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ORIGINAL ARTICLE

Diagnostic accuracy of contrast-enhanced FDG-PET/CT in primary staging of cutaneous malignant melanoma

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Abstract
Purpose To evaluate the diagnostic accuracy of contrast-enhanced FDG-PET/CT (ce-PET/CT), PET-only, and CT-only in patients with newly diagnosed and resected cutaneous malignant melanoma.
Methods A final group of 56 patients (mean age 62 years, range 23–86 years; 29 women, 27 men) were staged with ce-PET/CT after resection of the primary tumour. Histopathology as well as clinical follow-up (mean 780 days, range 102–1,390 days) served as the standards of reference. Differences between the staging modalities were tested for statistical significance with McNemar's test.
Results All imaging procedures provided low sensitivities in the detection of lymph nodes (sensitivity N-stage: PET/CT and PET-only 38.5%; CT-only 23.1%) and distant metastases (sensitivity M-stage: PET/CT 41.7%, PET-only 33.3%, CT-only 25.0%) in initial staging after resection of the primary tumour. No statistically significant differences were detected between the imaging procedures ($p>0.05$). PET/CT resulted in an alteration in further treatment in two patients compared to PET-only and in four patients compared to CT-only.
Conclusion All imaging modalities had a low sensitivity on initial staging of patients with malignant melanoma. Thus, close patient follow-up must be considered mandatory.

Keywords ce-PET/CT · Cutaneous melanoma · Staging · Follow-up · Diagnostic accuracy

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Introduction

The incidence of melanoma has been increasing worldwide, especially in the Caucasian population [1]. In 2007 approximately 60,000 new cases of melanoma were diagnosed and over 8,000 patients were expected to die from this disease in the United States. The patients' prognosis strongly depends on the tumour depth (tumour thickness and Breslow index), potential ulceration, and the presence of metastases [2, 3]. Cutaneous melanoma is considered curable in patients if the tumour is <2 mm deep, is without ulceration, and is without lymph node metastases. Tumours of higher tumour stages are considered to have an advanced likelihood of metastatic spread. Thus, overall survival is heavily dependent on the stage of the primary tumour [4, 5].

Several imaging methods are considered appropriate for imaging patients with malignant melanoma and potential metastatic spread. Computed tomography (CT) is widely accepted and recommended for detection of organ metastases [6, 7]. However, CT has a limited sensitivity for the detection of lymph node metastases because of its strict morphological nature. Locoregional ultrasonography has been used for assessment of lymph nodes, but is investigator-dependent and strictly morphological.

To overcome the lack of functional data, positron emission tomography (PET) using [^{18}F]-fluoro-2-deoxy-D-glucose (FDG) as a radioactive tracer has gained wide acceptance in patients with malignant melanoma in particular in patients with clinical suspicion of systemic metastatic spread [8, 9]. However, the accuracy of FDG-PET in initial staging of malignant melanoma has rarely been assessed. PET-only imaging can be impaired based on its lack of anatomical resolution. Hence, complementary anatomical imaging is often required, especially for surgical therapy planning. Coregistered PET/CT has been available since 2001 and provides such anatometabolic datasets in a single examination. PET/CT has been found to be superior to CT alone and PET alone in staging and evaluation of therapy response in several oncological diseases including malignant melanoma [10–12]. However, as mentioned above, there is currently only little knowledge concerning the accuracy of FDG-PET/CT compared to CT alone and PET alone for initial staging of malignant melanoma. Thus, the aim of our study was (1) to evaluate the accuracy of FDG-PET/CT, CT-only, and PET-only for initial staging of malignant melanoma using long-term follow-up and histopathology as the standards of reference, and (2) to assess the potential impact of FDG-PET/CT on patient management.

Materials and methods

Patients

Seventy-four patients were included based on their order of referral without further selection. All patients were referred for a combined FDG-PET/CT examination after surgical resection of a primary malignant melanoma. This prospective study was performed in accordance with the regulations of the local institutional review board and ethics committee. All patients were included consecutively based on the time of referral without further selection. Patients were excluded from the analysis if no sufficient follow-up data were available (e.g. patient did not attend for follow-up examinations or decided to have follow-up at another institution). Informed consent was obtained from all patients prior to the examination.

