

Patterns of disease detection using ^{18}F -DCFPyL PET/CT imaging in men with biochemical recurrence post prostatectomy being considered for salvage radiotherapy: a prospective trial

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Abstract

Purpose Prostate specific membrane antigen (PSMA) PET/CT is increasingly used in men with biochemical recurrence post-prostatectomy to detect local recurrence and metastatic disease at low PSA levels. The aim of this study was to assess patterns of disease detection, predictive factors and safety using ^{18}F -DCFPyL PET/CT versus diagnostic CT in men being considered for salvage radiotherapy with biochemical recurrence post-prostatectomy.

Methods We conducted a prospective trial recruiting 100 patients with biochemical failure post-prostatectomy (PSA 0.2-2.0ng/mL) in men referred for salvage radiotherapy from August 2018 to July 2020. All patients underwent a PSMA PET/CT using the ^{18}F -DCFPyL tracer and a diagnostic CT. The detection rates of ^{18}F -DCFPyL PET/CT vs diagnostic CT were compared and patterns of disease are reported. Clinical patient and tumour characteristics were analysed for predictive utility. Thirty-day post-scan safety is reported.

Results Of 100 patients recruited, 98 were suitable for analysis with a median PSA of 0.32ng/mL. ^{18}F -DCFPyL PET/CT was positive or equivocal in 52% compared to 19.6% for diagnostic CT. Local recurrence was detected on ^{18}F -DCFPyL PET/CT in 29.2%, nodal disease was seen in 29.6% and bony metastases in 7.1%. Both ISUP grade group ($p = 0.003$) and pre-scan PSA ($p = 0.061$) were significant predictors of ^{18}F -DCFPyL PET/CT positivity, and logistic regression generated probabilities combining the two showed improved prediction rates. No significant safety events were reported post ^{18}F -DCFPyL administration.

Conclusions ^{18}F -DCFPyL PET/CT increases detection of disease in men with biochemical recurrence post-prostatectomy compared to diagnostic CT. Men being considered for salvage radiotherapy with a PSA >0.2ng/mL should be considered for ^{18}F -DCFPyL PET/CT scan.

Clinical Trial Registration Australian New Zealand Clinical Trials Registry Number: ACTRN12618001530213. Registration date 13.9.2018
<http://www.anzctr.org.au/Trial/Registration/TrialReview.aspx?id=375932&isReview=true>

Introduction

Following radical prostatectomy (RP) for localised prostate cancer, biochemical recurrence (BCR) is defined as prostate-specific antigen (PSA) levels exceeding 0.2ng/ml [1]. These men are often referred for salvage radiotherapy (RT) once this PSA threshold is reached, however the five-year freedom from biochemical failure rate is on average only 56% with prostate bed radiation and is superior with lower pre-radiotherapy PSA [2]. Failure to achieve biochemical control may be caused by failure to detect and treat disease outside the standard prostate bed and/or treated pelvic lymph node radiation fields. Conventional imaging with computed tomography (CT), whole-body bone scan, and magnetic resonance imaging are limited by poor sensitivity to detect low volume disease, particularly when referral for radiation is made at very low PSA levels [3].

Prostate-specific membrane antigen (PSMA) is a type II cell-surface glycoprotein overexpressed in more than 90% of prostate cancer epithelial cells [4, 5] but lower expression in most benign tissue. Positron emission tomography (PET) using a variety of tracers can reliably detect sites of prostate cancer before abnormalities can be appreciated using conventional imaging, particularly with respect to local recurrence and metastatic disease. ⁶⁸Ga labelled PSMA (⁶⁸Ga-PSMA-11) remains the most widely used and reported tracer [6], however ¹⁸F labelled PSMA agents (¹⁸F-DCFPyL, ¹⁸F-PSMA-1007) appear to offer non-inferior diagnostic assessment of men with biochemical recurrence [7, 8].

We aim to evaluate disease localisation using ¹⁸F-DCFPyL PET/CT when compared to diagnostic CT of chest, abdomen and pelvis (CTCAP) in this prospective cohort of men with BCR post RP being considered for salvage RT, determine biochemical and histopathological predictors of ¹⁸F-DCFPyL PET/CT positivity, and safety of the ¹⁸F-DCFPyL tracer.

Methods

Study design and participants

We performed a prospective non-randomised trial at nine GenesisCare sites within Victoria, Australia. Between August 2018 and July 2020, 100 men were recruited with evidence of BCR post-RP with or without pelvic lymph node dissection, after referral to a radiation oncologist for consideration of salvage RT with a PSA between 0.2-2.0ng/ml. Exclusion criteria included established distant metastases prior to enrolment, previous pelvic RT and previous androgen deprivation therapy. The protocol was approved by the St Vincent's Hospital Melbourne Human Research Ethics Committee and was registered under Australian New Zealand Clinical Trials Registry (ACTRN12618001530213).

Imaging acquisition

All patients underwent a CTCAP and ¹⁸F-DCFPyL PET/CT at the Department of Nuclear Medicine, St Vincent's Hospital, Fitzroy. Both scans were performed on a GE Discovery 710 PET/CT (General Electric Medical Systems, Milwaukee, WI) at a single session, combining a 64-slice multidetector CT scanner with a dedicated, full ring PET scanner. For the diagnostic CTCAP, 100ml of intravenous contrast was administered, and patients scanned from apex of the lungs to lesser trochanters 70 seconds post contrast. An additional 10-minute delayed pelvis CT was also obtained to assist in distinction between ureters and lymph nodes. For the PET/CT, 250MBq of GMP quality ¹⁸F-DCFPyL manufactured by Cyclotek Australia, was administered with an uptake time of 120 minutes post injection. Patients were scanned from mid-upper thighs to vertex in a supine position, and images were reconstructed using the Q.Clear GE reconstruction method with a β -value of 400.

