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Original Article

Accuracy of whole-body HDP SPECT/CT, FDG PET/CT, and their combination for detecting bone metastases in breast cancer: an intra-personal comparison

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Abstract: New generation SPECT/CT scanners allow rapid whole-body imaging, and potentially facilitate significantly improved diagnostic accuracy. Thus, the aim of this study was to compare the diagnostic accuracy of whole-body Tc-99m-HDP SPECT/CT, F-18-FDG PET/CT, and their combination for detecting bone metastases in breast cancer. Women with biopsy-proven breast cancer that were referred for whole-body SPECT/CT and FDG PET/CT were consecutively included in this retrospective study. Two blinded readers independently interpreted all scans. In a per-patient analysis, the diagnostic performances of whole-body SPECT/CT, FDG PET/CT, and their combination were compared using *receiver operating characteristic* (ROC) analysis. In a per-lesion analysis, the performances were compared using figures of merit (FoM) differences in *Jackknife alternative free-response* ROC analysis, which considers the location information. Follow-up served as reference standard. Overall, 25 consecutive women (median age: 55; range 38-82) with 117 lesions were included. The median follow-up was 21 months (2-46 months). The per-patient analysis revealed no significant differences in diagnostic performance (P = 0.16), while the per-lesion analysis revealed a diagnostic superiority of whole-body SPECT/CT over FDG PET/CT (P = 0.004). Specifically, the PET/CT FoM was significantly lower than the SPECT/CT FoM (FoM difference = -0.11, 95% CI [-0.21; -0.02], P = 0.021). No significant difference was observed between SPECT/CT and the combination of SPECT/CT and PET/CT. The per-lesion analysis suggest that SPECT/CT has a higher diagnostic accuracy than FDG PET/CT for the detection of bone metastases. Thus, SPECT/CT may be a useful adjunct to FDG PET/CT for staging of breast cancer patients.

Keywords: ^{99m}Tc HDP, ^{18}F FDG, bone scan, breast cancer, bone metastases, molecular imaging, oncology, hybrid imaging, diagnostic work-up

Introduction

Breast cancer is the most common cancer, and the leading cause of cancer mortality among women worldwide [1]. The most frequent site of metastasis is to the bone, occurring as the sole site in 28% to 44% of cases and occurring in 50% to 70% of those who relapse through the course of their disease [2-4]. According to the 2015 guidelines of the National Comprehensive Cancer Network (NCCN), an imaging work-up including FDG PET/CT can be considered in breast cancer patients with stage III disease, or when standard staging studies are equivocal or suspicious [5]. Others reports have demonstrated that FDG PET/CT may change staging in patients with otherwise presumed earlier stage disease, and therefore alter clinical management [6-9]. Imaging options for the skeleton include bone scans, which can be supplemented with single-photon emission computed tomography (SPECT) or SPECT/computed

tomography (CT) and 2-deoxy-2-(^{18}F)fluoro-D-glucose (FDG) positron emission tomography (PET)/CT. SPECT/CT has gained a wide acceptance for bone scanning, and many studies have shown that it reduces the rate of equivocal lesions and increases diagnostic accuracy over SPECT alone or planar scintigraphy alone [10-17]. Nevertheless, no prior studies have compared FDG PET/CT to the latest generation whole-body SPECT/CT or to the combination of both modalities. The aim of this study was to compare whole body SPECT/CT images to F-18 FDG PET/CT in differentiating between benign and metastatic radiotracer uptake on a per-lesion and a per-patient analysis, and to evaluate the potential added benefit of both modalities in combination.

Material and methods

Patients

Women with biopsy-proven breast cancer referred for routine clinical work-up with whole-body SPECT/CT and FDG PET/CT within 90 days were consecutively included in this retrospective study. Patients with a second malignancy were excluded. The findings from whole-body SPECT/CT and FDG PET/CT were compared with the results of subsequent imaging follow-up as the reference standard including CT, MRI, and a subsequent PET or a subsequent scintigraphy ± SPECT/CT in some cases.

