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# Combination of MRI prostate and 18F-DCFPyI PSMA PET/CT detects all clinically significant prostate cancers in treatment-naive patients: An international multicentre retrospective study

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## Background

Prostate cancer is the most commonly diagnosed cancer amongst males and has traditionally relied upon clinical and biochemical assessment followed by systematic biopsy. These are imperfect tools and are known to miss

## Abstract

**Introduction:** Clinical and biochemical assessment and biopsies can miss clinically significant prostate cancers (csPCa) in up to 20% of patients and diagnose clinically insignificant tumours leading to overtreatment. This retrospective study analyses the accuracy of <sup>18</sup>F-DCFPyL PET/CT in detecting csPCa as a primary diagnostic tool and directly compares it with mpMRI prostate in treatment-naive patients. The two modalities are then correlated to determine whether they are better in combination, than either alone.

**Methods:** This is a retrospective dual-institution study of patients who underwent contemporaneous MRI and PSMA-PET between January 2017 and March 2020 with histologic confirmation. The images were re-reviewed and concordance between modalities assessed. Results were compared with histopathology to determine the ability of MRI and PSMA-PET to detect csPCA.

**Results:** MRI and PSMA-PET detected the same index lesion in 90.8% of cases with a kappa of 0.82. PET detected an additional 6.2% of index lesions which were MRI occult. MRI detected an additional 3.1% which were PET occult. No additional csPCa was identified on pathology which was not seen on imaging. The sensitivity of PSMA-PET in detecting csPCa is 96.7% and that of MRI is 93.4% with no statistically significant difference between the two ( $P = 0.232$ ). Both modalities detected all four cases of non-csPCa with these being considered false positives.

**Conclusion:** Both mpMRI and 18F-DCFPyL-PSMA-PET/CT have high sensitivity for detecting csPCa with high agreement between modalities. There were no synchronous csPCa lesions detected on pathology that were not detected on imaging too.

**Key words:** nuclear medicine; oncologic imaging; uroradiology.

clinically significant prostate cancer (csPCa) in up to 20% of patients, as well as diagnose clinically insignificant tumours.<sup>1</sup> Clinically insignificant tumours are defined histopathologically as organ confined Gleason 3 + 3 tumours with no Gleason 4 or 5 disease. Hence, these tend to be indolent leading to potential

overtreatment.<sup>2</sup> Multiparametric prostate MRI (mpMRI) has an established role in both detection and active surveillance of prostate cancer. It has been shown to increase the rates of diagnosis of csPCa while reducing the rates of detection of clinically insignificant tumours, providing vital information allowing targeted biopsy, either with ultrasound or in-bore MRI-guided biopsy.<sup>3</sup>

MRI has a high negative predictive value for csPCa. However, up to 10% of csPCa remains occult on MRI.<sup>4-6</sup> A significant proportion of these MRI negative tumours are situated within the central (CZ) and transition zones (TZ),<sup>7</sup> areas which are more challenging to assess, even for experienced genitourinary radiologists.<sup>8</sup>

Prostate-specific membrane antigen (PSMA) is a type 2 transmembrane glycoprotein that is highly expressed in almost all prostate cancer cells. Only 5–10% of cancers do not express PSMA on immunohistochemistry.<sup>9</sup> PSMA-PET/CT has an established role in prostate cancer initial staging and biochemical failure; however, its role in diagnosis and characterisation of suspected prostate cancer is not yet clear. <sup>68</sup>Gallium-PSMA-11 tracers are more widely represented in the literature. However, 2-(3-{1-carboxy-5-[(6-<sup>18</sup>F]fluoro-pyridine 3-carbonyl)-amino]-pentyl}-ureido)-pentanedioic acid (<sup>18</sup>F-DCFPyL) is a newer ligand used at our institutions and confers some advantages with longer half-life, amenability for large-scale batch production and improved tumour-to-background ratio. <sup>18</sup>F also has a lower positron energy than <sup>68</sup>Ga, theoretically resulting in improved spatial resolution.<sup>10,11</sup>

This retrospective review analyses the accuracy of <sup>18</sup>F-DCFPyL PET/CT in detecting csPCa as a primary diagnostic tool and directly compares it with mpMRI prostate in treatment-naïve patients. The two modalities are then correlated to determine whether they are better in combination, than either alone.

