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Prospective Evaluation in an Academic Center of ^{18}F-DCFPyL PET/CT in Biochemically Recurrent Prostate Cancer: A Focus on Localizing Disease and Changes in Management

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Abstract

^{18}F-DCFPyL is a promising PET radiopharmaceutical targeting prostate specific membrane antigen (PSMA). We present our experience in this single academic center prospective study evaluating the positivity rate of ^{18}F-DCFPyL PET/CT in patients with biochemical recurrence (BCR) of prostate cancer (PC).

Methods: We prospectively enrolled 72 men (52-91 years old, mean±SD: 71.5±7.2) with BCR after primary definitive treatment with prostatectomy (*n*=42) or radiotherapy (*n*=30). The presence of lesions compatible with PC was evaluated by two independent readers. Fifty-nine patients had concurrent scans with at least one other conventional scan: bone scan (24), CT (21), MR (20), ^{18}F-Fluciclovine PET/CT (18) and/or ^{18}F-NaF PET (14). Findings from ^{18}F-DCFPyL PET/CT were compared with those from other modalities. Impact on patient management based on ^{18}F-DCFPyL PET/CT was recorded from clinical chart review.

Results: ^{18}F-DCFPyL PET/CT had an overall positivity rate of 85%, which increased with higher prostate specific antigen (PSA) levels (ng/mL): 50% (PSA<0.5), 69% (0.5≤PSA<1), 100% (1≤PSA<2), 91% (2≤PSA<5) and 96% (PSA≥5), respectively. ^{18}F-DCFPyL PET detected more lesions than conventional imaging. For anatomic imaging, 20/41 (49%) CT/MRI had congruent findings with ^{18}F-DCFPyL, while ^{18}F-DCFPyL PET was positive in 17/41 (41%) cases with negative CT/MRI. For bone imaging, 26/38 (68%) bone scan/^{18}F-NaF PET were congruent with ^{18}F-DCFPyL PET, while ^{18}F-DCFPyL PET localized bone lesions in 8/38 (21%) patients with negative bone scan/^{18}F-NaF PET. In 8/18 (44%) patients, ^{18}F-Fluciclovine PET had located the same lesions as the ^{18}F-DCFPyL PET, while 5/18 (28%) patients with negative ^{18}F-Fluciclovine had positive ^{18}F-DCFPyL PET findings and 1/18 (6%) patient with negative ^{18}F-DCFPyL had uptake in the prostate bed on ^{18}F-Fluciclovine PET. In the remaining 4/18 (22%) patients, ^{18}F-DCFPyL and ^{18}F-Fluciclovine scans showed different lesions. Lastly, 43/72 (60%) patients had

treatment changes after ^{18}F-DCFPyL PET and, most noticeably, 17 of these patients (24% total) had lesion localization only on ^{18}F-DCFPyL PET, despite negative conventional imaging. **Conclusion:** ^{18}F-DCFPyL PET/CT is a promising diagnostic tool in the work-up of biochemically recurrent prostate cancer given the high positivity rate as compared to FDA-approved currently available imaging modalities and its impact on clinical management in 60% of patients.

Key words: ^{18}F-DCFPyL, prostate-specific membrane antigen, prostate cancer, biochemical recurrence

Introduction

Patients with localized PC who underwent primary definitive treatment may subsequently experience a rise in PSA levels, known as BCR. Approximately 20-40% of patients treated with radical prostatectomy (*1*) or 30-50% patients who underwent radiation therapy (*2*) will experience BCR within 10 years (*3*). Although rising PSA can predict recurrent disease or metastasis, not all BCR patients have the same prognosis based on PSA level alone. Oncologists thus need to balance rising PSA level with the efficacy and side effects of subsequent treatment options. Common clinical decisions made by oncologists include active surveillance, androgen deprivation therapy (ADT), salvage radiation therapy/prostatectomy or both. However, there is no uniform guideline regarding treatment choice and its timing (*4*). Therefore, effective imaging that is able to localize recurrence or distant metastasis in BCR patients with high sensitivity and specificity is critical for selection of different treatments.

Imaging such as CT/MR, or bone scintigraphy generally have low sensitivity in detecting sites of recurrent disease (*5*). The FDA approved ^{11}C-choline in 2012 and ^{18}F-fluciclovine (Blue Earth Diagnostics Ltd., United Kingdom) in 2016 for use in patients with BCR. Recent prospective trials have shown significant impact of ^{18}F-fluciclovine PET on clinical decision making in BCR (*6*). However, a common criticism is that the detection rate of ^{18}F-fluciclovine is relatively lower in patients with PSA<2.0 ng/mL (*7*).

PSMA expression is upregulated in PC and associated with high-grade PC and androgen deprivation (*8*). Several PSMA-based radiopharmaceuticals, including ^{68}Ga-PSMA-11 (*9-11*) and ^{18}F-PSMA-1007 (*12*) have better rates of detection when compared to ^{11}C- or ^{18}F-choline. ^{18}F-DCFPyL is a PSMA-targeting PET radiopharmaceutical with greater affinity than the previous generation (*13-15*). A direct comparison of ^{18}F-DCFPyL with ^{68}Ga-PSMA-11 showed that ^{18}F-DCFPyL is non-inferior and may even have higher sensitivity (*16*). A recent prospective study also showed that ^{18}F-DCFPyL PET/CT is safe and sensitive for detection of BCR and changed clinical management in the majority of the patients (*17*). Here, we report our

experience in an academic center prospective evaluation of ^{18}F-DCFPyL PET/CT in patients with BCR PC.

