Is there an added clinical value of "true" whole body ^{18}F-FDG PET/CT imaging in patients with malignant melanoma?

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Keywords: Metastatic malignant melanoma - "True" whole body scanning - PET/CT scan

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Received:
7 August 2012
Accepted revised:
3 September 2012

Abstract

Accurate and reliable staging of disease extent in patients with malignant MM is essential to ensure appropriate treatment planning. The detection of recurrent or residual malignancy after primary treatment is important to allow for early intervention and to optimise patient survival. 2-deoxy-2-[^{18}F]fluoro-D-g1ucose (^{18}F-FDG) PET or PET computed tomography (PET/CT) is indicated for surveillance of malignant MM due to its high sensitivity and specificity for soft-tissue or nodal recurrences and metastases. It has been claimed that including lower extremities and skull in addition to 'eyes to thigh' images in PET/CT evaluation of metastatic MM routinely is warranted. *We have studied* retrospectively the reports of whole-body PET/CT scans in all patients with MM scanned in our Department from April 2005 to December 2010. All PET abnormalities in the brain/scalp and lower extremities were tabulated by location and whether they were 'expected' or 'unexpected'. Findings were correlated with pathology, other imaging studies, and clinical follow-up. In this study, 398 PET/CT examinations in 361 patients with MM were included. *Results showed that* twelve of the 398 (3%) scans had brain/scalp abnormalities, with only 4 (1.0%) showing unexpected abnormalities. Twenty nine of the 398 (7.2%) scans showed lower extremity abnormalities, with only 5 (1.2%) showing unexpected abnormalities. In no case was an isolated unexpected malignant lesion identified in the brain/scalp or lower extremities. *In conclusion*, whole body PET/CT scan showed about 1% unexpected primary or metastatic MM lesions involving the head or lower extremities, which seldom offered significant additional clinical benefit and were unlikely to change clinical management. No clinically significant change in staging would have occurred. Routine 'eyes to thighs' images were adequate for this subset of patients.

Hell J Nucl Med 2012; 15(3): 202-205 *Epub ahead of print: 26-10-2012* *Published on line: 2 December 2012*

Introduction

Malignant melanoma (MM) is one of the most lethal cancers worldwide. Though it represents only 4% of dermatological cancers, MM is responsible for up to 80% of deaths from skin cancer. Among patients with metastatic MM, 5 years survival is only 15% [1]. Accurate and reliable staging of disease extent is essential to ensure appropriate treatment planning. The detection of occult, recurrent or residual malignancy after primary treatment is important to allow for early intervention and to optimise patient survival.

Fluorine-18 fluoro-2-deoxy-D-glucose positron emission tomography (^{18}F-FDG PET) or PET/computed tomography (PET/CT) is indicated for staging, restaging and surveillance of MM due to its proven high sensitivity (83%-100% in metastases >78mm^3) for soft-tissue or nodal recurrences and metastases which are inaccessible by clinical examination and/or not associated with detectable morphological changes on conventional imaging [2]. In primary staging (with very small volume metastatic disease in lymph nodes), a meta-analysis of 20 publications [3] showed sentinel node biopsy to be superior to PET in all cases with PET showing sensitivity of 0-55% with small volume disease.

The imaging field of view used for most oncological ^{18}F-FDG PET or PET/CT studies is from the skull base to upper thigh, however, it is not standardised and varies among institutions [4-6]. Researchers have proposed that true whole body (skull vertex to feet) PET/CT should be adopted as the standard of care in imaging of cancer patients and given the propensity of MM to metastasise anywhere in the body, many nuclear medicine departments routinely perform true whole-body PET/CT imaging in patients with MM. However, this requires nearly doubling the emission scanning time with resultant decrease in throughput important for busy units. The aim of this study was to assess the added benefit of scanning lower extremities and skull in addition to 'eyes to thigh' images in PET/CT evaluation of metastatic MM.

Patients and methods

The reports of all consecutive PET/CT studies performed at the Royal Adelaide Hospital between April 2005 to December 2010 for staging, restaging or surveillance in patients with histologically proven malignant MM were retrospectively reviewed. Positron emission tomography abnormalities in the brain/scalp and lower extremities were tabulated by location and whether they were 'expected' or 'unexpected'. Findings were correlated with pathology, other imaging studies, and clinical follow-up.

Criteria for inclusion into the study were: (a) the patient had at least one PET/CT scan performed for staging, restaging or surveillance of MM, (b) the PET/CT scan was performed as a true whole-body scan from the skull vertex to the feet; and (c) sufficient outcome data were available from the patient's electronic medical record to determine the result of abnormalities identified by PET/CT.

All PET/CT scans were acquired using a Philips Gemini PET/CT. Sixty minutes following intravenous administration of 260-320MBq of ^{18}F-FDG, a whole body PET/CT acquisition was initiated. A non-contrast CT scan for use in attenuation correction and anatomical localisation of ^{18}F-FDG activity was acquired from the top of the head through to the feet (with the arms down to accomplish true whole-body imaging), followed by an emission scan of the same region. The fusion PET/CT images were reviewed using axial, sagittal and coronal reformations.