## Methods

### Study population

This is a retrospective dual institution study involving St Vincent's Hospital Melbourne (STV), a university affiliated tertiary hospital and Pacific Radiology, Canterbury, New Zealand (PRC). Both centre databases were reviewed to identify patients who underwent MRI and PSMA-PET between January 2017 and March 2020. These patients were initially referred from our urology units with clinically suspected or biopsy proven cancer.

The inclusion criteria includes both studies being performed within 3 months with available histologic confirmation by either radical prostatectomy or biopsy. The exclusion criteria includes patients on androgen deprivation therapy before imaging and those who have had prior prostate surgery, embolisation or radiotherapy. Sixty-five patients were included (STV = 25, PRC = 40). At the time of referral to mpMRI, 22(33.8%) patients

had biopsy proven cancer and 43(66.2%) had clinical suspicion of cancer.

Clinically significant prostate cancer was defined as Internal Society of Urological Pathology (ISUP) grade group 2 and above.

### PET/CT and MRI acquisition

#### *Radiosynthesis, quality control and application of <sup>18</sup>F-DCFPyL PET/CT*

<sup>18</sup>F-DCPyL is a commercially available tracer with large-scale batch production and an excellent safety profile. It is also held to high quality control standards. All patients were administered 250 MBq ( $\pm 50$  MBq) of <sup>18</sup>F-DCFPyL intravenously in accordance with reference standards outlined by the Australian Radiation Protection and Nuclear Safety Agency (ARPANSA). Imaging was performed at 120 minutes ( $\pm 10$  min) after injection to ensure high uptake by prostate cancers and reduce background signal.

#### *PSMA imaging protocols and reconstruction*

PRC: Patients were imaged on a GE Discovery 690 (General Electric Medical Systems, Milwaukee WI). Low-dose attenuation correction CT images were acquired and reconstructed to 3.75 mm slice thickness with increment of 3.27 mm using iterative reconstruction (50% ASiR). Images were reconstructed from time of flight emission data using VUE Point FX and Q-Clear™ "GE Healthcare" iterative technique with  $\beta$  value of 400. Sharp IR function was applied with no Z-axis filter. PET images were reconstructed on a 256 matrix.

STV: Patients were imaged on a GE Discovery 710 PET/CT (General Electric Medical Systems, Milwaukee WI). Otherwise scanning parameters match those described above.

#### *MRI imaging protocols*

Multiparametric MR was performed using a 3 T scanner (Siemens Skyra STV and PRG, Siemens Magnetom Vida PRC) and a 1.5 T scanner (General Electric Signa Explorer PRC). The scan factors fulfilled the minimum technical requirements of the Prostate Imaging Reporting and Data system version 2 (PIRADS v2).<sup>12</sup> The sequences obtained include T2-weighted in axial, coronal and sagittal planes, DWI up to 2000 B value with correlating ADC maps. Lesions scored as PIRADS 3 or above were considered positive studies. No endorectal coil was used at either site.

#### *Biopsy and radical prostatectomy*

The histology was obtained either *via* a transperineal biopsy under ultrasound guidance with MRI fusion, or *via*

a radical prostatectomy (RP). Where both biopsy and RP were available, RP was used as the reference standard. Forty-four (67.7%) patients had radical prostatectomy, and 21 (32.3%) had targeted biopsy as the reference standard for histopathological assessment.

### Evaluation of imaging

Both  $^{18}\text{F}$ -DCFPyL PET/CT and MRIs were blindly re-reported with lesions suspicious for csPCa annotated on the PIRADS template map. Each index lesion on MRI was measured and scored as per PIRADS v2.<sup>12</sup> The index lesion was defined as the lesion with the highest PIRADS score or the largest lesion if there were multiple lesions with the same score. The MRI was reported as positive if the PIRADS score was  $\geq 3$ . Quantitative ADC (qADC) was measured in  $10^{-6} \text{ mm}^2/\text{s}$ .

