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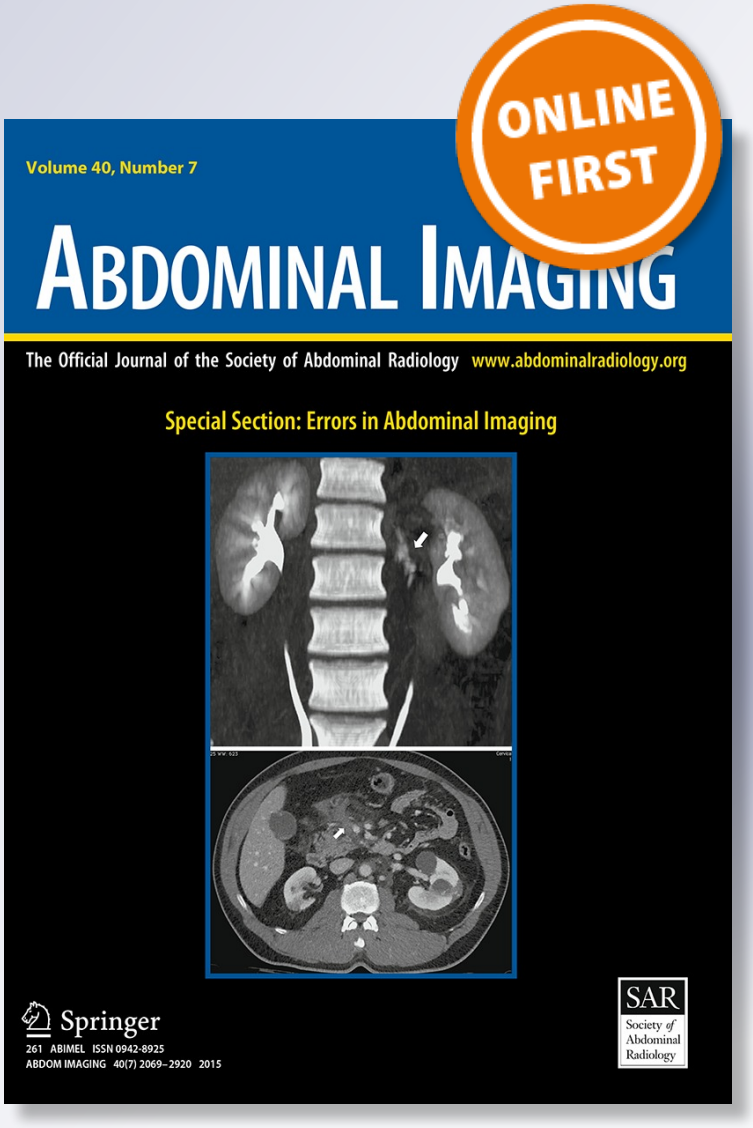

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The ability of 18F-choline PET/CT to identify local recurrence of prostate cancer

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Abstract

Purpose: To determine when 18F-choline PET/CT can truly identify local recurrence of prostate cancer.
Methods: 1031 patients from 3 European centers underwent ^{18}F-choline PET/CT (FCH PET/CT) for recurrent disease; 131 subjects (12.7%) showed a positive FCH uptake in the prostatic gland or prostatic fossa. Median age was 72 years (range 48–87 years), and the median PSA level at the time of FCH PET/CT scan was 4.41 ng/mL (0.22–18.13 ng/mL). 45 patients (34.4%) had a Gleason score (GS) >7, and the residual subjects had a GS ≤ 7. The assessment of true or false-positive FCH PET/CT findings was made by magnetic resonance imaging ($n = 34$) and/or biopsy in 75/131 cases. A χ^2 test and a Z Kolmogorov–Smirnov test were used to assess the correlation between clinical variables (age, PSA, GS, type of therapy) and FCH PET/CT findings.
Results: FCH PET/CT resulted truly positive (TP) for recurrent disease in the prostatic gland/fossa in 59/75 patients (79%) and falsely positive (FP) in 16 subjects (21%). The median value of PSA at the time of FCH PET/CT scan was higher in TP as compared to FP, although not statistically significant (4.76 vs. 3.04 ng/mL $p > 0.05$). Similarly, median age, GS categories, and the type of therapy were similar between the two groups ($p > 0.05$). However, when matching GS categories and PSA values, we found that the number of patients with TP findings were higher in the case of a PSA >2 ng/mL, independently from the GS (ranging between 74% and 92%). Conversely, FP rate ranged between 50% and 65% in patients with a PSA ≤ 2 ng/mL, especially in the case of GS ≤ 7, whereas FP was around 25% in those with a GS >7 and PSA >2 ng/mL.
Conclusions: FCH PET/CT has a limited role in evaluation of prostatic gland/fossa recurrence, due to the physiological biodistribution of the radiopharmaceutical agent. However, in 70–90% of patients with a PSA >2 ng/mL, independently from GS, a focal FCH uptake is compatible with a true local recurrence.

