

First imaging results of an intraindividual comparison of ^{11}C -acetate and ^{18}F -fluorocholine PET/CT in patients with prostate cancer at early biochemical first or second relapse after prostatectomy or radiotherapy

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Abstract

Purpose ^{18}F -Fluorocholine (FCH) and ^{11}C -acetate (ACE) PET are widely used for detection of recurrent prostate cancer (PC). We present the first results of a comparative, prospective PET/CT study of both tracers evaluated in the same patients presenting with recurrence and low PSA to compare the diagnostic information provided by the two tracers.

Methods The study group comprised 23 patients studied for a rising PSA level after radical prostatectomy (RP, 7 patients, PSA ≤ 3 ng/ml), curative radiotherapy (RT, 7 patients, PSA ≤ 5 ng/ml) or RP and salvage RT (9 patients, PSA ≤ 5 ng/ml). Both FCH and ACE PET/CT scans were performed in a random sequence a median of 4 days (range 0 to 11 days) apart. FCH PET/CT was started at injection (307 ± 16 MBq) with a 10-min dynamic acquisition of the prostate bed, followed by a whole-body PET scan and late (45 min) imaging of the

pelvis. ACE PET/CT was performed as a double whole-body PET scan starting 5 and 22 min after injection (994 ± 72 MBq), and a late view (45 min) of the prostate bed. PET/CT scans were blindly reviewed by two independent pairs of two experienced nuclear medicine physicians, discordant subgroup results being discussed to reach a consensus for positive, negative end equivocal results.

Results PET results were concordant in 88 out of 92 local, regional and distant findings (Cohen's kappa 0.929). In particular, results were concordant in all patients concerning local status, bone metastases and distant findings. Lymph-node results were concordant in 19 patients and different in 4 patients. On a per-patient basis results were concordant in 22 of 23 patients (14 positive, 5 negative and 3 equivocal). In only one patient was ACE PET/CT positive for nodal metastases while FCH PET/CT was overall negative; interestingly, the ACE-positive and FCH-negative lymph nodes became positive in a second FCH PET/CT scan performed a few months later.

Conclusion Overall, ACE and FCH PET/CT showed excellent concordance, on both a per-lesion and a per-patient basis, suggesting that both tracers perform equally for recurrent prostate cancer staging.

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Introduction

Promising results in the detection of recurrent prostate cancer (PC) have been obtained with different PET tracers such as ^{11}C -acetate (ACE), ^{11}C -choline, and ^{18}F -fluorocholine (FCH) [1, 2]. Prostate-specific antigen (PSA) is a sensitive early blood

marker for PC recurrence particularly after radical prostatectomy (RP) when PSA is expected to become undetectable. After surgery recurrence of cancer can be suspected at the earliest rise in PSA [3, 4]. PSA values of between 0.01 and 0.1 ng/ml after RP represent a probability for a further rise in PSA and tumour recurrence of 67 %, and this probability rises to 90 % with PSA values >0.1 ng/ml [5]. After primary radiation therapy (RT), a PSA value ≥ 2 ng/ml above the nadir is a robust standard for recurrence reliably predicting distant metastases, and cause-specific and overall mortality [6].

In this study we compared the performance of ACE and FCH for diagnosing early recurrent PC by assessing the correlation between the blinded reading of the two imaging sets. Early localization of recurrences might allow a still curative salvage treatment to be undertaken [7], although a consensus has not yet been defined for the indication for PET/CT in this situation [8–10]. Our group favours PET/CT very early after the definition of recurrence. Having experience with both ACE [11] and FCH [12–14], we aimed to evaluate both tracers in a comparative assessment to determine if one is superior to the other in the setting of early biochemical recurrence of PC.

Materials and methods

This prospective feasibility study was approved by the Ethics Committee of the University Hospital of Geneva, Swissmedic and OFSP, Section of Radioprotection, and was performed in conformance with Swiss legislation and Good Clinical Practice (GCP) rules and with the ethical standards of the Declaration of Helsinki and later amendments. All patients provided written informed consent to the study protocol foreseeing two PET/CT scans, one with FCH and the other with ACE in random order. In case of positive findings, the patients were investigated by complementary imaging (MR, bone scintigraphy) and biopsying the suspected local relapse, when indicated and feasible.

Patients

Up to the time of this report, 23 patients had been studied. The patients' characteristics are summarized in Table 1.

Inclusion criteria were:

- biochemical relapse after RP (group A), curative RT with or without androgen deprivation (AD, group B) or RP and salvage RT (with or without AD, group C)
- PSA values ≤ 3 ng/ml for group A and C and ≤ 5 ng/ml for group B
- signed written informed consent

Exclusion criteria were:

- patients under AD

- patients with active major inflammatory/infectious process

Compliance with further investigations (biopsy of suspected recurrence, complementary MR and bone scintigraphy) was not an inclusion criterion. Seven patients were included in group A, 7 in group B and 9 in group C. Mean PSA values at study entry were lowest in group A (1.1 ± 0.9 ng/ml), highest in group B (3.5 ± 0.9 ng/ml), and intermediate in group C (2.4 ± 1.0 ng/ml).

