Metabolic activity in bone metastases of breast and prostate cancer were similar as studied by ^{18}F-FDG PET/CT. The role of ^{99m}Tc-MDP

Agata Pietrzak[1] Msc,
Rafal Czepczynski[3] MD, PhD,
Ewa Wierzchoslawska[2] MD, PhD,
Witold Cholewinski[2] MD, PhD

1. Nuclear Medicine Department, Greater Poland Cancer Centre
2. Electroradiology Department, University of Medical Science.
3. Department of Endocrinology, Poznan University of Medical Sciences, Poznan, Poland

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Corresponding author:
Agata Pietrzak,
MSc Nuclear Medicine
Department, Greater Poland Cancer Centre, Garbary 15 Street, 60-101 Poznan, Poland
Agata.pietrzakk@gmail.com

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Abstract

Objective: The aim of this study was to compare the metabolic activity of metastatic foci from breast and prostate cancer patients as scanned by fluorine-18-fluorodeoxyglucose positron emission tomography/computed tomography (^{18}F-FDG PET/CT) and by technetium-99m methyl diphosphonate (^{99m}Tc-MDP) bone scan (BS). **Subjects and Methods:** Forty one patients were studied, divided into 2 groups based on histologically confirmed diagnosis: a) Breast cancer group, 23 women, mean age: 61±12 years, range: 37-79 years and, b) Prostate cancer group, 18 men, mean age 68±8 years, range: 52-82 years. Another group of 17 non cancer atherosclerotic subjects 9 women and 8 men, of mean age and age range similar to the above were also studied for comparison. The R index (the total count rate in bone metastases divided by the total count rate in a contralateral area), the maximum semi-quantitative standardized uptake value (SUVmax) of BS lesions and the mean number of metastases were evaluated. For the metastatic findings in the PET/CT scans the automatic method of contouring with 50% background cut-off was used, while for the ^{99m}Tc-MDP BS metastases were delineated manually. **Results:** The mean R index of the bone metastatic foci studied by ^{18}F-FDG PET/CT was 1.89±0.69 for Groups I and II patients. There was no significant difference of the R index between prostate cancer and breast cancer metastases (1.95±0.86 vs 1.83±0.52). The average SUVmax value was significantly higher in breast cancer patients than in prostate cancer patients (5.15±2.54 vs 4.01±1.71; P<0.05). There was no significant correlation in both cancer groups between R index and SUVmax values. The number of metastatic foci diagnosed by the ^{99m}Tc-MDP BS scan was much less than by the ^{18}F-FDG PET/CT. **Conclusion:** No significant correlation was noticed in the metabolic activity-glucose utilization of metastatic bone foci between breast and prostate cancer cases. This observation validates the independent value of analyzed diagnostic methods and suggests negligible influence of glucose utilization in bone re-modeling in the above metastatic cancer cells. The ^{18}F-FDG PET/CT bone scan was much better in diagnosing metastases compared to the ^{99m}Tc-MDP scan.

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Introduction

The skeleton is the main target of distant metastases in breast and prostate cancers. Bone scintigraphy (BS) using technetium-99 labeled methyl diphosphonates (^{99m}Tc-MDP) and fluorine-18-fluorodeoxyglucose positron emission tomography (^{18}F-FDG PET/CT) is routinely used for detecting distant bone metastases [1]. Staging of malignant diseases is based on the number and the size, of distant metastases detected by the above mentioned modalities [1-6].

Increased uptake of the radiopharmaceutical shows the metabolic activity of the bone affected by the metastatic tissue as shown by the above mentioned scans in the region of interest (ROI) studied. Although, due to higher spatial resolution and three dimensional acquisition, ^{18}F-FDG PET/CT is potentially more accurate than ^{99m}Tc-MDP BS in detecting bone metastases [3, 5, 6] some papers consider these modalities equally sensitive [7, 8].

The aim of this study was to compare BS metastatic findings obtained by the ^{18}F- FDG PET/CT scan in breast and in prostate cancer patients that may characterize these metastases. This study did not focus on the sensitivity and specificity of each method, as it has been widely investigated before. The overall number of metastases shown between the two methods, as above, was also studied.

Subjects and Methods

All patients were admitted and consulted in the Greater Poland Cancer Centre in Poznan, Poland, between 2012-2016.