FDG-PET/CT imaging procedure

Patients were instructed to fast for at least 4 h prior to the PET/CT procedure. Glucose levels in all patients were measured prior to FDG injection to ensure they were in the normal range. PET/CT imaging was conducted on a Biograph Duo PET/CT system (Siemens Molecular Imaging, Hoffman Estates, IL). The system integrates a dual-slice CT scanner (Somatom Emotion, Siemens Medical Solutions, Forchheim, Germany) and a full-ring, BGO-based PET tomograph (Siemens Molecular Imaging). The axial field-of-view of the PET scanner is 15.5 cm per bed position, and the in-plane spatial resolution is 4.6 mm, respectively. The average FDG activity administered 60 min prior to the PET/CT examination was 330–350 MBq. During the uptake time, 1,500 ml of a water-based, water-equivalent oral contrast agent was administered to all patients for small-bowel distension [13].

During the whole-body CT examination (part of the PET/CT examination), 140 ml of iodinated contrast agent (300 mmol/ml, Xenetix 300; Guerbet, Sulzbach, Germany) was administered intravenously according to a standardized protocol [14]. The CT scan was performed in the caudocranial direction. A start delay of 50 s was chosen for the CT acquisition after the start of the contrast agent injection. The first 90 ml of contrast agent were injected at a rate of 3 ml/s, and the remaining 50 ml were injected at a rate of 1.5 ml/s. The dual-phase injection was intended to ensure fully diagnostic (portal venous phase) CT data in the abdomen. The contrast-enhanced CT scan was used for attenuation correction of the PET data. The PET acquisition time per bed position was 3–5 min, depending on the weight of the patient. PET images were corrected for scatter and attenuation based on the available CT transmission images. Corrected PET images were reconstructed iteratively (FORE-OSEM, two iterations, eight subsets, 128× 128 matrix with 5-mm gaussian smoothing). CT images as well as PET data sets were viewed separately (CT-only, PET-only), and in fused mode (PET/CT) on a commercially available computer workstation (Siemens Molecular Imaging). Therefore, all imaging modalities compared were derived from the same dataset.

Image evaluation

N-staging and M-staging

The T-stage was documented from the histological specimens from the surgical resection, which was performed not more than 1 week prior to the imaging procedure. N-staging and M-staging evaluation were performed for CT-only, PET-only, and coregistered FDG-PET/CT. The PET images were evaluated with and without attenuation correction by

two nuclear medicine specialists in consensus. The CT images were evaluated by two radiologists in consensus. Contrast-enhanced PET/CT (ce-PET/CT) images were evaluated by a different radiologist and nuclear medicine specialist in consensus. The participating readers were informed about the patient-specific clinical background (first diagnosis of melanoma, postsurgical resection status, location of the resection site), but blinded to the results of histopathology of the primary tumour, and blinded to the other imaging procedures and to clinical examination.

Distant metastases were assessed based on the detection of soft-tissue masses (or focal cutaneous thickening) with contrast enhancement in different body compartments and in conjunction with focally increased glucose metabolism above the surrounding tissue level on FDG-PET/CT. The diagnosis of a distant metastasis was also supported by an maximum standardized uptake value (SUVmax) of at least 1.5 for cutaneous lesions, 2.5 for other extrahepatic lesions, and 3.5 for intrahepatic lesions [15]. However, the SUVmax was not taken as the absolute threshold to differentiate between malignant and benign findings. In fact, the qualitative assessment was taken as the most important parameter. If a lesion showed clear focal FDG avidity but displayed a lower SUVmax (e.g. due to small size), the lesion was rated malignant. In cases of malignant findings on CT-only without focally increased glucose metabolism, the lesions were evaluated based on CT criteria (see below). Lymph nodes were assessed for metastatic spread based on an increased glucose metabolism and independent of their size on PET/CT images.