MATERIALS AND METHODS

This study was approved by the Stanford Institutional Review Board and the Stanford Cancer Institute Scientific Review Committee. All subjects signed a written informed consent. The study was registered on clinicaltrials.gov (NCT03501940).

All participants had BCR after primary definitive treatment with radical prostatectomy with or without adjuvant pelvic radiation or radiation therapy alone. Rising PSA after definitive therapy with prostatectomy or radiation therapy (external beam or brachytherapy) was defined as follows. For post radical prostatectomy (American Urological Association recommendation) (*18*): PSA greater or equal to 0.2 ng/mL measured after at least 6 weeks following radical prostatectomy or confirmatory persistent PSA greater than or equal to 0.2 ng/mL (total of two PSA measurements greater than 0.2 ng/mL). For post radiation therapy (American Society for Radiation Oncology-Phoenix consensus definition) (*19*): A rise of PSA measurement of 2 or more ng/mL over the nadir. Time to first BCR was calculated from the date of primary definitive treatment to the date of the first BCR.

Imaging Protocol

^{18}F-DCFPyL was provided by Progenics Pharmaceuticals, Inc. (New York, NY, USA) as part of a research access program, for use in an investigator-initiated protocol. ^{18}F-DCFPyL dosage ranged 270.1-370 MBq (mean±SD: 338.8±25.3 MBq). Imaging started 60 minutes (mean±SD: 74.4±10.4 mins) following IV administration of the radiopharmaceutical. A low-dose CT scan was performed for attenuation correction and anatomic correlation. PET followed immediately after, starting from the mid-thighs to the vertex of the skull. All patients were scanned using a state-of-the-art time-of-flight enabled, silicon photomultipliers based Discovery

MI PET/CT scanner (GE Healthcare, Waukesha, WI, USA). PET data were reconstructed using a block sequential regularized expectation maximization penalized likelihood reconstruction (Q.Clear®, GE Healthcare). Beta, the noise penalizing determining factor in Q.Clear®, was set at 400 per local preference.

Image Analysis and Correlation with Biopsy Results

PET/CT images were reviewed independently by two nuclear medicine physicians using MIMvista version 6.7 (MIMvista, Cleveland, OH, USA). Positive lesions (uptake above adjacent background in putative sites of disease) were categorized based on their location in the prostate bed, pelvic lymph nodes, abdominal and retroperitoneal lymph nodes, osseous lesions and other visceral/soft tissue lesions (such as hepatic or pulmonary lesions). Imaging findings on other conventional imaging modalities including CT, MR, bone scan, ^{18}F-NaF PET/CT and ^{18}F-Fluciclovine PET/CT were also reviewed and compared to the findings on ^{18}F-DCFPyL PET/CT. Findings were considered congruent if both scans compared were negative or if the same lesions were identified on both scans. Impact on patient management after ^{18}F-DCFPyL PET/CT scan was recorded from prospective chart review of clinical notes.

Pathological confirmation of the ^{18}F-DCFPyL findings was only available in a small number of cases (*n*=4). Biopsy was not required by the study design and was often difficult since the lesions detected on ^{18}F-DCFPyL PET were frequently sub-centimeter in size.

Statistical Analysis

The positivity rate was defined as percentage of patients with focal ^{18}F-DCFPyL PET/CT in putative sites of disease. The positivity rates for different PSA levels and doubling time were compared with chi-square test with significant *P* value set at < 0.05.

RESULTS

Study Participants

We prospectively enrolled 72 men (52-91 year-old, mean±SD: 71.5±7.2) between May, 2018 and July, 2019. Primary definitive treatment included radical prostatectomy with or without adjuvant pelvic radiation in 42 participants and radiation therapy in 30 participants. The clinical data is summarized in Table 1. Fifty-nine patients (82%) had at least one of the following conventional imaging scans during the work-up for biochemical recurrence: bone scan (*n*=24), CT (*n*=21), MR (*n*=20), ^{18}F-Fluciclovine PET/CT (*n*=18) and/or ^{18}F-NaF PET (*n*=14).

PSA Levels and Positivity Rates on ^{18}F-DCFPyL PET/CT

The PSA level at the time of ^{18}F-DCFPyL PET/CT ranged 0.23-698.4 ng/mL (median 3.0 ng/mL, mean±SD: 15.8±83.2 ng/mL). Twenty-one patients (29%) had PSA<1.0 ng/mL at time of ^{18}F-DCFPyL PET/CT. The median PSA level for patients treated with radical prostatectomy or radiation therapy was 1.4 ng/mL (range: 0.2-18.3 ng/mL) and 5.4 ng/mL (range: 0.4-698.4 ng/mL), respectively.

