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TECHNICAL NOTE

Normal uptake of ^{18}F-FDG in the testis: an assessment by PET/CT

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Abstract
Objective The aim of this study was to assess the physiological uptake of ^{18}F-fluoro-2-deoxyglucose (FDG) by an apparently normal testis with combined positron emission tomography–computed tomography (PET/CT) and its correlation with age, blood glucose level, and testicular volume.
Methods The testicular uptake of ^{18}F-FDG, expressed as the standardized uptake value (SUV), was measured on PET/CT images in 203 men. The correlation between SUV and age, blood glucose level, and testicular volume was assessed.
Results The SUV in the total of 406 testes was 2.44 ± 0.45 (range 1.23–3.85). The SUV was 2.81 ± 0.43 (2.28–3.85) for 30–39 years (n = 12), 2.63 ± 0.45 (1.77–3.75) for 40–49 years (n = 64), 2.46 ± 0.35 (1.44–3.15) for 50–59 years (n = 82), 2.51 ± 0.41 (1.50–3.46) for 60–69 years (n = 86), 2.43 ± 0.47 (1.42–3.29) for 70–79 years (n = 86), and 2.18 ± 0.45 (1.23–3.03) for 80–89 years (n = 76). When we calculated the mean SUV of bilateral testes in each patient, there were significant statistical differences between those in the age group of 30–39 years and 80–89 years, 40–49 years and 80–89 years, and 50–60 years and 80–89 years, when using an unpaired test with Bonferroni correction. The laterality index ($|L - R|/(L + R) \times 2$) in 203 men was 0.066 ± 0.067 (0–0.522). There was a mild correlation between the mean SUV and age (r = –0.284, $P < 0.001$) as well as between the mean SUV and mean volume (r = +0.368, $P < 0.001$). There was no correlation between the mean SUV and glucose blood level (r = –0.065, P = 0.358).
Conclusions Some uptake of FDG is observed in the normal testis and declines slightly with age. Physiological FDG uptake in the testis should not be confused with pathological accumulation.

Keywords Testis · ^{18}F-FDG · Physiological uptake · PET/CT

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Introduction

^{18}F-fluoro-2-deoxyglucose (FDG) position emission tomography (PET) has been widely used for the evaluation of patients with cancer. Although FDG generally accumulates in malignant lesions, it can also accumulate in normal tissues [1, 2]. Hence, knowledge of the normal physiological and variant distribution of FDG is important for the proper interpretation of FDG-PET scans. In the literature, there have been some reports on normal

FDG accumulation in various regions such as the gastrointestinal tract [3], head and neck [4], endometrium and ovary [5, 6], and breast [7]. Kosuda et al. [8] discussed the physiological uptake in the testis, but testicular uptake has not been fully evaluated.

Combined PET/computed tomography (CT) scanners that enable highly precise localization of the metabolic abnormalities seen on PET and high-spatial-resolution CT images have been developed [9]. We believe that the evaluation of normal tracer uptake in the testis would be easier, more precise, and reliable with PET/CT.

In this study, we retrospectively evaluated FDG distribution in apparently normal testis in a large number of subjects and looked into the correlation with age, blood glucose level, and testicular volume, using an inline PET/CT system.

Materials and methods

Subjects

A total of 360 consecutive men underwent diagnostic FDG-PET/CT scans in our PET center between April 2006 and June 2006. Of these patients, 157 were excluded because accumulation in the testis may have been influenced: 153 men had received chemotherapy earlier for various cancers, 2 had received orchiectomy before PET/CT scan, and 2 showed a blood glucose level of more than 160 mg/dl. The remaining 203 men comprised the study population and had no history of malignancy in the testis and no abnormal findings in the testis on CT images of PET/CT and their clinical records. Of the 203 men, 117 were referred for the evaluation of lung cancer, 16 for cancer in the head and neck region, 12 for colorectal cancer, 6 for gastric cancer, 5 for melanoma, 4 for pancreas cancer, 3 for esophagus cancer, 5 for other cancers, and 35 for cancer screening. The 203 men were divided into six groups: Group A, 30–39 years (n = 6); Group B, 40–49 years (n = 32); Group C, 50–59 years (n = 41); Group D, 60–69 years (n = 43); Group E, 70–79 years (n = 43); and Group F, 80–89 years (n = 38). The mean age of the study cohort was 64.5 ± 13.7 years, ranging from 36 years to 89 years.