Imaging interpretation

Blinded interpretation of the diagnostic CTCAP and ¹⁸F-DCFPyL PET/CT was performed separately by two independent readers. CTCAP images were interpreted by an experienced genitourinary radiologist,

and ^{18}F -DCFPyL PET/CT images were reported by two experienced nuclear medicine physicians. Reporting physicians did not have access to the images or reports of the other modality, except for the delayed pelvis CT to allow the nuclear medicine physician localisation of the ureters and bladder anastomosis on PET.

Both scans were reported using a standardised template that encompassed local, nodal and distant disease, with each section being designated as positive, equivocal or negative. Positive disease was defined as focal uptake of ^{18}F -DCFPyL on PET/CT that was not physiological and 2-3 times higher than surrounding background activity, similar to previous reported studies.[9-11]. SUV_{max} was recorded for each lesion. Equivocal disease was defined as very low-grade uptake <2 times background uptake in lesions with an anatomical correlate, or low-grade uptake in non-draining nodes or bone.

Local recurrence was sub-classified into prostate bed (which includes the anastomosis) or seminal vesicle bed (bilateral rectovesical areas on CT where soft tissue densities are seen, and seminal vesicles are usually located +/- surgical clips). The prostate bed was reviewed for abnormal areas of enhancing soft tissue with these typically being asymmetric, homogenous, greater density than typical granulation tissue and with evidence of positive mass effect. Lymph node involvement on CTCAP was defined based on size and morphology and designated as positive, equivocal or negative. Particularly, nodes greater than 4mm were assessed for morphologic changes such as shape, loss of fatty hilum, cortical thickness and cortical irregularity. Size (mm) of each positive or equivocal nodal and distant lesion was also measured using short axis diameter on CT.

All positive and equivocal ^{18}F -DCFPyL PET/CT scans were reviewed in a consensus meeting comprising a radiation oncologist and two nuclear medicine physicians to corroborate positivity and anatomical location.

Safety

Adverse events were assessed using The National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE) Version 4.03 and were reported from the day of ^{18}F -DCFPyL administration until 30 days post.

Statistical analysis

The analysis used information on pre-operative test results, post-operative histopathology, diagnostic CTCAP and ^{18}F -DCFPyL PET/CT results along with post-operative PSA results. Summary statistics, tabulations and plots were carried out using SPSS 26 [12] and R 4.0 software [13]. Binary logistic regression was used to select significant marker variables which were then used in a further logistic regression to construct a linear predictor for subsequent ROC analysis. All ROC analyses were carried out using the R packages ROCR [14] and pROC [15].

Results

From August 2018 to July 2020, 100 participants were enrolled across nine sites (Figure 1). Two patients were excluded as their pre-scan PSA level was outside the eligibility criteria ($PSA \geq 2.0$) leaving 98 patients suitable for final analysis. A further one patient was excluded from comparison between diagnostic CTCAP and ^{18}F -DCFPyL PET/CT as he could not undergo CT, leaving 97 patients eligible for analysis in this context.

Baseline characteristics (Table 1a) included a median age of 68.0 years, median pre-scan PSA of 0.32ng/ml, and median time between RP and imaging of 951.5 days. Over half our cohort, 58.9%, had ISUP grade group ≥ 3 disease. Pelvic nodal sampling/dissection was performed in 32.7% of patients with median nodal count 5.0 (95% CI 4.1-7.9) and 5.1% overall had N1 disease. Histopathological characteristics revealed extraprostatic extension in 68.4%, seminal vesicle invasion in 24.5%, positive surgical margin in 37%, presence of intraductal carcinoma in 31.3% and perineural invasion in 82.6%.

Patterns of ^{18}F -DCFPyL avid disease

Overall, 46.9% (n=46) of our cohort had positive ^{18}F -DCFPyL PET/CT scans and a further 5.1% (n=5) were equivocal. Taking these together, 52% (n=51) demonstrated positive or equivocal disease with ^{18}F -DCFPyL uptake, the patterns of which are described in Table 2 and illustrated in Figure 2.

Local disease recurrence was identified in 28 patients (29.2%), 16 designated as prostate bed and 12 at seminal vesicle bed. Nodal disease was identified in 29 patients (29.6%), and distant bony metastases were seen in 7 (7.1%).

Overall, 71 nodal lesions were identified, with 3 designated as equivocal. Mean SUV_{max} of nodal lesions was 17.8 and mean size was 5.3mm. The majority of ^{18}F -DCFPyL avid nodes were located along the internal, external and common iliac vessels which accounted for 57.7% (n=41). Presacral and mesorectal nodes accounted for 20.6% and 11% respectively, and no patients had detected para-aortic nodes. Of 29 patients with node positive or equivocal disease, 12 (41%) had a solitary node, 14 (48%) had 2-3 nodes, and 3 had ≥ 4 nodes detected.

Overall, 11 bony metastases were reported on ^{18}F -DCFPyL PET/CT, with one being equivocal, in a total of 7 patients (7.1%). Location of bony sites of disease included pelvis, femur, ribs, scapula and thoracic spine. No distant metastases were identified in visceral sites.