On CT-only images, detection of soft-tissue masses (or focal cutaneous thickening) with contrast enhancement characterized malignancy. Lymph node assessment was based on lesion size: a short-axis diameter threshold of 1.5 cm was used for jugulodigastric lymph nodes and precarinal lymph nodes. A short-axis diameter threshold of 1 cm was used for all other lymph nodes of the neck, thorax, and abdomen [16]. Central necrosis was defined as a sign of malignancy as well, independent of lymph node size. Furthermore, according to standard CT criteria, a fatty hilum and calcifications were used as benign criteria on CT-only images.

PET-only images were assessed qualitatively and quantitatively for areas of increased FDG uptake. Lesions (distant metastasis and lymph nodes) were called malignant if the glucose utilization exceeded the surrounding tissue or blood pool level. As in evaluation of the PET/CT images, the diagnosis of metastases was also supported by a SUVmax of more than 1.5 for cutaneous lesions, more than 2.5 for extrahepatic lesions, and more than 3.5 for intrahepatic lesions. The N-stage and M-stage in all patients were assessed based on the current AJCC criteria for all imaging modalities [17].

The impact of FDG-PET/CT imaging on patient management as compared to PET-only and CT-only was assessed in consensus by the referring physicians and a radiologist and nuclear medicine specialist each, and evaluation was based on international clinical guidelines [6, 18].

Standard of reference

Initial clinical staging derived from histopathological examination of the primary tumour (T-stage) after resection, from sentinel lymph node resection within 4 weeks of PET/CT imaging and all other available clinical studies and imaging studies (MRI, radiography, ultrasonography, tumour markers). Because PET/CT imaging was the modality to be evaluated, the results of the PET/CT imaging were not taken into account for the definition of the initial clinical stage. Sentinel lymph node imaging and resection were performed within 4 weeks of initial PET/CT imaging. In all patients with suspected metastases on imaging, histopathological evaluation and the resected surgical specimen (tumours and/or lymph nodes) of at least one metastatic site served as the standard of reference for both N-stage and M-stage during the clinical course. For all other patients, clinical follow-up including all clinically available data (imaging, tumour markers, physical examination) served as the standard of reference.

Statistical analysis

The primary endpoint of the study was the correct classification of the N-stage and M-stage using CT-only or PET-only in comparison to fused PET/CT. Differences in the assessment of the N-stage and M-stage between the different imaging procedures were tested for significance by McNemar's test (exact). Bonferroni correction was applied to account for multiple comparisons. To maintain a global significance level of 0.05 the nominal significance level to evaluate the four hypotheses of the primary analysis had to be 0.0125. We calculated 95% confidence intervals (CI) according to the method of Tango for the difference in correlated proportions of the correct N-stage and M-stage [19]. Sensitivities, specificities, negative predictive values (NPV), positive predictive values (PPV), and accuracies (with exact 95% confidence intervals) for all modalities were determined for N-stage assessment and for M-stage assessment using histology and/or clinical follow-up as the standard of reference.

Statistical analyses were performed with SAS statistical software (version 9.1; SAS Institute, Cary, NC).

Results

Patients

Included in this prospective study were 74 consecutive patients who underwent combined PET/CT imaging in a University Hospital setting. Of these 74 patients, 18 were excluded because of a lack of sufficient follow-up, leaving 56 patients for final evaluation (mean age 62 years, range 23–86 years; 29 women, 27 men) (Table 1). The T-stage of the primary, melanoma location, histological type of the melanoma and the clinical stages according to the standard of reference are given in Table 1 for the 56 evaluated patients. Overall, the mean follow-up time was 780 days (range 102–1,390 days). A total 18 patients had metastases, in 12 detected at initial staging (clinical stage III or IV), and in the other 6 during the clinical course. Sentinel lymph node imaging and resection was performed within 4 weeks of the initial PET/CT procedure in 14 patients. Overall, at least one suspicious lesion was confirmed histologically in all patients suspected of harbouring metastases in lymph nodes or distant organs during the clinical course. During the follow-up 28 patients remained disease-free. Four patients died during the clinical course. In one patient, a secondary cancer (breast cancer) was detected at initial staging. All patients tolerated the PET/CT procedures well.