Dual PET/CT studies

FCH and ACE PET/CT studies were performed according to a random sequence in 21 patients, while 2 patients had both PET/CT scans performed on the same day (ACE in the morning and FCH in the afternoon, the two studies separated by a minimum of 2.5 h). The median interval between the two scans was 4.0 days (range 0 to 11 days).

^{18}F -Fluorocholine PET/CT

FCH (*N,N*-dimethyl-*N*-[^{18}F]fluoromethylethanolammonium) was prepared according to GMP rules at AAA (Advanced Accelerator Applications), St Genis-Pouilly, France.

Dual PET/CT studies were performed on either a Biograph 64 scanner (18 patients) or a Biograph 16 scanner (5 patients) (Siemens Medical Solutions, Erlangen, Germany). All patients fasted for at least 4 h before the FCH and ACE PET studies. After bladder voiding, patients underwent an initial low-dose CT scan from the mid thigh to the skull performed under a standard protocol (arms held above the head and shallow breathing) using 120 kVp, 60 mAs, pitch 1.5 and 1 s per rotation. Under these conditions, the mean effective radiation dose for an adult patient was estimated at 4.5 mSv, as calculated using the IMPACT CT patient dosimetry calculator (<http://www.impactscan.org/ctdosimetry.htm>).

After the CT scan, patients received a standard activity of 307 ± 16 MBq ^{18}F -FCH injected intravenously, and a continuous list-mode PET acquisition centred on the prostate bed was recorded over 10 min starting immediately with the tracer injection. The 10-min list mode data were used for generating 3×3 -min time frames corresponding to 0 to 3 min, 3 to 6 min and 6 to 9 min after injection. Following the list-mode acquisition, a standard whole-body PET study was performed from the mid thigh to the skull over seven to eight bed positions of 3 to 4 min each depending on patient size and weight. Two additional late images of 5 min each of the pelvis were acquired immediately after the whole-body PET scan (about 45 min after tracer injection).

Following Fourier rebinning and model-based scatter correction, PET images were reconstructed using two-dimensional iterative normalized attenuation-weighted

Table 1 Characteristics of 23 patients according to initial treatment

| Characteristic | Radical prostatectomy | Primary radiotherapy with or without androgen deprivation | Radical prostatectomy and salvage radiotherapy |
|--------------------------------|-----------------------|---|--|
| Number of patients | 7 | 7 | 9 |
| Age (years) | | | |
| Mean | 67.4 | | |
| SD | 7.5 | | |
| Range | 51.0 to 80.4 | | |
| Initial stage, <i>n</i> | | | |
| T1c | 0 | 1 | 0 |
| T2a | 0 | 1 | 0 |
| T2b | 0 | 1 | 1 |
| T2c | 6 | 0 | 2 |
| T3a | 0 | 3 | 3 |
| T3b | 1 | 1 | 3 |
| Gleason score summed, <i>n</i> | | | |
| 6 (low grade) | 2 | 1 | 1 |
| 7 (intermediate grade) | 4 | 4 | 4 |
| 8 or 9 (high grade) | 1 | 2 | 4 |
| PSA (ng/ml) | | | |
| At diagnosis | | | |
| Mean | 11.1 | 20.3 | 15.7 |
| SD | 4.8 | 7.7 | 9.5 |
| Nadir | | | |
| Mean | 0.1 | 0.7 | 0.2 |
| SD | 0.2 | 0.7 | 0.2 |
| At PET | | | |
| Mean | 1.1 | 3.5 | 2.4 |
| SD | 0.9 | 0.9 | 1.0 |

ordered subsets expectation maximization (NAW-OSEM) [15]. The CT-based attenuation map was used to correct emission data. The default reconstruction parameters of four iterations and eight subsets followed by a postprocessing gaussian filter (kernel size 5 mm, full-width at half-maximum) were applied. Images of the three phases of FCH PET/CT are shown in Fig. 1.

¹¹C-Acetate PET/CT

ACE was prepared at the Cyclotron Unit, University Hospital of Geneva, according to GMP rules. For the ACE PET/CT scan, which was identical to the FCH PET scan performed either on the Biograph 64 (18 patients) or the Biograph 16 (5 patients), patients fasted for at least 4 h before the study. After bladder voiding, patients received a standard activity of 994 ± 72 MBq ACE injected intravenously. After ACE injection they underwent a low-dose CT scan from the mid thigh to the skull performed under identical conditions to those used for the FCH PET scan using 120 kVp, 60 mAs, pitch 1.5 and 1 s per rotation.

