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Salvage Radiotherapy Management Decision in Post-prostatectomy Patients with Recurrent Prostate Cancer Based on ^{18}F-Fluciclovine PET/CT Guidance.

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Abstract

This study evaluated the impact of ^{18}F-fluciclovine positron emission tomography/computed tomography (PET/CT) on salvage radiotherapy management decisions in patients with recurrent prostate cancer (PCa) post-prostatectomy.

Methods: Patients with detectable prostate-specific antigen (PSA) post-prostatectomy were randomized to undergo either conventional imaging (CI) only (Arm A) or CI plus ^{18}F-fluciclovine PET/CT (Arm B) prior to radiotherapy. In Arm B, positivity rates on CI and ^{18}F-fluciclovine PET/CT for detection of recurrent PCa were determined. Final radiotherapy decisions, a) to offer radiotherapy or not and b) extent of radiotherapy field - prostate bed only or to include pelvis, were based on ^{18}F-fluciclovine PET/CT findings. Radiotherapy decisions before and after ^{18}F-fluciclovine PET/CT were compared. Statistical significance of decision changes was determined using Clopper-Pearson (exact) binomial method. Prognostic factors were compared between patients with and without decision changes.

Results: All 165 patients enrolled in the study had standard-of-care CI and were initially planned for radiotherapy. Sixty-three of 79 (79.7%) patients (median PSA 0.33 ng/mL) who underwent ^{18}F-fluciclovine PET/CT (Arm B) had positive findings. ^{18}F-Fluciclovine PET/CT had significantly higher positivity rate than CI for whole body (79.7% vs 13.9%; $p < 0.001$), prostate bed (69.6% vs 5.1%; $p < 0.001$), and pelvic lymph nodes (38.0% vs 10.1%; $p < 0.001$).

Twenty-eight of 79 (35.4%) patients had overall radiotherapy decision changed following ^{18}F-fluciclovine PET/CT; 4 of 79 (5.1%) had radiotherapy decisions withdrawn due to extrapelvic disease detected on ^{18}F-fluciclovine PET/CT. Twenty-four of 75 (32.0%) patients with the final decision to undergo radiotherapy had radiotherapy fields changed. Changes in overall radiotherapy decision and radiotherapy fields were statistically significant ($p < 0.001$). Overall mean PSA at PET was significantly different between patients with and without radiotherapy decision changes ($p=0.033$).

Conclusion: ^{18}F-fluciclovine PET/CT significantly altered salvage radiotherapy decisions in patients with recurrent prostate cancer post-prostatectomy. Further analysis to determine the impact of ^{18}F-fluciclovine PET/CT guidance on clinical outcomes post-radiotherapy is in progress.

Keywords

^{18}F-Fluciclovine; PET/CT; prostate cancer; radiotherapy; management change.

INTRODUCTION

Despite advances in prostate cancer (PCa) treatment, approximately 40% of patients treated with prostatectomy experience a rise in prostate-specific antigen (PSA) levels (*1,2*). Radiotherapy with or without hormone therapy has been the mainstay of recurrent PCa treatment post-prostatectomy (*3,4*). Nonetheless, PSA failure is noted in about 50% of patients after salvage radiotherapy (*5*), partly due to inappropriate patient selection and nontargeted therapy (*3,6*).

Imaging has played an essential role in disease localization and treatment planning for salvage radiotherapy in patients with recurrent PCa (*7-9*). Conventional imaging (CI), including bone scan, computed tomography (CT), and magnetic resonance imaging (MRI), has been the standard-of-care for PCa restaging and radiotherapy planning (*7,10,11*). Yet, CI has limited ability to accurately define the location and extent of recurrent disease, especially in patients with low PSA levels (*6,12-14*).

Imaging with novel PET radiotracers has significantly influenced radiotherapy decision-making and radiation planning in patients with recurrent PCa (*3,9,15,16*). ^{18}F-Fluciclovine (Axumin® (fluciclovine F 18); Blue Earth Diagnostics, Ltd, Oxford UK) is a non-natural amino acid PET radiotracer that is approved by the Food and Drug Administration, for the detection of recurrent PCa in patients with rising PSA. Due to its high specificity for extraprostatic disease, ^{18}F-fluciclovine is able to identify both prostatic and extraprostatic recurrence across all PSA levels (*17,18*). In a preliminary/interim analysis of this study, at 87/165 accrual, a 40.5% change in salvage radiotherapy management was seen in post-prostatectomy patients following guidance with ^{18}F-fluciclovine PET/CT (*19*). The purpose of this analysis was to report the final results of management decision change, and determine if the decision change trend remained after completion of accrual.

MATERIALS AND METHODS

This prospective randomized clinical trial (Clinical Trials.Gov ID: NCT01666808) - Emory Molecular Prostate Imaging for Radiotherapy Enhancement (EMPIRE-1) consisting of two groups (Arms A and B) was conducted in accordance with Health Insurance Portability and Accountability Act and approved by the Institutional Review Board.

Patients 18 years or older with a history of prostate adenocarcinoma, detectable PSA post-prostatectomy, no evidence of extrapelvic disease on CI, and Eastern Cooperative Oncology Group performance status of 0-2 were enrolled. Exclusion criteria include contraindications to radiotherapy, prior pelvic radiotherapy, previous invasive malignancy (unless disease-free for at least 3 years), and severe acute morbidity. All patients provided written informed consent.