Each subject gave written informed consent before scanning as required by our PET center.

FDG-PET/CT study

Whole-body FDG-PET/CT scanning was performed with one of the two combined PET/CT scanners (Discovery ST8 and ST16, GE Medical Systems, Waukesha, WI, USA). This scanner allows simultaneous acquisition of 47 transaxial PET images with interslice spacing of 3.75 mm in one bed position and provides an image from the head to the thigh with 7–8 bed positions. The transaxial field of view and pixel size of the PET images reconstructed for fusion were 70 cm and 5.47 mm, respectively, with a matrix size of 128 × 128. The CT part was either an 8- or 16-detector row helical CT scanner. The technical parameters used for CT imaging were as follows: a pitch of 6 (high-speed mode), a gantry rotation speed of 0.6 s, a table speed of 33.5 mm per gantry rotation, 140 kVp, and 40 mA, 3.75 mm slice thickness and no specific breath-holding instructions. After at least 4 h of fasting, patients received an intravenous injection of 3.33 MBq/kg body weight of FDG. The blood glucose levels were checked in all patients before FDG injection. About 50 min later, CT images from the meatus of the ear to the mid-thigh for 32 s were obtained. A whole-body emission PET scan for the same axial coverage was performed with 2 min acquisition per bed position using the 3D acquisition mode. CT images were used not only for image fusion but also to generate an attenuation map with the use of measured attenuation correction. PET images were reconstructed using an ordered-subset expectation maximization iterative reconstruction algorithm. PET, CT, and fused PET/CT images were generated for a review on a computer workstation (eXeleris).

Image analysis

The testis was identified as spherical or discoid-shaped soft tissue on axial CT images of PET/CT. For each slice showing the testis, a region of interest was placed for the testis, and the volume (mm^3) was calculated by multiplying area (mm^2) by slice thickness (3.75 mm). The total volume of the testis was then calculated by summation. The testicular uptake of ^{18}F-FDG showing the corresponding regions of interest on axial PET images was expressed as the maximal standardized uptake value (SUV). SUV was calculated as the ratio of decay-corrected activity per cubic centimeter of tissue to the injected dosage per body weight.

Statistical analysis

We defined "laterality index" by calculating ($|L - R|/(L + R) \times 2$), where L = left testicular SUV, R = right testicular SUV, and the mean SUV and volume of bilateral testes in each subject. We assessed the correlation between mean SUV and parameters such as age, plasma glucose levels, and testicular volume in 203 men as well as between mean testicular volume and age using Pearson's correlation coefficient test. Moreover, we

examined whether there was a significant difference in mean SUV among the six age groups, 30–39 years, 40–49 years, 50–59 years, 60–69 years, 70–79 years, and 80–89 years, using the *t*-test with Bonferroni correction. A *P* value of less than 0.05 was regarded as statistically significant.

Results

Figure 1 shows pelvic ant-post maximum intensity projection images, and axial PET and CT images at the testicular level of a typical subject, representing testicular uptake (SUV = 2.82 (*L*), 2.78 (*R*), laterality index = 0.014).