SPECT/CT acquisition

All patients received an intravenous dose of 10 MBq/Kg of ^{99m}Tc-hydroxymethylene diphosphonate (HDP). Three hours after injection, a whole-body planar scintigraphy in the anterior and posterior views followed by two consecutive SPECT/CT acquisitions were performed in the supine position with the arms elevated on a double-head SPECT/CT gamma camera (Symbia T6, Siemens Medical Solutions, Erlangen, Germany), allowing coverage of the skeleton from the skull base to the proximal femurs, with some slight variations due to patient height. Immediately after SPECT acquisition, the unenhanced CT scan was acquired. For SPECT acquisition, counts from the 15% energy windows at 140 keV were acquired into a 128 × 128 matrix. The axial field of view of the camera was 38.7 cm (75.4 cm for two SPECT with 2 cm overlap). A total of 64 15-second projections were acquired over 360 degrees using a non-circular orbit (auto-contouring) in the step-and-shoot mode. The camera heads were equipped with a high resolution, low energy, parallel hole collimator. Iterative reconstruction was performed using ordered-subsets expectation maximization with eight iterations and eight subsets (Flash3D™, Siemens Healthcare, Erlangen, Germany). Images were smoothed with a 3D spatial Gaussian filter (10.0 mm full width at half maximum). The unenhanced CT was acquired with the following parameters: 512 × 512 matrix, 110 kVp, 0.8-s rotation time, 0.5 pitch, and 6 × 2 mm collimation. Because only bone structures required analysis, the tube current was reduced to 40 mAs with intensity modulation (Caredose 4D, Siemens Healthcare) to minimize radiation exposure. Image reconstruction using a high resolution, sharp filter (B70 kernel) reconstruction algorithm resulted in images with a slice thickness of 3 mm for a 2 mm reconstruction increment. CT-based attenuation correction was used.

The average CTDIvol ± SD for the whole body SPECT/CT was 3.75 ± 0.93 mGy. Dosimetry was estimated to 4.2 ± 1.0 mSv for CT using ImPACT CT Patients Dosimetry Calculator (version 1.0.4, Imaging Performance Assessment on Computed tomography, www.impactscan.org) and to 3.99 mSv for radiotracer for a 70 kg adult (0.0057 mSv/MBq) according to ICRP [18].

PET/CT acquisition

PET/CT examinations were performed on an integrated PET/CT scanner (Biograph 16-slice PET/CT scanner, Siemens Healthcare, Erlangen, Germany). Prior to the exam, all patients fasted for at least six hours, with serum glucose level measured prior to study initiation at less than 8.5 mmol/L. PET data acquisition was started 60 minutes after injection of 370 MBq of FDG with three minutes per bed position, for a total of seven to nine bed positions scanning from the vertex to the proximal thigh. CT data acquisition for attenuation correction was performed using the following parameters: 120 kV, 80 mAs, 16 × 1.5 mm collimation, 0.8 pitch, and 0.5-s rotation time. PET image reconstruction was performed using an attenuation-weighted ordered subset expectation maximization iterative reconstruction algorithm with a

Table 1. Tumor Characteristics of the 25 patients

	n	%
Histology		
Invasive ductal carcinoma	18	72
Invasive lobulare carcinoma	3	24
Medullar carcinoma	1	4
Grade		
1	3	12
2	18	72
3	4	16
Estrogen receptor status		
+	21	84
-	4	16
Progesterone receptor status		
+	18	72
-	7	28
HER2 status		
+	7	28
-	18	72

Table 2. Anatomical location of the 115 scored lesions

	n	%
Cervical vertebrae	2	1.7
Thoracic vertebrae	34	29.6
Lumbar vertebrae	14	12.2
Sacrum	6	5.2
Pelvis	12	10.4
Scapula	3	2.6
Clavicle	2	1.7
Sternum	2	1.7
Ribs	27	23.5
Cranium	1	0.9
Femur	1	0.9
Humerus	5	4.3
No lesion	6	5.2
Total	115	100.0

matrix of 168 × 168 and a slice thickness of 5 mm. The reconstruction parameters were set to the default values (four iterations, eight subsets, and a post-processing Gaussian kernel with a full-width at half-maximum of 5 mm). The slice thickness of the reconstructed CT images was 2 mm, and the reconstruction interval was 1.5 mm. No intravenous or oral contrast material was administered.

The average CTDIvol ± SD for the PET/CT was 5.72 ± 1.79 mGy. Dosimetry was estimated to 6.73 ± 1.2 mSv for CT using ImPACT CT Patients Dosimetry Calculator (version 1.0.4, Imaging Performance Assessment on Computed tomography, www.impactscan.org) and to 7.03 mSv for radiotracer (0.019 mSv/MBq) according to ICRP [18].