Prior to randomization, the treating radiation oncologist completed an intention-to-treat form. Patients were randomized to receive either CI (abdominopelvic CT or MRI) only (Arm A) or CI plus ^{18}F-fluciclovine PET/CT (Arm B) prior to radiotherapy using a computer-generated schedule. All patients had standard-of-care ^{99m}Tc-methylene diphosphonate bone scan. Patient follow-up for a minimum of three years with PSA and other clinical parameters (every six months) is ongoing. This current report will focus mainly on management decision changes based on ^{18}F-fluciclovine PET/CT guidance (Arm B only), which are available earlier than cancer control outcomes.

^{18}F-Fluciclovine PET/CT Imaging Protocol

^{18}F-Fluciclovine was prepared as reported (*20*). After at least 4 hours of fasting, patients ingested oral contrast. One hour later, abdominopelvic CT (slice thickness, 3.75 mm; spacing, 3.25 mm) was completed for anatomic imaging and attenuation correction (~100 mAs and 120 kVp). Following this, 370 ± 11.1 MBq (10.1 ± 0.3 mCi) ^{18}F-fluciclovine was injected intravenously. Afterward, dual time-point (5-15.5 minute and 16-27.5 minute) imaging was completed, using 4 consecutive 2.5 min/bed PET acquisitions from pelvis to diaphragm. PET/CT images were

acquired on a GE Discovery MV690 16 slice integrated scanner (GE Healthcare, Waukesha, WI). Images were reconstructed with iterative technique (VUE Point Fx [GE Healthcare]; 3 iterations, 24 subsets, 6.4-mm filter cutoff), and transferred to a MIMVista workstation (MIM Software; Cleveland, OH) for interpretation.

Image Analysis

CI was performed and interpreted per institutional protocol before the ^{18}F-fluciclovine PET/CT scan. ^{18}F-Fluciclovine PET/CT images were interpreted independently by two board-certified nuclear medicine physicians (over 20 years experience each), with consensus agreement on discordant interpretations. Readers were blinded to patient's clinical history (beyond inclusion criteria) and other imaging results to avoid interpretation bias. ^{18}F-Fluciclovine PET positivity in prostate bed, lymph nodes, or bone was identified as persistent non-physiologic moderate (greater than marrow) focal uptake (*17*).

Management Decision Criteria

Prostate bed and pelvic lymph nodes were defined using the Radiation Therapy Oncology Group contouring guidelines (*21*). Initial (pre-fluciclovine) radiotherapy decisions were based on clinical history, histopathology findings at prostatectomy (lymph node+, margin+, seminal vesicle+, and extracapsular extension), PSA trajectory, and CI findings using well-recognized clinical criteria (*22*). Final radiotherapy decisions were based on ^{18}F-fluciclovine PET/CT findings: a) no uptake or uptake in prostate bed only - radiotherapy to prostate (surgical) bed only [64.8-70.2 Gy in 1.8 Gy fractions] as standard field or to include activity, respectively; b) pelvic nodal uptake or pN1 (regional node involvement) - radiotherapy to pelvis [45.0-50.4 Gy in 1.8 Gy fractions] + prostate (surgical) bed; c) extrapelvic uptake - no radiotherapy; systemic therapy offered.

Statistical Analysis

We calculated that a sample of 146 patients (73 in each Arm) were needed to test a 20% difference in 3-year failure-free survival [50% vs 70%] between Arms at a 0.05 level of significance with 80% power (*23*). Assuming a withdrawal/dropout rate of 10%, the overall target enrollment was a minimum of 162 subjects. Positivity rates on CI and ^{18}F-fluciclovine PET/CT for detection of recurrent PCa were determined and compared using chi-square or Fisher's exact test. Kappa was used to determine inter-reader agreement for ^{18}F-fluciclovine PET/CT.

Treatment plans before and after ^{18}F-fluciclovine PET/CT were compared and changes noted. Statistical significance of decision changes in: a) overall radiotherapy decision b) decision to offer radiotherapy or not, and c) extent of radiotherapy field i.e., treat prostate bed only or include pelvic nodes, was calculated using Clopper-Pearson (exact) binomial method. Two-sample t-test and Kruskal-Wallis test were used to determine the differences in mean PSA at PET, Gleason scores, and prostatectomy-PET interval between patients with and without decision changes. P-value <0.05 was regarded statistically significant. Data were analyzed using SAS Version 9.4 (SAS Institute Inc. Cary, NC, USA).

RESULTS

Patient Characteristics

Eighty-three of 165 patients enrolled in the study between September 2012 and March 2019 were randomized into Arm B. Four of 83 patients did not undergo ^{18}F-fluciclovine PET scan. Therefore, only 79 patients were analyzed. Median (range) PSA at PET was 0.33 ng/mL (0.02-31.00 ng/mL). Patient characteristics are outlined in Table 1. Supplemental Table 1 describes Arm A (CI only) demographics.