Metastases at initial staging

At initial staging, 12 patients were diagnosed with lymph node and/or distant metastases. The initial clinical stages were stage IV in eight patients and stage III in four patients. Combining the T-stage from histopathology with the staging results from FDG-PET/CT, PET-only and CT-only, the tumour stage was correctly classified in six patients with PET/CT, in five patients with PET, and in three patients with CT. No statistically significant difference was detected concerning the N-stage and the M-stage when comparing PET/CT and PET-only ($p>0.05$), PET/CT and CT-only ($p>0.05$) in this subgroup of patients.

Overall N-staging/M-staging

A comparison of the N-stages and M-stages for all imaging modalities are shown in Table 2. Overall, no statistically significant differences were detected concerning the N-stage between PET/CT and PET-only (difference 0%; 95% CI −10–10%; $p>0.05$) or between PET/CT and CT-only (difference 4%; 95% CI −15–7%; $p>0.05$). Additionally, no statistically significant differences were found concerning the M-stage between PET/CT and PET-only (difference −2%; 95% CI −12–8%; $p>0.05$) or between PET/CT and CT-only (difference −2%; 95% CI −12–8%; $p>0.05$).

Therapy alteration, occurrence of metastases and side findings

N-stage

In two patients, PET/CT and PET-only were superior to CT-only because lymph nodes with focal FDG avidity were not evaluated as malignant on CT-only due to size criteria. In these two patients these findings were therapeutically relevant, because both lymph node metastases were identified and treated consecutively after the initial scan.

Overall (during the whole clinical course including initial staging), eight patients were falsely staged as negative on PET/CT and PET-only concerning lymph node metastases and ten patients were falsely staged as negative on CT-only (Table 2). Two of these patients had micrometastases at initial staging which were overlooked on all imaging modalities but detected by sentinel lymph node resection after PET/CT imaging.

M-stage

Overall, in four patients, therapeutically relevant advantages arose from PET/CT imaging concerning the M-stage. In one patient, PET/CT detected small pulmonary nodules without FDG activity, which were evaluated as lung metastases based on the CT part of the PET/CT scan. However, these lesions were overlooked on PET-only (but detected by CT-only), based on their size and lack of FDG activity. Pulmonary metastases were confirmed on clinical follow-up.

In another patient, PET-only imaging showed an increased FDG uptake in an adrenal gland, but the CT component of the PET/CT scan showed no morphological correlate. Thus, on the PET/CT image, the readers evaluated this finding as not pathological, while on the PET-only image the readers considered the possibility of adrenal gland metastases. During the following clinical course, no adrenal gland metastasis was detected in this patient.

PET/CT had a therapeutically relevant advantage in another patient, in whom a pathologically enlarged inguinal lymph node was evaluated as malignant on CT-only. PET/CT showed no increased glucose metabolism. Thus, the lymph node was evaluated as normal on PET/CT which was confirmed during the clinical course. PET/CT had a therapeutically relevant advantage in another patient in whom (vice versa) the readers detected increased glucose metabolism in a lymph node that was not pathologically enlarged on PET/CT. The PET/CT image was evaluated correctly as malignant, while the CT-only image was evaluated falsely as negative (Fig. 1).

Table 1 Patient characteristics, locations of the primary tumour, histological type of melanoma, and clinical stage