Image data analysis

Interpretation of SPECT/CT and FDG PET/CT was performed on a diagnostic quality platform equipped with a DICOM viewing software (OsirixMD, pixeo SARL, Switzerland). Whole body SPECT/CT and PET/CT were reviewed independently and in random order by two different teams composed of one nuclear medicine physician and one radiologist each. The only clinical information provided to the interpreting physicians was the type of primary cancer.

Each team of readers recorded the degree of confidence for SPECT/CT and PET/CT on a per lesion analysis with a three-point scale: 1 benign or probably benign, 2 equivocal, 3 malignant or probably malignant lesion. A lesion was categorized as 1 if it did not follow the physiologic uptake pattern but was not thought to represent a tumour site. These lesions showed uptake of low intensity or were located in anatomical regions or structures that could be associated with non-tumoral uptake. Lesions categorized as 3 did not follow the physiological uptake pattern but had focal uptake corresponding to a suspicious metastatic site or pattern. If readers could not decide whether a lesion was benign or malignant on the basis of the previous criteria, the lesion was scored as 2. As the purpose was to study the diagnostic accuracy to detect metastases, when a lesion was detected only on one modality, it was automatically rated as “benign” on the other modality. The anatomical assignment of tumour lesions was made as detailed as possible. Secondly, each reader recorded his degree of confidence on per patient analysis using a three-point scale: 1 patient with no lesion or only benign or probably benign lesion, 2 patient with a least one equivocal lesion without any malignant lesion, 3 patients with at least one malignant or probably malignant lesion. In a third step, the two teams of readers had to reach a

Table 3. JAFROC and ROC Figures of Merit (FoM) and 95% confidence intervals (CI) for the detection of bone metastases with each modality: SPECT/CT, PET/CT and SPECT/CT + PET/CT

	ROC				JAFROC			
	FoM	[95% CI]	F	pval	FoM	[95% CI]	F	p
SPECT/CT	0.994	[0.98-1.01]	1.88	0.164	0.954	[0.91-1.00]	6.14	0.004
PET/CT	0.910	[0.78-1.04]			0.840	[0.74-0.94]		
SPECT/CT + PET/CT	1.00	[1.00-1.00]			0.997	[0.99-1.00]		

Table 4. JAFROC and ROC 95% confidence intervals (CI) for the difference in Figures of Merit (FoM) between all pairing modalities

FoM	M1	M2	M1-M2 [95% CI]	P
JAFROC	SPECT/CT	PET/CT	0.11 [0.02-0.21]	0.021
	SPECT/CT	SPECT/CT + PET/CT	-0.04 [-0.14-0.05]	0.367
	PET/CT	SPECT/CT + PET/CT	-0.16 [-0.25-0.06]	0.002
ROC	SPECT/CT	PET/CT	0.08 [-0.02-0.19]	0.120
	SPECT/CT	SPECT/CT + PET/CT	-0.01 [-0.11-0.10]	0.902
	PET/CT	SPECT/CT + PET/CT	-0.09 [-0.20-0.02]	0.095

consensus using SPECT/CT and PET/CT findings according to the same three-point scales on a per-lesion and on a per-patient analysis.

Statistical analysis

Our study relates to a free-response paradigm in that each team of readers, when asked to interpret the image, was free to mark as many regions as they believed were suspicious for disease [19-22]. In such a study, the number of suspected lesions is *a priori* unknown and should be regarded as a random variable. Free-response Receiver Operating Characteristic (FROC) methods, by taking into account this source of randomness, in addition to the usual randomness of the ratings, have higher statistical power than classical ROC methodology to detect differences between the diagnostic performances of modalities (i.e. data image acquisition in our study) [23, 24]. The performance of a modality is defined as the reader-averaged figure-of-merit (FoM), an objective measure of performance (e.g. the area under the ROC curve is a commonly used FoM in ROC analysis) taking values between 0 and 1, with a higher score indicating better diagnostic performance.

The primary analysis of this free-response study was the weighted version of Jacknife Alternative Free-response Receiver Operating Characteristic (JAFROC) to compare the FoM (i.e. diagnostic performance) of SPECT/CT and FDG PET/CT on a per-lesion analysis [25]. In the JAFROC approach, the FoM is the area under the alternative FROC curve and represents the probability that a lesion has a higher rate than all non-lesions of a normal image. We used the JAFROC software version 4.2.1 (available from htpp://www.devchakraborty.com) to compare the FoM of our single team of readers and we report the fixed-reader random-case model results. Complementary investigation was an inferred ROC analysis, which is equivalent to a patient-based ROC analysis: the inferred ROC uses the highest rated mark on an image as the equivalent ROC rating of that image. Sensitivity, specificity, and accuracy of SPECT/CT and FDG PET/CT were finally calculated on a lesion-based and patient-based analysis. Statistical significance was assessed at the two-tailed 0.05 level for all analyses. Except for the weighted JAFROC analysis, data were analyzed using the R software (R Foundation for Statistical Computing, version R-3.1.0, Vienna, Austria; www.R-project.org).

