Accumulation of [11C]acetate in normal prostate and benign prostatic hyperplasia: comparison with prostate cancer

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Received 10 August 2001 and in revised form 7 May 2002 / Published online: 21 August 2002

Abstract. Carbon-11 acetate positron emission tomography (PET) has been reported to be of clinical value for the diagnosis of prostate cancer. However, no detailed analysis has yet been carried out on the physiological accumulation of [11C]acetate in the prostate. The purpose of this study was to elucidate the physiological accumulation of [11C]acetate in the prostate using dynamic PET. The study included 30 subjects without prostate cancer [21 with normal prostate and nine with benign prostatic hyperplasia (BPH)] and six patients with prostate cancer. A dynamic PET study was performed for 20 min after intravenous administration of 555 MBq of [11C]acetate. The standardised uptake value (SUV) at 16–20 min post tracer administration and the early-to-late-activity ratio of the SUV (E/L ratio), which was determined by dividing the $SUV_{6–10\ min}$ by the $SUV_{16–20min}$, were calculated to evaluate the accumulation of [11C]acetate. The prostate was clearly visualised and distinguished from adjacent organs in PET images in most of the cases. The SUV of the prostate (2.6±0.8) was significantly higher than that of the rectum (1.7±0.4) or bone marrow (1.3±0.3) (P<0.0001 in each case). The SUV of the normal prostate of subjects aged <50 years (3.4±0.7) was significantly higher than both the SUV for the normal prostate of subjects aged ≥50 years (2.3±0.7) and that of subjects with BPH (2.1±0.6) (P<0.01 in each case). The primary prostate cancer in six cases was visualised by [11C]acetate PET. However, the difference in the SUV between subjects aged ≥50 with normal prostate or with BPH and the patients with prostate cancer (1.9±0.6) was not statistically significant. There was also no significant difference in the E/L ratio between subjects aged ≥50 with normal prostate (0.98±0.04) or BPH (0.96±0.08) and patients with prostate cancer (1.02±0.12). In conclusion, a normal prostate exhibits age-related physiological accumulation of [11C]acetate. Careful interpretation of [11C]acetate PET images of prostate cancer is necessary because the SUV and the E/L ratio for the normal prostate and for BPH overlap significantly with those for prostate cancer.

Keywords: Prostate – Prostate cancer – [11C]acetate – PET

Eur J Nucl Med (2002) 29:1492–1495
DOI 10.1007/s00259-002-0885-3

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Introduction

Carbon-11 acetate is a promising tracer for estimation of the growth activity of tumour cells. Positron emission tomography (PET) using [11C]acetate has been expected to serve as a means of assessing malignant tumours [1]. Recently, [11C]acetate PET has been reported to be of clinical value for the diagnosis of prostate cancer [2]. However, to the best of our knowledge, no detailed analysis of the physiological accumulation of [11C]acetate in the prostate has yet been carried out. Without knowledge of the physiological accumulation of [11C]acetate in the prostate, accurate diagnosis of prostate cancer is not possible by means of [11C]acetate PET. The purpose of this study was to elucidate the physiological accumulation of [11C]acetate in the prostate using dynamic PET.

Materials and methods

Subjects and patients. This study included 19 healthy male volunteers without a history of urological disease or symptoms of pollakiuria or ischuria, and 11 patients with malignant tumours (seven with oesophageal cancer, two with pancreatic cancer, one with colon cancer and one with gastric cancer) who had no history of prostate cancer and no malignant findings in the pelvis on computed tomography (CT). The serum PSA levels of all 30 subjects were within the normal range. Among these subjects, nine were suffering from benign prostatic hyperplasia (BPH), confirmed by palpation by an experienced urologist. In addition, six patients with prostate cancer were studied. Five of them were diagnosed as having prostate cancer by histopathology of biopsy specimens. In the remaining patient, a final diagnosis of prostate cancer was made on the basis of clinical findings. All volunteers except one underwent magnetic resonance imaging (MRI) of the pelvis within 1 month of the PET study to obtain anatomical information. In all the patients, correlative CT of the pelvis was performed within 4 weeks before PET study. Written informed consent to participation in the study was obtained from all participants before the study. The study was approved by the ethical committee of Hokkaido University Graduate School of Medicine.