Patient no.	Age (years)	Location	Histological type	S-100 (mg/l)[a]	Clinical stage[b]
1	59	Left back	Nodular	0.11	I A
2	53	Right breast	Superficial spreading	0.15	I A
3	58	Left shoulder	Superficial spreading	0.057	III
4	48	Left thigh	Nodular	0.016	I B
5	69	Right lower leg	Superficial spreading		II A
6	45	Left lower leg	Superficial spreading	0.168	II A
7	69	Left upper arm	Superficial spreading	0.132	II A
8	79	Left face	Lentigo maligna	0.027	I A
9	71	Right upper arm	Nodular		IV
10	47	Right thigh	Superficial spreading		I A
11	83	Right foot	Nodular	0.093	II A
12	35	Right forearm	Lentigo maligna	0.042	II A
13	69	Right knee	Superficial spreading	0.07	I B
14	70	Right hand	Superficial spreading	0.136	IV
15	86	Right lower leg	Nodular	0.402	IV
16	59	Right upper arm	Nodular		IV
17	46	Right lower back	Superficial spreading	<0.15	IV
18	48	middle back	Lentigo maligna	0.024	I B
19	69	Right thorax	Nodular	0.087	II A
20	65	Right thorax	Nodular		IV
21	57	Right abdomen	Superficial spreading		I A
22	65	Right upper arm	Superficial spreading	0.078	I A
23	46	Left back	Superficial spreading		IV
24	48	Right knee	Nodular	0.066	II C
25	53	Left back	Superficial spreading	0.038	I B
26	73	Right face	Nodular	0.075	II B
27	39	Left hip	Superficial spreading		I A
28	83	Left forearm	Nodular		II A
29	79	Right back	Superficial spreading		I A
30	41	Right lower back	Superficial spreading		I B
31	42	Left thorax	Superficial spreading	0.045	I A
32	59	Left thorax	Nodular	0.095	IV
33	57	Right thorax	Nodular		IV
34	77	Right forearm	Nodular	0.116	I B
35	65	Right thorax	Superficial spreading		IV
36	23	Right lower leg	Superficial spreading	0.117	I A
37	82	Right groin	Nodular		II B
38	62	Right upper arm	Nodular		I B
39	79	Right foot	Acrolentiginous		II B
40	75	Left abdomen	Superficial spreading	0.139	II B
41	66	Right thigh	Nodular		III
42	76	Right back	Superficial spreading	0.056	I B
43	79	Left back	Acrolentiginous		III
44	68	Right back	Superficial spreading	0.12	I B
45	70	Right thorax	Superficial spreading	0.092	IV
46	56	Left knee	Nodular		I B
47	73	Right shoulder	Superficial spreading	0.086	II A
48	71	Right lower leg	Superficial spreading	0.133	IV
49	55	Right lower leg	Nodular		II A
50	74	Left shoulder	Superficial spreading	0.075	IV
51	60	Left upper arm	Superficial spreading		I A
52	40	Right abdomen	Superficial spreading		I B
53	59	Left thigh	Lentigo maligna		III
54	84	Left upper arm	Nodular	0.08	I B
55	32	Right thorax	Superficial spreading		IV
56	49	Left thigh	Nodular		II C

[a] Standard tumour marker measured at initial diagnosis.
[b] Evaluated based on the standard of reference; thus, clinical results within the follow-up time were also included.

Table 2 Staging results

Stage	Modality	Correctly staged	Overstaged	Understaged	Sensitivity (95% CI) (%)	Specificity (95% CI) (%)	Accuracy (95% CI) (%)	NPV (95% CI) (%)	PPV (95% CI) (%)
N	PET/CT	48/56	0/56	8/56	38.5 (14–68)	100 (92–100)	85.6 (74–94)	84.3 (71–93)	100 (48–100)
	PET-only	48/56	0/56	8/56	38.5 (14–68)	100 (92–100)	85.7 (74–94)	84.3 (71–93)	100 (48–100)
	CT-only	46/56	0/56	10/56	23.1 (5–53)	100 (92–100)	82.1 (70–91)	81.1 (68–91)	100 (48–100)
M	PET/CT	46/56	3/56	7/56	41.7 (15–72)	93.2 (81–99)	82.1 (70–91)	85.4 (72–94)	62.5 (24–91)
	PET-only	44/56	4/56	8/56	33.3 (9–65)	90.9 (78–97)	78.6 (66–88)	83.3 (70–93)	50.0 (16–84)
	CT-only	44/56	3/56	9/56	25.0 (5–57)	93.2 (81–99)	78.6 (66–88)	82.0 (69–91)	50.0 (12–88)

Overall, 18/56 patients (32%) had either metastases at initial staging (12 patients) or developed metastases during the clinical course. Of these 18 patients, 12 (21%) presented initially with clinical stage III or IV, and 6 (11%) initially staged as clinical stage I or II, developed local lymph node metastases and/or distant metastases (Fig. 2).