Results

Patients analysed

During the time period from the 1st December 2012 to the 30th October 2014, 25 women with biopsy-proven breast cancer were scanned with HDP SPECT/CT and FDG PET/CT at our department, and consecutively included in our study. No patient was excluded due to a second malignancy. Eight patients were referred for staging and 17 for re-staging. The characteristics of the patients are presented in **Table 1**. The median time between SPECT/CT and FDG PET/CT was 10 days (range, 1-69 days). During the median follow-up period of 21 months (range, 2-46 months) bone metastases

Table 5. Sensitivity, Specificity and Accuracy (positive test if rated 3) of SPECT/CT, PET/CT and SPECT/CT + PET/CT analyzed on a per patient and on a per lesion basis

	Patient			Lesion*		
	Sensitivity (N = 12)	Specificity (N = 13)	Accuracy (N = 25)	Sensitivity (N = 91)	Specificity (N = 18)	Accuracy (N = 109)
SPECT/CT	11 (92%)	13 (100%)	24 (96%)	78 (86%)	18 (100%)	96 (88%)
PETCT	10 (83%)	13 (100%)	23 (92%)	43 (47%)	18 (100%)	61 (56%)
SPECT/CT + PET/CT	12 (100%)	13 (100%)	25 (100%)	86 (95%)	18 (100%)	104 (95%)

*The 109 lesions were observed in 19 patients (6 patients without lesion).

Table 6. JAFROC and ROC Figures of Merit (FoM) and 95% confidence intervals (CI) for the detection of bone metastases with each modality: SPECT, PET and SPECT + PET in staging patients

	ROC				JAFROC			
	FoM	[95% CI]	F	p	FoM	[95% CI]	F	p
SPECT/CT	1	[1.00-1.00]	-	-	0.83	[0.77-0.90]	18.1	<0.001
PET/CT	1	[1.00-1.00]			0.85	[0.80-0.90]		
SPECT/CT + PET/CT	1	[1.00-1.00]			1	[1.00-1.00]		

Table 7. JAFROC 95% confidence intervals (CI) for the difference in Figures of Merit (FoM) between all pairing modalities in staging patients

FoM	M1	M2	M1-M2 [95% CI]	p
JAFROC	SPECT/CT	PET/CT	-0.02 [-0.09-0.04]	0.501
	SPECT/CT	SPECT/CT + PET/CT	-0.17 [-0.23-0.10]	<0.001
	PET/CT	SPECT/CT + PET/CT	-0.15 [-0.21-0.08]	<0.001

were confirmed in 12 patients (48%) and excluded in 13 patients (52%).

Lesion analysed

A total of 117 scored lesions were evaluated. Six patients had no lesions and were assigned one "scored lesion" each. The reference standard could not be established for two lesions (located in two patients, each having four other established malignant lesions) due to incomplete imaging follow up data. Therefore, these two lesions were excluded from all analyses, for a total of 115 lesions in 25 patients. Most lesions were located in the thoracic vertebrae and in the ribs (**Table 2**). According to SPECT/CT, out of 115 scored lesions, 21 (18.3%) were classified as benign, 10 (8.7%) as equivocal, and 78 (67.8%) as malignant. According to FDG PET/CT, the corresponding values were 58 (50.4%), eight (7.0%), and 43 (37.4%). With the addition of SPECT/CT and FDG PET/CT, the corresponding values were 14 (12.2%), nine (7.8%) and 86 (74.8%). In six (5.2%) cases, no lesion could be found on any modality.

SPECT/CT was generally superior to FDG PET/CT

In the 12 patients with confirmed bone metastases based on follow-up imaging, the total number of malignant lesions was 91, for an average of 7.6 lesions per patient (range, 1-24). Three of these patients also had one or more benign lesions in addition to the malignant metastases. In the 13 patients without confirmed bone metastases, six patients had no lesions. In the remaining seven patients, the total number of benign lesions was 13, for an average per patient of 1.9 (range, 1-4).