Key words: Prostate cancer recurrence—18F-choline PET/CT—False positive—True positive—Salvage treatments

From 27% to 53% of all, patients who undergo radical prostatectomy (RP) or external beam radiation therapy (RT) as the first-line treatment of prostate cancer (PCa) develop a biochemical recurrence [1]. Regarding local disease relapse after surgery, about 50% high-risk patients (those with wide positive margins and/or pT3) and approximately 10% of those with low risk (negative margins and pT2) will develop a local relapse within 15 years from surgery [2]. After RP, the most common sites of local recurrence are vesical–urethral anastomosis and peri-anastomotic tissues [3, 4]. Other sites include the anterior and the posterior bladder neck and, less frequently, the retrovesical space (posterior to the bladder neck). Conversely, after RT, morphological changes in the prostate include inflammation, glandular atrophy, fibrosis, and shrinkage [5, 6].

A large number of studies have shown that magnetic resonance imaging (MRI) is a powerful tool for early detection of local recurrence after surgery [7–12] and

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external beam radiation therapy (EBRT) [13–17]. However, the introduction of Choline PET/CT, labeled with ^{11}C or ^{18}F, has deeply changed the management of patients with biochemical recurrence. In fact, Choline PET/CT is able to detect the recurrence of disease with high sensitivity (82%) [18], thus, guaranteeing the restaging of disease in a single session. Nevertheless, the detection rate and the sensitivity of Choline PET/CT for the local recurrence of disease, particularly ^{18}F-Choline (FCH), are significantly lower than MRI [19].

The aim of this study was to determine when FCH PET/CT can truly identify the presence of local prostate cancer recurrence, and it was carried out in a cohort of patients who showed a significant uptake of FCH only in the prostate gland or prostatic fossa.

Materials and methods

Patients

Between October 2004 and June 2013, 1031 men underwent FCH PET/CT scan, in three different centers, for biochemical recurrence of PCa and after potentially curative treatment: RP or EBRT (PSA ≥0.2 ng/mL in the case of RP and a PSA level above the previous PSA nadir measured at 3 months after EBRT). The median time between the first treatment and the biochemical relapse was 34 months (3–88 months). FCH PET/CT was performed within 2–3 months from biochemical recurrence. In this study, we retrospectively evaluated patients according to predefined inclusion criteria: (1) Gleason score (GS) (of biopsy in case of no surgery or of surgical specimen), (2) record of current and past therapies (surgery, radiotherapy and/or systemic therapy), (3) serum PSA level (ng/mL) at the time of the FCH PET/CT scan, and (4) a positive FCH uptake in prostatic gland or prostatic fossa. Exclusion criteria were (1) a significant FCH uptake in lymph nodes (i.e., the presence of focal FCH uptake corresponding to abdominal-pelvic lymph nodes, including lymph nodes <1 cm in size) and (2) a significant FCH uptake in the distant organs (such as in bone, lung, and other common metastatic sites). According to institutional policies, all patients had given their informed consent before undergoing a FCH PET/CT scan and for subsequent, anonymous analysis of data. The study was performed in accordance with the Declaration of Helsinki.

