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Whole-Body versus Routine Skull Base to Mid-thigh ^{18}F-Fluorodeoxyglucose Positron Emission Tomography/Computed Tomography in Patients with Malignant Melanoma

Savas Ozdemir[1], Barry McCook[1], Christopher Klassen[1]

[1]Department of Radiology, University of Florida College of Medicine - Jacksonville, Jacksonville, Florida, United States.

***Corresponding author:**
Savas Ozdemir,
Department of Radiology,
University of Florida College of Medicine - Jacksonville,
855 W 8th St., Jacksonville,
Florida 32209, United States.

savas.ozdemir@jax.ufl.edu

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ABSTRACT

Objectives: The objectives of this study are to assess the utility of whole-body ^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography (^{18}F-FDG PET/CT) (skull vertex to toes) imaging relative to the standard field of view (skull base to mid-thigh) in patients with primary melanoma site that is not located in the lower extremities.

Material and Methods: The primary site of the melanoma and metastatic disease was determined based on ^{18}F-FDG PET/CT findings in 26 patients. The FDG avid sites were tabulated as the primary site, lower extremity, brain, and other sites. The hypothesis is that routine skull base to mid-thigh versus whole-body ^{18}F-FDG PET/CT in patients with malignant melanoma will not change management.

Results: Patients (26) were divided into those with primary melanoma site in either the lower extremities (six patients) or other site (20 patients). Four of the six patients with the primary site in the lower extremities also had positive findings in the ipsilateral inguinal lymph nodes. One of the patients with a positive inguinal lymph node had metastatic sites in the external iliac region and lungs on the initial study. On follow-up imaging, this patient also exhibited diffuse metastatic disease, including a lower extremity. None of the remaining patients in this group had positive findings other than the primary site in the lower extremity. Of the remaining 20 patients with the primary site not in the lower extremity, one had diffuse metastatic disease that included a lower extremity. However, lower extremity involvement would not change patient management in this case. A second patient in this group had diffuse metastatic disease that also involved the brain. However, no metastatic disease was present in the lower extremities in this patient. None of the remaining 18 patients in this group had metastatic disease in a lower extremity. Two patients in the entire study group of 26 had brain metastasis on contrast-enhanced head CT, with one having multiple brain metastasis. PET failed to demonstrate some of the brain lesions. In the other patient with solitary brain metastasis detected on contrast-enhanced head CT, PET was negative.

Conclusion: ^{18}F-FDG PET/CT imaging of the lower extremity may not be justified if the primary neoplasm is not located in the lower extremities. Elimination of lower extremity imaging will reduce scanning time and additional radiation exposure. Similarly, PET/CT imaging of the brain may not be justified if contrast-enhanced CT or magnetic resonance imaging of the head is already obtained since these are more sensitive.

Keywords: Melanoma, ^{18}F-Fluorodeoxyglucose, Whole-body positron emission tomography/computed tomography

INTRODUCTION

In the United States, cutaneous melanoma is the fifth most common type of new cancer diagnosis in men and the seventh most common in women, with continually increasing new cases. The estimated new melanoma cases for 2020 are 100,350, which are 5.6% of all new cancer cases. Estimated death from cutaneous melanoma for 2020 is 6850, which is 1.1% of all cancer-related deaths.[1] Although ^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography (^{18}F-FDG PET/CT) is inferior to sentinel lymph node biopsy in the evaluation of regional disease, it could be useful in the detection of distant metastases in patients with advanced-stage or high-risk melanoma.[2-5] It has a high diagnostic value in the routine follow-up of melanoma.[6] There is also an improved prediction of patient survival with PET/CT imaging.[7]

MATERIAL AND METHODS

Patients selected for inclusion received whole-body ^{18}F-FDG PET/CT from January 10, 2007, to January 1, 2018, with a diagnosis of malignant melanoma. These patients were identified by running a query of the PACS system. All ^{18}F-FDG PET/CT images were acquired using Siemens Biograph 40 TruePoint PET/CT (Knoxville, TN). The PET component was composed of lutetium oxyortho-silicate (LSO) crystals. The CT component had 40 slice multidetector-row with 70 cm transverse field of view. The acquisition parameters consist of 120 kV, 60 mAs, 0.5 s rotation time, 5 mm slice thickness, and 0.8 pitch.

The image acquisition involved two fields, one from the vertex of the skull to pelvis with 3–4 min per bed position (range for incubation period 56–102 min, mean 113 min) and second from the pelvis to toes with 1–2 min per bed position (range for incubation period 90–207 min, and mean 121 min). The time interval between the two fields of the study ranged from 29 to 56 min (mean 37 min). The patient's arms were positioned down during acquisition.

