The effect of patients' body mass indices on PET/CT images with 68Ga-labeled prostate-specific membrane antigen on a TruFlight PET/CT system

Y. Parlak*, G. Mutevelizade, C. Sezgin, D. Goksoy, G. Gumuser, E. Sayit

[1]*Department of Nuclear Medicine, Manisa, Turkey*

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***Corresponding author:**
Yasemin Parlak, Ph.D.,
E-mail:
yasemin.gultekin@hotmail.com

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ABSTRACT

Background**:** The aim of our study was to determine the appropriate scanning time for 68Ga-labeled PSMA PET/CT imaging by using the BMI of the patients. ***Materials and Methods*****:** Fifty-seven patients who were included to the study were divided into 4 groups according to their BMI. In addition to the routine imaging protocol, further imaging focused on the patient's liver was performed. PET images were reconstructed from the reference image obtained for the images at 60, 90, 120, 180, 240, and 300 s/bp. To evaluate PET/CT with 68Ga-PSMA image quality, SNRnorm was calculated using the SNR in the liver. The correlations and differences between scanning times according to BMI were calculated. ***Results*****:** The SUVmax values of the reconstructed images were obtained and the changes observed in SUVmax were statistically significant ($p<0.05$). Our results showed that the SUVmax in the liver decreases with increasing scan time. We calculated that SNR decreased with scan time in all groups. The SNR difference was statistically significant only for 60 and 90 s/bp ($p=0.045$, $p=0.02$, respectively). No difference in SNRnorm values was determined between the groups ($p\geq0.05$). ***Conclusion*****:** If the same amount of radioactivity is injected into patients, the liver SUVmax of the overweight patient would be expected to be higher than underweights. Since SUV calculations are standardized according to body weight, BMI and body composition may cause variability in SUV measurements. As the BMI increased, the background activity in 68Ga-PSMA PET/CT images improved. However, due to the longer imaging time, patient movement should be considered.

INTRODUCTION

Prostate cancer is one of the most common types of cancer in men. In recent years, positron emission tomography/computed tomography (PET/CT) imaging with 68Ga PSMA has been widely used in prostate cancer patients, providing early treatment opportunities [1]. This imaging method is a non-invasive diagnostic technique to image prostate cancer with increased PSMA expression [2]. PET systems provide excellent sensitivity but poor spatial resolution. In contrast, CT systems have excellent spatial resolution but greatly reduced sensitivity. To overcome the limitations of individual modalities, combined PET/CT systems allow the visualization of molecular processes with both high sensitivity and high spatial resolution [3].

The TruFlight systems have lutetium with yttrium orthosilicate crystals that provide a high level of PET performance with the additional benefits of time-of-flight. With time-of-flight imaging, the actual time difference between the detection of the two coincident gamma rays is measured. This time difference is then used in the data reconstruction to more accurately localize the origin of the annihilation. PET/CT systems with time-of-flight performance allow shorter PET acquisition times and improvements in image quality [4].

High image quality has a very important influence on clinical image interpretation. Moreover, a high PET image quality depends on many factors (biodistribution of the tracer, the amount of activity administered, patient size, reconstruction methods, the acquisition time, etc.) [5].

PET/CT imaging produces inconsistent quality between patients of different body mass index (BMI), requiring higher patient dose and/or longer acquisition times for larger patients. As the patient's weight increases, image quality may degrade due to attenuation by excessive soft tissue and a high scatter fraction. In overweight patients, as the activity is increased, the detected count rate increases, resulting in improved image statistics for a given acquisition time. In addition, the activity administered should be minimized for radiation safety. However, the activity should be sufficient to provide optimal image quality for diagnosis [6].

For heavier patients, it may be beneficial to acquire images for a little longer, e.g., 2-3 minutes per frame rather than 1 minute per frame. In this case the

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acquisition may take up to 10 minutes longer, but image quality will be improved. If images are acquired over longer durations, they will still be available for review within minutes following completion of the acquisition [6].

The signal-to-noise ratio (SNR) is defined as the ratio of the mean pixel value (mean) to the standard deviation (SD) in the observed region. The PET/CT image quality is related to the amount of activity administered to the patient and the scan time per bed position.