FCH PET/CT imaging

[18F]fluorocholine as [18F]fluoromethylcholine ([18F]fluoromethyldimethyl-2-hydroxyethylammonium [FCH]) was provided by IASON Labormedizin GesmbH & Co. KG (Feldkirchner Straße 4, A-8054 Graz-Seiersberg, Austria). [18F]fluoride is produced in an 18O(p,n)18F reaction by the bombardment of 1.7 mL [18O]water with a 16-MeV proton beam using a GE PET trace cyclotron. The synthesis of [18F]fluorocholine consists of two steps. In the first step, [18F] bromofluoromethane is produced by the nucleophilic substitution of dibromomethane with [18F]fluoride. Subsequently, [18F]bromofluoromethane is converted online to [18F]fluoromethyl triflate. In the second step, dimethylaminoethanol is alkylated with [18F]fluoromethyl triflate to [18F]fluoromethylcholine. The production of [18F] fluorocholine is performed in a fully automated synthesis module of the ARGOS Zyklotron Company. Before synthesis, the module is tested by an automated leak check. The radiochemical purity of [18F] fluorocholine by high-pressure liquid chromatography was $>95\%$ ([18F]fluoromethyl triflate $<5\%$). The integrated PET/CT systems employed at the three centers were a Discovery LS scanner (GE Healthcare, Milwaukee, USA) in Aviano, a Biograph 16 HT PET/CT scanner (Siemens Medical Solutions, IL, USA) in Padua, and a Biograph mCT PET/CT scanner in Ljubljana (Siemens Medical Solution, IL, USA). FCH PET/CT included a delayed whole-body PET scan (6–8 beds, 2–3 min per bed position) performed 45–60 min after the i.v. administration of 3.0–3.5 MBq/kg of FCH (IASOcholine, IASON GmbH, Graz, Austria) and a co-registered low-dose CT whole-body scan (140 kV, 80–120 mA) without contrast enhancement. In each institution, two specialists in nuclear medicine independently reviewed the scans, according to visual assessment. In particular, local relapse was recorded in the presence of clear focal FCH uptake in the prostatic bed.

FCH PET/CT diagnostic performance

Positive FCH PET/CT findings were compared with the results of biopsy, salvage surgery performed after PET/CT, and with MRI. Follow-up duration ranged between 1 and 12 months. Positive FCH PET/CT findings were considered true positive (TP) when any of the following criteria was met: (1) confirmation on histology, in case of salvage surgical approach; (2) confirmation on peri-urethral anastomosis biopsy; and (3) confirmation on MRI either at baseline or during follow-up.

Statistical analysis

Continuous data are presented as median and range, and categorical data as numbers and percentages. A Kolmogorov–Smirnov test was used to assess the correlation between continuous clinical variables and FCH PET/CT findings. The differences between categorical data were assessed using Yates-corrected χ^2 test. A univariate logistic regression analysis was performed to identify the independent predictors of TP and FP findings at PET/CT. Two-tailed p values <0.05 were considered statistically significant. Statistical analysis was performed with SPSS software for Windows (Chicago, IL).

Table 1. Characteristics of study population

	FCH uptake in prostate gland (n = 83)	FCH uptake in prostatic fossae (n = 48)	P value
Median age, years	73 (5.21)	69 (56–86)	0.059*
Median PSA pre-PET (ng/mL)	4.8 (0.25–18.13)	3.6 (0.22–14.6)	0.142*
PSA categories, n (%)			0.232**
1≤ ng/mL	6 (7.2)	8 (16.7)	
1> PSA ≤2 ng/mL	10 (12.1)	6 (12.5)	
≥2 ng/mL	67 (80.7)	34 (70.8)	
GS, n (%)			0.614**
≤6	26 (31.3)	16 (33.3)	
=7	26 (31.3)	18 (37.5)	
≥7	31 (37.4)	14 (29.2)	
Therapy, n (%)			<0.0001**
RP ± LAD (alone)	–	24 (50)	
RP + EBRT (±ADT)	–	7 (14.6)	
EBRT (±ADT)	28 (33.7)	–	
ADT alone	31 (37.3)	–	
NA	24 (28.9)	17 (35.4)	
Ongoing ADT			0.135**
No	43 (51.8)	27 (56.3)	
Yes	22 (26.5)	6 (12.5)	
NA	18 (21.7)	15 (31.3)	
Site of FCH PET/CT			0.982
Prostatic gland	26 (44)	7 (43.7)	
Prostatic fossae	33 (56)	9 (56.3)	

GS Gleason score, *RP* radical prostatectomy, *LAD* lymphadenectomy dissection, *EBRT* external beam radiotherapy, *ADT* androgen deprivation therapy, *NA* not available
* Kolmogorov–Smirnov test; ** χ^2 test

