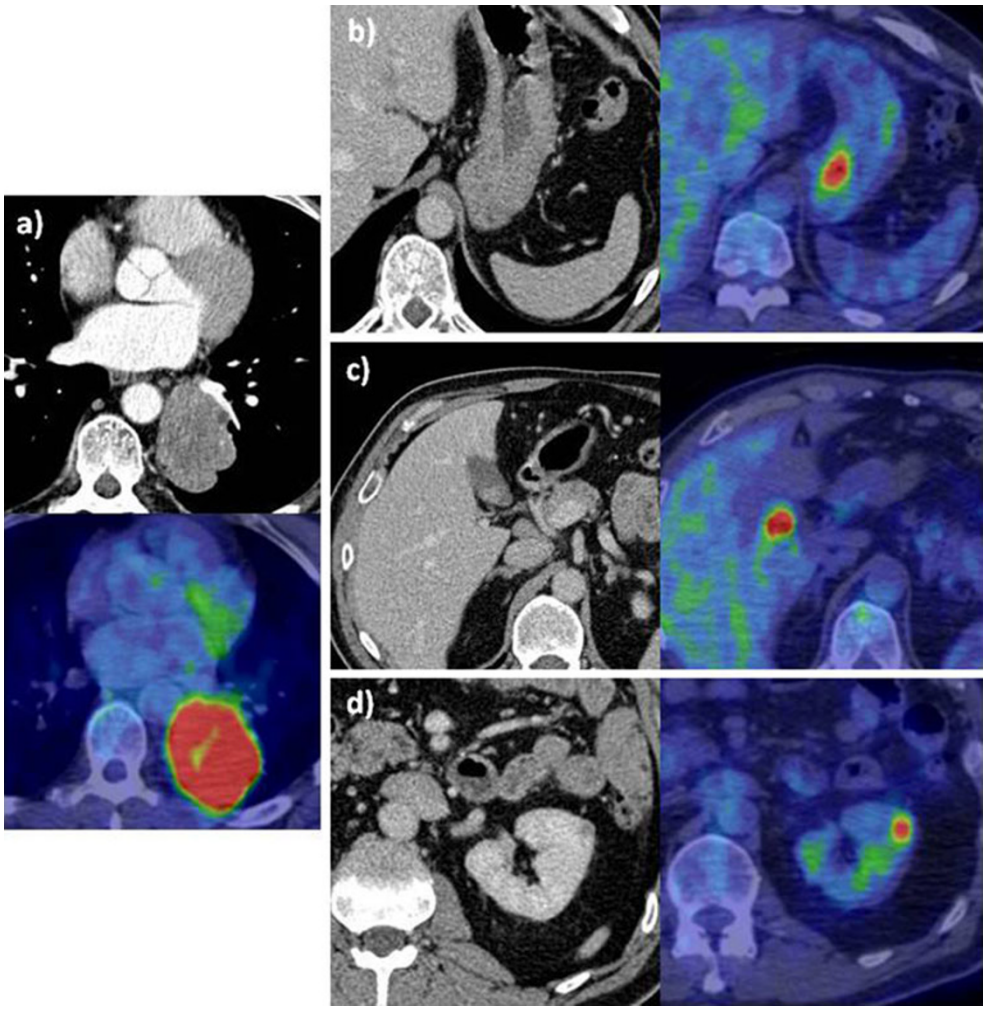

Fig. 2 A 62-year-old man diagnosed with MM 14 years previously re-presented with a biopsy proven left lower lobe recurrence (**a**) and a suspicious enlarged portocaval lymph node (not shown) on a restaging CT. Incidental findings of 'gallstones' and 'hyperdense renal cysts' were also noted. A subsequent FDG PET-CT revealed multiple sites of markedly FDG-avid disease in the chest, abdomen and pelvis including an intramural gastric cardia metastasis (**b**), an intraluminal gallbladder metastasis ('gallstone') (**c**) and a 3-mm left renal metastasis ('hyperdense renal cyst') (**d**) as seen on the axial PET images and corresponding axial sections from the prior CECT. This resulted in a change from potential radical surgery to chemotherapy—a major clinical impact

predominated as the site of first recurrence in 44 % of patients. Secondly, the majority of management decision alterations were made in patients with oligometastatic stage IV disease, indicating that haematogenous seeding of the tumour had already occurred [2]. Both of these factors resulted in a high pre-test probability that further sites of metastatic disease were present. The number of treatment decision alterations made through detection of additional sites of disease was therefore likely to reflect a combination of this high pre-test probability in addition to the improved detection of metastases, in particular subcutaneous and intra-muscular metastases, sub-centimetre nodal disease, intra-abdominal metastases including solid visceral, gastrointestinal tract and peritoneal deposits and bone metastases, afforded by FDG PET-CT [10, 13].