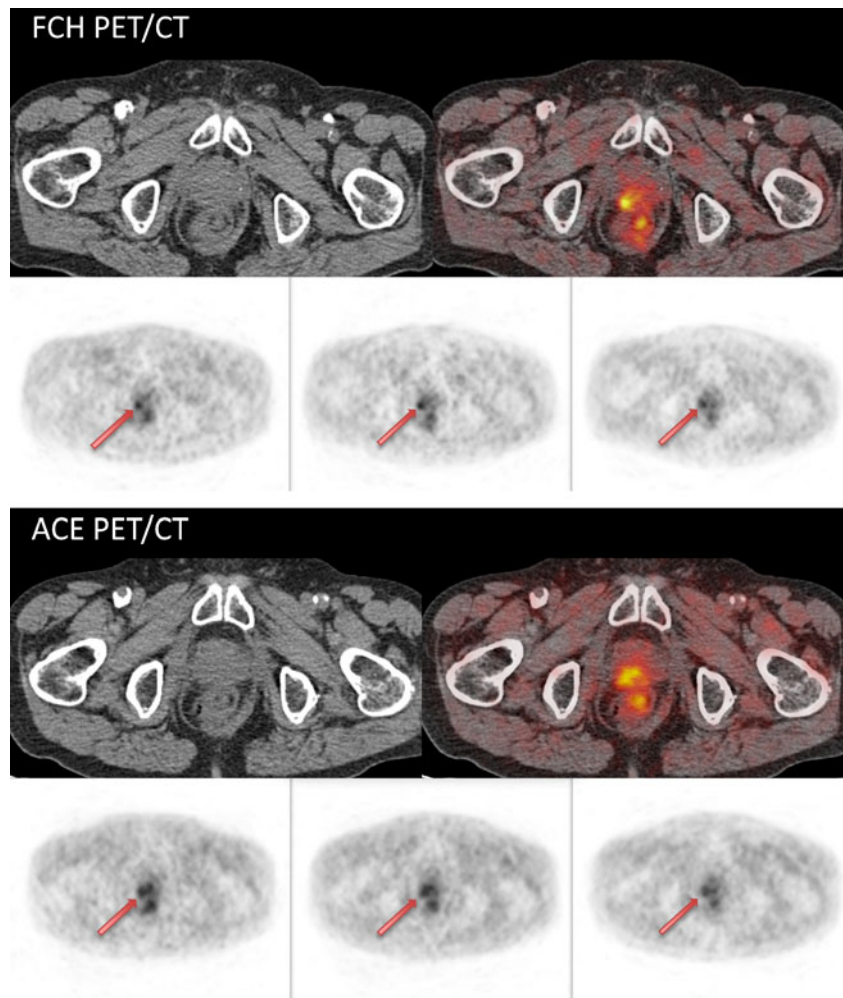
A first whole-body PET study was performed 5 min after tracer injection from the mid thigh to the skull over seven to

eight bed positions of 2 min each, followed immediately (about 22 min after injection) by a second whole-body PET scan of 3 min per bed position and finally a late PET scan of the prostate bed was recorded about 45 min after injection. ACE PET images were reconstructed using the same procedure described above for FCH PET. Images of the three phases of ACE PET/CT are shown in Fig. 1.

PET/CT interpretation

Each patient's PET/CT scans were interpreted blindly by two pairs of two experienced nuclear medicine physicians who graded either the FCH or ACE PET scans for the presence of recurrent tumour as positive, equivocal or negative. FCH PET scans were graded according to the typical time-course of activity in malignant and benign lesions. Focal FCH hyperactivity above background that persisted throughout the examination with typical kinetics was considered a positive lesion [13]. For the ACE PET scans, focal ACE hyperactivity confirmed in the first and second whole-body scan was considered positive. The third ACE acquisition centred on the prostate bed was not retained for interpretation since hyperactivities decreased in all patients to a

Fig. 1 Three-phase FCH and three-phase ACE PET/CT showing concordant local recurrence (*arrows*)



marked degree. Negative ACE and FCH PET scans were those that did not show any focal persistent activity higher than background. Equivocal was defined as any lesion with an activity between the two categories “positive” and “negative”.

Specifically:

- Local relapses corresponded to focal, persistent uptake over the three FCH sequences and the two ACE sequences in the prostate or prostatic bed. In order to avoid possible interference of bladder activity, particularly for FCH PET, on the assessment of local relapse after RP, we systematically assessed early dynamic images acquired before urine accumulation [13].
- Lymph nodes were considered positive if they showed persistent uptake over the three FCH sequences and the two ACE sequences, higher than surrounding tissue. Inguinal lymph nodes that showed transient tracer uptake and presenting a lipid centre on CT were interpreted as negative.
- CT images were used for localization and morphological analysis, discriminating between intestinal and lymph node uptakes and allowing the characterization of lesions,

such as bone hypodensity or hyperdensity and lung nodules.

Maximum standard uptake values (SUVmax) were calculated within regions of interest drawn over focal hyperactivities using a standard formula [16]. The reported values were measured on the whole-body FCH PET/CT study and on the first whole-body ACE PET/CT study. SUVmax values were evaluated since SUVmax is widely used in the literature and because it is not dependent on lesion size or operator. Since the two PET/CT scanners used in this study were from the same provider (Siemens) and had been installed simultaneously, and acquisition, treatment protocols and software evaluation were identical, images and SUV calculations were comparable.