Results

From the 1031 subjects who underwent FCH PET/CT, 131 patients (12.7%) showed a positive FCH exclusively in the prostatic gland or fossa (n = 83; 63.3% in the prostatic gland and n = 48; 36.7% in the prostatic fossa). Median age was 72 years (range 48–87 years), and the median PSA level at the time of FCH PET/CT scan was 4.41 ng/mL (0.22–18.13 ng/mL). Moreover, 45 patients (34.4%) had a GS >7, and the residual subjects had a GS ≤7. Table 1 reports the correlations between clinical data and the site of FCH PET/CT uptake. As shown, no differences between the site of FCH uptake and clinical variables were found. However, in patients with a PSA ≤1 ng/mL, the detection rates of recurrent prostate cancer in the gland and in the fossa were 7.2% vs. 16.7%, respectively. Moreover, the detection of recurrent local disease appeared lower in patients under androgen deprivation therapy (ADT) than their counterpart (21.4% vs. 53.4%).

The correlations among FCH PET/CT findings, MRI, and/or histology were available in 75 cases (57%). In particular, 34 subjects had MRI examination. FCH PET/CT resulted TP in 59 patients (79%) and FP in 16 subjects (21%) (Table 2). The number of patients with true-positive PET/CT findings was 43 and 28, respectively, for histology and MRI. Conversely, the number of false positives was 10 and 6 patients, respectively, for histology and MRI. The median value of PSA at the time of PET/CT scan was higher in TP as compared to FP, although not statistically significant (4.76 vs. 3.04 ng/mL $p > 0.05$). Similarly, median age, GS categories, and the type of therapy were similar between the two groups ($p > 0.05$). However, when matching GS categories and PSA values, we found that the rates of TP were higher in patients with a PSA >2 ng/mL independently from GS (ranging between 74% and 92%). Conversely, the rates of FP ranged between 50% and 65% in patients with a PSA ≤ 2 ng/mL, especially in those with a GS ≤ 7 (n = 7/11; 63.6%), whereas FP findings were around 25% in those with a GS >7 and PSA >2 ng/mL (Table 3). Figures 1 and 2 present examples of a true-positive and false-positive FCH PET/CT in the prostatic fossa, respectively.

From the univariate analysis, none of the clinical parameters correlated with TP or FP results at FCH PET/CT, although, as shown in Table 4, the odds of FP findings in patients who were treated with RP and adjuvant RT were higher (OR 3.695; IC 95% 0.837–15.703) than those of patients treated with RP alone. Similarly, the odds of TP findings were higher in patients who were treated by ADT alone (OR 2.069; IC 95% 0.218–19.629) as compared to the other subset of patients.

Discussion

Time to PSA relapse, pathological stage, and GS are the main factors related to the likelihood of local vs. distant relapse. In general, PSA detectable after 1 year, negative

Table 2. Correlation between clinical variables and FCH PET/CT findings

	True-positive finding (n = 59)	False-positive finding (n = 16)	p value
Median age, years	72 (54–86)	69 (59–82)	0.688*
Median PSA pre-PET (ng/mL)	4.76 (0.25–18.13)	3.04 (2.35–3.74)	0.852*
PSA categories, n (%)			0.444**
1≤ ng/mL	6 (10.2)	3 (18.8)	
1> PSA ≤2 ng/mL	7 (11.9)	3 (18.8)	
≥2 ng/mL	46 (78)	10 (62.5)	
GS, n (%)			0.689**
≤6	16 (27)	3 (18.8)	
=7	20 (34)	5 (31.3)	
≥7	23 (39)	8 (49.9)	
Therapy, n (%)			0.427**
RP ± LAD (alone)	8 (13.6)	4 (25)	
RP + EBRT (±ADT)	4 (6.8)	1 (6.3)	
EBRT (±ADT)	12 (20.3)	5 (31.3)	
HT alone	6 (10.2)	6 (37.4)	
NA	29 (49.1)	0	
Ongoing ADT			0.086**
No	25 (42.3)	10 (62.5)	
Yes	9 (15.4)	4 (25)	
NA	25 (42.3)	2 (12.5)	

GS Gleason score, *RP* radical prostatectomy, *LAD* lymphadenectomy dissection, *EBRT* external beam radiotherapy, *ADT* androgen deprivation therapy, *NA* not available
* Kolmogorov–Smirnov test; ** χ^2 test

Table 3. Correlation between Gleason score/PSA categories and FCH PET/CT findings