Regarding exclusive sites of disease, 16 patients (16.3%) had local recurrence only, 17 patients demonstrated nodal disease only (17.3%), and 2 patients (2.0%) had bone oligometastases only. A combination of local recurrence and nodal disease was identified in 8 patients (8.2%), and local recurrence with bony metastases in 1 patient.

Diagnostic CTCAP vs ^{18}F -DCFPyL PET/CT positivity.

97 patients were eligible for comparison between diagnostic CTCAP and ^{18}F -DCFPyL PET/CT after one patient was unable to complete the CT component. ^{18}F -DCFPyL PET/CT scans were positive in 46.4% (n=45), compared to 15.5% (n=15) for diagnostic CTCAP (Table 3). This increased to 51.6% (n=50) and 19.6% (n=19) respectively, when including overall equivocal results of each modality.

Of the 80.4% (n=78) with a negative diagnostic CTCAP, 38 of these had a positive or equivocal ^{18}F -DCFPyL PET/CT. Of the 19.6% (n=19) with a positive or equivocal CTCAP, 12 of these had a positive or equivocal ^{18}F -DCFPyL PET/CT. In 4.1% (n=4), diagnostic CTCAP was positive whilst ^{18}F -DCFPyL PET/CT was negative. Disease was identified on CT at the prostate bed in three of these patients, and an external iliac node in the other patient.

When comparing diagnostic CTCAP and ^{18}F -DCFPyL PET/CT for detection of local recurrence only, the latter had higher rates of detection with 26 patients having ^{18}F -DCFPyL avid local disease compared to 9 patients with positive or equivocal disease on CT. In 88 patients with no evidence of local disease on CT, 23 (26%) of these demonstrated positive or equivocal ^{18}F -DCFPyL uptake at either the prostate bed or SV bed on PET/CT.

Comparison of the imaging modalities for detection of nodal disease demonstrated higher rates with ^{18}F -DCFPyL avid nodes in 29 patients compared to 11 patients on CTCAP. In 86 patients with no evidence of nodal disease on CT, 24 (28%) of these demonstrated positive or equivocal ^{18}F -DCFPyL uptake within pelvic nodes. This comparison was similar in distant bony disease, with higher rates of detection on ^{18}F -DCFPyL PET/CT. In 96 patients with no evidence of bony metastases on CT, 7 demonstrated positive or equivocal ^{18}F -DCFPyL uptake in distant sites.

Predictors of ^{18}F -DCFPyL PET/CT positivity.

The majority of patients with a positive or equivocal ^{18}F -DCFPyL PET/CT had a pre-scan PSA between 0.2-0.49ng/ml, with a positive detection rate of 48% (37/77) in this PSA band (Table 4). Further analysis of this PSA band showed a positive ^{18}F -DCFPyL PET/CT detection rate of 39.5% (19/48) for PSA 0.2-0.29ng/mL, 62% (15/24) for 0.3-0.39ng/mL, and 60% (3/5) for 0.4-0.49ng/mL.

The majority of our patients had ISUP grade group 2-3 disease, with a positive or equivocal detection rate on ^{18}F -DCFPyL PET/CT of 27.7% and 58.9% respectively (Table 5).

Table 6 demonstrates results of tests of association between potential predictors of ^{18}F -DCFPyL positivity. The significant factors were then used as predictors of ^{18}F -DCFPyL positivity in logistic regression analysis, which demonstrated that ISUP grade group is a highly significant predictor (p=0.003) and pre-scan PSA is a moderately significant predictor (p=0.061).

ROC analysis was performed using the classifier ^{18}F -DCFPyL PET/CT positivity and the markers ISUP grade group, log(PSA) and the probability predictions from the logistic regression denoted as the

composite marker. The composite marker was calculated using the equation in Figure 3 to determine the probability of ^{18}F -DCFPyL PET/CT based on these variables. For example, if PSA is 0.3ng/mL and ISUP grade group is 2, the predicted probability of a positive scan is 31.6%, whereas if the PSA is 1.0ng/mL and ISUP grade group 4, the probability is 81.0%. Figure 4 demonstrates the ROC curves showing improved prediction rate using combined ISUP and PSA rather than individually.

Safety of ^{18}F -DCFPyL PET/CT

Within 30 days of ^{18}F -DCFPyL administration, there were 5 adverse events in the original 100 patients (5%). This included chest pain, extravasation of tracer, headache, rash and vomiting. Only the extravasation was considered related to administration of ^{18}F -DCFPyL, and the only Grade ≥ 3 event was chest pain. All 5 cases resolved without further intervention.

Discussion

Accurate identification of disease sites in men with biochemical recurrence (BCR) post radical prostatectomy (RP) is critical for assessing suitability for salvage treatments and achievement of long-term biochemical control. The sensitivity of PSMA PET/CT using ^{68}Ga -PSMA to detect disease within and outside the prostatic fossa at low PSA levels is well established, with 45% of scans positive when PSA is 0.2-0.49ng/ml, 59% when PSA is 0.5-0.99ng/ml, 75% when PSA is 1.0-1.99ng/ml, and 95% when PSA is ≥ 2.0 ng/ml [16]. Our prospective study is in keeping with this meta-analysis, with a median PSA 0.32ng/ml, 46.4% of ^{18}F -DCFPyL PET/CT scans positive, and the positivity rate substantially exceeding that of diagnostic CT.