We studied retrospectively, 58 subjects. Twenty three women had breast cancer, mean age: 61±12 years, age range: 37 to 79 years. Eighteen men had prostate cancers, mean age 68±8 years, age range: 52 to 82 years and 17 subjects had atherosclerosis aged 66±3 years old, age range 58±71 years were examined for various other reasons and their ^{18}F-FDG PET/CT and ^{99m}Tc-MPD scans were negative. These patients had undergone only a PET/CT scan for other re-asons except cancer. All other patients had undergone ^{18}F-FDG PET/CT scan and ^{99m}Tc-MDP BS within four weeks. All breast and prostate cancers were histopathologically confirmed [9-11].

Study protocol

Whole body PET/CT scans (by Gemini TF 16, Philips, Cleveland, USA) were performed 60 minutes after the intravenous (i.v.) injection of up to 400MBq of ^{18}F-FDG (range: 240-400MBq). Patients were asked to have a low carbohydrate diet, intensive exercise, avoid cold environment for 48 hours and were fasted for more than 6h. Patients layed supine with arms beside their body for up to 30 minutes. Computed tomography (CT) was performed before PET acquisition with 120kV peak and 100mA per second. No contrast agent was used. Emission images were acquired for 1 minute and 30 seconds [4, 12-15].

Bone scans were performed with dual head gamma camera (BrightView XCT, Philips, Cleveland, USA), 3 hours after the i.v. injection of up to 800MBq of ^{99m}Tc-MDP (range: 650-800 MBq). Whole body scans were performed simultaneously in anterior and posterior positions with low energy, high resolution collimators with a speed of 15cm/min. The 256x 1024 pixels matrix was used.

Dataset analysis

The R index was calculated as an inversely related proportion between the total counts rate in a metastatic lesion and in an equal in size contralateral physiologic bone area:

$$R\ index = \frac{\text{total count rate in a metastatic bone lesion}}{\text{total count rate in a symmetrical area}}$$

The semiquantitative assessment of tracer uptake in the PET/CT scan was based on SUVmax and SUVmean values [16, 17]. The SUVmax value of the metastases was calculated by the equation:

$$SUVmax = \frac{\text{maximum tissue concentration}[\frac{\text{MBq}}{\text{kg}}]}{\frac{\text{injected dose[MBq]}}{\text{body weight [kg]}}}$$

The maximum pixel as the surrogate to SUVmax value factor was measured and evaluated. The mean SUV was also calculated.

Statistica (StatSoft) commercial software was used.

Results

Statistical analysis

For statistical analysis we used: Groups were evaluated in interval scale. According to Shapiro-Wilk test results, all variables had Gaussian distribution. Thus, Students' t-test for statistical significance assessment was used. The homogeneity of groups was considered.

The differences between age, number of patients and numbered lesions were statistically insignificant, thus both groups were homogenic and comparable.

The R index, SUVmax and SUVmean values in breast cancer patients (Group 1), and in prostate cancer patients (Group 2) were not different. The statistical limit accepted was $P<0.05$.

The dataset characteristics

Table 1 shows our patients characteristics.

Table 1. *The patients characteristics*

Characteristics	Value
Breast cancer	
Number of patients	23
Women/men	23/0
Mean age	61±12
Range (years)	37-79
Prostate cancer	
Number of patients	18
Mean age	68±8
Range (years)	52-82

In each patient, 1-3 metastatic lesions were studied within rectangular regions of interest (ROI). From the 39 lesions studied in Group I, 16 were in the vertebral column.

From the 41 lesions analyzed in Group 2, 11 were in the vertebral column.

Methods of contouring

The manual method of contouring on BS scans was used (Figure 1). The ROI delineations on PET/CT images were performed with 50% background cut-off (Figure 2).

According to Student's t-test results, the mean R index within bone metastatic foci was 1.89±0.69 in Groups I and II and was insignificantly higher in patients with prostate cancer than in breast cancer patients (1.95±0.86 vs 1.83±0.52; P=0.48). The average SUVmax was significantly higher in breast patients than in prostate cancer patients (5.15±2.54 vs 4.01±1.71; P=0.04).

There was no significant correlation between R and SUV max values (correlation coefficient in the whole group, in prostatic and breast patients was 0.10, 0.47 and 0.25, respectively). The highest correlation coefficient was observed in prostate cancer patients.

Comparison of ^{18}F-FDG PET/CT and ^{99m}Tc-MDP BS findings

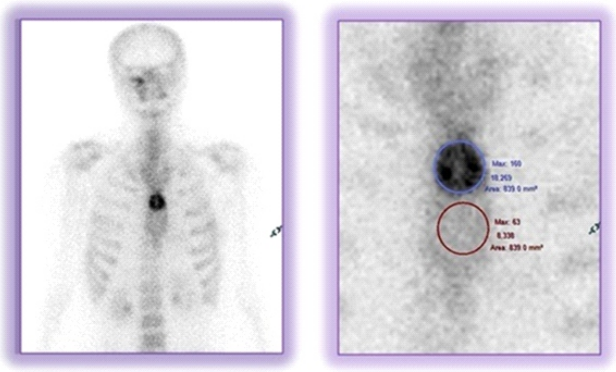

Figure 1. A large metastatic bone lesion in the sternum shown in the ^{99m}Tc-MDP bone scan.