	N pts	True-positive FCH PET/CT finding	False-positive FCH PET/CT finding	p value
GS ≤6 and PSA <1 ng/mL	3	3 (100)	0	0.382
GS ≤6 and 1> PSA ≤2 ng/mL	4	2 (50)	2 (50)	
GS ≤6 and PSA >2 ng/mL	12	11 (91.7)	1 (8.3)	
GS = 7 and PSA <1 ng/mL	3	1 (33.3)	2 (66.7)	
GS = 7 and 1> PSA ≤2 ng/mL	1	1 (33.3)	0	
GS = 7 and PSA >2 ng/mL	21	18 (85.7)	3 (14.3)	
GS >7 and PSA <1 ng/mL	3	2 (66.7)	1 (33.3)	
GS >7 and 1> PSA ≤2 ng/mL	5	4 (80)	1 (33.3)	
GS >7 and PSA >2 ng/mL	23	17 (73.9)	6 (26.1)	

GS Gleason score, *PSA* prostatic specific antigen

lymph nodes, no seminal vesicle invasion, positive margins, and GS <7 are all factors related to a higher risk of local relapse, while PSA detectable before 1 year, positive lymph nodes, seminal vesicle invasion, and GS >6 are related to systemic relapse. However, in clinical practice, it is not so easy to identify the origin of PSA. As suggested by Paparo et al. [1], the combination of multi parametric magnetic resonance imaging (mpMRI) and Choline PET/CT provides a comprehensive assessment for the restaging of patients with biochemical recurrence after RP and RT, thus allowing local recurrence to be distinguished from metastatic disease.

From our results, it emerged that the detection rate of FCH PET/CT for local recurrent disease, in a population of more than 1000 people, is at least 13%. From the analysis of published literature, the detection rate of FCH PET/CT in prostatic bed ranged between 17% and 100% (see Table 5; Ref. [19–27]). Unfortunately, few data on PSA levels are available to evaluate the correlation between biochemical recurrence and FCH PET/CT detection rate. In addition, we found that FCH PET/CT detection of local recurrence seems higher for the prostate gland as compared to prostatic fossa, probably related to our older patient population who were mainly treated by non-invasive approaches (brachytherapy or EBRT) as primary treatment, due to the presence of comorbidities (high Charlson Comorbidity index). However, the numbers of FP and TP findings were similar for both patients with FCH uptake in prostate gland and those with FCH uptake in prostatic fossa.

Picchio et al. [28] reported that false-positive findings could occur in the prostatectomy bed, although false-negative results are the greatest concern at this anatomical location. As reported by Richter et al. [29], ^{11}C-choline would be more useful than FCH PET for the detection of primary PCa and recurrent disease in prostatic fossa according to its physiological elimination. As largely discussed in the literature, 11C-Choline has the

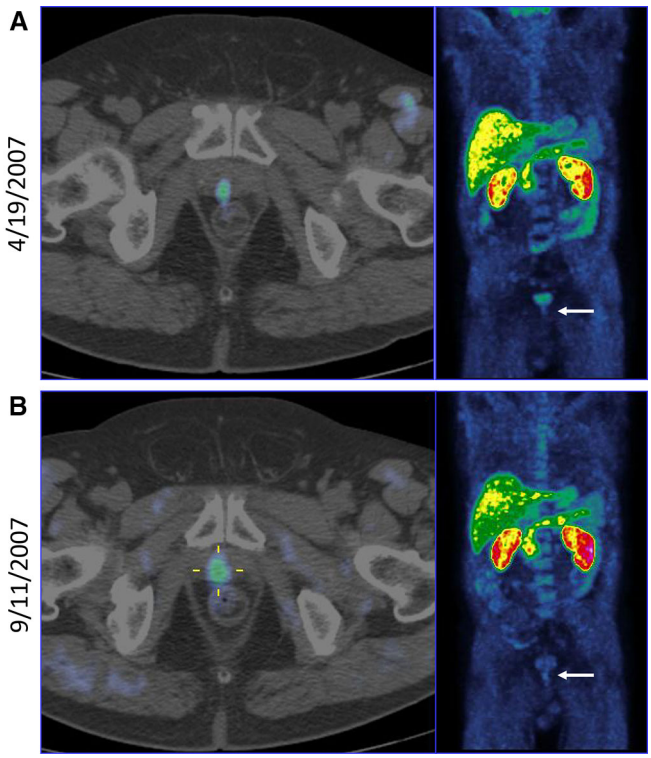

Fig. 1. A patient with suspected local recurrence after radical prostatectomy (GS = 7). **A** Focal uptake of FCH in the vesical–urethral anastomosis (PSA level was 2.4 ng/mL); **B** increase in focal FCH uptake after 7 months from the previous scan (PSA level was: 4.25 ng/mL) that confirmed the local recurrence of disease.

advantage of detecting prostate recurrence due to its physiological elimination, mainly by the intestinal tract rather than urinary one. On the contrary, FCH presents a variable urinary excretion with high accumulation in the bladder that can compromise the evaluation of the prostatic region. However, to date, comparative data are still missing.