Several recently published studies have assessed ^{18}F -DCFPyL PET/CT in biochemically recurrent prostate cancer, with all demonstrating sensitive disease detection [8, 17-22], although none prospectively investigated ^{18}F -DCFPyL PET/CT within a large homogenous prospective cohort of post-RP patients without previous radiation, and where all had a pre-scan PSA < 2.0 ng/ml. Of note, Rousseau et al., published a mixed cohort of recurrence post-RP and external beam radiotherapy (EBRT) [21]. In the subgroup of 92 men post-RP with mean PSA baseline 3.03-3.40ng/mL, 79.3% scans were positive with 14.1% local recurrence, 44.6% regional nodes and 21.7% bone metastases reported. Wondergem et al., also published a mixed cohort post-RP or EBRT [19]. In their subgroup of 43 men post-RP with PSA 0.5-1.0ng/mL, detection of disease outside the prostatic bed was 50%. Lindenberg et al., reported 77 men with BCR post-RP and a median PSA 2.27ng/mL where more pelvic nodal disease was detected with ^{18}F -DCFPyL PET/CT than MRI (128 vs 23 nodes) [8]. Rowe et al., published 31 patients with BCR post-RP but was the most similar to our study with a median PSA 0.4ng/ml and 67% having positive ^{18}F -DCFPyL PET/CT [20]. Perry et al published the largest series to date of 222 patients undergoing ^{18}F -DCFPyL PET/CT, with a 69.8% of men having a positive scan, with a detection rate of 47.6% in the cohort of PSA < 0.5 ng/mL similar to our study.[9]

Our patterns of PSMA avid disease are similar to published studies using the ^{68}Ga -PSMA tracer. Local recurrence was demonstrated as positive or equivocal in 28.6% of our cohort, which is comparable to the 22% reported by Perera et al., [16] and 21.5% seen in a recent prospective Australian study of 260 men post-RP [23]. The majority of studies examining PSMA PET/CT in this BCR post-RP context, categorise local recurrence as within the prostatic fossa. We further described our 28 patients with ^{18}F -DCFPyL-avid local recurrence by site, with 12 patients having disease in the seminal vesicle bed compared to 16 within the prostate bed. Our rate of nodal disease was similar to larger cohorts at 29.6%, compared to 26.2% reported by Emmett et al., [23], although our rate of distant metastases was much lower at 7.1% compared to 17.7%. This is likely a consequence of our cohort having lower numbers of high-risk ISUP grade group disease (19.4% vs 42.0% with grade group 4-5 disease) and pre-scan PSA (<2.0ng/mL vs <5.0ng/mL upper limit).

^{18}F -labelled PSMA compounds have optimal nuclear decay characteristics, translating to higher spatial resolution, better tumour-to-background ratio and more refined imaging quality than ^{68}Ga -PSMA [24]. Dietlein et al., published a preliminary study directly comparing ^{18}F -DCFPyL with ^{68}Ga -PSMA-11, showing noninferiority although 3/14 patients had additional lesions detected by ^{18}F -DCFPyL [25]. Our study adds to the literature to establish ^{18}F labelled compounds as alternative to ^{68}Ga -PSMA, particularly the manufacturing advantages of ^{18}F tracers with large scale production capacity and longer half-life to allow centres to introduce PSMA PET/CT scans without a GA-68 generator. Newer ^{18}F tracers such as ^{18}F -PSMA-1007 or ^{18}F -rhPSMA7 offer advantages of lower urinary excretion that could improve detection of prostate bed recurrences.[26, 27]

Just under a third of our patients had ^{18}F -DCFPyL-avid nodal disease, all located within the pelvis, which would not have been incorporated into traditional prostate bed radiotherapy fields. Boreta et al., [28] identified that 42% of ^{68}Ga -PSMA-11 avid lesions in their cohort would fall outside these boundaries, with sites predominantly extra-pelvic nodal and distant. Roach et al., [29] demonstrated significantly increased use of pelvic radiotherapy in their biochemical failure group related to PSMA-avid disease outside traditional prostate bed fields. The majority of nodal disease in our cohort was along the iliac vessels and presacral region which is covered by recommended elective nodal radiotherapy fields [30], however there were patients with mesorectal and peri-vesical nodal disease that are not routinely included. Considering 29% had pelvic nodal disease, ^{18}F -DCFPyL PET/CT would have impacted management by targeting the pelvic nodes with or without prostate bed irradiation. With nearly 50% of our cohort having a negative ^{18}F -DCFPyL PET/CT, this lends support to the use of elective nodal radiotherapy to prostate bed radiation [31]. Also, 7.1% of patients in our study could avoid salvage prostate bed radiotherapy due to detection of distant metastases by ^{18}F -DCFPyL PET/CT.

We demonstrated pre-scan PSA and ISUP grade group to be predictors of ^{18}F -DCFPyL PET/CT positivity in our cohort whereas other histopathological and biochemical factors were not. Many studies have similarly shown PSA to correlate with PSMA PET/CT positivity [19, 21, 23, 28, 32], although many included men with PSA >2.0 ng/mL. ISUP grade group correlation has not been widely explored although

was not predictive in one study [33]. We have provided a nomogram to predict ^{18}F -DCFPyL PET/CT positivity using these two variables which could be tested in larger cohorts and provides a starting point for selecting patients most likely to derive benefit from ^{18}F -DCFPyL PET/CT scan prior to radiotherapy. Rauscher et al provided nomograms to predict a positive ^{68}Ga -PSMA scan from a series of 272 post-prostatectomy patients.[34] Similarly PSA and grade were predictive factors, but previous radiotherapy and androgen deprivation use was predictive as well reflecting a different post-surgical cohort compared to our cohort who were being considered for salvage radiotherapy.