Study design

This retrospective study was approved by the Institutional Review Board of University of Florida – Jacksonville. A query of the PACS system identified 42 patients that received whole-body ^{18}F-FDG PET/CT (skull vertex to toes) from January 10, 2017, to January 1, 2018. Of these, 26 patients were identified as patients with malignant melanoma with PET/CT imaging used for initial staging or restaging. The age of the patients ranged from 48 to 83, with the median age of 57 and mean age of 60 years old. There was an equal female to male ratio. The patients fasted a minimum of 4 h (range 4–20 h, mean 12.7 h) before intravenous injection of the prescribed dose of 555 MBq [15 mCi] of ^{18}F-FDG (range 476.93–604.95 MBq [12.89–16.35 mCi], and mean 560.55 MBq [15.15 mCi]). Blood glucose levels of the patients were measured before the injection of ^{18}F-FDG (range 4.67–11.28 mmol/l, and mean 6.29 mmol/l). All ^{18}F-FDG PET/CT images were acquired using Siemens Biograph 40 TruePoint PET/CT (Knoxville, TN). The PET component was composed of LSO crystals. The CT component had 40 slice multidetector-row with 70 cm transverse field of view. The acquisition parameters consisted of 120 kV, 60 mAs, 0.5 s rotation time, 5 mm slice thickness, and 0.8 pitch. The image acquisition consisted of two fields, one from the vertex of the skull to pelvis with 3–4 min per bed position (range for incubation period 56–102 min, and mean 113 min) and second field from the pelvis to toes with 1 to 2 min per bed position (range for incubation period 90–207 min, and mean 121 min). The time interval between the two parts of the study ranged from 29 to 56 min (mean 37 min).

RESULTS

The results consisted of identifying and tabulating the primary site of melanoma and the presence of metastatic disease in the lower extremities and other locations [Table 1].

Six of the 26 patients had the primary site of melanoma in the lower extremities (three in thighs, one in calf, and two in feet). Four of these six patients had metastatic disease. Three patients with metastatic disease had ipsilateral inguinal lymph node involvement. The fourth patient had ipsilateral inguinal nodes, ipsilateral external iliac nodes, and lungs metastasis on the initial study and diffuse metastasis, including a lower extremity on a follow-up study.

In the remaining 20 patients with the primary site not involving the lower extremity, four had the primary site in the upper extremities, seven in the head and neck, and nine in torso. One of these patients had a primary site located in the upper back also had a diffuse metastatic disease that involved the lower extremity [Figure 1]. However, this would not have changed management due to metastatic disease. Another patient in this group had primary vulvar melanoma with diffuse metastatic disease, including brain temporal lobe involvement. Additional brain metastatic foci were visible on contrast-enhanced head CT but were not discernible on PET [Figure 2]. However, no metastatic disease was present in the lower extremities in this patient. None of the remaining 18 patients in this group had metastatic disease in the lower extremities. In summary, whole-body imaging would not have changed patient management in the two patients that exhibited involvement outside standard PET/CT field of view, one in the lower extremity with diffuse metastatic disease and one in the brain already detected with contrast-enhanced head CT.

Ten patients of the entire group of 26 had head CT within 1 month of the whole-body ^{18}F-FDG PET/CT (eight of them

Table 1: Patient characteristics: Primary melanoma and metastatic sites.

Patient number	Primary melanoma site	Metastatic sites excluding lower extremities and brain	Lower extremity metastasis	Brain metastasis PET	Brain metastasis head CT	Date of head CT
1	Left axilla	None	No	No	No	Same day
2	Right and left groin	None	No	No		
3	Left groin	None	No	No	No	Same day
4	Upper back	Multiple diffuse metastasis	Yes	No		
5	Left cheek	None	No	No	No	27 days prior
6	Left thigh	None	No	No		
7	Vagina	None	No	No		
8	Left orbit	None	No	No		
9	Vulva	Multiple metastasis	No	Yes	Yes	2 days prior
10	Left calf	None	No	No		
11	Left foot	Left inguinal node	No	No		
12	Right thigh	Right inguinal, right external iliac nodes and lungs metastasis on the initial study, diffuse metastasis including lower extremities on follow-up study	Yes	No		
13	Right chest	None	No	No		
14	Left-arm	Left axillary node	No	No	No	Same day
15	Left neck	None	No	No	No	Same day
16	Left face	None	No	No	No	Same day
17	Left back	None	No	No	No	Same day
18	Right elbow	None	No	No		
19	Left eye	None	No	No		
20	Left thigh	Right inguinal node, Right breast (primary versus metastasis)	No	No	Yes	Same day
21	Right temporal region	None (Incidentally found colon cancer)	No	No		
22	Left ear	Bilateral neck nodes	No	No		
23	Left anterior chest and back	None	No	No		
24	Right foot	Right inguinal node	No	No		
25	Left upper arm	Left axillary node	No	No	No	Same day
26	Right and left upper extremity	Right axillary node	No	No		

PET: Positron emission tomography, CT: Computed tomography

on the same day, one 2 days prior, and one 27 days before whole ^{18}F-FDG PET/CT). Two patients had metastatic disease involving the brain. In one patient, as discussed above, ^{18}F-FDG PET was positive only in one cerebral lesion and failed to demonstrate additional lesions. In the second case, ^{18}F-FDG PET did not demonstrate the solitary lesion detected on contrast-enhanced head CT.