^{18}F-DCFPyL PET showed focal uptake in putative sites of disease in 61 patients (85%). This positivity rate increased significantly with PSA levels. ^{18}F-DCFPyL PET was positive in 62% of participants with PSA levels <1.0 ng/mL and 94% of participants with PSA levels ≥1.0 ng/mL ($P < 0.001$). The positivity rate for different PSA levels (ng/mL) was 50% (PSA<0.5), 69% (0.5≤PSA<1), 100% (1≤PSA<2), 91% (2≤PSA<5) and 96% (PSA≥5). These findings are summarized in Table 2. ^{18}F-DCFPyL PET positivity rate for different PSA doubling time was 87%, 85%, 92% and 79% for doubling time of 0-3 month, 3-6 months, 6-12 months and greater than 12 months, respectively ($P>0.05$). Four biopsies were performed and all four confirmed prostate adenocarcinoma at the sites of ^{18}F-DCFPyL uptake. Three of the biopsy sites evaluated uptake in the prostate gland and one biopsy targeted the left pubic bone.

The ^{18}F-DCFPyL PET positivity rate was 89% for the 28 patients with prior BCR and treatment, compared to 82% in 44 patients evaluated at first BCR (P<0.01). This difference may be partially explained by the fact that fewer patients with prior BCR had pre-scan PSA that was less than 1.0 (7 out of 28 patients, 25%) compared to patients at first BCR (13 out of 44, 30%) since overall positivity rate is lower in patients with pre-scan PSA<1.0.

Sites of Disease Detection with ^{18}F-DCFPyL PET/CT

The most common sites of disease that were detected by ^{18}F-DCFPyL PET/CT in this cohort included prostate bed (31% of positive scans) and pelvic lymph nodes (48% of positive scans). In addition, a high percentage of patients had extra-pelvic findings on ^{18}F-DCFPyL PET/CT, including 46% with bone lesions, 28% with abdominal and retroperitoneal lymph nodes and 16% with soft tissue lesions in other organs such as liver and lungs. Fig. 1 shows pelvic lymph nodes as sites of recurrent disease, while Fig. 2 shows a small osseous lesion. As expected, more lesions were detected in the prostate bed when patients were treated with radiation therapy (15/30 patients, 50%) vs. radical prostatectomy (4/42 patients, 10%) (P < 0.001). No significant difference in percentage of detected extra-pelvic disease (abdominal and retroperitoneal lymph node lesions, bone and other sites including lungs and liver) was seen between prostatectomy or radiation therapy (P>0.05).

Comparison with Other Imaging Modalities

When ^{18}F-DCFPyL PET was compared to CT, 7/21 (33%) CT scans showed congruent findings with ^{18}F-DCFPyL PET, while 12/21 (57%) patients with negative CT had positive ^{18}F-DCFPyL PET finding(s). In addition, a higher percentage (13/20, 65%) of MR scans had congruent findings with ^{18}F-DCFPyL PET, while 5/20 (25%) patients with negative MR had positive ^{18}F-DCFPyL PET finding(s). These findings are shown in Supplemental Table 1. The main explanation of ^{18}F-DCFPyL's advantage over conventional CT/MR is that ^{18}F-DCFPyL PET

often results in uptake in subcentimeter lesions that do not meet size criteria on cross-sectional imaging. Figure 1 shows an example of a patient with DCFPyL uptake in sub-centimeter pelvic wall lymph nodes seen on CT but not meeting size criteria. Moreover, 1/18 (6%) MR scan showed a single suspicious L1 lesion with spinal stenosis confirmed by bone scan; the patient was initially scheduled for laminectomy. However, ^{18}F-DCFPyL PET showed uptake in additional lesions in L2 and L5 vertebrae; therefore, treatment was changed to ADT. This case demonstrates the advantage of ^{18}F-DCFPyL PET over MR in identifying small marrow lesions.

For dedicated bone imaging, 16/24 (67%) ^{99m}Tc-MDP bone scans had congruent findings with ^{18}F-DCFPyL PET while 6/24 (25%) patients with negative bone scans had bone metastases identified on ^{18}F-DCFPyL PET. Fig. 3 shows an ^{18}F-DCFPyL PET with extensive bone metastasis including left iliac wing lesion that had no uptake on bone scan. On the other hand, one of the patients had uptake in a sclerotic rib lesion on bone scan, but no uptake was seen on ^{18}F-DCFPyL PET. This patient continued active surveillance under the assumption that it was non-specific uptake on bone scan. In another participant with focal ^{99m}Tc-MDP uptake in an iliac crest lesion, ^{18}F-DCFPyL PET found no uptake in the iliac lesion; instead there was uptake in a sclerotic rib lesion, as well as in multiple abdominal lymph nodes. This patient received ADT and the PSA has been down-trending. Similarly, 10/14 (71%) ^{18}F-NaF PET had congruent findings with ^{18}F-DCFPyL PET, while 2/14 (14%) patients with positive ^{18}F-DCFPyL PET for bone metastasis had negative ^{18}F-NaF PET. In a patient who had different findings on^{18}F-NaF and ^{8}F-DCFPyL PET, ^{18}F-NaF PET showed uptake in a left iliac lesion, but no bony uptake was seen on ^{18}F-DCFPyL; instead, ^{18}F-DCFPyL uptake was seen in several abdominal soft tissue nodules and hepatic lesions. This patient started ADT and the PSA has decreased to undetectable levels.