Overall, in patients classified as false-negative, lymph node metastases were detected after a mean follow-up time of 150 days (range 15–425 days), and distant metastases were detected after a mean follow-up time of 204 days (range 71–558 days).

Discussion

Both functional and morphological imaging procedures have a low sensitivity when assessing patients with cutaneous malignant melanoma for locoregional and distant metastases at initial diagnosis. In metastasis-negative patients this has to be taken into account and should mandate a close patient follow-up.

Currently there is only little knowledge about FDG-PET/CT and its role as a first-line diagnostic tool or follow-up imaging modality in malignant melanoma. However, different studies have found a benefit of PET-only when compared with CT imaging in patients with recurrent melanoma [8]. Fuster et al. reported an FDG-PET sensitivity and specificity of 74% and 86% for lesion detection in patients with melanoma compared with 58% and 54% for standard imaging [20]. Crippa et al. found an even higher accuracy of FDG-PET imaging. In their study the sensitivity, specificity and accuracy, and the PPV and NPV for detection and characterization of lymph node metastases were 95%, 84%, 91%, 92%, and 89%, respectively [21]. In another patient population with a primary diagnosis of melanoma, which may thus be comparable to our population, a lesion-based sensitivity of 94.9% was found [22]. These overall promising results of PET imaging were confirmed by Reinhardt et al. who evaluated a mixed patient population comprising 250 patients with a primary diagnosis, therapy control, recurrence, and follow-up on FDG-PET/CT imaging [10]. The sensitivity, specificity, and accuracy for the N-stage and M-stage in the entire patient population ranged between 95% and 100% for PET/CT imaging. The substantial differences between previously reported sensitivities and the sensitivities in our study can be attributed to several factors. Most previous studies included a limited follow-up time. We followed our patients over a mean period of over 2 years, compared to 1 year in the study by Reinhardt et al. and most of the other studies.

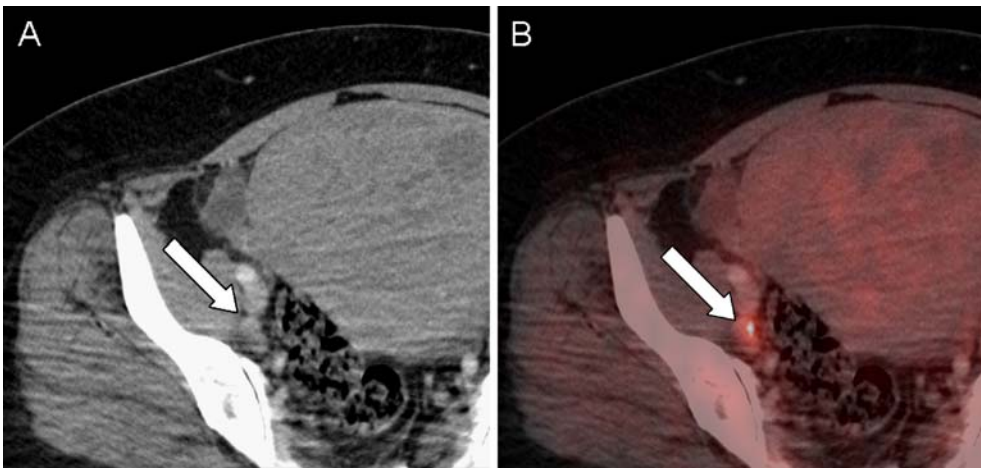

Fig. 1 A 66-year-old female after resection of a malignant melanoma of the right thigh. **a** A small lymph node that is not pathologically enlarged is seen on the CT-only image dorsal to the right external iliac vessels. However, based on size criteria, the lymph node was not evaluated as malignant. **b** On the corresponding PET/CT image, the same lymph node is seen as FDG avid and was thus evaluated as metastasis