Imaging. PET was performed using an ECAT Exact 47 scanner (Siemens-CTI, Knoxville, Tenn.). All the subjects and patients fasted for more than 4 h before the PET study. Transmission scanning using externally rotating germanium-68 rod sources was performed for attenuation correction before tracer administration. After intravenous injection of 555 MBq of [^{11}C]acetate, dynamic imaging of the pelvis was performed for 20 min with ten 30-s frames and fifteen 60-s frames.

Analysis. Attenuation- and decay-corrected images were reconstructed by standard filtered back-projection using a Hann filter. The region of interest (ROI) was placed over the prostate or prostate cancer on the merged image obtained at 16–20 min post tracer administration in the dynamic PET study (area of 50% cut-off of maximal count). The MRI or CT images were compared with the PET images to aid in locating the ROI of the prostate or prostate cancer. Two parameters for evaluating the accumulation of [^{11}C]acetate in the prostate were calculated. First, the mean standardised uptake value (SUV = decay-corrected activity concentration/injected dose/body weight) at 16–20 min post tracer administration was calculated within an ROI. Second, the early-to-late activity ratio of SUV (E/L ratio) was calculated by dividing the $SUV_{6–10\ min}$ by the $SUV_{16–20\ min}$. The SUVs and E/L ratios of the rectum, bladder and bone marrow of the pubic bone were obtained in the same manner as for the prostate. The 30 subjects without prostate cancer were divided into three groups as follows: those aged <50 years with normal prostate, those aged ≥50 years with normal prostate and those with BPH. All results are represented as means ± standard deviation, and the Mann-Whitney test was applied to determine the significance of differences. A value of $P<0.05$ was considered statistically significant.

Results

In [^{11}C]acetate PET images, the prostate was clearly distinguished from adjacent organs in most cases (Figs. 1, 2). Table 1 shows the SUV and E/L ratio of each organ. The SUV of the prostate was significantly higher than that of the rectum or bone marrow ($P<0.0001$ in each case). Although there was no significant difference between the SUV of the prostate and bladder, the E/L ratio of the prostate was significantly higher than that of the bladder ($P<0.0001$) (Table 1). Table 2 shows the SUV and E/L ratio of the prostate of each group. The SUV of the normal prostate in subjects aged <50 was significantly higher than the SUVs for subjects aged ≥50 and for those with BPH ($P<0.01$ in each case) (Table 2). There was no significant difference in the SUV or E/L ratio between subjects aged ≥50 with normal prostate and those with BPH (Table 2).

The characteristics of the six patients with prostate cancer are shown in Table 3. In three of them, multiple bone metastases were detected by bone scintigraphy, and one of them had lymph node metastasis detected by CT of the pelvis (Fig. 3). The primary prostate cancer in these six cases was visualised by [^{11}C]acetate PET (Fig. 3). However, the difference in the SUV or E/L ratio between subjects aged ≥50 with normal prostate or those with BPH and the patients with prostate cancer was not statistically significant (Table 2).

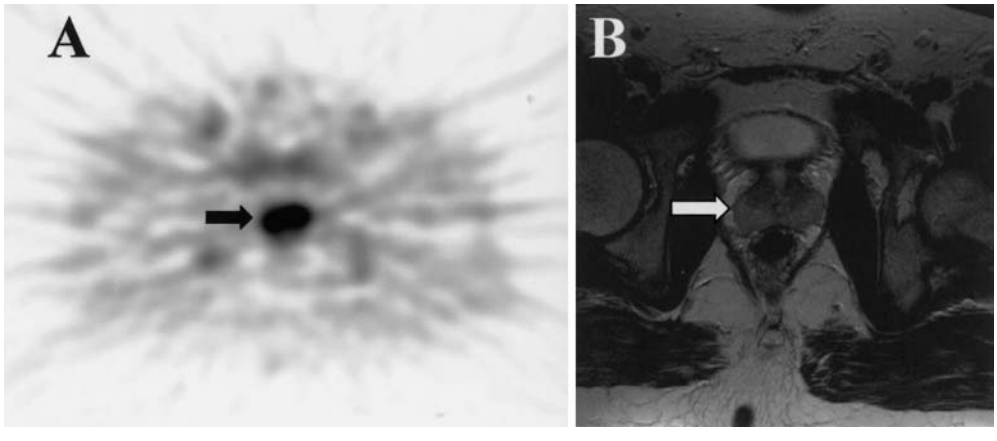

Fig. 1. A [^{11}C]acetate PET image of a 26-year-old normal volunteer. The prostate is clearly visualised (*black arrow*) (SUV=4.4). **B** Corresponding T2-weighted MRI shows no abnormality of the prostate (*white arrow*)