A total of 18 patients had ^{18}F-Fluciclovine PET/CT as part of standard of care work-up of BCR. Eight out of 18 (44%) ^{18}F-Fluciclovine PET scans showed the same lesions as the ^{18}F-DCFPyL PET. However, in 5/18 (28%) patients with negative ^{18}F-Fluciclovine PET, ^{18}F-DCFPyL

PET identified putative sites of disease, including three cases with uptake in pelvic side wall lymph nodes and two cases with uptake in multiple sclerotic bone lesions. In comparison, 1/18 (6%) patients had negative ^{18}F- DCFPyL while ^{18}F-Fluciclovine showed uptake in the prostate bed. In the remaining 4/18 (22%) patients, ^{18}F-DCFPyL and ^{18}F-Fluciclovine scans had different findings. For example, in one patient post-radical prostatectomy, ^{18}F-DCFPyL PET showed uptake in multiple pelvic and abdominal lymph nodes as well as focal uptake in the T7 vertebral body, and no uptake in the prostate bed whereas ^{18}F-Fluciclovine PET showed uptake in the prostate bed but not in other nodal and bone lesions seen on ^{18}F-DCFPyL PET (Fig. 4). Based on the fact that the patient had high grade PC at diagnosis and there was a positive margin at prostatectomy, the oncologist took into account findings on both PET scans and treated the patient with ADT and focal radiation to the prostate bed. The patient's PSA has decreased to undetectable levels.

Impact of ^{18}F-DCFPyL PET/CT on Patient Management

A total of 43 (60%) patients started new treatment after ^{18}F-DCFPyL PET. These included 20 patients (47%) referred for radiation therapy with or without concurrent ADT and 23 patients (53%) who started ADT without RT. This data is summarized in Supplemental Table 2. Among the 20 patients who received RT, 7 had targeted extra-pelvic lesions (including ribs, vertebral bodies, retroperitoneal lymph nodes, sternum and calvaria) and 13 had targeted pelvic lesions (6 prostate bed and 7 pelvic lymph nodes). Nine patients had confirmed PSA decrease after radiation therapy at the time of manuscript write-up.

^{18}F-DCFPyL PET identified lesions in 26 patients (36%) without findings on conventional imaging modalities. This led to changes in clinical management in 17 patients (24% of total participants), including 6 patients who received targeted radiotherapy and 11 patients who started ADT. Three of the 26 patients remained under active surveillance despite positive findings on ^{18}F-DCFPyL PET due to relatively low PSA levels at time of imaging (0.38 and 0.59

ng/mL) or patient preference. Four recently scanned patients had no documented clinical decision after ^{18}F-DCFPyL PET.

DISCUSSION

^{18}F-labeled PSMA targeting PET radiopharmaceuticals have the advantage of higher spatial resolution due to shorter positron range and potentially improved commercial availability due to longer half-life when compared to ^{68}Ga-labeled tracers. Here, ^{18}F-DCFPyL PET had a high overall positivity rate of 85%. ^{18}F-DCFPyL PET detected more lesions than conventional imaging, ranging from 25% in bone imaging to 57% in CT. Overall, 26 patients (36%) had lesion localization only on ^{18}F-DCFPyL PET with no findings on other conventional imaging. Similar diagnostic advantage was shown previously where 138 lesions were detected on ^{18}F-DCFPyL PET while only 30 lesions were detected on conventional imaging (*14*). One of the reasons for this advantage over anatomic imaging is that ^{18}F-DCFPyL uptake is detected in lesions (e.g. lymph nodes) before anatomic diagnostic criteria are met. Moreover, for bone lesions, ^{18}F-DCFPyL PET may be able to detect small marrow lesions that have not caused detectable reactive bony changes typically seen on bone scintigraphy.

No statistically significant higher positivity rate of ^{18}F-DCFPyL PET were found in patients with shorter PSA doubling time although a trend was observed. This may be attributed to the relatively small cohort size. Other PET radiotracers targeting PC have shown increased positivity rate with shorter PSA doubling time. In a meta-analysis of 1309 patients, ^{68}Ga-PSMA PET positivity was found to be associated with shorter PSA doubling time (*20*).

^{18}F-DCFPyL PET altered clinical management in 43 patients (60%) treated with targeted radiotherapy and/or ADT, including 17 patients (24% overall) without findings identified on conventional imaging. This level of impact on clinical management has been observed in other studies using PSMA-targeting radiopharmaceuticals (*9,17*). One difference in methodology is that several prior studies used a survey of oncologists to determine change of intended clinical

management, whereas we conducted a review of clinical charts to determine the impact of ^{18}F-DCFPyL PET on clinical management. This approach, although based on actual changes, not intent, has the limitation that it is difficult to determine whether the decisions made by the treating physicians were based on imaging alone or other contributing factors such as PSA, risk and benefit of treatments and patient preference. Adding the survey approach with pre-scan and post-scan questionnaires to the treating physicians regarding patient management is planned for future prospective trials and may help validate these initial findings.

One limitation of our study is that there was only a small number of histopathological confirmation available for positive ^{18}F-DCFPyL scans. ^{18}F-DCFPyL PET/CT often detects subcentimeter lesions in the setting of BCR that are difficulty to biopsy. When multiple lesions are detected on ^{18}F-DCFPyL PET in putative sites of disease for PC recurrence or metastases, treating physicians often rely on post-treatment PSA changes as alternative for confirmation of positive DCFPyL lesions rather than on biopsy. Overall, there is still not enough data in our cohort to evaluate the rate of ^{18}F-DCFPyL false positive lesions. We previously showed that ^{68}Ga-PSMA-11 had specificity of 87.5% for prostate lesions and 98.4 % for metastatic lymph nodes in initial staging using histopathology as the gold standard (*11*).