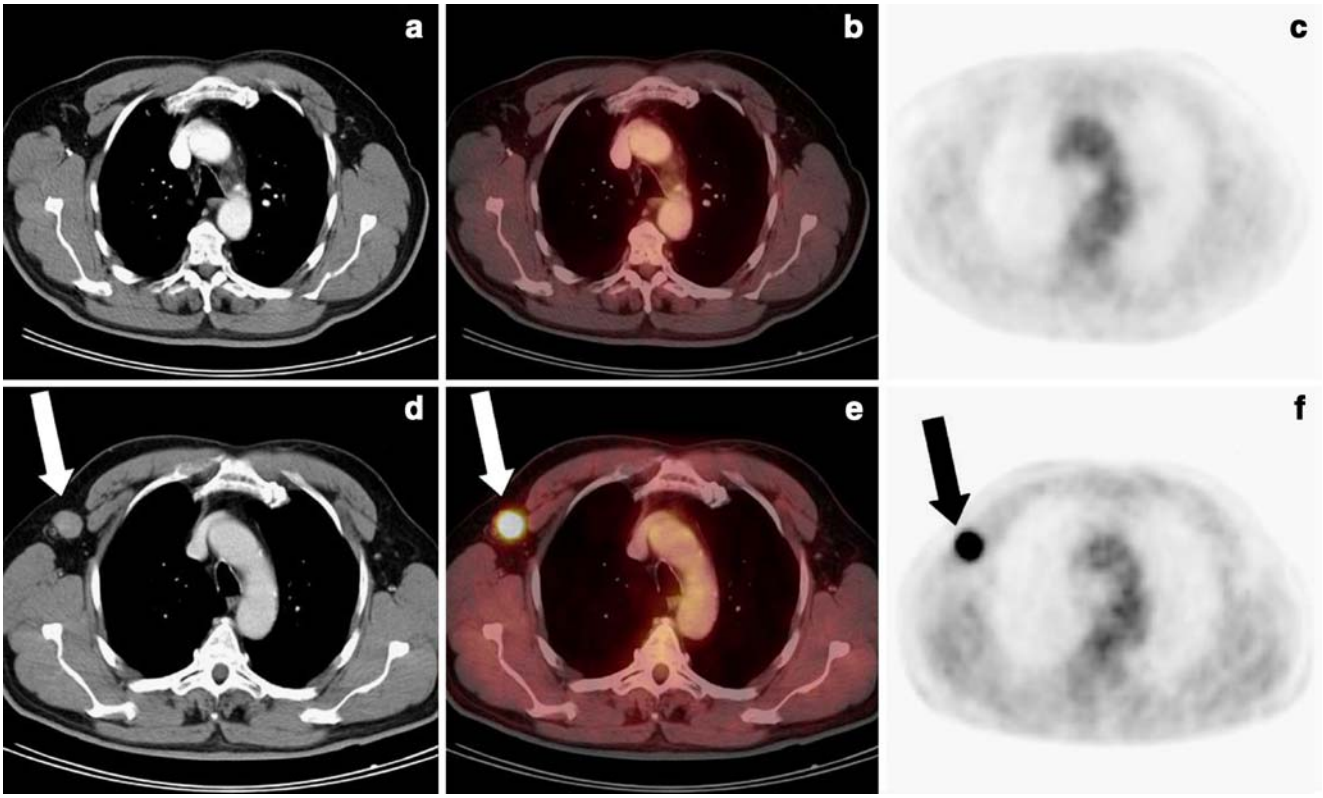

Fig. 2 A 59-year-old male after resection of a malignant melanoma of the left dorsal thorax (initial clinical stage II). **a–c** On initial staging 12 days after resection of the primary tumour, no right axillary distant metastases are seen on the CT-only (**a**), PET/CT (**b**) or PET-only (**c**) images. **d–f** During follow-up, a distant metastasis in the right axilla is seen on the CT-only (**d**), PET/CT (**e**) and PET-only (**f**) images