All reported abnormal PET/CT findings in the brain, scalp/skull and lower extremities (ie outside of the typical skull base to upper thigh field of view) were identified and tabulated according to location and whether the abnormality was 'expected' (either because of the known location of the primary tumor site or because the patient had known metastases in that region) or 'unexpected'. All suspected lesions in the brain, scalp/skull and lower extremities were correlated with available pathology data, the results of other imaging studies such as CT, magnetic resonance imaging (MRI) or whole body bone scan (WBBS), and clinical follow-up.

Reported PET/CT abnormalities were subclassified as 'likely benign', 'equivocal' or 'likely malignant'. Any reported PET/CT abnormalities in the 'equivocal' or 'likely malignant' categories which were determined to represent MM by subsequent studies or follow-up were classified as true positive. Abnormalities in PET/CT scan in these categories subsequently determined to represent a process unrelated to MM were classified as false positive for MM.

A total of 398 PET/CT examinations performed in 361 patients with MM met inclusion criteria for this study. Mean patients' age was 56.7 years (range 26-90 years). Of these 398 studies, 328 were performed for staging, 64 for restaging and 6 for surveillance of MM. 58 (16.1%) of 361 patients had two or more PET/CT scans.

Results

The distribution of primary tumour sites in our 361 patients is shown in Table 1.

Abnormal uptake was found on PET/CT of the brain (within the cranium) and scalp (outside the cranium) in 12 of 398 scans (3%) as shown in the PET images in Figures 1 and 2. Multiple other hypermetetabolic "hot" lesions suggestive of metastatic MM were identified on the PET/CT scan in the usual skull base to upper thigh field of view as shown in Figure 1D of a 78 year old man referred for staging 18 months after resection of a primary MM of the left arm. Five of these abnormal scans showed abnormalities which had been identified prior to the study, either on physical examination or by another imaging modality such as magnetic resonance imaging (MRI). Overall, unexpected abnormalities were identified on PET/CT in only 4 (1.0%) of all scans. In each of these 4 patients, a subsequent metastasis in the brain was subsequently confirmed on brain MRI (Table 2).

Table 1. *Distribution of primary tumour sites*

Primary site	No. of patients	Percentage of total
Scalp	17	4.7
Face	26	7.2
Ear	5	1.4
Neck	41	11.4
Torso/Back	120	33.2
Arms	30	8.3
Legs	106	29.4
Unknown	16	4.4
Total	361	100

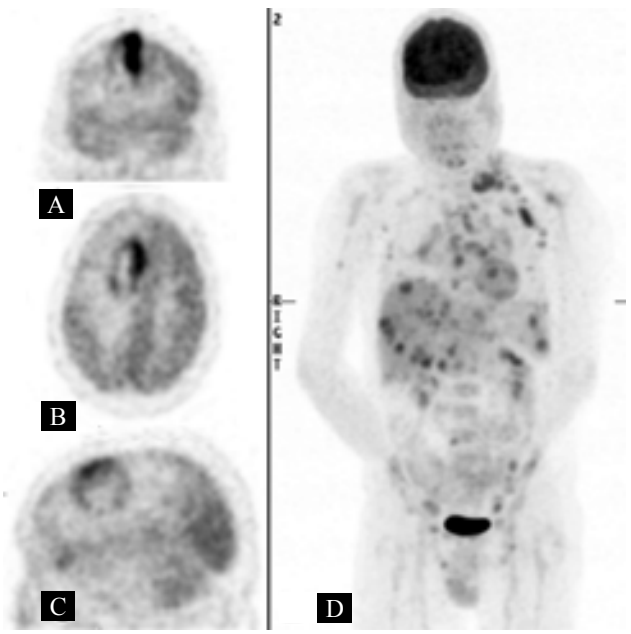

Figure 1. (A) Coronal, (B) Transaxial and (C) Parasagittal PET images of the brain showing a focal 'hot' lesions in the right frontal lobe medially with a central photopenic deficit. (D) ^{18}F-FDG PET maximal intensity projection image demonstrating extensive metastatic disease.

In 29 of the 398 scans (7.2%), abnormal uptake typical of metastatic disease was identified in the lower extremities outside of the usual skull base to upper thigh field of view. Other (non-metastatic) causes of increased uptake were excluded on the distribution (pattern recognition) historical or clinical grounds. Twenty-four scans showed expected abnormalities in the lower extremities outside this region, either because the primary tumor was located on the legs or

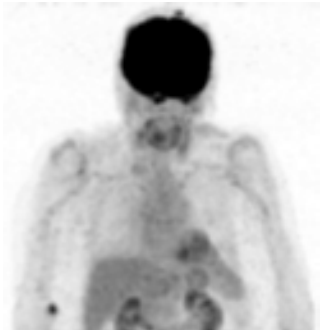

Figure 2. Maximum intensity projection showing isolated scalp MM metastasis.

because of known metastatic lesions in this region on prior studies. In only 5 of the 398 scans (1.2% of all scans) unexpected abnormalities were identified in the lower extremities which would not have been identified using the routine imaging field of view (Table 2). The PET and CT images in Figure 3, are of a 57 years old female referred for staging from an unknown primary MM which showed focal intense tracer uptake in the right distal tibia. In only 19/29 scans metabolically active lesions on PET/CT were thought to represent MM, either by clinical follow-up or further imaging studies. In all of these 19 patients, other multiple "hot" lesions suggestive of MM were identified on PET/CT in the usual whole-body field of view.