Three recently published studies of ^{18}F-DCFPyL showed overall positivity rate of 84.6%, 67.7% and 86.3% (*17,21,22*). When comparing to a recent prospective two-center trial of ^{68}Ga-PSMA11 PET in BCR with a large patient cohort (635 patients) (*9*), ^{18}F-DCFPyL PET has better or similar positivity rates for PSA<0.5 ng/mL (50% vs. 38% for ^{68}Ga-PSMA11 PET), for PSA 0.5≤PSA<1.0 ng/mL (69% vs. 57%), for PSA 1.0≤PSA<5.0 (93% vs. 85%) and for PSA≥5 ng/mL (96% vs. 97%). Similar overall positivity rate of 80.3% was found for ^{18}F-PSMA-1007 in the setting of BCR (*12*).

In our study, ^{18}F-DCFPyL PET had a higher positivity rate compared to ^{18}F-Fluciclovine PET in a small sub-group who underwent both PET imaging tests (89% vs. 67%, P<0.01). The overall positivity rate of ^{18}F-Fluciclovine PET was 59% in a published study (*6*). Similarly, higher

positivity rates of PSMA-based radiotracers were seen in head-to-head direct comparisons of ^{68}Ga-PSMA-11 to ^{18}F-Fluciclovine (*23,24*). Interestingly, we report three patients with prostate bed uptake on ^{18}F-Fluciclovine PET who had multiple extra-pelvic lesions but no prostate bed lesion identified on ^{18}F-DCFPyL PET. This oraises the possibilities that various radiopharmaceuticals may be complementary in detecting lesions in patients with BCR.

Improved detection of recurrence by ^{18}F-DCFPyL PET is only clinically significant if subsequently changed clinical management can improve progression free survival or overall survival. These long-term benefits have yet to be evaluated. A multicenter phase III trial (SPPORT trial) in patients with BCR showed freedom-from-progression rate increased from 71.7% in patients who received prostate bed radiation alone to 89.1% in patients who received prostate bed radiation, pelvic lymph node radiation and short term ADT (*25*). This management decision did not use input of any imaging finding instead was solely based on rising PSA. Such changes in practice by radiation oncologists could mean that ^{18}F-DCFPyL PET may add most value when extra-pelvic oligometastatic lesions are detected that may benefit from targeted radiation (*26*). More clinical trials are needed to evaluate survival benefits of PSMA based PET radiotracer in BCR.

The assessment of ^{18}F-DCFPyL PET accuracy in localizing disease in patients with BCR and negative baseline imaging (including ^{18}F-fluciclovine PET) according to institutional standard of care work-up is currently under investigation in a multi-center, multi-reader prospective trial (ClinicalTrials.gov identifier, NCT03739684).

CONCLUSION

^{18}F-DCFPyL PET/CT is a promising diagnostic tool in the work-up of patients with biochemically recurrent prostate cancer, with an overall positivity rate of 85% in this cohort and impact on clinical management in 60% of patients, including 24% without abnormal findings on conventional imaging.

DISCLOSURE

^{18}F-DCFPyL was provided by Progenics Pharmaceuticals, Inc. (New York, NY, USA) as part of a research access program. No potential conflicts of interest relevant to this article exist.

KEY POINTS

QUESTION: Is ^{18}F-DCFPyL PET/CT useful in the evaluation of patients with BCR PC?

PERTINENT FINDINGS: In a prospective study of 60 men with BCR after primary definitive treatment, ^{18}F-DCFPyL PET/CT had an overall positivity rate of 83%, which increased with higher PSA levels (ng/mL): 43% (PSA<0.5), 64% (0.5≤PSA<1), 100% (1≤PSA<2), 94% (2≤PSA<5) and 96% (PSA≥5), respectively. A total of 36/60 patients (60%) had treatment changes after ^{18}F-DCFPyL PET and, most noticeably, 14 of these patients (23% total) had lesion localization only on ^{18}F-DCFPyL PET, despite negative conventional imaging.

IMPLICATIONS FOR PATIENT CARE: ^{18}F-DCFPyL PET/CT is a promising diagnostic tool in the work-up of BCR patients given the high positivity rate as compared to other currently FDA-approved imaging modalities and its impact on clinical management.

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FIGURE LEGENGS:

Figure 1: 68 year-old man with BCR (PSA 5.4 ng/mL). Maximum intensity projection (MIP) image from ^{18}F-DCFPyL PET (A) shows uptake in bilateral pelvic wall lymph nodes (arrows), also seen on axial PET (B), CT (C) and fused PET/CT (D). These are below the CT size threshold for pathology.