As Cimitan et al. [30] demonstrated, delayed FCH PET/CT images (such as after 60 min) could reduce the rate of false-positive lymph node uptake. Recently, Chondroggianis et al. [31, 32] reported that the inclusion of early static images can improve the detection of local recurrence of prostate cancer, thus reducing the rate of FN and FP findings. Alonso et al. [33] investigated 64 prostate cancer patients with PSA relapse under ADT by 68Ga-DOTATATE PET/CT and 11C-Choline PET/CT. The authors found five false-positive lesions for both tracers, which were located in the prostate bed ($n = 1$) and regional lymph nodes ($n = 4$), respectively. Pathology revealed non-specific inflammatory lesions in all cases. Furthermore, in 2010, Le et al. described a case of active inflammation by FCH PET/CT in a patient with pulmonary infection, thus confirming that active infection is choline avid [34].

Unfortunately, none of the clinical parameters that we have evaluated in this setting can be useful to predict TP or FP FCH PET/CT. In our study, FCH PET/CT was able to identify true recurrence of prostate cancer in prostatic gland/fossa in 59/75 (79%) patients with available standard of reference (i.e., histology or MRI). As shown in Table 2, higher PSA values seem to be linked to a TP FCH uptake, although this result was not statistically significant ($p = 0.852$). Moreover, we found that the rates of TP FCH PET/CT for local recurrence were higher in patients with a PSA >2 ng/mL independently from GS. Conversely, the rates of FP ranged between 50% and 65% in patients with a PSA ≤ 2 ng/mL, particularly in 63.6% of those with a GS ≤ 7. At univariate analysis, we found that the odds of FP findings in patients who were treated by RP and adjuvant RT were 3.695 higher than those of patients treated with RP alone. This result can be associated with an increase in inflammation and/or a different anatomical conformation that can be associated with urinary residual.

As reported in the literature, after local primary treatments, patients who showed a confined recurrence of disease in prostate gland (in case of a previous EBRT) or in prostatic fossa (in case of RP) can benefit from salvage RP or pulse dose-rate brachytherapy with Ir-192 and salvage EBRT, respectively [35, 36]. Moreover, local therapies can be indicated after neo-adjuvant ADT [37], because men given neo-adjuvant hormone therapy prior to EBRT, showed significant improvements in clinical disease-free survival as well as overall survival [38]. Breeuwsma et al. [39] reported that in a cohort of 70 patients undergoing 11C-Choline PET/CT after EBRT, a significant FCH uptake in the prostatic gland was found in 41/57 (72%) patients with a positive PET scan. In this subgroup of patients, PSAdt and PSAvel were significantly higher than those with lymph node or distant metastases. Alongi et al. [40] analyzed 15 patients who underwent salvage EBRT due to a biochemical recurrence after high intensity focused ultrasound (HIFU). In these selected patients, 11C-Choline showed a positive intraprostatic-alone failure, thus being able to give information about the target definition in salvage EBRT, although it would still be considered an experimental procedure. D'Angelillo et al. [20] evaluated the utility of FCH dynamic PET imaging for the definition of recurrences in patients previously treated by RP and who were candidates for EBRT. In the analysis of 60 patients, the authors found that FCH PET/CT was able to recognize a local recurrence in all patients and also recorded a nodal disease in five subjects with low median PSA levels (median: 0.9 ng/mL; 0.2–11.7). Therefore, the identification of clinical data that are linked to a positive FCH uptake in prostatic bed could be useful to determine salvage treatments.