The FoM according to the JAFROC analysis and the inferred ROC analysis are presented in **Table 3**. The FoM differences between the three modalities was statistically significant on a per-lesion JAFROC analysis (P = 0.004), whereas it was not in the inferred per-patient ROC analysis (P = 0.16). In pairwise comparisons two differences were statistically significant in JAFROC analysis: the PET/CT FoM was significantly lower than the SPECT/CT (FoM difference = -0.11, 95% CI [-0.21; -0.02], P = 0.021), and then the combination of SPECT/CT and PET/CT (FoM difference = -0.16, 95% CI [-0.25; -0.06], P = 0.002) (**Table 4**). No significant difference was observed between SPECT/CT and the combination of SPECT/CT and PET/CT. The absolute values, as well as sensitivities and specificities, on a per-patient and on a per-lesion analysis are presented in **Table 5**. The analysis was performed using score 3 as the cut-off for malignancy.

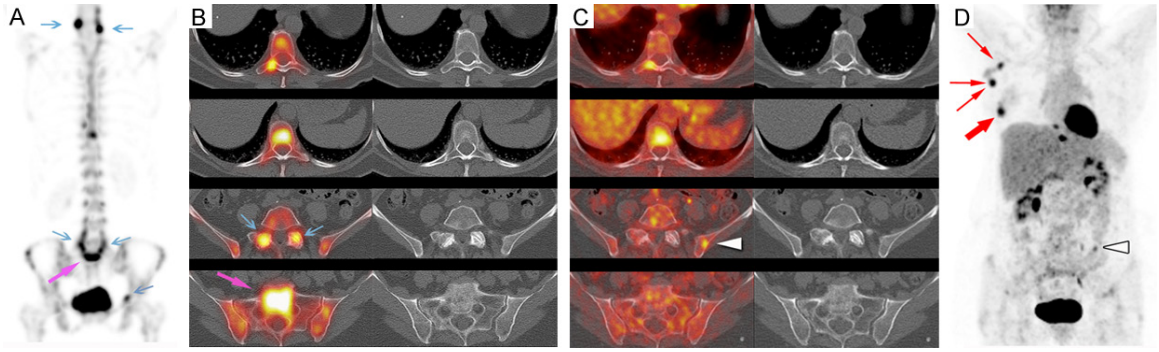

Figure 1. Added value of SPECT/CT to FDG PET/CT. Initial staging in a 62-year-old woman with T2 N2 Mx (stage IIIA) invasive ductal carcinoma of the right breast (ER positive, PR positive, and HER2 non-amplified). SPECT MIP (A), transaxial SPECT CT (B), transaxial PET/CT (C), and PET MIP (D) identified concordant focal uptake in the right laminar process of T9 and the vertebral body of T10. Focal uptake of S1 was seen only on SPECT/CT (pink arrow) (A, B), and a small focal uptake in the left iliac wing was seen only on PET/CT (arrow head) (C, D). These four lesions were established as osseous metastases on imaging follow-up. Interestingly, none of these lesions were visible on CT. SPECT/CT also identified uptake corresponding to degenerative disease in the cervical spine, posterior L5-S1, and left hip (blue arrows, A, B). PET/CT MIP (D) showed the primary tumor (thick red arrow), as well as several axillary lymph nodes (thin red arrows).

Table 8. JAFROC and ROC Figures of Merit (FoM) and 95% confidence intervals (CI) for the detection of bone metastases with each modality: SPECT, PET and SPECT + PET in re-staging patients

	ROC				JAFROC			
	FoM	[95% CI]	F	p	FoM	[95% CI]	F	p
SPECT/CT	1.00	[1.00-1.00]	2.15	0.133	0.97	[0.91-1.02]	7.77	0.002
PET/CT	0.90	[0.76-1.04]			0.78	[0.64-0.91]		
SPECT/CT + PET/CT	1.00	[1.00-1.00]			1.00	[1.00-1.00]		