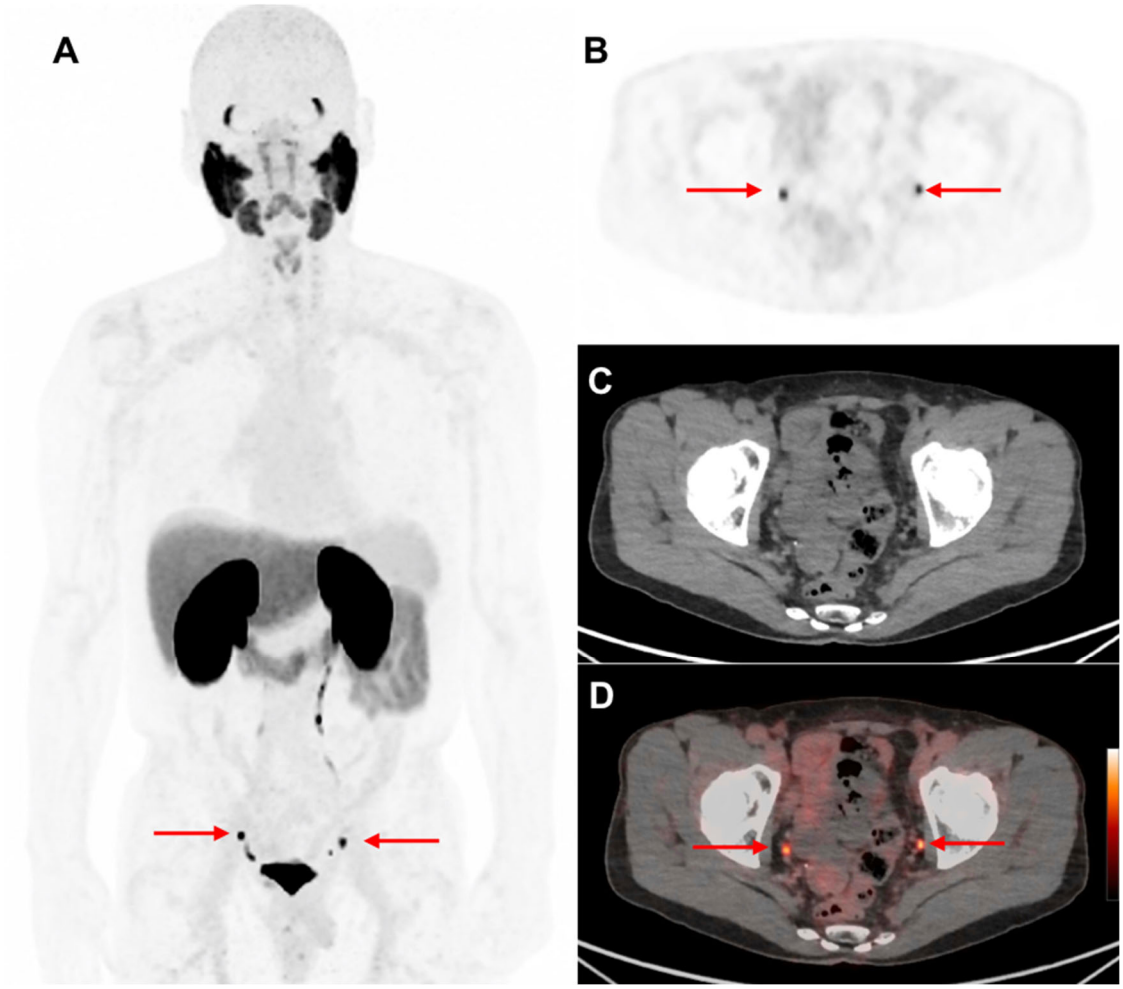

Figure 2: 69 year-old man with BCR (PSA 0.4 ng/mL). ^{18}F-DCFPyL PET MIP (A) shows several small bone lesions and a pelvic lymph node. Focal ^{18}F-DCFPyL uptake in the right ischium (arrow) is seen on axial PET (C), CT (D) and fused PET/CT (E).