To compare the quantitative information provided by the two PET/CT scanners, we report the SUVmax of the positive lesions found in the two studies. In order to provide a measure of the contrast provided by the ACE and FCH PET images we also calculated target-to-background ratios (TBR). As a background measure with a high reproducibility across studies we chose the blood-pool activity in the abdominal aorta.

Table 2 PET results in 23 patients with relapse (on a per-patient basis) according to initial treatment and PSA value at the time of the PET scan

| PSA (ng/ml) | Radical prostatectomy | | | Primary radiotherapy with or without androgen deprivation | | Radical prostatectomy and salvage radiotherapy | | | All | | | |
|-------------|-----------------------|-----------|----------|---|-----------|--|----------|----------------|-----------|-----------|----------|------------|
| | Positive | Equivocal | Negative | Positive | Equivocal | Positive | Negative | Discordant | Positive | Equivocal | Negative | Discordant |
| <1 | 2 | 1 | 2 | | | 1 | | | 3 (50 %) | 1 | 2 | |
| 1–3 | | | 2 | 2 | | 4 | 1 | | 6 (67 %) | | 3 | |
| >3–5 | – | | | 3 | 2 | 2 | | 1 ^a | 5 (63 %) | 2 | 0 | 1 |
| All | 2 | 1 | 4 | 5 | 2 | 7 | 1 | 1 | 14 (61 %) | 3 | 5 | 1 |

^a Patient positive on ACE PET/CT and negative on FCH PET/CT

Furthermore, a Jaszack phantom-based calibration was carried out to ensure compatibility between the two scanners. A radiologist interpreted the low-dose CT scans for distant sites.

Standard of reference

All findings were evaluated on both PET and CT images acquired in the same session. Thus, CT images without contrast enhancement were consistently available and allowed identification of lymph nodes and distant unrelated findings. As mentioned above, if findings were positive complementary imaging with MR and bone scintigraphy and biopsies of the suspected local recurrences were performed, when indicated and feasible. Planned patient follow-up was 2 years, and at the time of this report follow-up was ongoing with a current median of 11 months (range 1 to 20 months).

Statistical analysis

We measured the agreement between the two tracers considering the results of each imaging test as positive, negative or equivocal for local recurrence, locoregional nodal status, bone metastasis and other distant findings (lung and other organs),

by using Cohen's kappa coefficient [17]. We also used Cohen's kappa to evaluate agreement between the two readers interpreting the ACE PET and FCH PET data. SUVmax and TBRs obtained for positive lesions in the two PET/CT studies were compared using a paired Student's *t* test.

Results

Overall, we observed remarkable agreement between the two PET/CT imaging procedures, with a Cohen's kappa of 0.929 (above the suggested cut-off of 0.8 [18]). The interrater agreement was slightly lower for ACE (0.657) than for FCH (0.771), but in both cases was above the conventionally accepted threshold of 0.6 for substantial interrater agreement [18].

For both PET/CT studies, positive, equivocal, or negative results on a per-patient basis were identical in 22 patients (Table 2). In only one patient was an ACE PET/CT scan positive for nodal metastases while the corresponding FCH PET/CT scan was negative. In a second FCH PET/CT scan performed a few months later (once the PSA value had increased from 3.84 to 15 ng/ml), the previously negative lymph nodes this time showed tracer take-up reproducing the positive result of the previous ACE

Table 3 PET results in 23 patients with relapse (on a per-patient basis) according to initial treatment and PSA doubling time

| PSA doubling time (months) | Radical prostatectomy | | | Primary radiotherapy with or without androgen deprivation | | Radical prostatectomy and salvage radiotherapy | | | All | | | |
|----------------------------|-----------------------|-----------|----------|---|-----------|--|----------|------------|-----------|-----------|----------|------------|
| | Positive | Equivocal | Negative | Positive | Equivocal | Positive | Negative | Discordant | Positive | Equivocal | Negative | Discordant |
| <5 | | 1 | 2 | | | 4 | | 1 | 4 (50 %) | 1 | 2 | 1 |
| 5–10 | | | 1 | 3 | | 3 | 1 | | 6 (75 %) | | 2 | |
| >10 | 2 ^a | | 1 | 2 | 2 | | | | 4 (57 %) | 2 | 1 | |
| All | 2 | 1 | 4 | 5 | 2 | 7 | 1 | 1 | 14 (61 %) | 3 | 5 | 1 |

^a Two patients in the surgery group had a positive PET scan (one local, one adenopathy) while presenting with particularly high doubling times of 86 and 35 months and low PSA of 0.96 and 0.4 ng/ml

Table 4 PET results according to localization and concordance between ACE and FCH PET expressed as the numbers of double-positive, double-equivocal, double-negative and discordant PET results per site

| Recurrence | Concordant PET results | | | Discordant PET results | Total per site |
|-----------------------|------------------------|----------------|---------------|------------------------|----------------|
| | Both positive | Both equivocal | Both negative | | |
| Local | 6 | 3 | 14 | 0 | 23 |
| Lymph node | 9 | 2 | 8 | 4 | 23 |
| Bone metastasis | 2 | 0 | 21 | 0 | 23 |
| Total | 17 ^a | 5 | 43 | 4 | 69 |
| Unrelated pathologies | 4 ^b | 0 | 19 | 0 | 23 |

^a Two patients were simultaneously double-positive for lymph nodes and bone metastases, one patient simultaneously had a double-positive local recurrence and lymph nodes. With regard to Tables 2 and 3, a total of 14 patients had double-positive PET results.