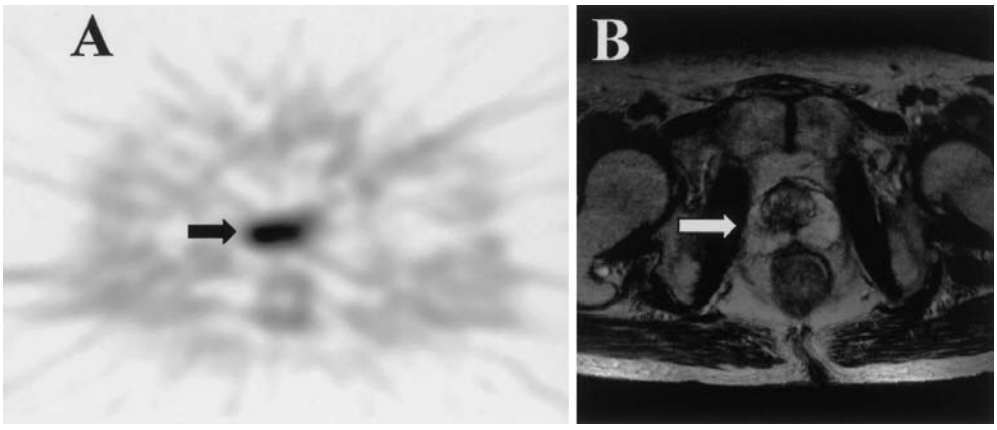

Fig. 2. A [^{11}C]acetate PET image of an 85-year-old patient with BPH. The prostate is clearly visualised (*black arrow*) (SUV=2.9). **B** Corresponding T2-weighted MRI shows enlargement of the central gland of the prostate which is compatible with BPH (*white arrow*)

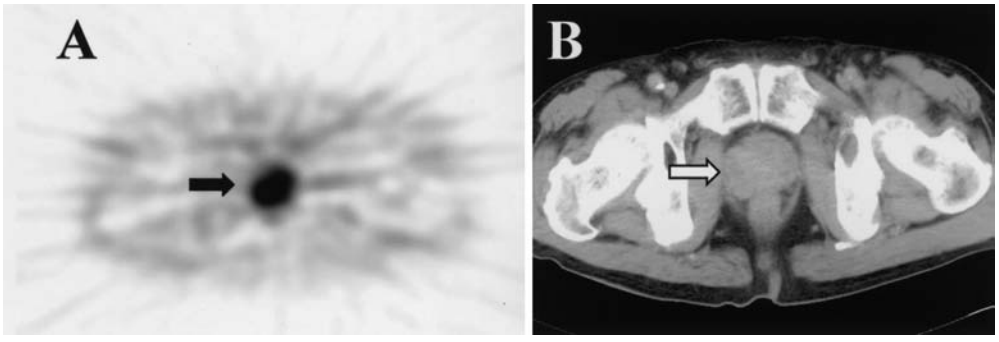

Fig. 3. A [^{11}C]acetate PET image (**A**) of an 83-year-old patient with prostate cancer. The prostate cancer is clearly visualised (*black arrow*) (SUV=2.1). **B** Corresponding CT image shows irregular swelling of the prostate which is indicative of prostate cancer (*white arrow*)

Table 1. SUV and E/L ratio of each organ in the 30 subjects with normal prostate or BPH

	SUV	E/L ratio
Prostate	2.6±0.8*	0.98±0.07
Rectum	1.7±0.4	0.92±0.06
Bladder	3.2±2.0	0.53±0.23**
Bone marrow	1.3±0.3	0.97±0.07

* The SUV of the prostate was significantly higher than that of the rectum or bone marrow (P<0.0001 in each case)
** The E/L ratio of the bladder was significantly lower than that of the prostate, rectum or bone marrow (P<0.0001 in each case)

Table 2. SUVs and E/L ratios of normal prostate, BPH and prostate cancer

	No.	Age (yrs)	SUV	E/L ratio
Normal prostate				
Age <50 yrs	10	35±8	3.4±0.7*	0.98±0.11
Age ≥50 yrs	11	61±7	2.3±0.7	0.98±0.04
BPH	9	70±8	2.1±0.6	0.96±0.08
Prostate cancer	6	74±8	1.9±0.6	1.02±0.12

* The SUV of normal prostate of subjects aged <50 years was significantly higher than the SUVs of subjects aged ≥50 years, subjects with BPH and patients with prostate cancer