On the other hand, the SNR norm is assumed to be independent of the scan time and the activity applied. The amount of radioactivity obtained from the gallium generator has limited production during the day due to its relatively short half-life. Compared to FDG, imaging is performed with more restricted radioactivity. Therefore, it is more appropriate to extend the scan time rather than increasing the activity in 68Ga-PSMA imaging. For this reason, it is necessary to optimize the scanning time and activity according to the BMI of the patients. To the best of our knowledge, neither scan duration nor activity optimization has yet been explored for PET/CT with 68Ga-PSMA. As 68Ga-PSMA imaging is performed with increasing frequency, providing good image quality is important for clinical interpretation. Accordingly, the effects of scan duration or administered activity reduction in 68Ga-PSMA PET/CT imaging on TruFlight PET/CT systems on quantitative imaging parameters and its influence on clinical image interpretation were evaluated in the present study.

MATERIALS AND METHODS

Patient-based parameters

Fifty-seven patients with prostate cancer (mean age 70.22 ± 9.1 years) admitted to our department for 68Ga-PSMA PET/CT were included. The study was approved by the Local Ethics Committee dated 01.12.2021 and numbered 1057. Written consent was obtained from all patients. Table 1 summarizes the demographic information (age, number of patients, BMI) and PSMA PET/CT parameters (mean administered activity) of the patients. The body mass (kg) and height (m) of all patients were measured and BMI was calculated by dividing body mass (kg) by the square of height (m^2). The patients were distributed according to their BMI into 4 different groups (group 1 BMI≤24.9, group 2 BMI 25-29.9, group 3 BMI 30-34.9, and group 4 BMI≥35).

Gallium-68-PSMA PET/CT imaging protocol

Patient preparation, acquisition protocols, and reconstruction parameters were standardized for all patients. For hydration, they were asked to drink about 1 liter of water during the 1 h prior to injection. After the intravenous injection of 2.2 MBq/kg 68Ga PSMA, the patients were taken to special waiting rooms to rest. After an average of 60 minutes, the patient was positioned in the supine position with the arms up and was scanned from the vertex to the proximal thigh, and low-dose CT (120 kVp and 80 mAs) and PET (Philips Healthcare, TruFlight Select, Cleveland, OH, lutetium yttrium orthosilicate crystals; 3-dimensional acquisition; 90 s per bed position (s/bp); 5-6 bed positions)) images were obtained. CT was performed for attenuation correction. The ordered subsets expectation maximization reconstruction algorithm was used with reconstruction parameters of 3 iterations and 33 subsets, which are also used in the routine for all patients.

Further imaging focused on the patient's liver was performed, with a reference image (360 s/bp, one bed positions) obtained.

Table 1. The mean (± SD) values of administered activities and patient demographic data according to their groups.

Patient Groups		Age (years)	Patient number	Activity (MBq)	Body mass index
1	BMI<25	73.6±8.45	13	140±32.9	23.2±1.24
2	25<BMI<29.9	69.6±8.8	22	141±25.9	27.1±1.2
3	30<BMI<34.9	68.7±10.3	18	138±18.5	32.3±1.3
4	BMI≥35	69.2±6.1	4	145±13.3	37.3±2.1
Total	All	70.2±9.1	57	141±25.9	29.6±4.8

MBq: megabecquerel, BMI: Body mass index, SD: Standard deviation

Quantitative image analysis

PET images were reconstructed using 3D ordered subset expectation maximization (OSEM) as appropriate, in conjunction with the parameters described for the clinical protocol. The OSEM reconstruction algorithm was used with 3 iterations 33 subset, matrix size of 144×144, and voxels of 4×4×4 mm reconstruction parameters referred to as clinical. No Gaussian filter was applied.

PET scans of 60, 90, 120, 180, 240, and 300 s/bp were extracted from the 360 s/bp images using list mode data.

As a measure of 68Ga-PSMA PET/CT image quality, the SNR due to the relative homogeneous 68Ga uptake in the liver was calculated [5,6]. The lesion and high activity regions of interest (ROIs) were excluded from the axial fusion images obtained after imaging and 2D ROIs were plotted to calculate the average SUV in the right lobe of the liver (figure 1). All ROIs were placed at the same location for all 6 PET reconstructions. The 360 s/bed PET reconstruction served as the reference for comparing the SNR and SNRnorm between reconstructions. The correlation between the SNRnorm and the BMIs of the patients was calculated.

A SNRnorm normalized for the administered dose and scan time per bed position was defined as follows [7]:

$$SNR_{norm} = \frac{SNR}{\sqrt{A.t}},$$

Where; A is the administered dose (MBq) and t is the acquisition time per bed position (min).

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Figure 1. 2D ROI plotted on right lobe of liver Min: minimum, max: maximum, SUV: standard uptake value, StdDev: standard deviation, ROI: region of interest.