The SSMDT at our tertiary institution is a double professorial unit (Dermatology and Clinical Oncology) and consists of a number of other healthcare professionals, including dermatologists, plastic surgeons, medical and clinical oncologists, radiologists, histopathologists and specialist nurses. It provides direct access to highly specialist plastic surgery and oncological services and the option for potential treatment within clinical trials, all of which are only available in larger centres. Every patient referred to the SSMDT has their pathology and relevant imaging reviewed and, through open discussion, a consensus decision is reached with regards to further potential surgical, oncological and radiological management, including referral for FDG PET-CT. A unique feature related to our SSMDT is the availability of parallel clinic working, whereby a joint clinic approach with dermatologists, medical and clinical oncologists and plastic surgeons who are all in attendance in one locality, enables expedient clinical discussion and decision-making.

Examples where unique options available to our SSMDT may have resulted in higher clinical impact include several instances where surgery was being contemplated in patients with more than one potential site of distant metastatic disease. This reflects a more radical surgical approach adopted by a tertiary centre SSMDT and the subsequent increased utilisation of FDG PET-CT to optimise management in a patient group that would not be routinely offered surgery. Similarly, two cases of major clinical impact where FDG PET-CT was used to determine eligibility for entry into a

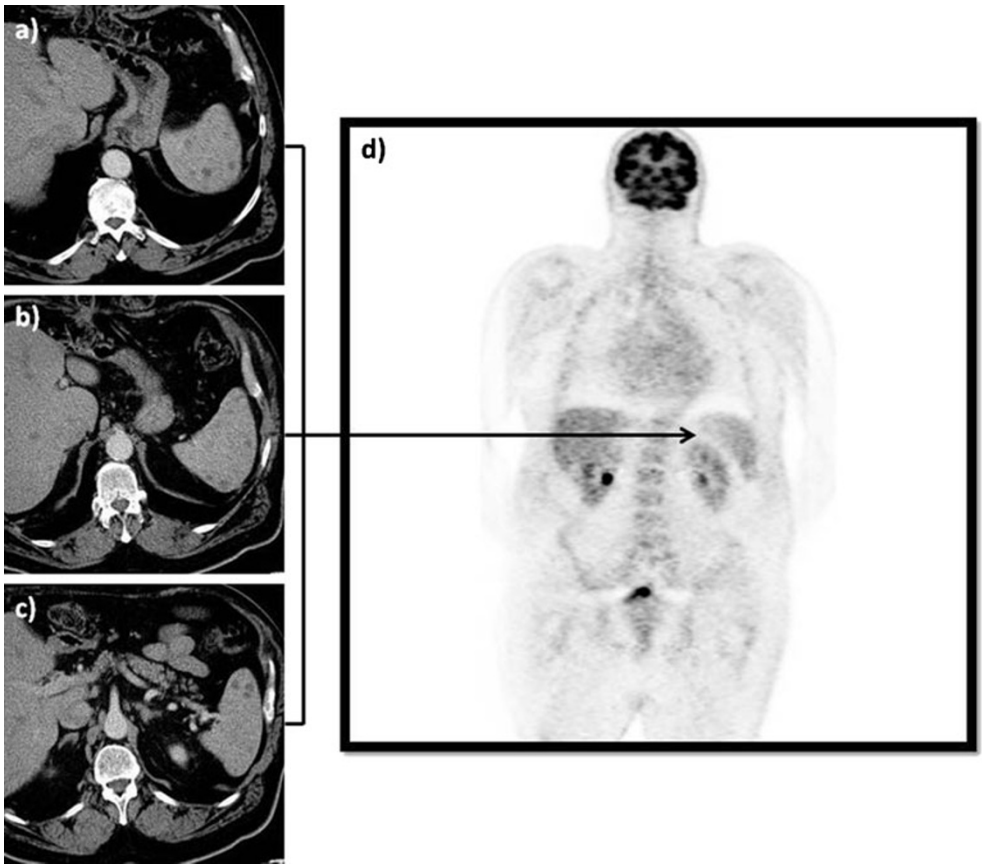

Fig. 3 A 67-year-old man with previously treated lower limb primary MM 7 months ago was found to have suspicious pelvic lymph nodes and multiple low attenuation splenic lesions, concerning for metastases on a surveillance CT (**a**–**c**). A subsequent FDG PET-CT revealed a necrotic right pelvic lymph node (not shown) and normal appearances of the spleen, as seen on the coronal PET image (**d**). This resulted in a change from potential chemotherapy to radical surgery—a major clinical impact

chemotherapeutic clinical trial, illustrate the unique options available for treatment via a tertiary centre SSMDT and also the fact that patients with inoperable late-stage MM undergoing chemotherapy would not routinely undergo FDG PET-CT examination.