SUV and age

The relationship between uptake of ^{18}F-FDG and age in 406 testes is summarized in Table 1. The mean ± standard deviation (minimum–maximum) SUV of 406 testes in the 203 men was 2.44 ± 0.45 (1.23–3.85): 2.81 ± 0.43 (2.28–3.85) in group A (n = 12), 2.63 ± 0.45 (1.77–3.75) in group B (n = 64), 2.46 ± 0.35 (1.44–3.15) in group C (n = 82), 2.51 ± 0.41 (1.50–3.46) in group D (n = 86), 2.43 ± 0.47 (1.42–3.29) in group E (n = 86), and 2.18 ± 0.45 (1.23–3.03) in group F (n = 76). When we calculated the mean SUV of bilateral testes in each patient, there were significant statistical differences between group A and group F, group B and group F, and group D and group F in comparison with the Bonferroni correction. The laterality index ($|L - R|/(L + R) \times 2$) in the 203 men was 0.066 ± 0.067 (range 0–0.522) with 5% from the top being 0.193. As shown in Fig. 2, the correlation between the mean SUV of bilateral testes and age in the 203 men was statistically significant (r = –0.284, $P < 0.0001$).

SUV and blood glucose level

The blood glucose level before FDG injection in the 203 men was 111.4 ± 15.6 mg/dl (range 70–159). No subject received an insulin injection before the scan. Blood

Table 1 Testicular ^{18}F-fluoro-2-deoxyglucose uptake and volume in 406 testes of 203 men

Group	Age	No. of testes	SUV		Volume (cm^3)	
			Mean ± SD	Range	Mean ± SD	Range
A	30–39	12	2.81 ± 0.43	2.28–3.85	27.9 ± 6.6	19.2–41.1
B	40–49	64	2.63 ± 0.45	1.77–3.75	24.5 ± 6.9	3.8–41.5
C	50–59	82	2.46 ± 0.35	1.44–3.15	22.8 ± 6.9	12.3–38.1
D	60–69	86	2.51 ± 0.41	1.50–3.46	21.6 ± 6.4	9.6–39.2
E	70–79	86	2.42 ± 0.47	1.42–3.29	21.7 ± 7.9	10.5–35.4
F	80–89	76	2.18 ± 0.45	1.23–3.03	20.0 ± 7.7	8.2–35.7
Total		406	2.44 ± 0.45	1.23–3.85	22.1 ± 6.4	3.8–41.5

SUV, standardized uptake value

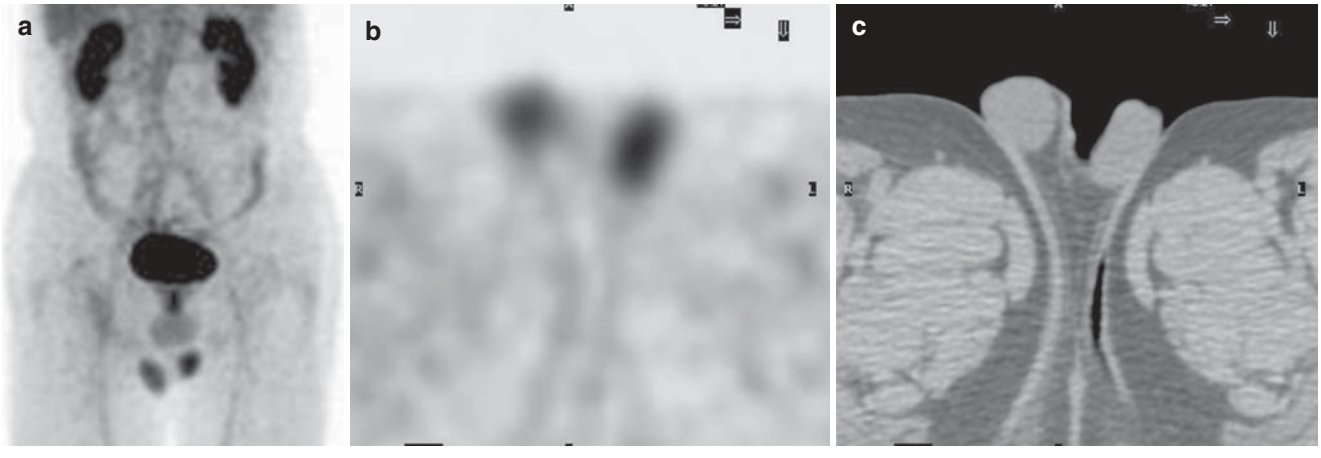

Fig. 1 A maximum intensity projection image (**a**), and axial positron emission tomography (**b**), and computed tomography (**c**) images at the testicular level are shown. Homogenous and moderate uptake is seen corresponding to the bilateral testes with a highest standardized uptake value (SUV) of 2.82 in the left and 2.78 in the right. The laterality index was calculated to be 0.014