Detection of Recurrence on ^{18}F-Fluciclovine PET/CT

Sixty-three of 79 (79.7%) patients had positive ^{18}F-fluciclovine PET/CT scans. On whole body analysis, positivity rate on ^{18}F-fluciclovine PET/CT was 75.4% for PSA ≤1 ng/mL and 90.9% for PSA >1 ng/mL (Table 2). Kappa was 0.59 in the prostate, 0.83 in the pelvis, and 0.67 in the extrapelvic regions.

Conventional Imaging Analysis

Seventy-one MRI and eight CT scans were performed. On whole body analysis, positivity rate on CI was 8.8% for PSA ≤1 ng/mL and 27.3% for PSA >1 ng/mL (Table 2). No patient had extrapelvic metastasis per inclusion criteria.

Comparison between Positivity Rates on ^{18}F-Fluciclovine PET/CT and CI

^{18}F-Fluciclovine PET/CT had significantly higher positivity rate than CI for whole body (79.7% vs 13.9%; p <0.001), prostate bed (69.6% vs 5.1%; p <0.001) and pelvic lymph nodes (38.0% vs 10.1%; p <0.001). These differences were significant across PSA levels (Figure 1; Table 2). ^{18}F-Fluciclovine PET/CT detected extrapelvic disease not previously seen on CI in 4 of 79 (5.1%) patients; 2 patients had uptake in extrapelvic lymph nodes, while 2 other patients had uptake in bone ± extrapelvic lymph nodes.

Management Decision Change

All 79 patients were initially planned for radiotherapy to either a) prostate bed only in 45 patients, or b) prostate bed and pelvis in 34 patients. Details of ^{18}F-fluciclovine uptake pattern, initial and final treatment decisions are shown in Figure 2.

*OVERALL DECISION CHANGE***.** Based on ^{18}F-fluciclovine PET/CT findings, 28 of 79 (35.4%) patients had overall radiotherapy decisions changed (Table 3). Subgroup analyses showed a 76.5% positivity rate on ^{18}F-fluciclovine PET/CT and 29.4% management change in patients with PSA <0.5 ng/mL. Additionally, androgen deprivation therapy (ADT) decisions were changed in 5

patients; 2 patients were offered ADT (no ADT pre-fluciclovine) and 3 patients initially planned for short-term ADT were offered long-term ADT due to extrapelvic disease detected on ^{18}F-fluciclovine PET/CT.

RADIOTHERAPY FIELD CHANGE. As shown in Table 3, 24 of 75 (32.0%) patients with the final decision to undergo radiotherapy had radiotherapy fields changed following ^{18}F-fluciclovine PET/CT. Changes in overall radiotherapy decision and radiotherapy field were both statistically significant ($p < 0.001$). Although there were four major decision changes to not offer radiotherapy due to extrapelvic disease detected on PET, this difference, when considered alone, did not reach statistical significance ($p=0.120$). Representative images showing extrapelvic, pelvic, and prostate bed ^{18}F-fluciclovine uptake are shown in Figures 3, 4, and 5, respectively.

Among the prognostic factors examined, overall mean PSA at PET was significantly higher in patients with radiotherapy decision changes than those without (Table 4).

DISCUSSION

Accurate localization and early detection of recurrent PCa are essential for patient selection, targeted therapy, and improved clinical outcomes. This prospective intention-to-treat clinical trial was designed to explore the influence of ^{18}F-fluciclovine PET/CT on radiotherapy planning in post-prostatectomy patients with PSA failure.

In this study, ^{18}F-fluciclovine PET/CT resulted in a significant 35.4% change in overall radiotherapy treatment decision and 32.0% change in radiotherapy fields. The decision to offer radiotherapy was withdrawn and systemic therapy offered in 5.1% of patients due to extrapelvic disease detected only on ^{18}F-fluciclovine PET/CT. In an interim analysis of this study of 42 patients who underwent ^{18}F-fluciclovine PET/CT, we reported 40.5% overall decision change and 37.5% radiotherapy field change (*19*), comparable to current findings.

Whole body positivity rate on ^{18}F-fluciclovine PET/CT was 79.7% in this study population, consistent with the reported positivity rate of 79.3% by Pernthaler (*24*) and 81% by Savir-Baruch (*25*). In contrast, relatively lower positivity rates on ^{18}F-fluciclovine PET/CT have been reported by other studies (*26,27*), likely related to differences in mean PSA and PSA kinetics. Similar to other studies, we found that the detection rate of recurrent PCa on ^{18}F-fluciclovine PET/CT improves with increased PSA levels; 75.4% and 90.9% for PSA ≤1 ng/mL and >1 ng/mL, respectively (*19,25,28,29*).

Radiotherapy field design in post-prostatectomy patients with recurrent PCa is primarily based on imaging findings (*8-11,17*). In this study, positive findings on ^{18}F-fluciclovine PET/CT were identified in 53 patients who had negative CI findings. Furthermore, 23 of 28 patients with management change had negative CI scans. Our results agree with previous studies that have reported ^{18}F-fluciclovine PET/CT performed better than CI in detection of recurrent PCa (*17,29*). Distant metastases on ^{18}F-fluciclovine PET/CT, not seen on CI, led to the decision to withdraw salvage radiotherapy and offer systemic therapy. These patients may have benefited from the early onset of systemic therapy and spared the side effects of salvage radiotherapy.