Discussion

Unexpected abnormalities were identified on PET/CT in the brain in only 1.0% and 1.2% in the lower extremities which would not have been identified using the routine imaging field of view. In no case was an unexpected *isolated* malignant lesion identified in the brain, scalp or lower extremities which is consistent with previously published findings by other researchers [7, 8].

Metastases from MM typically progress in an orderly fashion to regional lymph nodes [9]. However, extranodal metastases due to haematogenous spread may occur concurrently with nodal metastases or, in up to 30% of cases, in the absence of nodal metastases. Haematogenous spread can result in metastases to any part of the body. Given this propensity for distant metastatic spread, as well as the reality that the primary tumour can be located at both cutaneous

Table 2. *Location of unexpected PET/CT findings in the brain and the lower extremities, related to the primary site of MM and confirmed by MRI or CT. There was a single unexpected lesion in all patients. Change of stage was studied.*

Primary site	Location	Change of stage AJCC[13]
Ankle	Brain	Unchanged IV
Calf	»	» »
Leg	»	» »
Abdomen	»	» »
Thigh	Knee	Unchanged III
Groin	»	» »
Unknown	Tibia	Unchanged IV
Cheek	Toe	» III-IV
Calf	Fibula/Heel	Unchanged IV

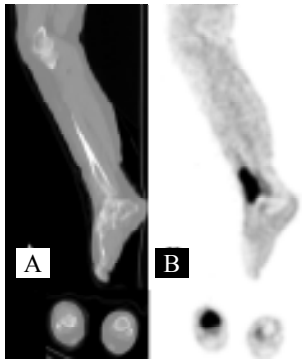

Figure 3. Sagittal and transaxial (**A**) CT and (**B**) PET images through right tibia indicating focal ^{18}F-FDG uptake in a lytic lesion due to metastatic MM.

and non-cutaneous sites anywhere in the body, true whole-body PET/CT imaging has been advocated and is frequently performed [10].

The majority of patients with locally recurrent or locoregionally advanced MM have non curable disseminated disease. In the presence of distant/extranodal metastatic disease, treatment is palliative and typically includes chemotherapy and/or local radiation. In the presence of distant/extranodal metastases which are surgically unresectable, the overall number of lesions does not usually affect the choice of systemic treatment. Thus in a patient with multiple hypermetabolic lesions throughout the torso on PET suggestive of metastatic MM, the presence or absence of additional lesions in the scalp and/or lower extremities likely has little influence on the type of treatment which will be prescribed.

Routine inclusion of the scalp/brain and lower extremities in the PET/CT imaging field of view has several disadvantages. It requires extending the scan by up to 30min and subsequently increased processing time. This added time decreases patient throughput and limits the total number of patients which can be scanned in a day. With the use of PET/CT, the additional radiation exposure incurred by the transmission CT scan used for attenuation correction and anatomical localisation is not negligible, particularly in patients for whom a scan is performed repeatedly for surveillance purposes or in the relatively young patients (without disease) in which MM frequently occurs. It is generally regarded that PET/CT is not sensitive (68%-82% compared with MRI) in the diagnosis of brain metastases [11], but Bochev (2012) [12] found that the inclusion of the brain in the routine field of view demonstrated metastatic disease in patients with a large range of malignancies (25 of 2502 mainly lung cancer) and this was asymptomatic in 23 of the 25. This 1% incidence is similar to that found in our study.

In patients with known primary or metastatic lesions involving the brain/scalp or lower extremities, true whole-body PET/CT (with the arms down to include them in the field of view) is reasonable as it may provide useful information regarding the presence of residual or locally recurrent malignancy. However, in this study we found, as have others [8, 10], that no patient had an unexpected isolated malignant lesion in the extended whole-body region. These data suggest that in patients such as ours with no known or suspected primary or metastatic MM involving the head or lower extremities, a true whole-body scan is of low yield and appears to offer little significant additional benefit. In patients with metastatic melanoma but unknown primary a "whole body" approach is still indicated if finding the primary will affect management.

In conclusion, whole body PET/CT scan showed about 1% unexpected primary or metastatic MM lesions involving the head or lower extremities, which seldom offered significant additional clinical benefit and were unlikely to change clinical management. Routine 'eyes to thighs' images were adequate for this subset of patients.

The authors declare that they have no conflicts of interest.

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