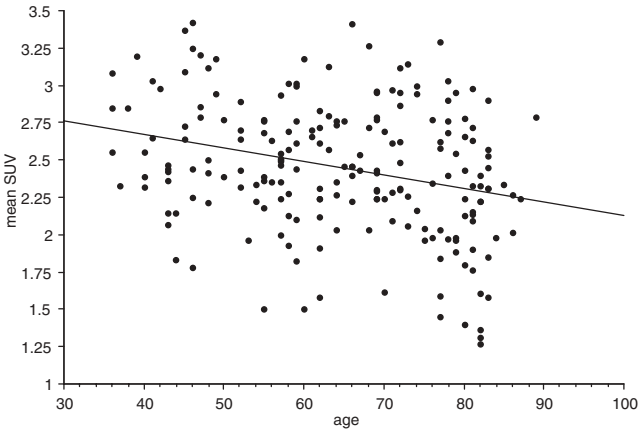

Fig. 2 Correlation between mean SUV of the bilateral testes and age in 203 men. A weak, but significant negative correlation is observed ($r = –0.284$, $P < 0.0001$)

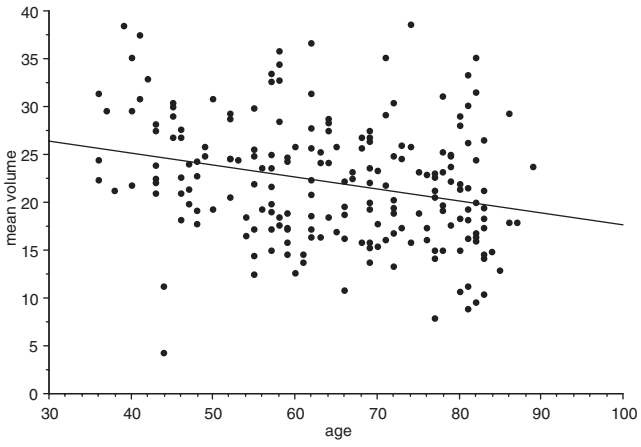

Fig. 3 Correlation between mean testicular volume and age. A weak, but significant negative correlation is observed ($r = –0.269$, $P = 0.0001$)

glucose level did not correlate with the mean SUV of bilateral testes ($r = –0.065$, $P = 0.358$).

Testicular volume and age

The relationship between testicular volume and age in 406 testes is summarized in Table 1. The mean ± standard deviation (minimum–maximum) volume of 406 testes in the 203 men was 22.1 ± 6.4 cm^3 (3.8–41.5): 27.9 ± 6.6 (19.2–41.1) in group A ($n = 12$), 24.5 ± 6.9 (3.8–41.5) in group B ($n = 64$), 22.8 ± 6.9 (12.3–38.1) in group C ($n = 82$), 21.6 ± 6.4 (9.6–39.2) in group D ($n = 86$), 21.7 ± 7.9 (10.5–35.4) in group E ($n = 86$), and 20.0 ± 7.7 (8.2–35.7) in group F ($n = 76$). When we calculated the mean SUV of bilateral testes in each patient, there were significant statistical differences between group B and group F in comparison with the Bonferroni correction. As shown in Fig. 3, the correlation between the mean volume of bilateral testes and age in the 203 men was statistically significant ($r = –0.269$, $P = 0.0001$).

SUV and testicular volume

The correlation between the mean SUV and mean volume of bilateral testes in the 203 men was statistically significant ($r = +0.368$, $P < 0.0001$).