In a prospective multicenter study of 104 men with biochemical recurrence (BCR) and median PSA 0.79 ng/mL, a 64% management change after ^{18}F-fluciclovine PET/CT was reported (*26*). The lower management change found in our study is likely due to the homogeneous patient population, lower median PSA, exclusion of patients with evidence of extrapelvic disease on CI, and strict pre-defined major treatment changes. Comparable to our finding, Solanki reported a 48% management change following ^{18}F-fluciclovine PET/CT in 114 post-prostatectomy patients with BCR (median PSA 0.42 ng/mL) intended for radiotherapy (*27*).

In studies evaluating the role of prostate-specific membrane antigen (PSMA) PET/CT in treatment planning, a range of 30.2%-76% has been reported (*30-32*). Our result of 29.4% management change in patients with PSA <0.5 ng/mL is similar to that of a retrospective study of

^{68}Ga-PSMA-11 PET/CT in patients with early PSA failure (PSA <0.5 ng/mL) post-prostatectomy, which reported intended treatment change in 30.2% of patients (*30*). Treatment modification was also found in 13%-46.7% patients with BCR after ^{11}C-choline or ^{18}F-fluorocholine PET (*33-35*). Thus, our finding of 35.4% management change is on the lower end of the reported PSMA range and higher end of choline range. In a recent preliminary report on the primary endpoint of this trial, cancer control, we found that ^{18}F-fluciclovine PET/CT resulted in significant improvement in failure-free survival between the two Arms at 3 and 4 years post-radiotherapy (*36*). Although other PET radiotracers have reported change in management comparable to ^{18}F-fluciclovine PET, clinical outcome as a primary endpoint in a prospective, randomized, controlled manner for these radiotracers is yet to be reported (*37,38*).

The randomized prospective design, two independent readers with consensus agreement, and the homogenous population of post-prostatectomy patients are strengths of this study. Our study has several limitations. First, pre-fluciclovine radiotherapy decisions were made by several radiotherapy providers. These decisions likely represent a cross-section of decisions made in the prostate radiotherapy community. However, it should be noted that our study is quite rigorous compared to virtually all other trials with respect to the handling of post-PET decisions, as these were clearly declared at the outset, and providers were held to these decisions. Second, most patients in this study did not have histologic investigation of imaging findings, as the study was not designed to validate the diagnostic performance of ^{18}F-fluciclovine. Prior studies have reported a high positive predictive value of ^{18}F-fluciclovine PET/CT using validated histology data (*28*). Finally, malignant extraprostatic lesions, especially osteoblastic bone lesions, may have been missed due to inherent radiotracer characteristics such as lower sensitivity in detection of small volume disease and lack of uptake in some indolent sclerotic lesions (*39*). However, ^{18}F-fluciclovine has demonstrated superior performance in the prostate bed due to very low urinary excretion (*24*).

In conclusion, this study shows that ^{18}F-fluciclovine PET/CT changes patient management even at low PSA levels. In the setting of treatment planning for salvage radiotherapy post-prostatectomy in patients with biochemical recurrence, our findings suggest that imaging with ^{18}F-fluciclovine PET/CT can guide treatment decisions. Follow-up of these patients continues, and further study is ongoing to determine the impact of ^{18}F-fluciclovine PET/CT-guided treatment on clinical outcomes post-radiotherapy.

FINANCIAL DISCLOSURE

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KEYPOINTS

QUESTION: Can ^{18}F-fluciclovine PET/CT influence salvage radiotherapy management decisions in patients with prostate cancer recurrence post-prostatectomy?

PERTINENT FINDINGS: In this prospective clinical trial exploring the influence of ^{18}F-fluciclovine PET/CT on salvage radiotherapy decision-planning in patients with prostate cancer recurrence post-prostatectomy, we found a significant 35.4% change in overall radiotherapy treatment decision and 32.0% change in radiotherapy fields.

IMPLICATIONS FOR PATIENT CARE: Appropriate patient selection and targeted therapy through advanced imaging are essential to reduce high biochemical failure rates following salvage radiotherapy.