The limitations of our study include the lack of histopathological confirmation or alternative methods of radiological confirmation of disease e.g. with MRI and/or bone scan. Many of the prostate bed lesions would be difficult to biopsy, as would many of the avid lymph nodes given their mean size on CT was 5.3mm. Strengths of our study include the largest prospective study in a homogenous cohort of men post-prostatectomy using ^{18}F -DCFPyL at a single imaging centre, sufficient numbers to generate a predictive model for positive ^{18}F -DCFPyL scans and we pragmatically selected PSA eligibility between 0.2-2.0ng/mL i.e. a common management issue in men who are referred for radiotherapy and felt to be salvageable with radiation. We also believe incorporating IV contrast for the CT component to highlight the bladder and ureters improves the ability to distinguish urine from PSMA avid disease in the prostate bed and lymph nodes, which is not always performed in other centres. In the future, we will report detailed change in radiotherapy management and biochemical outcomes at three years in men who receive radiotherapy that will help validate the accuracy of ^{18}F -DCFPyL PET/CT.

Conclusion

In summary, ^{18}F -DCFPyL PET/CT provides improved detection of recurrent disease in over half our cohort with biochemical failure (PSA >0.2 ng/mL), with improved detection compared to diagnostic CTCAP. With at least 30% of men having nodal disease, ^{18}F -DCFPyL PET/CT would allow inclusion of nodal disease with salvage prostate bed radiotherapy. All men being considered for salvage radiotherapy and a PSA >0.2 ng/mL should be considered for PSMA PET, or otherwise selective use in men with a higher pre-scan PSA and/or higher ISUP grade group.

Declarations

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Conflict of interest/Competing Interests -Not applicable

Availability of data and material - Not applicable

Code availability - Not applicable

Consent to participate – Not applicable.

Consent for publications- Not applicable

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Tables

All patients (n=98)	
Age, years	
Median (95% CI)	68.0 (66.0-71.0)
PSA, ng/ml	
Median (95% CI)	0.32 (0.28-0.36)
Time between RP and imaging, days	
Median (95% CI)	951.5 (755-1117)
Biochemical recurrence vs persistence	
Biochemical recurrence	59 (60.2%)
Biochemical persistence	39 (39.8%)
Pathological T stage	
T2	28 (28.6%)
T3a	46 (46.9%)
T3b	24 (24.5%)
ISUP grade group	
1	4 (4.1%)
2	36 (36.7%)
3	39 (39.8%)
4	3 (3.1%)
5	16 (16.3%)
Pelvic nodal dissection	
Not performed	66 (67.3%)
Unilateral	8 (8.2%)
Bilateral	24 (24.5%)
Pathological N stage	
Nx	66 (67.3%)
N0	27 (27.6%)
N1	5 (5.1%)

Table 1a: Baseline characteristics of our cohort.

Data are n (%) unless otherwise specified. PSA, prostate specific antigen; RP, radical prostatectomy, ISUP, International Society of Uro pathology.

All patients (n=98)	
Extraprostatic extension	
No	31 (31.6%)
Yes	67 (68.4%)
Seminal vesicle invasion	
No	74 (75.5%)
Unilateral	13 (13.3%)
Bilateral	11 (11.2%)
Positive surgical margin	
No	60 (61.0%)
Equivocal	2 (2.0%)
Yes	36 (37.0%)
Perineural invasion (PNI)	
No	17 (17.4%)
Yes	81 (82.6%)
Intraductal carcinoma	
No	68 (68.7%)
Yes	30 (31.3%)

Table 1b: Detailed histopathological characteristics of our cohort.

Data are n (%) unless otherwise specified.

Local recurrence (n=28 patients)	
Positive	27 lesions
<i>Prostate bed</i>	15 (55.6%)
<i>SV bed</i>	12 (44.4%)
Equivocal	1 lesion
<i>Prostate bed</i>	1 (100.0%)
Mean SUV _{max} (95% CI)	16.6 (8.5-24.6)
Nodal disease (n=29 patients)	
Positive	68 lesions
<i>Internal iliac</i>	20 (29.4%)
<i>External iliac</i>	18 (26.4%)
<i>Common iliac</i>	8 (11.8%)
<i>Obturator</i>	1 (1.5%)
<i>Presacral</i>	14 (20.6%)
<i>Mesorectal</i>	6 (8.8%)
<i>Perivesical</i>	1 (1.5%)
Equivocal	3 lesions
<i>Internal iliac</i>	1 (33.3%)
<i>Mesorectal</i>	2 (66.4%)
Mean SUV _{max} (95% CI)	17.8 (12.9-22.7)
Mean size (mm)	5.3 (4.7-6.0)
Distant metastases (n=7 patients)	
Positive	10 lesions
<i>Pelvis</i>	3 (30.0%)
<i>Femur</i>	4 (40.0%)
<i>Rib</i>	1 (10.0%)
<i>Scapula</i>	1 (10.0%)
<i>Thoracic spine</i>	1 (10.0%)
Equivocal	1 lesion
<i>Rib</i>	1 (100.0%)
Mean SUV _{max} (95% CI)	12.5 (6.3-18.7)
Mean size (mm)	4.9 (2.7-7.0)

Table 2: Patterns of ^{18}F -DCFPyL avid disease in 51 patients with positive or equivocal PET/CT.

Data are n (%) unless otherwise specified. SV, seminal vesicle; SUV_{max} maximum standardised uptake value.