Data analysis

In order to perform statistical analysis, all data such as BMI, SUVmax, SNR, and SNRnorm were obtained. Thereafter, mean value, percentage error, and standard deviation were calculated using statistical software. Pairwise comparisons were also performed to assess the differences between each reconstructed image derived from the 360 s/bp images.

Statistical analysis

The data obtained were entered into SPSS version 15.0 (IBM, Turkey) and a p value of less than 0.05 was considered significant.

RESULTS

In group 1 there were 13 patients (with an age range from 62 to 93 y), whose BMI was below 25. There were 22 patients (with an age range from 54 to 85 y) in group 2, whose BMI was 25-29.9; 18 patients (with an age range from 39 to 87 y) in group 3, whose BMI was 30-34.9; and 4 patients (with an age range from 54 to 85 y) in group 4, whose BMI was above 35.

The maximum standardized uptake value (SUVmax) changes for the groups are given in table 2. This table shows that the SUVmax in the liver decreases with increasing scanning time. Moreover, SUVmax in the liver rose with the increasing body mass of the patients. The highest SUVmax was obtained in group 4. The reductions in SUVmax detected for all scan times were considered. When all groups are evaluated, this change observed in SUVmax was statistically significant ($p<0.05$). Plots of the SUVmax measured in the liver against the acquisition time per bed position are given in figure 2. The SUVmax decrease detected between 60 and 360 s/bp in groups 1, 2, 3, and 4 was 21%, 24%, 22%, and 29%, respectively. The mean SUV reduction between 60 and 360 seconds was 22.4%.

For each bed position, the corresponding mean SUVmax, SNR, and SNRnorm values are shown in table 3. The interest in varying the time per bed position is clearly highlighted when looking at all SUVmax, SNR, and SNRnorm values as a function of bed position. Figure 3 shows the intergroup changes in SNR values. For the patients in groups 1, 2, 3, and 4 separated by BMI, the SNR decreases by a maximum of 37.5%, 32.5%, 34.6%, and 30.2%, respectively, between 60 and 360 s/bp. However, the SNR difference was significant for the 60 and 90 s/bp positions, but not for other scan times ($p<0.05$). There is a significant relationship between the duration of the scan and the SNR. While the SNR of the reference scanning period was 14 for group 1 (BMI below 25), it was 10.6 for group 4 (BMI above 35). The SNR reduction rate between these two groups was 24.2%.

The SNRnorm values for all groups are given in figure 4. There was no significant difference in SNRnorm values between the groups separated according to their BMI ($p\geq0.05$).

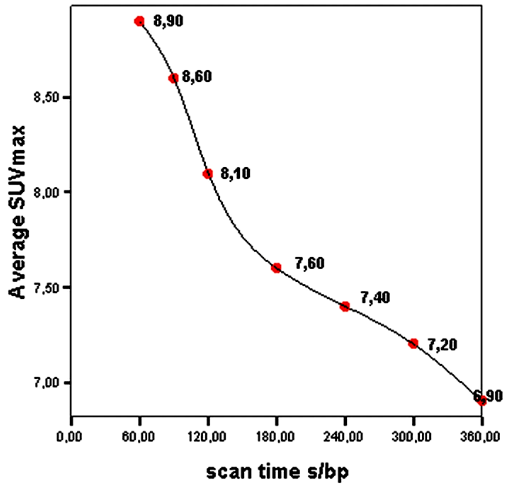

Figure 2. Average SUVmax obtained from image reconstructions at different scan durations.

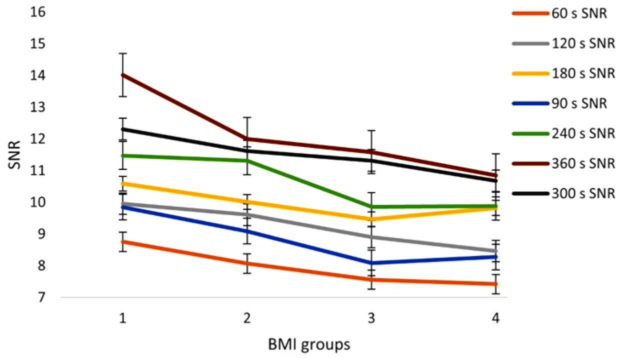

Figure 3. SNR values corresponding to varying scan times in different BMI groups. SNR: Signal-to-noise ratio, BMI: Body mass index The error bars represent two standard deviations.