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FIGURE LEGENDS

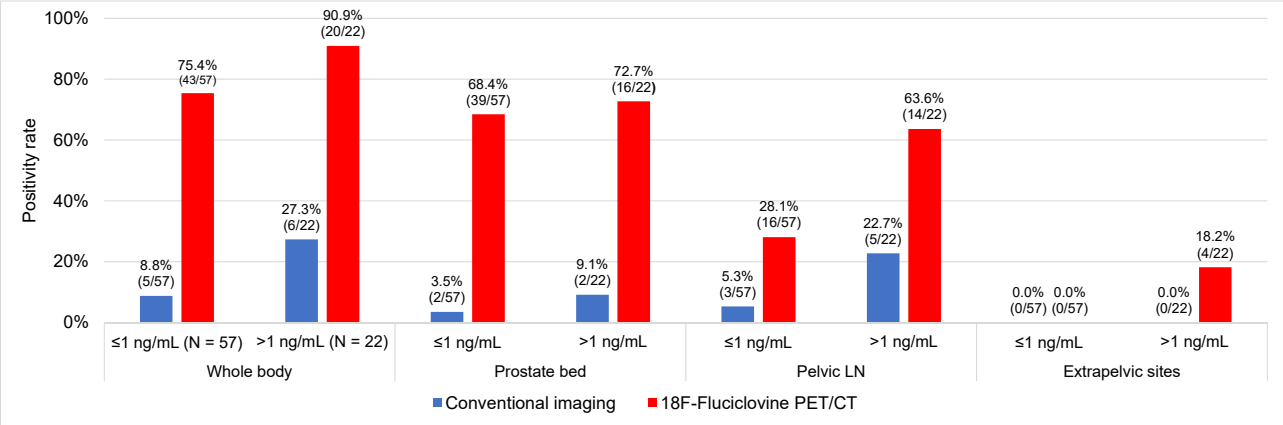


FIGURE 1: Comparison of positivity rates on conventional imaging and ^{18}F-fluciclovine PET/CT