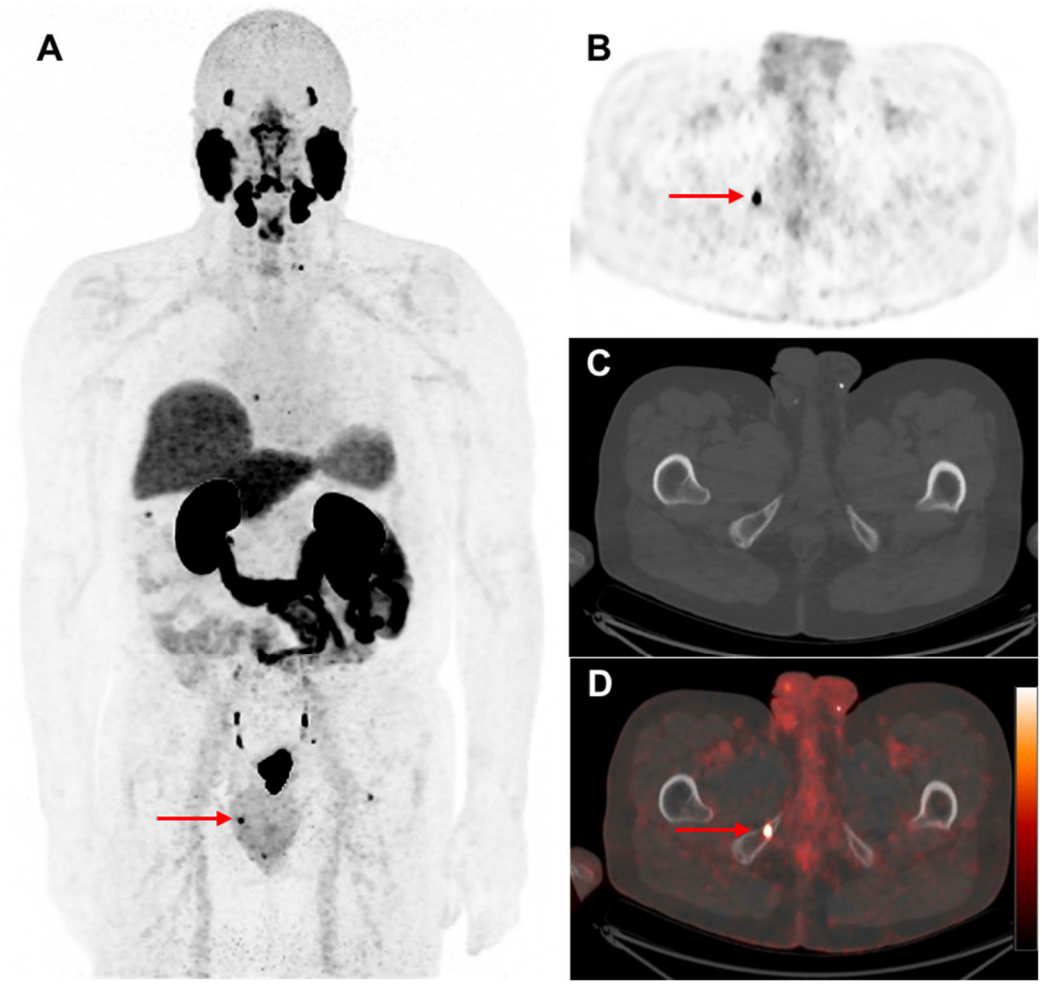

Figure 3: 69 year-old man with BCR (PSA 3.3 ng/mL) had a bone scan that was negative (A), but ^{18}F-DCFPyL PET MIP (B) showed extensive nodal and skeletal metastases. Focal ^{18}F-DCFPyL uptake in the left iliac wing (arrow) is seen on axial PET (C), CT (D) and fused PET/CT (E).

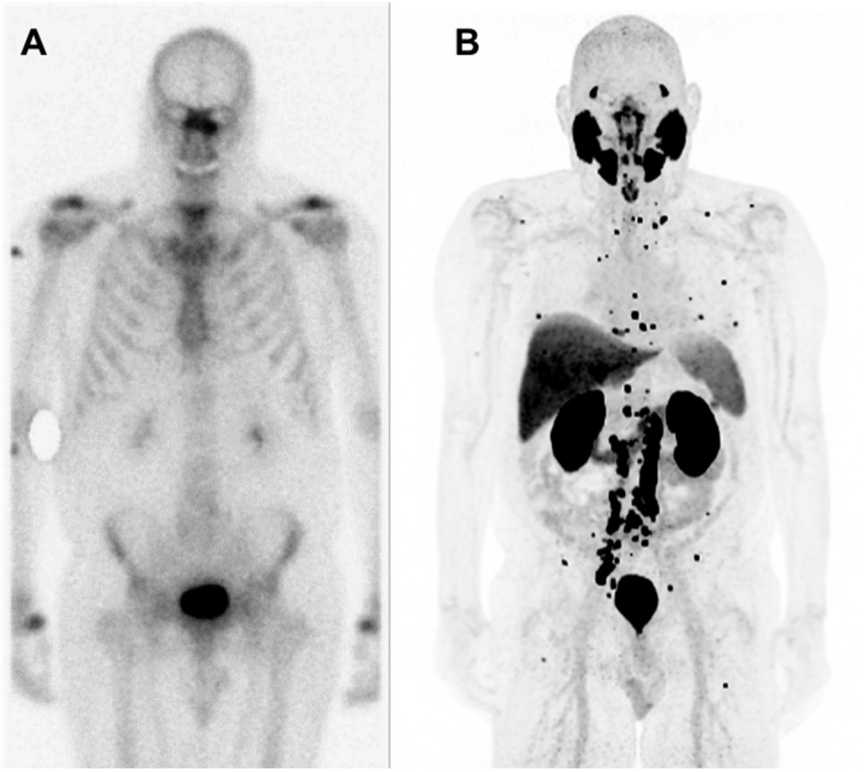

Figure 4: 64 year-old man with BCR (PSA 3.1 ng/mL) had different findings on ^{18}F-DCFPyL and ^{18}F-Fluciclovine PET. Axial fused ^{18}F-DCFPyL PET/CT (A bottom) and ^{18}F-DCFPyL PET (A top), show focal uptake in the T7 vertebral body (arrow) but no uptake in prostate bed (B bottom - fused PET/CT images, B top - PET). In comparison, axial fused ^{18}F-Fluciclovine PET/CT (C bottom) and ^{18}F-Fluciclovine PET (C top) show no uptake in the T7 vertebral body but focal uptake (arrowhead) in the left aspect of the prostate bed (D bottom - fused PET/CT images, D top - PET).