^b Three concordant hyperactivities unrelated to PC were observed in one hypophysis, one thyroid and one lung.

PET/CT scan. PET double positivity was lowest in patients with PSA <1 ng/ml, with three of six patients being positive in this subgroup. A higher positivity rate was observed in those with a PSA value between 1 and 3 ng/ml (67 % positive) and a PSA value between 3 and 5 ng/ml (63 % positive). A correlation between double PET positivity rate and PSA doubling time was not observed (Table 3); however, the subgroups were rather small.

Table 4 summarizes all PET results according to site and concordance for ACE and FCH PET studies. Both PET/CTs were similarly positive for local recurrences in 6 patients.

Four out of six local recurrences could be confirmed by the standard of reference investigations. In particular, three patients underwent biopsies of the prostate and/or prostatic bed, which in all patients confirmed the local recurrence, and one patient had an MR scan which identified a local recurrence corresponding to the focal uptake visible on PET images. The two bone metastases identified in two patients were confirmed as isolated lesions on CT images and on positive bone scans. Two examples of concordantly positive imaging for local recurrence and for bone metastasis are shown in Figs. 1 and 2. Concordant imaging of incidental pathologies was observed in four patients with both radiotracers positive: a pituitary tumour (confirmed by MR and subsequently by histology; Fig. 3), a thyroid nodule (confirmed by ultrasound imaging and biological evaluation as a parathyroid adenoma), a lung tumour (confirmed by follow-up CT imaging as a stable nodule), and a supraclavicular lymph node (visible on CT images and probably unrelated to the baseline PC). Concordant information concerning lymph node status was obtained in 19 patients (9 positive, 8 negative, 2 equivocal). An example of concordantly positive findings for a pelvic lymph node is presented in Fig. 4. For positive lymph nodes, the average SUVmax was 4.8 ± 2.7 and 5.6 ± 2.7 on ACE and FCH PET/CT, respectively.

Differences between ACE and FCH PET/CT were observed in four patients. Among these, two patients had a clearly positive lymph node on ACE PET/CT but negative on FCH PET, as shown in Fig. 5. In these two patients, the SUVmax values found on ACE PET/CT were 3.3 and 2.9, that is in the range of lower values for positive lesions. In one patient a subsequent repeat FCH PET/CT scan confirmed the earlier ACE PET/CT positivity. In the third patient an external