Table 2. The maximum standardized uptake values with scan time increased for all groups

Scan Time (s/bp)	Group 1 BMI<25	Group 2 25<BMI<29.9	Group 3 30<BMI<34.9	Group 4 BMI≥35	Mean± SD
60	6.2±1.6	9.3±3.2	9.8±2.5	11.9±2.9	8.9±3.1
90	5.9±1.3	8.6±3.3	9.8±2.5	11.1±2.5	8.6±3.1
120	5.8±1.3	8.4±3.2	8.9±2.5	10.6±2.7	8.1±2.9
180	5.5±1.2	7.7±2.9	8.6±2.5	8.9±1.6	7.6±2.7
240	5.2±1.1	7.6±3.0	8.1±2.6	8.9±1.6	7.4±2.8
300	5.1±1.2	7.3±2.9	7.8±2.4	9.1±1.8	7.2±2.6
360	4.9±1.1	7.1±3.3	7.6±2.5	8.4±1.0	6.9±2.8

BMI: Body mass index, SD: Standard deviation, s/bp: second/bed position

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Table 3. The mean (±SD) values of SUVmax, SNR, and SNRnorm as a function of scan time.

Scan Time (s/bp)	SUVmax (mean±SD)	SNR (mean±SD)	SNRnorm (mean±SD)
60	8.9±3	8.0±1.2	0.69±0.09
90	8.6±3	8.8±1.6	0.63±0.1
120	8.1±2.9	9.38±1.8	0.58±0.1
180	7.6±2.7	9.95±1.7	0.5±0.1
240	7.4±2.7	10.8±2.1	0.47±0.1
300	7.1±2.6	11.62±2.3	0.45±0.1
360	6.9±2.8	12.24±2.9	0.43±0.1

SD: Standard deviation, s/bp: second/bed position, SNR: signal-to-noise ratio, SNRnorm: Normalized signal-to-noise ratio, SUVmax: maximum standardized uptake values

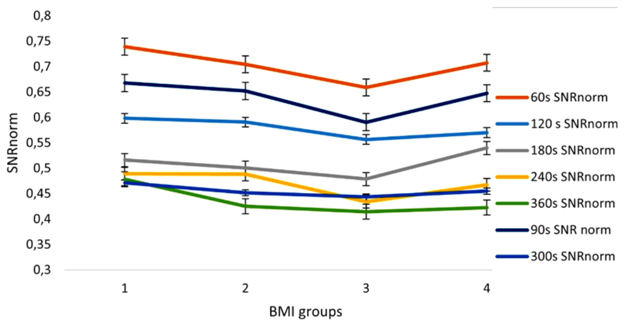

Figure 4. SNRnorm values corresponding to varying scan times in different BMI groups. SNRnorm: Normalized signal-to-noise ratio, BMI: Body mass index The error bars represent two standard deviations.

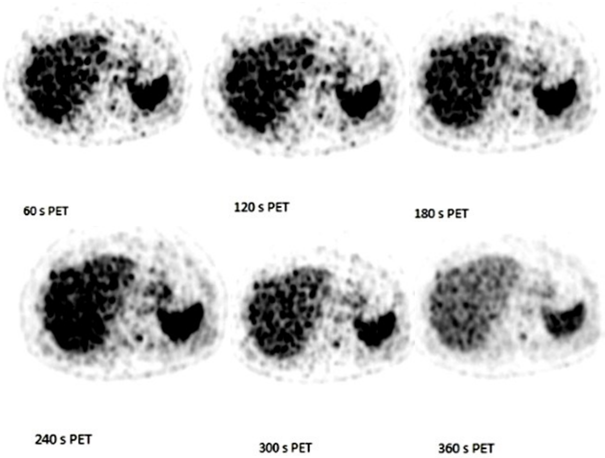

Figure 5. Visualization of reconstructions of a lesion in the liver.

DISCUSSION

PET/CT is a highly useful hybrid imaging modality for tumor diagnosis and staging and evaluation of treatment response. The major advantage of PET/CT is the ability to measure radiopharmaceutical uptake and it gives digital results in the form of standardized uptake values [8]. The optimal image quality for 68Ga-PSMA PET/CT is important for the clinical efficacy of PET-based measurement, a semi-quantitative imaging biomarker for treatment response and treatment planning in patients with prostate cancer [9, 10].

The major finding of the present study was that an extended acquisition time enabled an effective evaluation of the quality of 68Ga PSMA PET/CT images in patients with different BMI values. Therefore, the aim in the present study was to examine scan duration optimization parameters and how those choices can influence the final outcome in terms of the optimal image quality for PET/CT with 68Ga-PSMA.