Diagnostic CTCAP vs ^{18}F -DCFPyL PET/CT for disease detection (n=97)		^{18}F -DCFPyL PET/CT positivity			
		Positive	Equivocal	Negative	Total
Diagnostic CTCAP positivity	Positive	9 (9.3%)	2 (2.1%)	4 (4.1%)	15 (15.5%)
	Equivocal	1 (1.0%)	0 (0.0%)	3 (3.1%)	4 (4.1%)
	Negative	35 (36.1%)	3 (3.1%)	40 (41.2%)	78 (80.4%)
	Total	45 (46.4%)	5 (5.2%)	47 (48.5%)	97 (100.0%)

Table 3: Comparison of diagnostic CTCAP and ^{18}F -DCFPyL PET/CT positivity within the cohort.

Data are n (%) unless otherwise specified. CTCAP, computed tomography of chest, abdomen and pelvis; PET/CT, positron emission tomography/computed tomography.

PSA band (ng/ml)	^{18}F -DCFPyL PET/CT			
	Positive (n)	Equivocal (n)	Negative (n)	% Overall Positive or Equivocal
0.2 - 0.49	33	4	40	37/77 (48.0%)
0.5 - 0.99	4	1	5	5/10 (50.0%)
1.0 - 1.49	5	0	0	5/5 (100.0%)
1.5 - 2.0	4	0	2	4/6 (66.7%)
Total	46	5	47	51/98 (52.0%)

Table 4: Rates of detection of disease by ^{18}F -DCFPyL PET/CT based on pre-scan PSA.

Data are n (%) unless otherwise specified. PSA, prostate specific antigen; PET/CT, positron emission tomography/computed tomography.

ISUP grade group	^{18}F -DCFPyL PET/CT			
	Positive (n)	Equivocal (n)	Negative (n)	% Overall positive or equivocal
1	2	0	2	2/4 (50.0%)
2	9	1	26	10/36 (27.7%)
3	21	2	16	23/39 (58.9%)
4	3	0	0	3/3 (100.0%)
5	11	2	3	14/16 (87.5%)
Total	46	5	47	51/98 (52.0%)

Table 5: Rates of detection of disease by ^{18}F -DCFPyL PET/CT based on ISUP grade group.

Data are n (%) unless otherwise specified. PSA, prostate specific antigen; ISUP, International Society of Uro pathology; PET/CT, positron emission tomography/computed tomography.

Potential predictor of ¹⁸ F-DCFPyL PET/CT positivity	Association p-value
Intraductal carcinoma	0.268
Extraprostatic extension	0.188
Perineural invasion	0.432
Seminal vesicle invasion	0.237
Positive surgical margin	0.197
Biochemical persistence	0.977
Pre-scan PSA*	0.029
Log PSA doubling time*	0.120
ISUP grade group*	<0.001
Log days between RP and scan*	0.554

*Table 6: Variables assessed for association with ¹⁸F-DCFPyL PET/CT positivity. Variables marked with * denote p-values for point-biserial correlation, remaining variables were assessed with Fisher's exact test.*

Data are n (%) unless otherwise specified. PSA, prostate specific antigen; ISUP, International Society of Uro pathology; PET/CT, positron emission tomography/computed tomography.