Table 3. Characteristics of the six patients with prostate cancer

Patient no.	Age (yrs)	Pathology of primary tumour	Metastasis	PSA (ng/ml)	SUV
1	64	Adenocarcinoma	Multiple bone metastases[a]	3630.5	1.2
2	82	Not determined	Multiple bone metastases[a]	6954.8	1.2
3	83	Adenocarcinoma	Multiple bone metastases[a] Lymph node metastasis[b]	142.1	2.1
4	70	Adenocarcinoma	No metastasis	6.7	2.0
5	76	Adenocarcinoma	No metastasis	6.9	2.7
6	67	Adenocarcinoma	No metastasis	0.3	2.4

[a] Bone metastasis was detected by bone scintigraphy
[b] Lymph node metastasis was detected by CT

Discussion

This study indicates that a normal prostate or BPH can show enhanced accumulation of [^{11}C]acetate, especially in younger subjects. Since the SUV or E/L ratio of the physiological accumulation of [^{11}C]acetate in the normal prostate or BPH overlaps with that in prostate cancer, careful interpretation of [^{11}C]acetate PET images of prostate cancer is necessary.

Fluorine-18 fluoro-2-deoxy-D-glucose (FDG) PET has been shown to be a useful modality for the evaluation of several malignant tumours such as lung cancer, colorectal cancer and malignant lymphoma. However, Effert et al. [3] reported that there is low FDG uptake in untreated primary prostate cancer and that significant overlap exists between the FDG uptake values for prostate cancer and those for BPH. In addition, FDG-PET has been suggested not to be sensitive for the detection of metastases of prostate cancer [4, 5]. Another problem in using FDG-PET to evaluate the pelvic region is the high residual FDG activity in the bladder [3, 4]. The advantages of [^{11}C]acetate over FDG are (a) that [^{11}C]acetate is not excreted by the kidney [6] and (b) a small amount of tracer accumulation in the bladder may improve the quality of PET images of the pelvis. Although accumulation of [^{11}C]acetate in the bladder was shown in the PET images in our study, differentiation of uptake between the bladder and prostate cancer was not difficult because there was no accumulation in the bladder in the early phase of images (less than 10 min post tracer administration). Thus, [^{11}C]acetate is expected to be suitable as a new tracer for prostate cancer imaging.

Although the mechanism of acetate turnover in a normal prostate has not yet been fully evaluated, the pathways of lipid synthesis in the prostate gland may account for the long retention of the tracer in the prostate. In an in vivo study of rats, [^{14}C]acetate incorporation into free and esterified cholesterol in the ventral prostate was demonstrated [7]. In a [^{11}C]acetate PET study, the lipid synthetic pathway in acinar tissues of the pancreas was considered to cause the retention of tracer activity in the pancreas for more than 10 min post tracer administration[8].

In our study, normal prostate showed age-related accumulation of [^{11}C]acetate. The human prostate undergoes age-related histological changes. Berry et al. [9] reported that the prevalence of pathological BPH is only 8% in males in their 40s, but 50% in those aged 51–60 years. In our results, there was no significant difference in the SUV between subjects aged ≥50 with normal prostate and those with BPH. Although we did not perform histological evaluation of normal prostate or BPH, age-related accumulation of [^{11}C]acetate could not be explained by BPH only.

Some organs such as the kidney [6] or nasopharynx [10] have an [^{11}C]acetate turnover rate that is different from that of malignant tumour. Long retention of [^{11}C]acetate for more than 10 min post tracer administration is characteristic of renal cell carcinoma [6] and nasopharyngeal carcinoma [10]. However, the results of this study indicate that differentiation between normal tissue and prostate cancer is difficult because long retention of [^{11}C]acetate was observed in both normal prostate and prostate cancer. In addition, there was no significant difference in the SUV between subjects aged ≥50 with normal prostate or those with BPH and patients with prostate cancer. The number of patients with prostate cancer investigated in this study was small; further studies involving more patients are thus needed to confirm our results.

In conclusion, our preliminary results indicate that careful interpretation of [^{11}C]acetate PET images of prostate cancer is necessary because the SUVs and E/L ratios for normal prostate and BPH overlap significantly with those for prostate cancer. Elucidation of the physiological accumulation of [^{11}C]acetate in the prostate may lead to more effective application of [^{11}C]acetate PET for the diagnosis of prostate cancer.

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