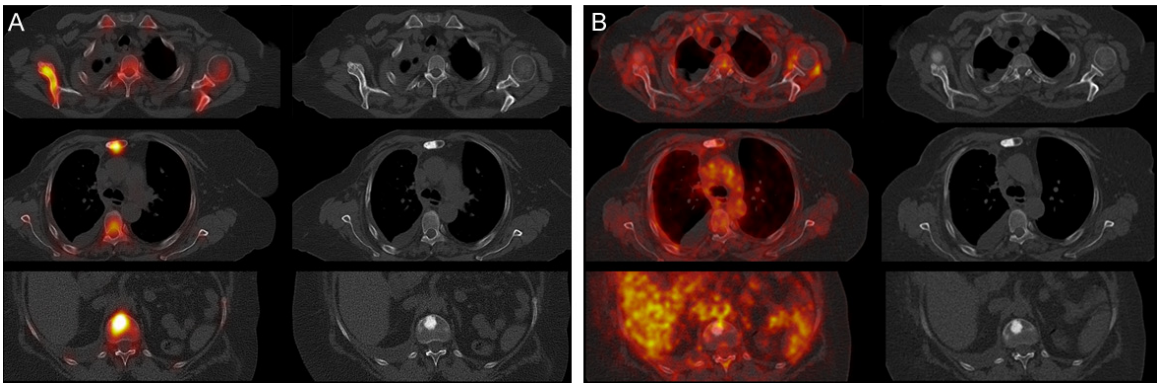

Figure 2. Superiority of SPECT/CT over PET/CT for restaging. Restaging in a 62-year-old woman 12 years after diagnosis of an invasive ductal carcinoma of the right breast (ER negative, PR negative, and HER2 non-amplified, T2 N1 M0), treated by surgical resection, axillary node dissection, and 6 cycles of chemotherapy. The patient had no treatment since then. Transaxial SPECT/CT (A) identified focal uptake in the right scapula, the sternum and in the vertebral body of L1, whereas there was no focal uptake on PET/CT (B). The first lesion had no morphological correlate on the CT scan, whereas the two others corresponded to sclerotic lesions. All three lesions were established as osseous metastases on imaging follow-up.

SPECT/CT plus FDG PET/CT was superior to each modality alone for staging

Among the eight patients referred for staging, five had clinical stage IIB (T2N1Mx), two had stage IIIA (T2N2Mx), and one had stage IIIB (T4N1Mx). The median follow up for the eight patients (median age: 54.5 years; range, 38-82 years) referred for staging was 28 months (range, 9-46 months). Two patients had con-

Table 9. JAFROC and ROC 95% confidence intervals (CI) for the difference in Figures of Merit (FoM) between all pairing modalities in re-staging patients

FoM	M1	M2	M1-M2 [95% CI]	p
JAFROC	SPECT/CT	PET/CT	0.19 [0.07-0.31]	0.004
	SPECT/CT	SPECT/CT + PET/CT	-0.03 [-0.16-0.09]	0.581
	PET/CT	SPECT/CT + PET/CT	-0.22 [-0.35-0.10]	0.001
ROC	SPECT/CT	PET/CT	0.10 [-0.01-0.21]	0.082
	SPECT/CT	SPECT/CT + PET/CT	-	-
	PET/CT	SPECT/CT + PET/CT	-0.10 [-0.21-0.01]	0.082

firmed bone metastases, each with four malignant lesions. In the six patients without confirmed bone metastases, three patients had no lesions. In the remaining three patients, the total number of benign lesions was four. The FoM differences between the three modalities were statistically significant on a per-lesion analysis in the JAFROC analysis (P<0.001), whereas it was not in the inferred per-patient ROC analysis (P = 1) (**Table 6**). In pairwise comparison, the FoM of the combined SPECT/CT + PET/CT was significantly higher than in PET/CT alone or than in SPECT/CT alone; nevertheless, no significant difference was observed between SPECT/CT and PET/CT (**Table 7**; **Figure 1**).

SPECT/CT was superior to FDG PET/CT for re-staging

The median follow up for the 17 patients (median age: 55 years, range, 40-77 years) referred for re-staging was 19.5 months (range, 2-39 months). Ten patients had confirmed bone metastases, with an average of 8.3 malignant lesions per patient, and seven patients were without confirmed bone metastases (three patients had no lesions and in the remaining four patients, the total of malignant lesions was nine). The FoM differences among the three modalities were statistically significant in the per-lesion JAFROC analysis (P = 0.002) whereas no significant difference was observed in the inferred per-lesion ROC analysis (P = 0.13, **Table 8**). In pairwise comparison, the PET/CT FoM was significantly lower than SPECT/CT FoM and than the combined SPECT/CT + PET/CT FoM (**Figure 2**). No significant difference was observed between SPECT/CT and the combination of SPECT/CT and PET/CT (**Table 9**).