Fig. 2 Bone lesion concordantly positive (arrows) on both FCH and ACE PET/CT

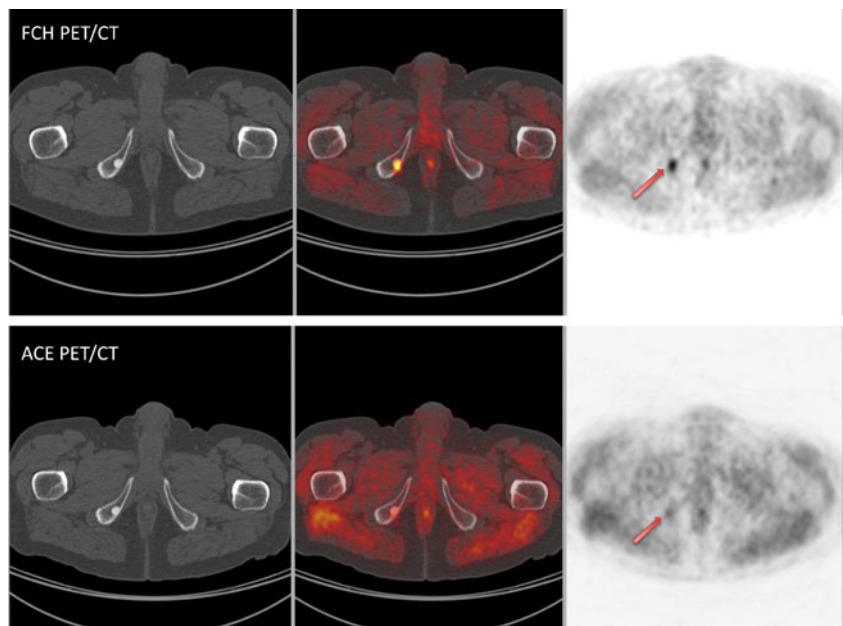
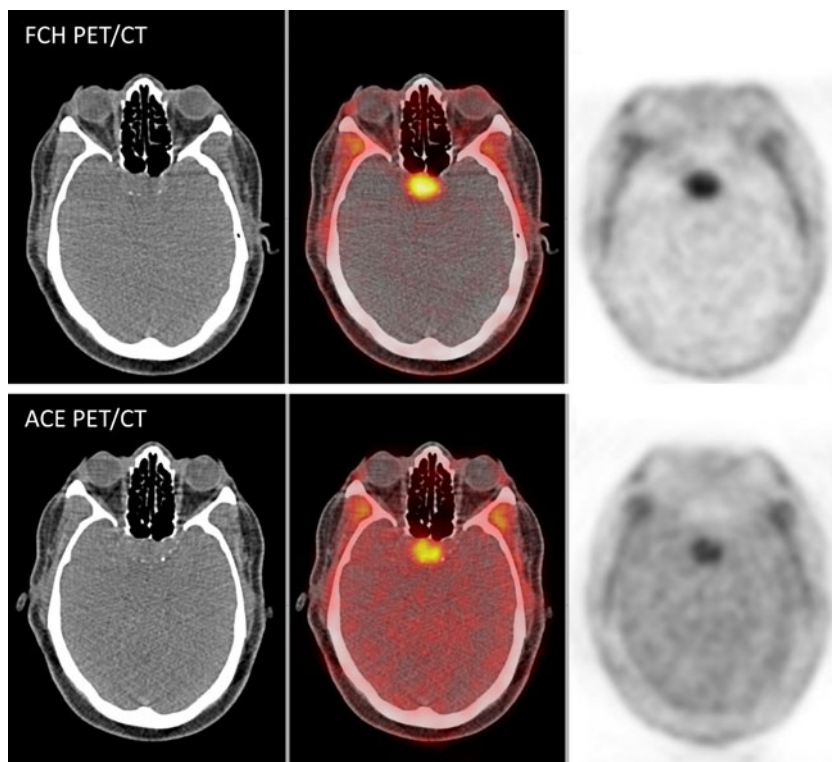


Fig. 3 Pituitary gland concordantly positive on whole-body FCH and ACE PET/CT acquisitions corresponding to a macroadenoma



iliac lymph node was equivocal on ACE PET and negative on FCH PET. In the fourth patient, retroperitoneal lymph nodes were equivocal on both FCH and ACE PET/CT, but some nodes were equivocal with one or the other of the radiotracers but not with both, although in this patient both PET scans were performed on the same day. Discordant lymph node PET/CT findings might occasionally reflect inflammatory situations, but in one patient an ACE-positive FCH-negative lymph node had progressed on imaging follow-up, suggesting a possible but small difference in sensitivity. No comparison with our

standard of reference was available for lymph node status, given that no biopsy could be performed and the follow-up at the time of this report was shorter than planned.

The SUVmax values of the concordantly positive lesions on ACE and FCH PET/CT studies were 4.4 ± 1.7 (mean \pm SD) and 5.3 ± 2 , respectively (Table 5). The values were significantly different between the two studies ($p = 0.017$). The TBR values, however, did not differ significantly between the two studies (4.4 ± 1.7 and 5.1 ± 2.1 on ACE and FCH PET/CT studies, respectively; $p = 0.089$).

Fig. 4 Pelvic lymph node concordantly positive (arrows) on both FCH and ACE PET/CT