Figures

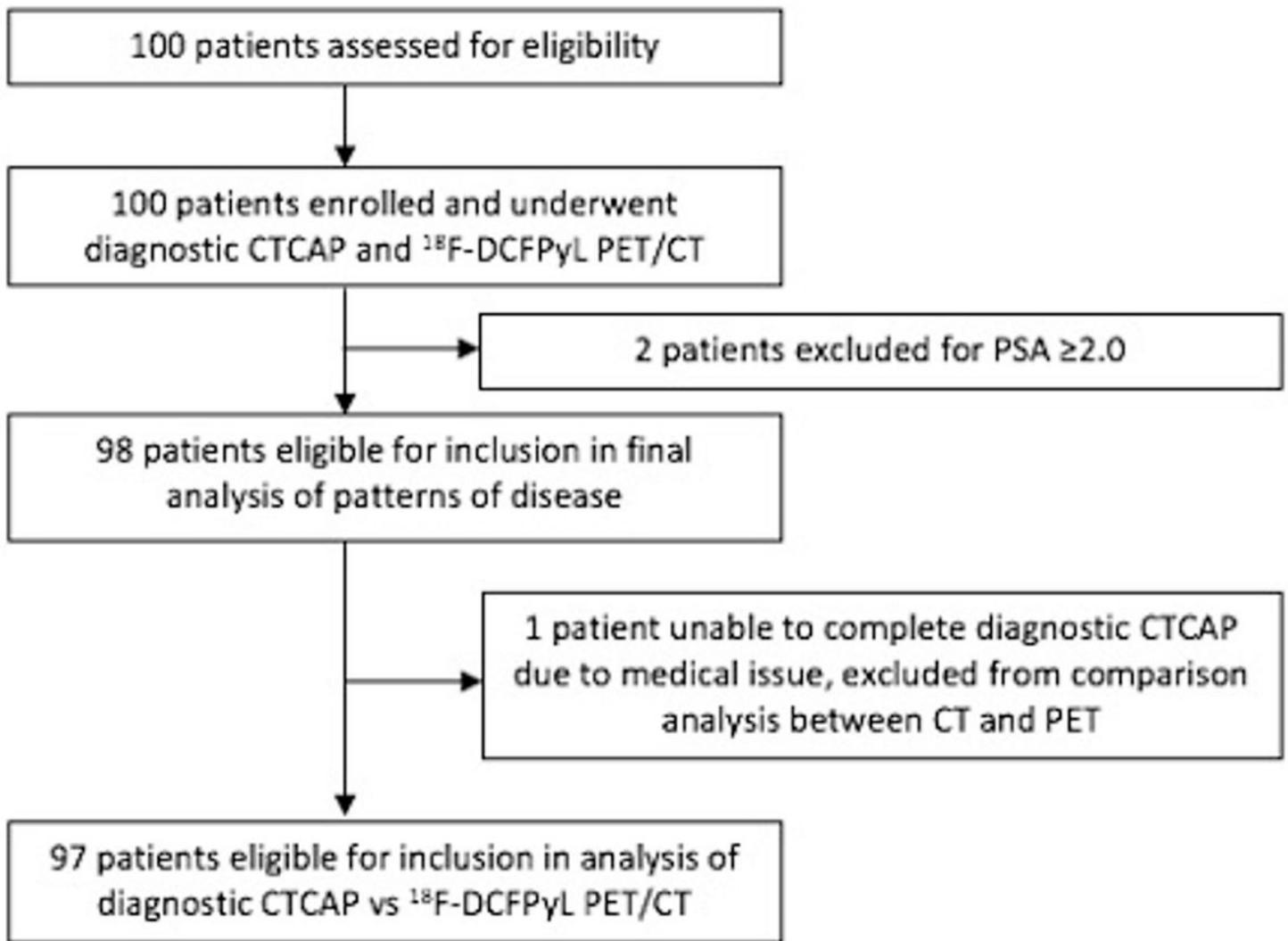


Figure 1

Eligible participants enrolled in the IMPPORT study.