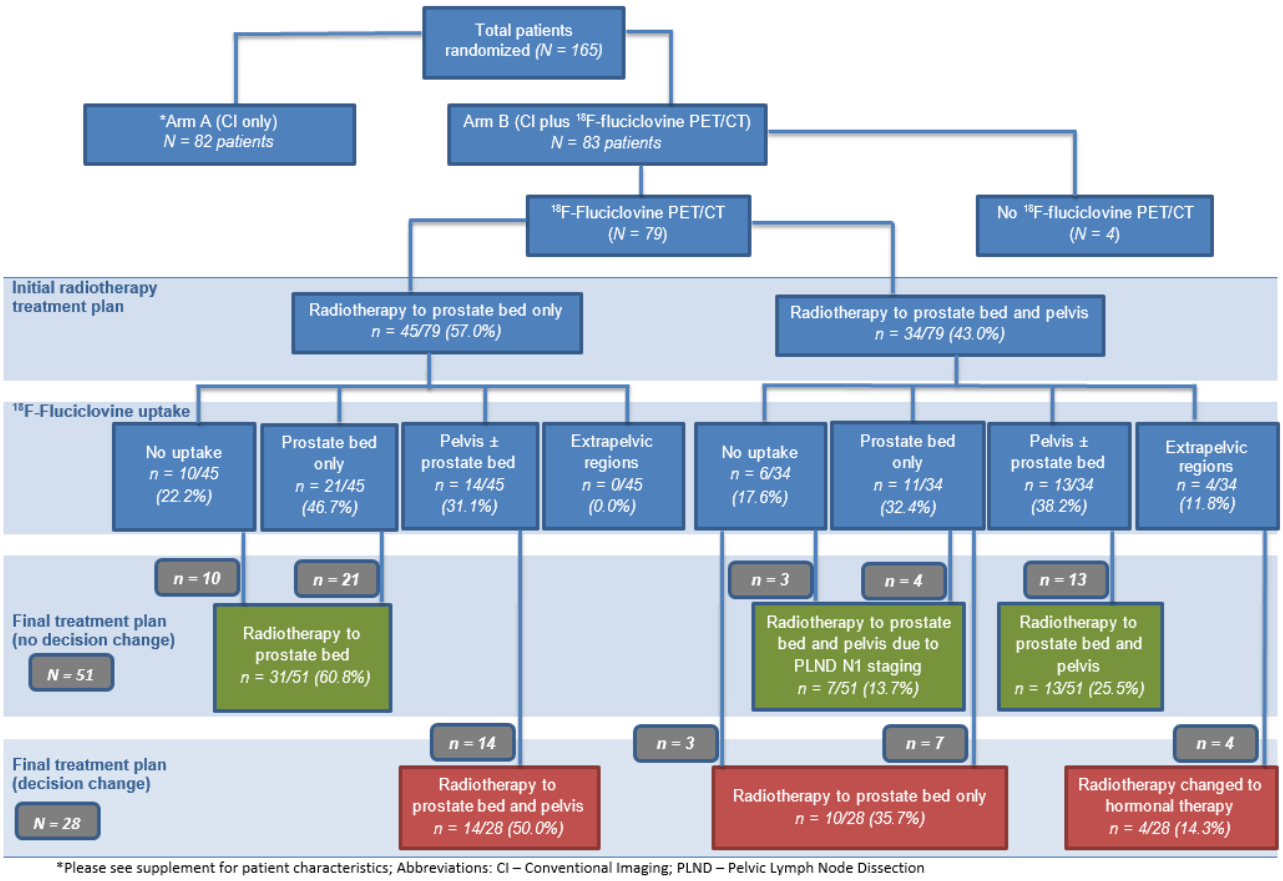


FIGURE 2: Study flow diagram showing initial and final radiotherapy decisions

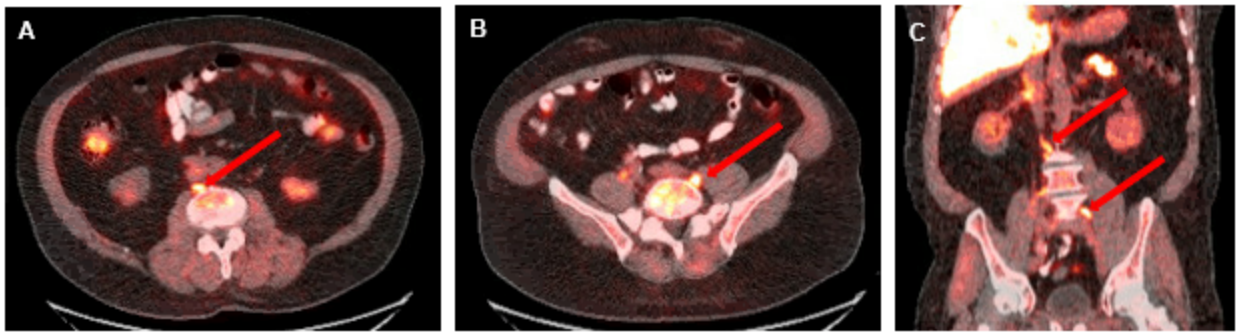


FIGURE 3: 72-y-old patient with biochemical recurrence post-prostatectomy (PSA 3.46 ng/mL; Gleason score 5+4=9; T3bN1M0). Fused transaxial (A, B) and coronal (C) PET/CT images show abnormal ^{18}F-fluciclovine uptake (arrows) in retroperitoneal lymph nodes. Radiotherapy decision was withdrawn and hormonal therapy only was offered.

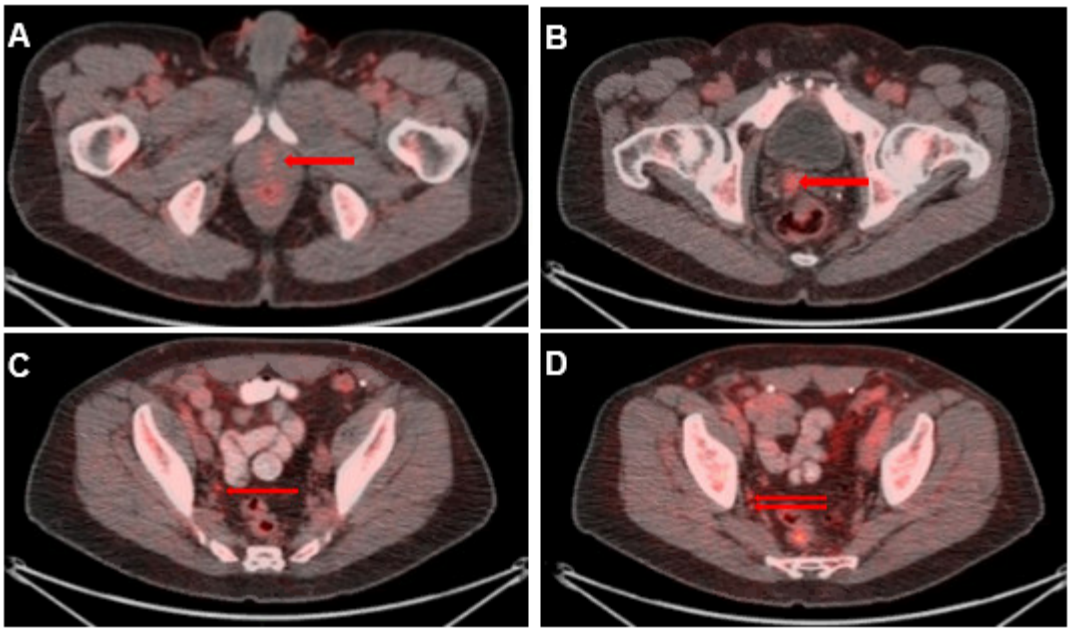


FIGURE 4: 64-y-old patient with biochemical recurrence post-prostatectomy (PSA 0.96 ng/mL; Gleason score 4+3=7; T3aN0M0). Fused transaxial PET/CT images (arrows, A–D) show abnormal ^{18}F-fluciclovine uptake at the vesicourethral anastomosis (A), right seminal vesicle (B), right internal iliac (C), and right obturator lymph nodes (D). Treatment decision changed from radiotherapy to prostate bed only to prostate bed and pelvis.