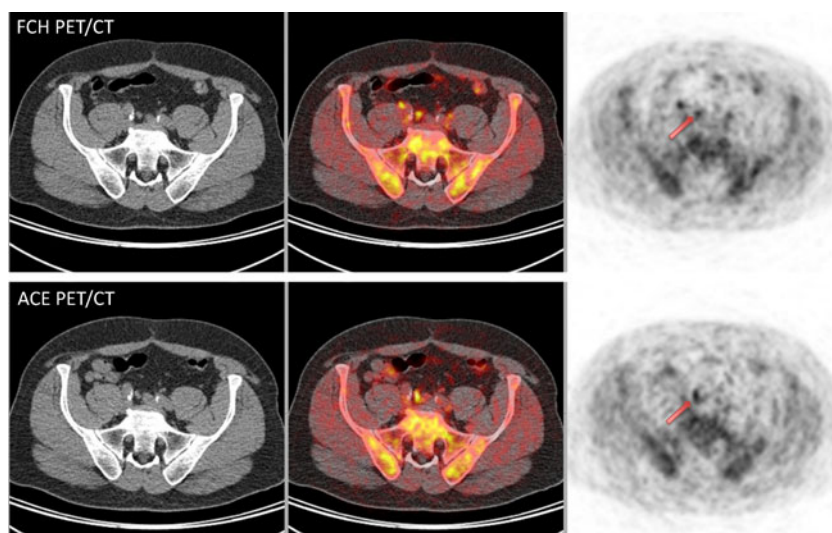
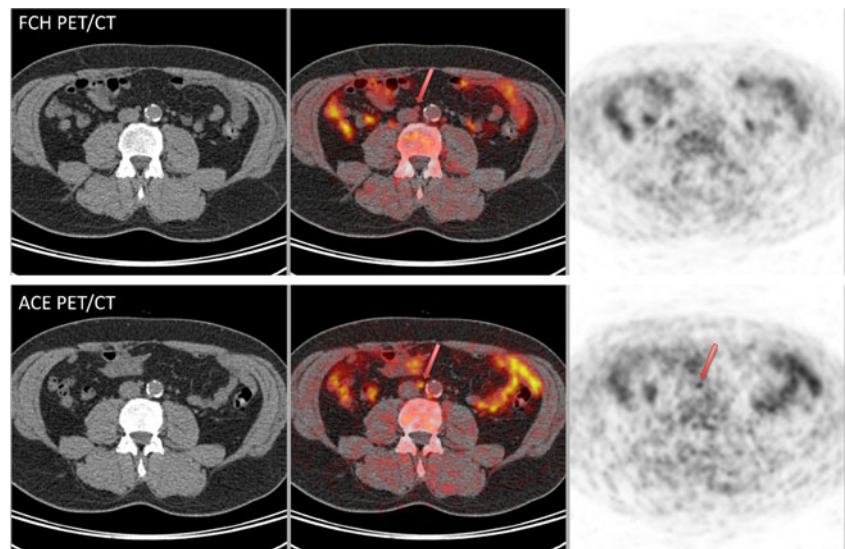


Fig. 5 Discordant interaortic lymph node, negative on FCH PET/CT (*above*) and positive on ACE PET/CT (first whole-body acquisition, *lower row*)



Discussion

¹¹C-Choline, ¹⁸F-choline and ¹¹C-acetate are major agents for PET imaging of PC [1, 2]. Only a few intraindividual comparisons of PET have been performed with these radiotracers. ¹¹C-Acetate and ¹¹C-choline PET have been directly compared in limited numbers of PC patients [19] and more recently by PET/CT in bladder cancer patients [20]. Both studies concluded that the performance of both tracers is similar. It has been reported that ¹¹C-acetate PET fused retrospectively with CT and MR scans is essential for the final diagnosis of recurrent PC, notably for uptake in the prostate region [21]. Our findings are concordant with these results, given that we had a high rate of histological confirmation of positive local findings (all patients biopsied showed local recurrence). In addition, all our studies obtained on an integrated PET/CT scanner systematically included a whole-body unenhanced CT scan for localization and morphological analysis, discriminating between intestinal lymph node uptake. We had a higher rate of negative findings in our study (39 % vs. 10 %), that could be explained by the lower mean PSA at inclusion (2.3 vs. 6.3 ng/ml),

Acetate and choline are taken up by proliferating cells and can be transformed to phosphatidylcholine and phosphocholine, respectively [22, 23]. Transmembrane transport of choline is dependent on the high-affinity choline transporter [24, 25], while transport of acetate is dependent on the monocarboxylate transporter-1 (MTC-1) or sodium-coupled MTC-1 (SMTC1) [26]. A relationship between ¹¹C-choline and choline kinase expression has also been described [27], and in that study, this tracer was highly specific and sensitive for staging pelvic lymph nodes. Phosphatidylcholine can be incorporated into nascent cell membranes. In a direct comparison of the two tracers, uptake was correlated with the tumour cell proliferation rate measured with tritiated thymidine, with an uptake advantage

being found in the in vitro situation for ACE [22]. However, acetate can also be metabolized, notably in active musculature which allows cardiac [28] and striate muscle imaging [29]. Similarly, choline can be oxidized to betain aldehyde and is

Table 5 SUVmax values and TBR for positive findings on ACE or FCH PET/CT or both

| | ACE PET/CT | | FCH PET/CT | | | |
|---------------------|------------|------------|------------|----------|------------|------|
| | SUVmax | | TBR | SUVmax | | TBR |
| | Target | Background | | Target | Background | |
| Prostate | | | | | | |
| 1 | 4.6 | 1.1 | 4.2 | 5.3 | 1.1 | 4.8 |
| 2 | 3.2 | 1.3 | 2.5 | 4.4 | 1.5 | 2.9 |
| 3 | 4.3 | 0.7 | 6.1 | 5.5 | 0.9 | 6.1 |
| 4 | 3.8 | 1.4 | 2.7 | 5.4 | 1.3 | 4.2 |
| 5 | 4 | 1 | 4.0 | 5.2 | 1.1 | 4.7 |
| 6 | 5.2 | 1 | 5.2 | 5 | 1.3 | 3.8 |
| Lymph nodes | | | | | | |
| 1 | 6.7 | 0.9 | 7.4 | 9.5 | 1 | 9.5 |
| 2 | 4.8 | 1.5 | 3.2 | 4.5 | 1 | 4.5 |
| 3 | 1.5 | 0.6 | 2.5 | 3.6 | 0.8 | 4.5 |
| 4 | 3.8 | 1.1 | 3.5 | 3.1 | 0.9 | 3.4 |
| 5 | 6.6 | 1 | 6.6 | 6.2 | 1.1 | 5.6 |
| 6 | 7.9 | 1.1 | 7.2 | 10.4 | 1 | 10.4 |
| 7 | 6.2 | 1.2 | 5.2 | 5.6 | 1 | 5.6 |
| 8 | 3 | 1 | 3.0 | 4.8 | 1.3 | 3.7 |
| 9 | 2.8 | 0.8 | 3.5 | 2.9 | 1.1 | 2.6 |
| 10 | 3.3 | 1.2 | 2.8 | Negative | Negative | – |
| 11 | 2.9 | 1 | 2.9 | Negative | Negative | – |
| Bone lesions | | | | | | |
| 1 | 4.8 | 0.9 | 5.3 | 3.5 | 1 | 3.5 |
| 2 | 1.8 | 0.6 | 3.0 | 5.3 | 0.8 | 6.6 |