Discussion

In this study, the diagnostic accuracy was 88% for whole-body SPECT/CT, 56% for FDG PET/CT, and 95% for the combination of both modalities on a per lesion analysis in the overall patients, This difference of performance was exclusively due to the higher sensitivity of 86% for whole body SPECT/CT and of 95% for the combined modalities compared to 47% for F-18 FDG PET/CT.

Comparison with previous studies

The high diagnostic accuracy of whole body SPECT/CT is concordant with the previous recent studies in which sensitivity and specificity are considered very high, with respective values of 97.7% and 94% in breast cancer on a per patient analysis, and with respective values of 95% and 100% on a per lesion analysis in another study [15, 17]. The accuracy of F-18-FDG PET/CT with values from 85% to 94% is more variable, depending on the population included, the reference standard used, or the follow-up length [26, 27].

Possible effects of therapy

The superiority of SPECT/CT over FDG PET/CT could be partially explained in re-staging patients by the effect of therapy, after which some lesions may be metabolically inactive on FDG PET/CT but still take up tracer on SPECT/CT [28]. On the other hand, in the staging patients sub-group, including only patients without previous therapy, the FoM of SPECT/CT and FDG PET/CT, with similar values of 0.83 and 0.85 respectively, were not significantly different. Nevertheless, the combination of SPECT/CT and FDG PET/CT was significantly better that each modality alone in these patients. These results suggest that SPECT/CT and FDG PET/CT provide complementary information for a comprehensive work-up of different osseous lesions (**Figure 1**) and that this difference is not due to the effect of therapy, since these patients did not receive prior treatment. Several studies have concluded that FDG PET/CT was more sensitive for the detection of osteolytic metastases in breast cancer patients, while SPECT/CT was more sensitive for osteoblastic metastases [26, 28]. The superiority of the combination of both modalities might be explained by the presence of osteolytic, osteoblastic lesions and mixed bone metastases in breast cancer patients [29].

Impact on clinic and research

Some publications have reported that FDG PET/CT is as accurate or more accurate than planar bone scan for the detection of bone metastases [27, 30, 31]. Based on these findings, bone scan is usually omitted in cases when a FDG PET/CT has already been performed. It is well established that SPECT/CT has a better accuracy than planar scintigraphy, even with SPECT alone (without CT) [10-14]. Some authors use SPECT/CT only to identify indeterminate lesions on planar scintigraphy, but others recommend acquiring systematic whole-body SPECT/CT [12, 15]. Our study is the first comparing head to head whole-body SPECT/CT versus FDG PET/CT for bone metastatic work-up in a population of stage IIB and stage III breast cancer with a relative long follow-up. Our results suggest that whole body SPECT/CT should be combined with FDG PET/CT which is also performed to detect extra-axillary nodal involvement and distant metastases.

In research, our results could be useful to determine the sample size required in future prospective studies.

Strengths and limitations

The strengths of our study include breast cancer diagnosis proven by biopsy in all patients, inclusion of consecutive patients, independent readers for SPECT/CT and FDG PET/CT, a follow-up with different imaging modalities in all patients, and the robustness of the statistical analyses.

The limitations of our study were inherent to its retrospective design and small sample population. We selected patients referred for SPECT/CT and FDG PET/CT for metastatic work-up of biopsy-proven breast cancer. The FDG PET/CT was required for routine indication in these patients, i.e. at initial work up for stage IIB or higher, but the bone scan is not automatically required at our institution and the reason for its request by clinicians had not been established in all patients. Furthermore, the reference standard based on imaging including CT, MRI, and in some cases a subsequent PET, or a subsequent scintigraphy ± SPECT/CT was inhomogeneous. Theoretically, the reference standard should be based on histology but that would have required a bone biopsy for every lesion, which is not practical or necessarily ethical. It will be necessary to validate these data in larger prospective series to evaluate the potential impact of SPECT/CT and F-18 FDG PET/CT on a per-patient analysis.

Conclusions

In conclusion, on a per-lesion analysis, our results suggest that SPECT/CT has a better diagnostic accuracy than FDG PET/CT for detection of bone metastases. In patients referred for staging, the combination of whole body SPECT/CT and FDG PET/CT could have a better diagnostic accuracy than each modality alone, suggesting that SPECT/CT may be a useful adjunct to FDG PET/CT for staging of breast cancer patients.

Disclosure of conflict of interest

None.

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