The retrospective nature of this study and the relatively small cohort coupled with an unequal proportion of examinations performed in stage IV disease are potential limitations as they may positively skew the results and contribute to the high estimation of the clinical impact of FDG PET-CT. Reporting of the FDG PET-CT examination with a lack of blinding to the result of the prior CECT was likely to influence the positive clinical impact of FDG PET-CT, but this methodology is reflective of real life, day-to-day practice. In addition, it could be argued that the median delay between CECT and subsequent FDG PET-CT examination of 32 days may have been sufficient time for new sites of disease to develop in the intervening period and become apparent on FDG PET-CT and thereby falsely result in a major clinical impact by detection of additional sites of disease. However, sub-group

Table 3 Details of false-positive and false-negative cases

Case	^{18}F-FDG PET-CT finding	SUV_{max}	Confirmed finding
	False positives		
1	FDG-avid cervical lymph nodes	4.6	Reactive lymphadenopathy only
2	FDG-avid soft-tissue lesion	2.8	Post-operative change
3	FDG-avid distal and (proximal) endobronchial lesions	18.1 (30.1)	Distal lesion = impacted mucus(Proximal lesion = MM)
4	FDG-avid lung nodule[a]	23	Lung adenocarcinoma
5	FDG-avid lung nodule[a]	4.3	Lung sarcoma
	False negatives		
6	FDG-negative lung nodule	N/A	Lung metastasis
7	FDG-negative liver lesion	N/A	Progressive hepatic disease on follow-up imaging

[a] Cases in which PET-CT was of benefit in non-melanoma lesions

analysis showed similar figures for change in management with differing time intervals between FDG PET-CT and CECT examinations.

A 41.2 % change in management represents a significant clinical impact of FDG PET-CT in recurrent stage III/IV MM. Despite similar results in the literature as detailed above and a recent meta-analysis confirming FDG PET-CT as the superior imaging modality for the detection of distant metastases in both staging and surveillance of MM [14], even allowing for its relative limitations in the detection of FDG-negative sub-centimetre lung metastases [17] and brain metastases [18], recommendations for its routine use are lacking in internationally published guidelines [27–31].

The lack of recognition in international guidelines is likely to reflect the absence of rigorous well-designed prospective trials to address the clinical utility of FDG PET-CT in patients with stage III/IV MM and, more importantly, its impact on overall patient outcome and survival. In addition, with a relatively expensive test, there are resultant cost implications that need to be considered prior to wholesale endorsement of this technique in guidelines.

Early studies have shown that FDG PET and FDG PET-CT in the context of metastatic/recurrent melanoma or in the specific context prior to pulmonary metastasectomy are cost-effective options resulting in net savings [32, 33]. Most recently, Bastiaannet et al. [34] performed a cost-effectiveness study assessing the additional costs of adding FDG-PET or CT to the diagnostic work-up of patients with stage III melanoma. They reported that FDG PET and CECT was the most diagnostically accurate combination, upstaging a large proportion of patients and thereby reducing the number of inappropriate surgical procedures. However, reduced costs associated with surgery and accompanying post-operative hospital stay were negated by increased costs associated with a greater number of patients receiving expensive systemic therapy options and the cost associated with FDG PET itself. The additional cost of PET and CT (with intravenous contrast) performed as separate examinations to diagnostic pathway was 15.1 % as costs for combined PET-CT were not yet established in The Netherlands.

However, the addition of FDG PET only to the diagnostic algorithm resulted in an additional cost of 7.2 %, which, in the era of financial austerity, the authors felt was justifiable in view of the benefits gained. One would expect that the additional costs of integrated PET-CT not to be too dissimilar to FDG PET alone as most centres perform a low-dose unenhanced CT, which avoids the additional costs associated with intravenous contrast. In addition to a cost reduction, the associated radiation exposure is significantly less and, importantly, the use of a low dose unenhanced CT does not significantly alter the diagnostic accuracy of integrated PET-CT for lesion detection/characterisation or staging compared with a contrast-enhanced CT component [35].

Conclusion

This study shows that FDG PET-CT has a significant clinical impact on management decisions in patients with stage III/IV MM through the detection of additional sites of distant metastatic disease and characterisation of indeterminate findings on CECT, which can alter or preclude potential surgical or chemotherapeutic management. In addition, it provides a unique insight into the experience of a highly specialised tertiary centre SSMDT, through which individual cases are discussed and patients are appropriately referred on for further evaluation with FDG PET-CT. It also illustrates the more radical surgical and chemotherapeutic options available via the SSMDT, settings in which FDG PET-CT can be of beneficial use. Prospective trials in stage-specific cohorts of patients in addition to further cost-effective analyses are required to develop consensus opinion on the utilisation of FDG PET-CT in MM.

Conflicts of interest The authors declare no conflicts of interest. No funding was received for this work. Written informed consent from all patients was waived by the Institutional Review Board.

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