therefore taken up particularly in the liver and kidneys [22]. The uptake of ^{18}F -choline by cells is similar to that of ^{11}C -labelled choline, but after phosphorylation via choline kinase, the phospho- ^{18}F -choline remains trapped in the cytoplasm without further metabolism [30]. In the present study, we compared FCH and ACE PET/CT intraindividually in patients with biochemical recurrence and low PSA values. We sought to determine whether an indication of higher sensitivity of one or the other agent would be observed in patients with low PSA levels or whether both tracers could be complementary. The localization of tumour recurrences in patients with low PSA levels is of clinical interest, since it could allow detection of tumours of restricted dissemination and therefore amenable to curative salvage therapy [7].

In contrast to ACE and ^{11}C -choline, FCH is a PET tracer with a half-life of 110 min and can be prepared on a commercial basis for distribution to PET centres without access to a cyclotron unit. FCH has become widely available and appears to be valuable for evaluation of PC patients with biochemical recurrence [13, 14, 31, 32]. With the use of early dynamic imaging centred on the prostate bed, the disadvantage of urinary excretion of ^{18}F can be partially compensated for since tumour uptake of FCH occurs earlier than urinary excretion [13, 33]. Furthermore, late imaging with FCH might allow discrimination between inflammatory lymph nodes and tumour-infiltrated lymph nodes [13, 33, 34].

ACE has the advantage of a low to only moderate urinary excretion of ^{11}C , catabolized tracer being exhaled as ^{11}C - CO_2 . On the other hand, its short half-life of 20 min does not allow the wider distribution of this tracer and requires a demanding and strict organization of tracer production and injection of patients. ACE PET/CT positivity in early recurrence appears to be correlated with blood PSA levels [35]. For PSA <1 ng/ml, different groups have reported detection rates between 18 % and 36 % [36–40]. Positivity rates of FCH PET/CT in patients with similarly low PSA values are in the same range as for ACE PET/CT [12, 13, 32], but occasionally a higher percentage positivity (49 %) has also been reported [41], as was the case in this study with, however, only a small number of patients in this group. Nevertheless, only small numbers of patients have been studied at very low PSA values by both ACE and FCH PET/CT, and thus comparison of the results from the literature would not be reliable. In addition, the above studies underscore the need for a careful intraindividual assessment of FCH versus ^{11}C -choline PET/CT.

The current results show excellent agreement between FCH and ACE PET/CT. This suggests that both tracers visualize similar features of PC cells either on tracer integration in lipid synthesis or catabolic energy provision. These concordant data are in line with previous reports on ACE and ^{11}C -choline [19, 20], implying that FCH would be a valid alternative to ^{11}C -choline, although this point still needs to be addressed by a direct comparison.

This study has a main limitation, namely the absence of adequate follow-up to provide a “standard of reference” for all PET/CT findings. While the two positive bone findings were confirmed as bone metastases on CT and bone scintigraphy, and four of six positive findings for local recurrence could be confirmed, for other localizations, notably for lymph nodes, a conclusive interpretation is currently not possible. The limitation of these tracers, however, for lymph node disease is known [8], as also shown recently for ^{11}C -choline [42] and reviewed with regard to PET/MR [43]. Thus neither tracer is the optimal tracer for recurrent PC, particularly for lymph node evaluation, as uptake is also observed in reactive mediastinal and inguinal nodes. It is thus not surprising that the few discordant data in 4 of 23 patients observed with ACE and FCH concern lymph node status. A longer follow-up is currently ongoing and is necessary to address this question. New tracers targeting specific molecules are currently under development for the diagnostic evaluation of PC, and some promising results have been shown in preliminary studies [1, 44, 45].

Conclusion

These findings demonstrated that three-phase FCH PET/CT and an analogous ACE PET/CT protocol performed equally for early recurrent PC staging show an overall excellent concordance on a per-patient and a per-lesion basis.

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Conflicts of interest None.

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