DISCUSSION

The most commonly used protocol for oncologic ^{18}F-FDG PET/CT imaging is routine skull base to mid-thigh imaging.[8] However, whole-body imaging is frequently obtained in patients with malignant melanoma. The rationale for whole-body imaging in patients with malignant melanoma is that it can metastasize to any organ.[8,9] Earlier reports in the literature demonstrate the effectiveness of this approach.[10] Whole-body imaging may reveal unsuspected malignancy outside the typical skull base to mid-thigh field of view in patients with various cancers.[11,12] However, although ^{18}F-FDG PET/CT imaging of the head may reveal additional lesions, the sensitivity of contrast-enhanced CT or magnetic resonance imaging (MRI) of the head is reported to be superior to ^{18}F-FDG PET/CT.[13] ^{18}F-FDG PET/CT did not demonstrate additional lesions in the two patients with brain metastasis

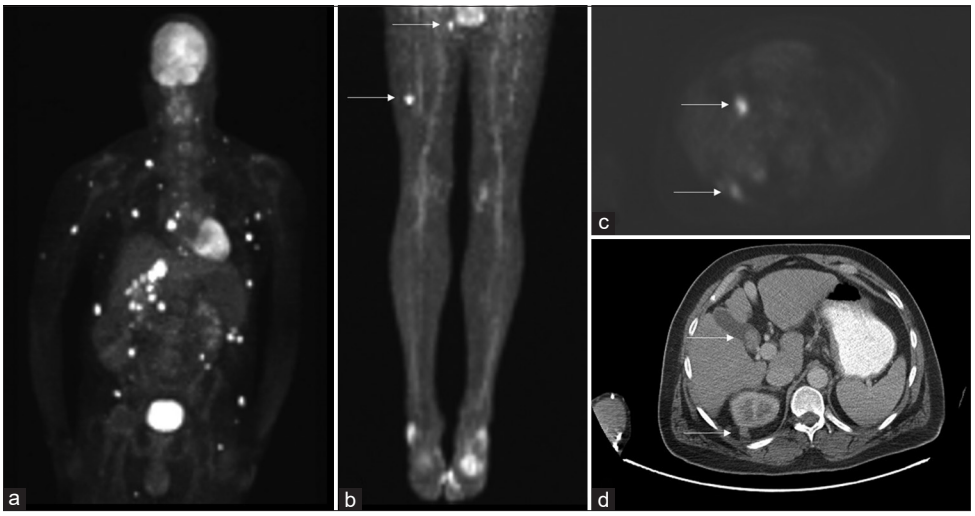

Figure 1: A 55-year-old male with primary melanoma site of the upper back. (a) Skull vertex to the upper thigh maximum intensity projection (MIP) image of ^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography (PET/CT) demonstrates diffuse metastatic disease. (b) Lower extremities MIP demonstrates two foci of increased uptake in the right thigh, consistent with metastatic disease (white arrows). (c) Axial attenuation corrected PET and (d) corresponding axial CT images demonstrates metastatic disease in the gallbladder and retroperitoneal region, posterior to the right kidney (white arrows).

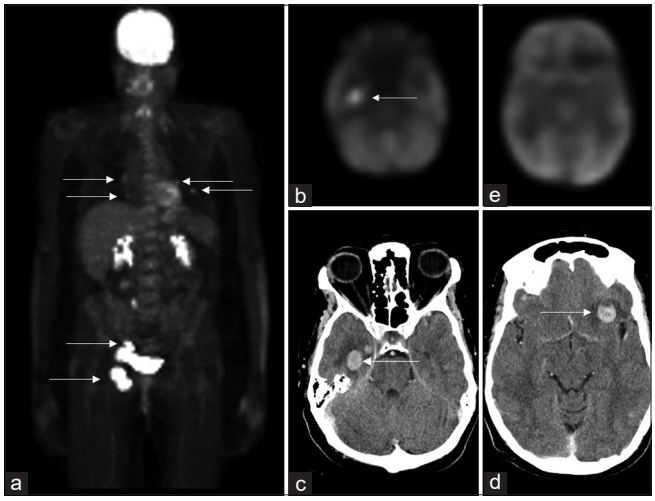

Figure 2: A 56-year-old female with primary melanoma site of vulva. (a) Skull vertex to the upper thigh maximum intensity projection image of ^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography (PET/CT) demonstrates right inguinal and pelvic lymph node involvement as well as bilateral pulmonary metastasis (white arrows). (b) Axial attenuation corrected PET and (c) axial contrast-enhanced CT show metastatic disease in the right temporal region (white arrows). (d) Axial contrast-enhanced head CT demonstrates metastatic disease in left frontal region (white arrows). (e) Corresponding attenuation corrected PET reveals no definite abnormality.

that CT already detected, and it failed to demonstrate some of the lesions detected on head CT. Therefore, a dedicated CT or MRI of the head is usually obtained for accurate staging regardless of whether the head is included or not with the ^{18}F-FDG PET/CT.