It is well known that with an increase in follow-up time, the incidence of metastases increases. Metastases which occurred during the clinical course and were not detected on initial FDG-PET/CT imaging were rated as false-negative in our analysis. We chose this approach because the primary melanoma had already been resected. Metastases developing in the further course of disease must, therefore, have been present as micrometastases before. Small metastatic cell deposits need to have a certain size to be detected by FDG-PET or FDG-PET/CT imaging. It has been shown that cell conglomerates of 78 mm^3 are needed for PET-only imaging to provide a sensitivity of 90% [23]. As the detectors of the PET component of PET/CT are similar to those in PET-only no additional sensitivity of FDG-PET/CT over FDG-PET can be expected. However, rating the imaging findings as false-negative in the presence of micrometastases has been a matter of controversy, as metastases detected at a later time may have resulted from small cell deposits in other organs. Yet metastatic cells might circulate over a certain period of time, probably depending on the immunological status of the patient. In this case, detection of lymph nodes or organ metastases must be considered impossible with current imaging techniques. However, this would still result in a false-negative assessment for metastatic spread on initial staging and stresses the need for a close follow-up in metastasis-negative patients.

Another major difference compared to the study of Rheinhardt et al. was the finding of metastases in 35% of the 76 patients at initial staging, while in our study only 21% of the patients (12/56) had metastases by the time of first diagnosis. Consequently, therapy changes occurred in a significantly higher percentage (43% in patients with primary diagnosis of melanoma) compared to our patient population. It is already known from PET imaging studies that the impact on therapy and staging increases in higher clinical stages [24]. However, there are also studies in the literature that have shown low sensitivities of FDG-PET in malignant melanoma. In a study including patients with early-stage melanoma, the sensitivity to detect lymph node metastases was only 21% [25]. Based on these results FDG-PET was not recommended as a first-line tool to stage malignant melanoma. Also in this study, the follow-up time was significantly longer than 1 year (>41 months).

As sentinel lymph node imaging and biopsy should be considered in stages I and II and is definitively recommended by staging guidelines in higher stages, it should be applied at least in patients with advanced clinical stages [6].

If positive, the next staging step and follow-up could be combined PET/CT imaging (PET imaging is recommended in staging guidelines anyway) for several reasons. First, it has already been shown (also partly in our study), that PET/CT imaging can correctly change the subsequent therapy and therefore might decrease rates of morbidity compared to CT-only and PET-only [10, 26]. PET/CT imaging has also been found to be useful for the follow-up of patients with resected melanoma because it provides detection of metastases, even when tumour markers are negative, and it can furthermore improve the detection of melanoma metastases compared to PET-alone [11, 12]. An efficient follow-up imaging algorithm (as proposed here) has to be collaboratively developed because 11% of our patients developed metastases despite the initially low clinical stage.

Our study has several limitations concerning comparability with other studies. Our whole-body CT protocol was different from that used in the study by Reinhardt et al. in which no intravenous contrast medium was administered. However, since PET/CT is a combined imaging modality, we believe that adequate image quality should be provided in both imaging parts (CT and PET). An additional reason for the differences was the relatively low number of patients with metastases at initial staging and during the clinical course in our study. However, we included our patients prospectively with no further selection thus, reflecting the clinical routine in our department.

Sentinel lymph node biopsy was not available in every patient because there are no strict guidelines recommending this in every melanoma case (see guidelines and discussion above). However, there is evidence that sentinel lymph node imaging and resection is more sensitive than PET imaging alone, especially in stage I and II disease [27–30]. Currently there is no study available comparing the sensitivity of sentinel lymph node imaging and PET/CT imaging (there are studies comparing sentinel lymph node imaging to PET-only), but since the CT part in PET/CT generally does not increase the sensitivity in lymph node detection, it can be assumed that these data are still valid.

We did not have the standard tumour marker available in every patient (S-100, see Table 1) because only lactate dehydrogenase is optionally included in a guideline-oriented standard work-up in advanced clinical stages. It has already been demonstrated, that the S-100 marker also has a limited ability to detect melanoma metastases compared to PET/CT imaging [12].

Conclusion

Based on our results, ce-FDG-PET/CT can only be recommended as a first-line diagnostic tool for selected melanoma patients in the high-risk group. Generally, ce-FDG-PET/CT and FDG-PET have low sensitivities on initial staging of patients with malignant melanoma. Thus, close patient follow-up must be considered mandatory.

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