The main limitation of the present study is the absence of PSA kinetic data. As largely reported in the

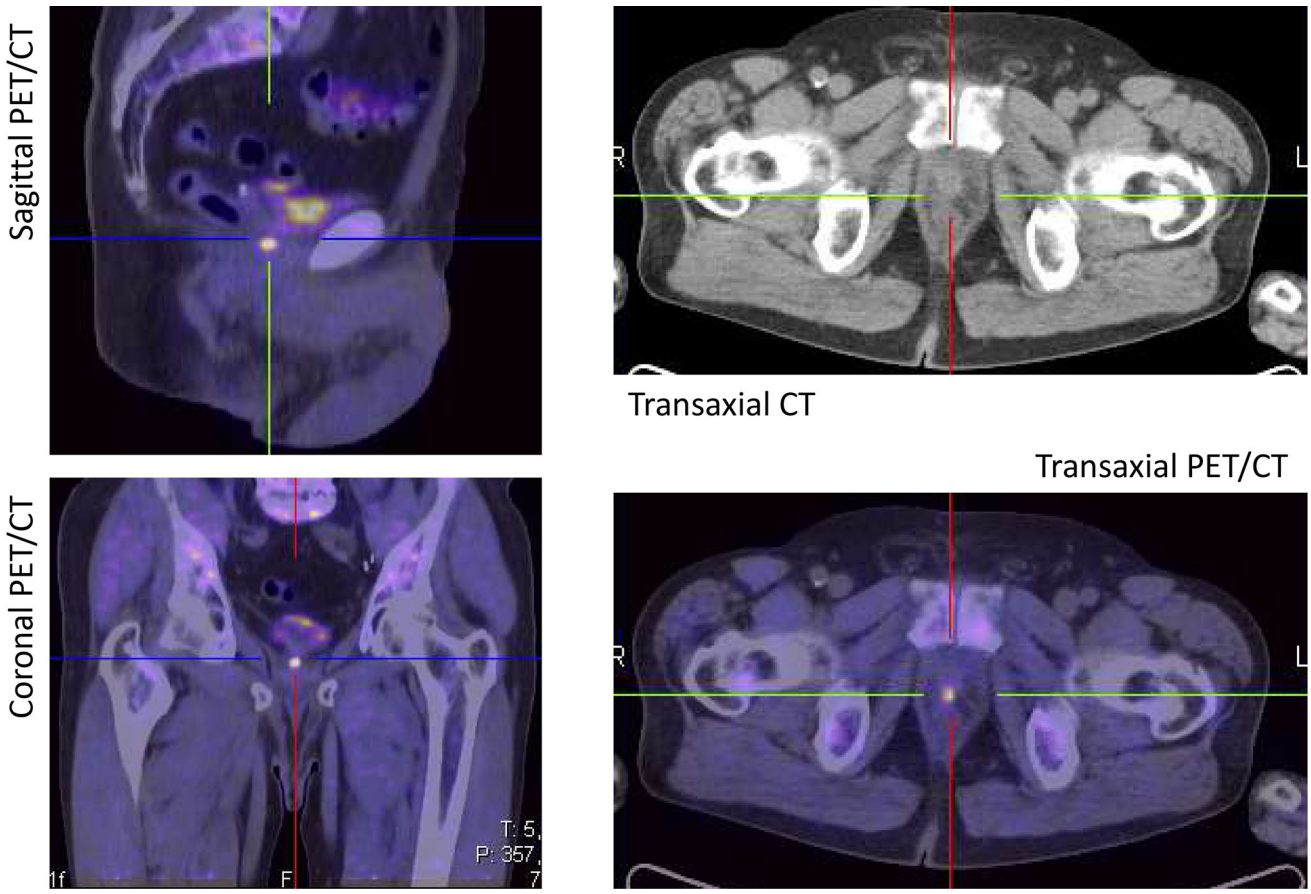

Fig. 2. A 78-year-old patient with a focal FCH uptake in prostatic fossa after robotic radical prostatectomy, in proximity of urethra (GS = 7; PSA level 0.7 ng/mL) at PET/CT scan. The suspicion was not confirmed by biopsy.