Imaging of the lower extremities requires more time, usually several additional bed positions. Although, more lesions can be detected by this approach, it may not necessarily change patient management. In our series, no metastatic disease was present in the lower extremities in 19 of 20 patients who had primary sites other than the lower extremities. Only one of the 20 patients had involvement of the lower extremities. However, this finding did not change patient management since diffuse metastatic disease was already present. Elimination of the brain and lower extremity imaging will reduce the length of scanning time and additional radiation exposure.

CONCLUSION

Although ^{18}F-FDG PET/CT is a sensitive technique for staging malignant melanoma, the value of lower extremity imaging remains controversial unless the primary site is located in the lower extremities. Similarly, its use for detecting brain metastasis is questionable since contrast-enhanced CT or MR has better sensitivity. Our findings support the hypothesis that whole-body imaging in patients with melanoma with the primary site not involving the lower extremity does not change patient management. There are many other studies that question the utility of including lower extremity and brain imaging in patients with melanoma. Niederkohr *et al*.[14] found no unanticipated isolated lesions in brain/scalp or lower extremities to change the clinical management in their retrospective analysis of 296 PET/CT examination of 173 patients. Querellau *et al*.[15] found no additional benefit of the lower extremity imaging in therapeutic decision-making in a retrospective study of

122 patients. Additional lesions in the lower extremities were either part of the disseminated metastatic disease or benign lesions. Lazaga *et al*.[16] found only three scans had positive findings in the lower extremities in their 200 patient series, one of the findings within the field of view of standard skull base to mid-thigh, one benign finding, and one incidental squamous cell carcinoma. Plouznikoff *et al*.[17] found 21 scans demonstrating findings attributed to melanoma in the lower limbs in their series of 461 whole-body scans. However, none of the lesions upstaged a patient. Tan *et al*.[18] found only four unexpected brain/scalp abnormalities and only five lower extremity abnormalities in their series of 398 PET/CT examinations of 361 patients. There are, however, other studies that support whole-body imaging for the detection of unsuspected metastasis that results in a change in patient management. Osman *et al*.[11] found that 59 of 500 patients had FDG PET/CT findings suggestive of malignancy outside the routine skull base to mid-thigh field of view in their retrospective study. However, their case series was not confined to melanoma patients. Within the 55 melanoma cases, only four of them had unexpected findings outside the skull base to mid-thigh field of view with no change in staging. In this study, whole-body PET/CT had a greater impact in changing staging and patient management in other malignancies such as lung cancer. Bronstein *et al*.[12] evaluated whole-body PET/CT in 32 patients with oligometastatic Stage IV and clinically evident Stage III patients with malignant melanoma who already had contrast-enhanced CT of the chest, abdomen, and pelvis and MRI of the brain. PET/CT changed the management of four patients because of unanticipated findings. In two of these cases, the findings were within gastric wall and bones, remaining within the fields of view of a standard skull base to mid-thigh PET/CT. In the third case, there were two unanticipated lower extremity findings with the larger one located in the upper thigh also within a standard field of view. The remaining additional finding was in a below the knee lower extremity and would probably not have changed patient management. However, in a final fourth case, a finding was detected in the soft tissue of the below the knee leg that did change management by adding adjuvant isolated limb perfusion.

This study supports our hypothesis and also existing reports that demonstrate a very small benefit of whole-body PET/CT compared with the standard skull base to mid-thigh PET/CT if the primary melanoma is not located in the lower extremities. The main benefits of the standard field of view include reduced scanner time and radiation dose. The limitations of this study include a small sample size and lack of pathologic correlation for each ^{18}F-FDG avid finding. Recent developments of mutation-driven therapy, immunotherapy, and targeted therapies such as BRAF blockade therapy have significantly improved survival of the patients with malignant melanoma.[19] ^{18}F-FDG PET/CT plays an integral role in the treatment and evaluation of therapy response with these new novel therapies. Prospective studies incorporating a larger number of patients and longer-term follow-up are needed to determine the optimal imaging protocol for patients with malignant melanoma.

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Declaration of patient consent

Institutional Review Board (IRB) permission obtained for the study.

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Conflicts of interest

There are no conflicts of interest.

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