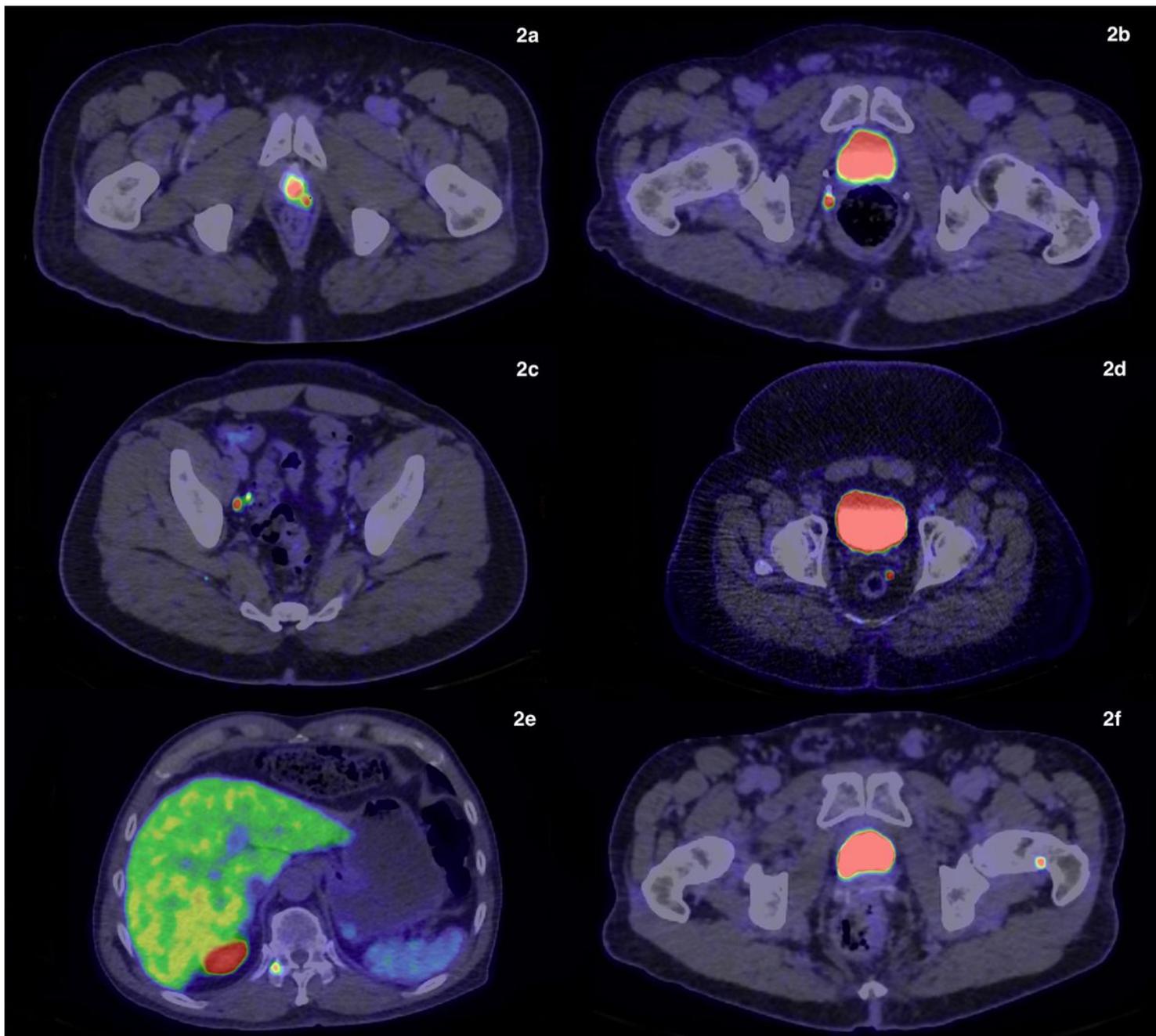


Figure 2

Examples of local, nodal and distant ^{18}F -DCFPyL avid disease on PET/CT. Local disease recurrence is seen in the top row, at the left posterior prostate bed in a patient with clear surgical margins at RP and PSA 0.35 (2a), and at the right SV bed adjacent to surgical clips in a patient with clear surgical margins and no SV invasion at RP and PSA 0.53. Nodal disease is seen in the middle row, in a right external iliac node in a patient with grade group 5 pT3b disease on RP and PSA 1.8 (2c), and in a mesorectal node in a patient with grade group 5 pT2 disease on RP and PSA 1.0 (2d). Distant bony metastases are seen in the bottom row, in the right transverse process of a T11 vertebra in a patient with grade group 5 disease and PSA 0.38 (2e), and in a left femur in a patient with grade group 3 disease and PSA 0.39 (2f).

$$\text{logit}(Y) = -1.229 + 0.809 \times \log(\text{PSA}) + 0.715 \times \text{ISUP}$$



$$Y = P(\text{positive } ^{18}\text{F} - \text{DCFPyL result}) = \frac{\exp(\text{logit}(Y))}{1 + \exp(\text{logit}(Y))}$$

Figure 3

Model using PSA and ISUP grade group to calculate probability of positive ¹⁸F-DCFPyL PET/CT in our cohort.

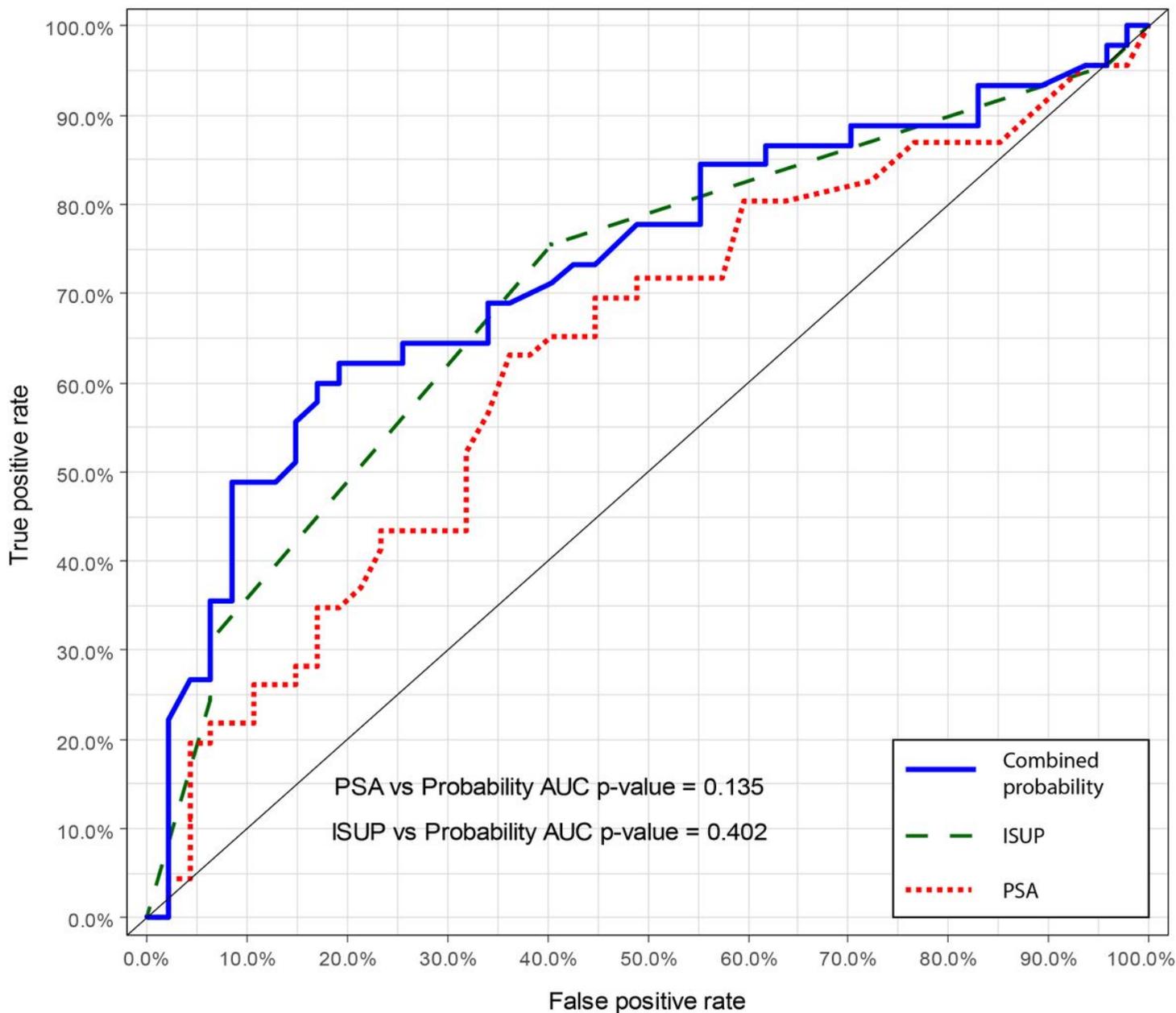


Figure 4

ROC curves for PSA (red dotted), ISUP grade group (green dashed) and logistic regression generated probabilities combined (blue solid), with the latter demonstrating the best prediction for 18F-DCFPyL PET/CT positivity.