Discussion

There has been one report on normal FDG uptake in testis [8], which demonstrated a statistically significant negative correlation between testicular uptake and age over 50 years, and that higher glucose metabolism in the testes of younger men might result in higher FDG uptake in their testes. According to our results on the basis of a larger number of data sets, a weak, but significant negative correlation between SUV and patient age was observed, which was consistent with the earlier report.

As there was a weak negative correlation between testicular volume and age, the effect of testicular volume was adjusted for. The partial correlation coefficient between SUV and age adjusted for volume was –0.206 ($P < 0.0005$, partial F test). Therefore, a part, but not all of the correlation between SUV and age may be attributed to age-associated atrophy and partial volume effect. Because the longitudinal length of the testis at the slice where maximal SUV is expressed is more than 20 mm in most patients, the partial volume effect may be small.

The laterality of bilateral testicular uptake was low in this study, as the laterality index in the 203 men was 0.066 ± 0.067 (0–0.522) with 95% of the subjects below 0.193. Laterality above this range may indicate a pathological process and requires further examination.

The testis is divided into the seminiferous tubules and interstitial tissue separated by the septum. The seminiferous tubules comprise germinal elements, spermatozoa, sertoli cells, and epithelium, and take up 70%–80% of the total testicular volume [10]. The interstitial tissue comprises Leydig cells producing testosterone, mast cells, macrophages as well as nerves and blood and lymph vessels, and takes up 20%–30% of the total testicular volume. In a healthy young man, the ovoid testis measures 15 ml to 25 ml [11] or 12 ml to 18 ml [12] in volume and has a longitudinal length of approximately 4.3 cm to 4.6 cm [13]. The volume of total testis is gradually reduced at ages greater than 50 years because of age-related reductions in total volume of seminiferous tubules, length of tubules, seminiferous epithelium volume, germinal elements [14–16], and the volume and

number of Leydig cells [17, 18]. Generally, reduced serum testosterone concentration is a hallmark of aging [19, 20], and it is known that the decreases in serum testosterone are accompanied by a constellation of symptoms, sometimes termed andropause, that includes sexual dysfunction, lack of energy, loss of muscle and bone mass, increased frailty, loss of balance, and cognitive impairment [21]. The reduced ability of aged Leydig cells of the testis to produce testosterone most likely results from defects in the luteinizing hormone (LH) signaling pathway leading to reduced cyclic adenosine monophosphate [22]. It has been reported by Amrolia et al. [23] that Leydig cells can take up glucose to produce testosterone by a transport system that appears to be similar to the facilitated-diffusion system of glucose uptake in most other mammalian cells. Therefore, reduced FDG uptake in the testis in elderly men may be caused by the reduced production ability of aged Leydig cells and also aging which decreases the number of Leydig cells. The mechanism by which Leydig cells become steroidigenically hypofunctional with age is still uncertain, although some researchers documented that the mechanism is because of factors such as impaired perfusion and metabolism [18, 24] and inefficient signal transduction [25].

Although there have been two reports on FDG uptake of retroperitoneal lymph node in testicular tumor before therapy [26, 27], there have been no reports of documenting SUV of testicular tumor before therapy. These two reports revealed that SUV of metastatic lymph nodes ranged from 1.8 to 17.3. The analysis of FDG uptake of testicular tumor before therapy is the next important step.

There are some limitations in this study. First, although we included only patients in whom no apparent disease of the testis had been detected on CT images and by clinical records, the population may have included subjects with pathological conditions. However, even if pathological testis were included, the percentage should be low and would not affect the statistical results. Second, only six of the subjects were aged below 40, and there were no teenagers or subjects in the 20–29 years age group. Although a negative correlation might have arisen if there had been more young subjects, we believe that this population was quite representative of men who are referred for clinical PET.

Conclusions

Some uptake of FDG is observed in the normal testis, and faintly declines with age. This physiological FDG uptake should not be confused with pathological accumulation.

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