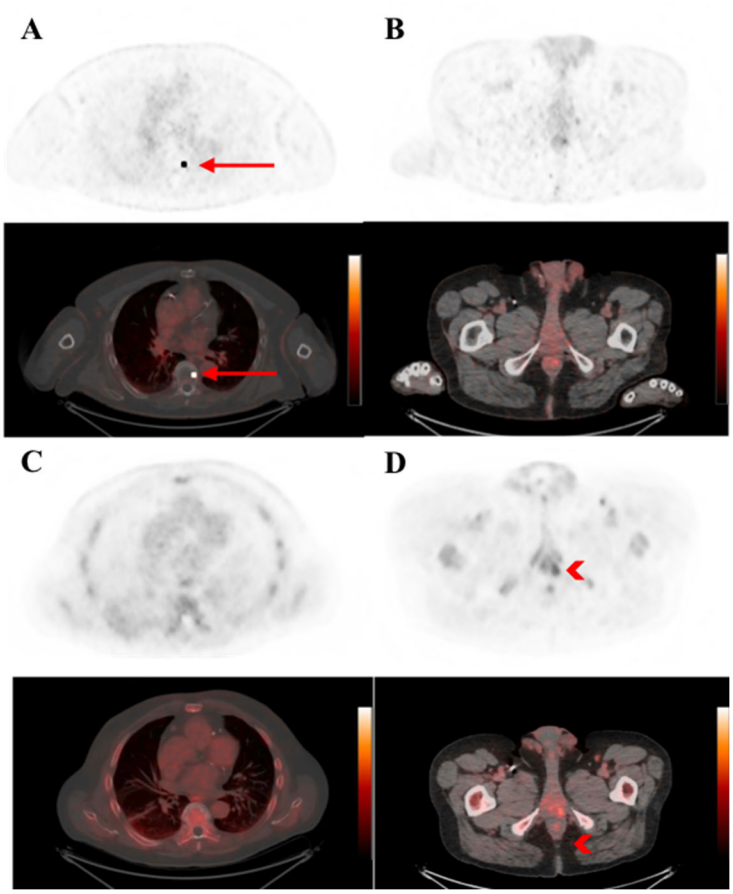

Table 1: Demographics and Characteristics of Participants

Characteristic	
Age (years) mean±SD	71.5±7.2
Primary definitive treatment, No. (%)	
Radical prostatectomy	42 (58)*
Radiation therapy	30 (42)
Gleason score at initial diagnosis	
6	6 (8)
7	37 (51)
8	11 (15)
9	17 (24)
10	1 (1)
Median time to first BCR† (months)	
Radical prostatectomy	36 (range 3-120)
Radiation therapy	48 (range 4-192)
^{18}F-DCFPyL activity (mean±SD, MBq)	338.8±25.3
Time to acquisition after injection (mean±SD, min)	74.4±10.4

*12 patients (17%) received adjuvant radiation to pelvis.
†28 patients (39%) had multiple recurrences with treatments.

Table 2: Positivity rates of ^{18}F-DCFPyL PET/CT based on PSA levels (ng/mL) and PSA doubling time (months)

	Positive PET scan (*n*)	Negative PET scan (*n*)	Percentage positive scan
PSA<0.5	4	4	50%
0.5≤PSA<1	9	4	69%
1≤PSA<2	5	0	100%
2≤PSA<5	20	2	91%
PSA ≥ 5	23	1	96%
Total	61	11	85%
PSA Doubling time*			
0-3	13	2	87%
3-6	17	3	85%
6-12	11	1	92%
>12	11	3	79%

*Two patients were treated with ADT before ^{18}F-DCFPyL PET/CT and PSA was down-trending. Six patients had fluctuating to down-trending PSA before the scan with no treatment. Three patients referred from outside hospital had no documented PSA trend or nadir.

Supplemental Table 1: Comparison of ^{18}F-DCFPyL PET/CT findings to conventional imaging

Number of scans (%)	CT	MR	^{99m}Tc MDP Bone Scan	^{18}F-NaF PET/CT	^{18}F-Fluciclovine PET/CT
Congruent	7 (33)	13 (65)	16 (67)	10 (71)	8 (44)
Non-Congruent	14 (67)	7 (35)	8 (33)	4 (29)	10 (56)
Positive ^{18}F-DCFPyL PET	12	5	6	2	5
Negative ^{18}F-DCFPyL PET	1		1	1	1
Different findings	1	2	1	1	4

Supplemental Table 2: Impact of ^{18}F-DCFPyL PET/CT on Patient Management

Number of patients (% total patients)	Positive ^{18}F-DCFPyL PET				Negative ^{18}F-DCFPyL PET
	Total	Prostatectomy	Radiation therapy	Negative conventional imaging†	Total
Radiation with or without ADT	20 (28)	15 (21)	5 (7)	6 (8)	3‡ (4)
ADT	23 (32)	12 (17)	11 (15)	11 (15)	3 (4)
Surveillance	5 (7)	3 (4)	2 (3)	3 (4)	5 (7)
Other	13* (18)	5 (7)	8 (11)	6 (8)	

*Six patients with no documented follow up management plan yet. Three patients started ADT before the scan and continued afterwards. Three patients need additional work-up. One patient had ^{18}F-DCFPyL PET as a requirement to participate in a clinical trial.

†Eight patients had not had any documented conventional imaging.

‡Two patients with negative ^{18}F-DCFPyL PET scans received radiation therapy to prostate bed and pelvic lymph nodes. One patient who had negative ^{18}F-DCFPyL PET but prostate bed uptake on ^{18}F-Fluciclovine PET received radiation therapy.