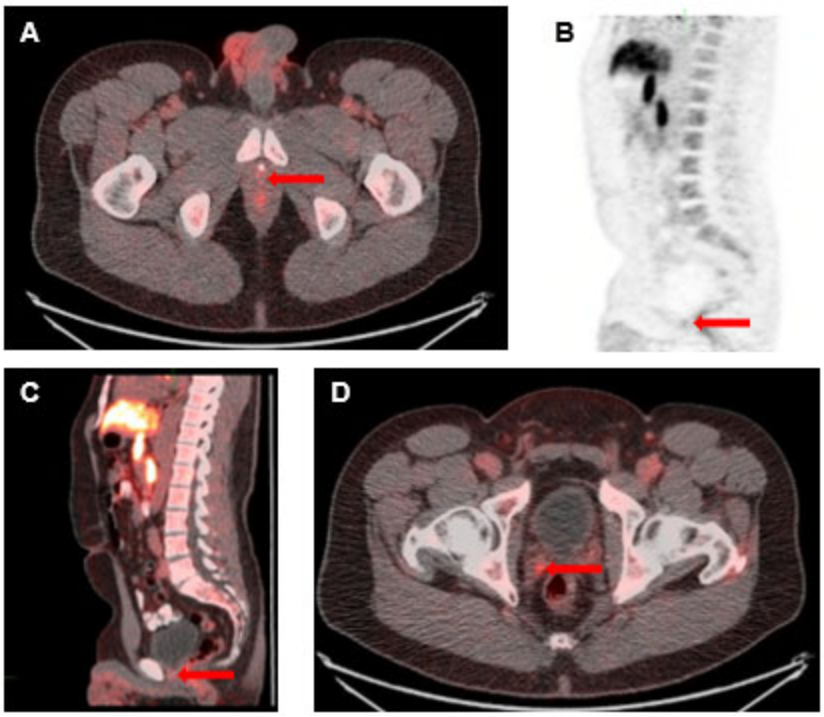


FIGURE 5: 53-y-old patient with biochemical recurrence post-prostatectomy (PSA 0.23 ng/mL; Gleason score 3+4=7; T2N0M0). Abnormal fluciclovine uptake seen at the vesicourethral anastomosis on fused transaxial PET/CT (A), sagittal PET (B) and fused PET/CT (C), and right seminal vesicle on fused transaxial PET/CT (D) images. Treatment decision changed from radiotherapy to prostate bed and pelvis to prostate bed only.

Table 1: Demographic, Clinical and Histopathologic Characteristics of Arm B (CI plus ^{18}F-fluciclovine PET) Study Participants (n=79)

Age (years)	
Mean (SD)	61.6 (7.6)
PSA at PET scan (ng/mL)	
Median (range)	0.33 (0.02-31.00)
Gleason score (GS), n (%)	
GS 3+3 (Grade group 1)	8 (10.1)
GS 3+4 (Grade group 2)	27 (34.2)
GS 4+3 (Grade group 3)	23 (29.1)
GS ≥ 4+4 (Grade groups 4 and 5)	21 (26.6)
Primary tumor stage, n (%)	
T1-T2	37 (46.8)
T3-T4	42 (53.2)
Extracapsular extension, n (%)	36 (45.6)
Seminal vesicle invasion, n (%)	24 (30.4)
Margin positive, n (%)	34 (43.0)
Node positive, n (%)	15 (19.0)
*Ongoing androgen deprivation therapy at PET, n (%)	12 (15.4)
Duration on ADT prior to PET (days)	
Mean (SD)	40 (31)
Prostatectomy-Conventional Imaging Interval (years)	
Median (range)	1.6 (0.0-11.3)
Prostatectomy-PET Interval (years)	
Median (range)	1.7 (0.2-11.5)

*n=78 patients

Table 2: Comparison of Positivity Rates on Conventional Imaging and ^{18}F-fluciclovine PET

	Whole body n (%)			Prostate bed n (%)			Pelvic lymph nodes n (%)		
	CI	PET	P-value	CI	PET	P-value	CI	PET	P-value
All patients (n=79)	11/79 (13.9)	63/79 (79.7)	<0.001	4/79 (5.1)	55/79 (69.6)	<0.001*	8/79 (10.1)	30/79 (38.0)	<0.001
≤1 ng/mL (n=57)	5/57 (8.8)	43/57 (75.4)	<0.001	2/57 (3.5)	39/57 (68.4)	<0.001*	3/57 (5.3)	16/57 (28.1)	0.002*
>1 ng/mL (n=22)	6/22 (27.3)	20/22 (90.9)	<0.001*	2/22 (9.1)	16/22 (72.7)	<0.001*	5/22 (22.7)	14/22 (63.6)	0.014

CI: conventional imaging; *Fisher's exact test

Table 3: Influence of ^{18}F-fluciclovine on Management Decision and Radiotherapy Field Recommendations

Pre-fluciclovine decision	**Post-fluciclovine decision**			**Decision change, n (%)**	**P-value**
Overall XRT decision (n=79)	Prostate bed only	Pelvis ± prostate bed	No XRT		
XRT to prostate bed only	31	14*	0	14/79 (17.7)	
XRT to Prostate bed + Pelvis	10*	20	4*	14/79 (17.7)	**<0.001**
No XRT	0	0	0	0/79 (0.0)	
				Overall decision change: 35.4%	
Radiotherapy Decision (n=79)	Offer XRT		No XRT		
Offer XRT	75		4	4/79 (5.1)	0.120
No XRT	0		0	0/79 (0.0)	
Radiotherapy field (n=75)†	Prostate bed only		Pelvis ± prostate bed		
Prostate bed only (n=45)	31		14*	14/75 (18.7)	**<0.001**
Prostate bed + Pelvis (n=30)	10*		20	10/75 (13.3)	
				Field change: 32.0%	