According to World Health Organization (WHO) data, the prevalence of obesity worldwide (BMI ≥30 kg/m^2) has increased approximately three-fold in the 40 years after 1975. In terms of numerical data, the overweight problem is seen almost equally in men and women (39% and 40%, respectively). Of those who are overweight, 650 million (13% worldwide; 11% in men and 15% in women) are obese. Approximately 2.8 million people die each year due to overweight or obesity. In the recently announced European Cardiovascular Disease Statistics (ATLAS) study, the rates reported for Turkish men and women are 35.8% and 22.9%, respectively [11]. Obesity causes artifacts in all nuclear medicine imaging modalities and thus can change the clinical efficacy of images. Since SUV calculations are standardized according to body weight, the patient's BMI and body composition may cause variability in SUV measurements. The quantitative measurements of PET/CT images are affected by patients with different BMIs [10].

Body mass can be used to estimate 68Ga-PSMA PET image duration and quality for overweight patients. It may be beneficial to increase the acquisition time. Even a small increase in bed time will raise the patient's total imaging time and image quality will be improved [10]. Scan time should be long enough to ensure accurate measurement of SUVmax. However, increased acquisition time may also cause artifacts, especially in patients with pain, due to the possibility of movement. In addition, patient comfort deteriorates with long scan times. This is more important, especially considering that the imaging was performed in the oncological patient group. Therefore, optimization of scan time is crucial.

In our study, when we increased the s/bp, SUVmax decreased in the liver in all groups. The average SUVmax reduction between 60 and 360 seconds was 22.4%.

According to the European Organisation for Research and Treatment of Cancer (EORTC) and Positron Emission Tomography Response Criteria in Solid Tumors (PERCIST) criteria, when evaluating the treatment response, 25% and 30% SUVmax changes were considered progression and regression, respectively [12]. The 22.4% change detected in our study may have had an impact on the treatment response decision. In fact, this change reaches 29% for group 4. This situation may have an impact on the physician's decision about disease progression/ regression in obese patients. For this reason, standardization should be ensured in imaging protocols in the follow-up of the same patient.

The ratio of the signal intensity to the noise level

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in the image is the definition of SNR. This ratio represents the detectability of an object. The lower the SNR, the noisier the image. An image with a lot of high frequency, high amplitude noise will have a very low SNR. A low SNR is in addition to a low signal [13].

The SNR decreases in obese patients as noise increases due to high photon attenuation and scattering [6, 14]. In our study, the SNR decreased with increasing BMI in all groups, which was consistent with the literature. On the other hand, the SNR difference was statistically significant for 60 and 90 s/bp positions, but not for the other scan times. This finding can be explained by the high noise level with short scan times. As the scanning time is increased, the noise level will decrease and the SNR will improve [16]. Cox *et al.* found significantly lower mean SNR for all other lower s/bp compared with 360 s/bp in 68Ga-DOTA-TATE PET images [5].

As expected, image quality measured by the SNRnorm in the liver increased with prolonged scanning time. In our study, SNRnorm decreased with increasing s/bp but there was no statistically significant difference between the groups. Halpern *et al.* stated that normalized image quality of 1 and 3-5 mbps does not show any significant difference compared to 6 mbps reconstruction [6]. This result is consistent with our study.

According to our calculated SUVmax, SNR, and SNRnorm results, 180-360 s/bp images are recommended for optimal image evaluation. However, Gallium-68 has a short half-life, increasing scan times will result in a long imaging time, and Gallium-68 will be halved while scanning the patient, resulting in image degradation. In addition, the patient's comfort will deteriorate and the patient may need to void. The increase in bladder fullness will cause artifacts in the pelvis, which is our most important evaluation area in prostate cancer patients. We recommend urinary catheterization in patients with longer scan times to prevent bladder fullness.

Pilz *et al.* reported that shortening the scanning time in PET/CT systems improves patient comfort, especially in elderly and anguished patients [16].

Based on our findings, the optimized scan time of at least 180 s/bp in the first 3 groups and 240 s/bp for the patients in group 4 will significantly increase image quality.

Although the present study included a small number of patients, our result is promising because it enables small lesion detection and clearer visualization of lesion borders, especially in obese patients. Our findings can be applied for TruFlight PET/CT Technology systems. New studies are needed for other PET/CT systems.

CONCLUSION

In 68Ga-PSMA PET/CT images, the patient's general medical condition and BMI and the half-life of the radionuclide should be taken into account. For this reason, we recommend that the time per bed position should not be less than 180 seconds to obtain adequate image quality in patients with prostate cancer.

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Conflict of interest: The authors have no conflicts of interest to declare.

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