Table2. *Lesions characteristic of the two Groups.*

Analysed parameters	Breast cancer	Prostate cancer
Total number of lesions	**39**	**41**
avg R index	1,83	1,95
SD	0,52	0,86
avg SUVmax value	5,15	4,01
SD	2,54	1,71
avg SUVmean value	3,24	2,39
SD	1,46	1,08
avg Max Px (BS, lesion)	148,85	111,58
SD	52,98	72,30
avg Max Px (BS, contralateral area)	89,06	54,13
SD	35,45	23,17
avg total count rate (BS, lesion)	6763,03	5307,71
SD	5909,39	5702,36
avg total count rate (BS, contralateral area)	3778,85	2694,48
SD	3245,12	2185,26
avg volume [mm^3] (PET/CT, lesion)	7721,49	6348,75
SD	10708,81	7512,81

Avg: average, SD: standard deviation, Max Px: maximum pixel, BS: bone scintigraphy

The number of lesions detected by the two modalities in the BS is shown in Table 3.

In every case, ^{18}F-FDG PET/CT was a more sensitive imaging tool than ^{99m}Tc-MDP BS. The number of lesions diagnosed by ^{18}F-FDG PET/CT was significantly more than by the ^{99m}Tc-MDP BS (P=0.04).

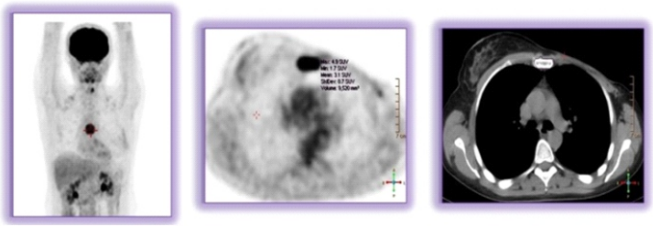

Figure 2. The same metastatic bone lesion in the sternum shown in the ^{18}F-FDG PET/CT scan.

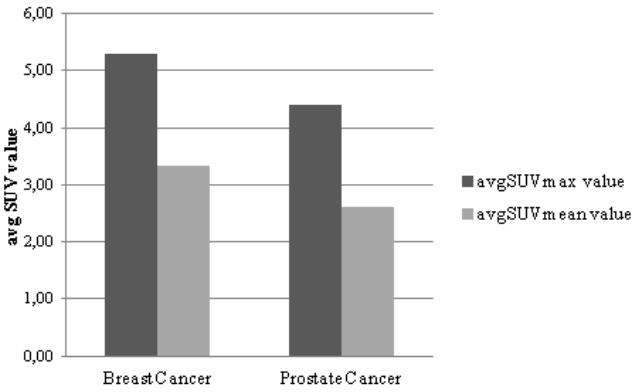

Figure 3. Comparison of SUVmax and SUVmean values in the 2 Groups.

Table3. *The total number and sensitivity of detected metastatic bone lesions by the two methods.*

Groups	Number of detected lesions
Breast cancer	**353**
^{99m}Tc-MDP BS	123
^{18}F-FDG PET/CT	230
Prostate Cancer	**55**
^{99m}Tc-MDP BS	21
^{18}F-FDG PET/CT	34

Discussion

The ^{18}F-FDG-PET/CT BS is considered more sensitive, specific and accurate diagnostic technique than the conventional planar ^{99m}Tc-MDP BS in detecting bone metastases in various cancer diseases [18], as was in this study shown, although other authors claimed that the sensitivity of these techniques is similar and close to 98% [2, 8, 11-15, 19].

As only for ^{18}F-FDG PET/CT for breast cancer, researchers described this method as an extremely efficient diagnostic procedure [20] while others considered it as having a limited value in detecting axillary, internal mammary and supraclavicular lymph nodes [21].

In conclusion, no significant correlation was noticed between the metabolic activity- glucose utilization in metastatic bone foci in cases of breast and prostate cancer. This observation validates the independent value of analyzed diagnostic methods and suggests negligible influence of glucose utilization in bone re-modeling in the above metastatic cancer cells. The ^{18}F-FDG PET/CT bone scan was much better in diagnosing the number of metastases compared to the ^{99m}Tc-MDP scan.

The authors of this study declare no conflicts of interest

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