literature, a PSA velocity <0.75 ng/mL/year and a PSA doubling time >6 months are related to higher risk of local relapse, while a PSA velocity >0.75 ng/mL/year and a PSA doubling time <6 months are related to systemic relapse [41]. Nevertheless, pathological stage and GS are the main factors related to the likelihood of local vs. distant relapse. Therefore, for the retrospective nature of the present study, we considered only two out of the four predictive parameters that often correspond to clinical practice. The lack of dynamic or early PET acquisitions represents another important limitation to the present study. As recently demonstrated by Chondroggianis et al. [31, 32] and later reported in a recent revision by Evangelista et al. [42], the prostatic region uptake is better visualized in the early phase than in the late images. In fact, an early static or dynamic pelvic acquisition allows studying the prostate region before physiological urinary excretion of FCH, thus identifying with more accuracy, the presence of prostatic fossa recurrence. However, dual phase acquisition of PET/CT is time consuming and increases the number of false-positive findings of local recurrence especially in older patients who are mainly treated by non-invasive approaches. Thus, in clinical practice, a whole-body late imaging is often preferred. Other limitations are the lack of data on patient outcome and that the study was based on a retrospective analysis of the data.

In conclusion, from the present study emerged that, although PET/CT with FCH has some limitations for the evaluation of prostatic gland/fossa, due to the physiological biodistribution of the radiopharmaceutical agent, in 70–90% of patients with a PSA level >2 ng/mL, independently from the GS, a focal FCH uptake could be compatible with local recurrence. Therefore, a careful lecture of FCH PET/CT images, especially in the pelvis, also in whole-body examination is recommended for avoiding the presence of a true recurrence of prostatic bed, in patients with already treated prostate cancer. A prospective comparative study between MRI and PET/CT with FCH by including a large number of patients, stratified for age, GS, PSA level, PSA kinetic values, and type of treatments is mandatory in order to assess the

Table 4. Univariate analysis

	True positive at FCH PET/CT			False positive at FCH PET/CT		
	OR	IC 95%	*p* value	OR	IC 95%	*p* value
Age	1.015	0.936–1.099	0.723	0.986	0.910–1.068	0.723
PSA pre-PET/CT	1.036	0.890–1.206	0.648	0.965	0.829–1.124	0.648
GS categories						
GS ≤6	Reference	Reference	Reference	Reference	Reference	Reference
GS = 7	1.855	0.426–8.027	0.411	0.539	0.124–2350	0.411
GS >7	1.391	0.392–4.944	0.610	0.719	0.202–2554	0.610
PSA categories						
PSA ≤1 ng/mL	Reference	Reference	Reference	Reference	Reference	Reference
1> PSA ≤2 ng/mL	0.435	0.093–2.039	0.291	2.300	0.490–10.787	0.291
PSA >2 ng/mL	0.597	0.511–2.309	0.380	1.971	0.433–8.974	0.380
Therapy						
RP ± LAD (alone)	Reference	Reference	Reference	Reference	Reference	Reference
RP + EBRT (±ADT)	0.276	0.664–1.195	0.085	3.625	0.837–15.703	0.085
EBRT (±ADT)	0	–	–	0	–	–
HT alone	2.069	0.218–19.629	0.527	0.483	0.051–4.586	0.527
NA	0.207	0.045–0.946	0.042	4.833	1.057–22.091	0.042
ADT ongoing						
No	Reference	Reference	Reference	Reference	Reference	Reference
Yes	0.200	0.040–1.007	0.051	5.000	0.993–25.170	0.051
NA	0.180	0.028–1.15	0.071	5.556	0.864–35.706	0.071

GS Gleason score, *RP* radical prostatectomy, *LAD* lymphadenectomy dissection, *EBRT* external beam radiotherapy, *ADT* androgen deprivation therapy, *NA* not available

Table 5. Detection rate of local recurrence of disease by FCH PET/CT in patients with prostate cancer

Authors, reference	N of pts	Detection Rate in prostatic fossae	PSA levels
D'Angellillo et al. [20]	60	60 (100%)	0.9 (0.2–11.7)
Piccardo et al. [21]	21	4 (19%)	No data
Beheshti et al. [22]	250	95 (38%)	6.6 ± 2.8 (ADT ongoing) 5.9 ± 2.0 (no ADT)
Panebianco et al. [19]	76	63 (83%)	No data
Henninger et al. [23]	35	17 (49%)	No data
Schillaci al [24]	49	33 (67%)	5.35 ± 5.04
Husarik et al. [25]	68	19 (28%)	No data
Pelosi et al. [26]	24	4 (17%)	No data
Vees et al. [27]	11	5 (45%)	No data

ADT androgen deprivation therapy

correct management of patients with suspicion for prostatic bed recurrence.

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Conflict of interest. None.

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