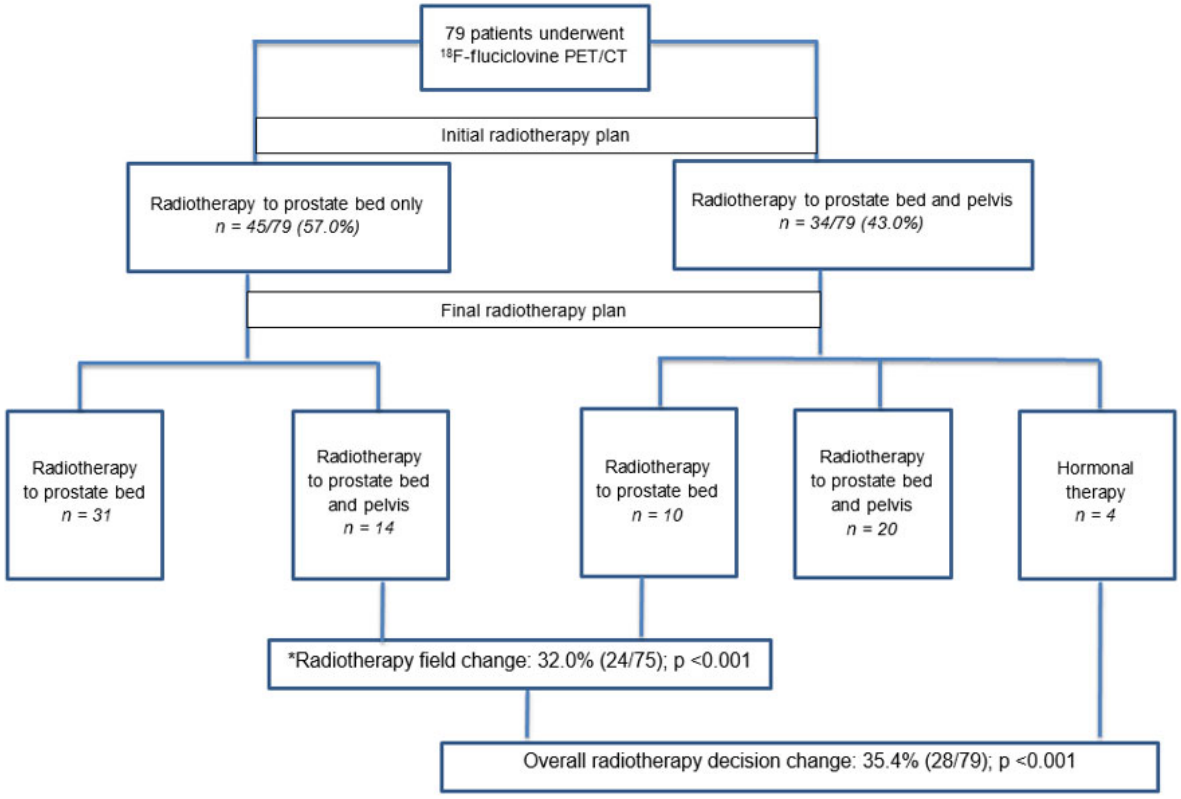
XRT: radiotherapy; *Decision change; †4 patients excluded due to extrapelvic uptake.

Table 4: Prognostic Factors and Radiotherapy Decision Change

Prognostic Factor	Decision Change (N=28) Mean (SD)	No Decision Change (N=51) Mean (SD)	p-value
PSA at PET (ng/mL)	2.67 (6.10)	1.21 (2.30)	**0.033***
≤1 (n=57)	0.36 (0.23)	0.25 (0.18)	0.054
>1 (n=22)	6.59 (7.43)	4.33 (3.18)	0.380
Gleason Score (GS)	7.25 (0.89)	7.39 (0.92)	0.507
GS ≤3+4 (n=35)	6.69 (0.48)	6.82 (0.40)	0.406
GS ≥4+3 (n=44)	7.73 (0.88)	7.83 (0.97)	0.754
Prostatectomy-PET Interval (years)	3.91 (3.64)	2.51 (2.69)	0.055
≤2 (n=45)	0.88 (0.61)	0.81 (0.52)	0.706
>2 (n=34)	6.53 (3.05)	5.36 (2.43)	0.223

*Kruskal-Wallis test

Graphical Abstract



*75 patients had radiotherapy

Supplemental Table 1. Demographic, Clinical and Histopathologic Characteristics of Arm A (Conventional Imaging only) Study Participants (n=82).

Age (years)	
Mean (SD)	61.7 (7.5)
PSA prior to radiotherapy (ng/mL)	
Median (range)	0.34 (0.01-27.14)
Gleason score (GS), n (%)	
GS 3+3 (Grade group 1)	4 (4.8)
GS 3+4 (Grade group 2)	30 (36.6)
GS 4+3 (Grade group 3)	19 (23.2)
GS ≥ 4+4 (Grade groups 4 and 5)	29 (35.4)
Primary tumor stage, n (%)	
T1-T2	35 (42.7)
T3-T4	47 (57.3)
Extracapsular extension, n (%)	43 (52.4)
Seminal vesicle invasion, n (%)	22 (26.8)
Margin positive, n (%)	41 (50.0)
Node positive, n (%)	14 (17.1)
Prostatectomy-Conventional Imaging Interval (years) Median (range)	0.94 (0.08-21.22)
Androgen deprivation therapy, n (%)	28 (34.6)
Radiotherapy Decisions*	
Prostate bed only	56
Prostate bed and pelvic nodes	25

*In total, 81 patients in Arm A received radiotherapy.