On PET/CT, the index lesion suspicious for malignancy was recorded as the lesion with highest focal uptake compared with the background prostate avidity as calculated by maximum standardised uptake value ( $\text{SUV}_{\text{max}}$ ) and as described in previous studies.<sup>13</sup> Lesions were also annotated on the PIRADS template map and  $\text{SUV}_{\text{max}}$  recorded. At STV, MRIs were reviewed by a single experienced radiologist with GU subspecialist practice (TS) and PET/CTs reviewed by a single nuclear medicine physician (KT) both with more than 10 years' experience reporting abdominal studies. At PRC, one of two experienced radiologists with GU subspecialist practice, cancer imaging fellowship training and >5 years PET/CT reporting experience (EP, JH) alternately reviewed all MRI and  $^{18}\text{F}$ -DCFPyL PET/CT blinded to the comparative study. All reviewers were blinded to the original reports and clinical details. The reviewers then met to compare the  $^{18}\text{F}$ -DCFPyL PET/CT and MRI and determine concordance between the studies. The histopathology was reviewed by genitourinary trained pathologists in both centres. The imaging results were then compared with the histology by a radiology fellow (NP).

### Statistical analysis

All statistical analysis was performed using Jamovi software, version 1.2.22.0. Patient demographic data and baseline characteristics were summarised using descriptive statistics. Mann–Whitney U tests were used to evaluate differences in groups with and without csPCa. The chi-square test was used to compare proportions. A level of 5% was used to confer statistical significance.

The sensitivity and positive predictive values for detecting clinically significant prostate tumours were calculated for MR and  $^{18}\text{F}$ -DCFPyL PET/CT, respectively.

Inter-reader agreement between mpMRI and PSMA-PET/CT reporting was calculated utilising the free-marginal kappa coefficient. The strength of agreement was interpreted based on kappa results as follows: poor, <0.00; slight, 0.00–0.20; fair, 0.21–0.40; moderate,

0.41–0.60; substantial, 0.61–0.80; and almost perfect, 0.81–1.00.

### Reference standard

All included patients had either undergone a radical prostatectomy or targeted biopsy as directed by the original MRI report. Histopathology reports were reviewed and compared with the template maps by a single investigator (NP). All pathology reports were reported as an ISUP grade group.

### Results

A total of 65 patients, with a median age of 67 years (range 44–80 years), were included in this retrospective dual-centre study. Baseline patient demographics and clinical features are summarised in Table 1.

#### Multiparametric MRI

93.8% (61/65) index lesions were detected as likely csPCa on MRI. 60.7% (37/61) of these lesions were scored as PIRADS 5; 36.1% (22/61) as PIRADS 4 and 3.3% (2/61) as PIRADS 3

#### $^{18}\text{F}$ -DCFPyL PET/CT

96.9% (63/65) index lesions were detected by PET/CT which had uptake suspicious for csPCa. The median  $\text{SUV}_{\text{max}}$  in positive cases was 18.2 (range 3.9–85). The box plots depicting  $\text{SUV}_{\text{max}}$  of all cases against the

**Table 1.** Baseline patient demographics and clinical features

Characteristic	Number (n, %)
Number of patients, total (%)	65 (100%)
Age (years), median (range)	67 (44–80)
PSA (ng/mL), mean $\pm$ SD	14.3 $\pm$ 11.6
PSA density (ng/mL/cc), mean $\pm$ SD	0.38 $\pm$ 0.40
Histopathological assessment	
Radical prostatectomy, total (%)	44 (67.7%)
Targeted biopsy, total (%)	21 (32.3%)
ISUP Grade Group, total (%)	
1	4 (6.2%)
2	18 (27.7%)
3	20 (30.8%)
4	9 (13.8%)
5	14 (21.5%)
Mean interval between MR and PET/CT, days (range)	48.6 (1–90)
PI-RADS, total (%)	
1–2	4 (6.2%)
3	2 (3.1%)
4	22 (33.8%)
5	37 (56.9%)
qADC, mean (range)	676 (378–1,205)
$\text{SUV}_{\text{max}}$ , median (range)	18.2 (3.9–85.0)

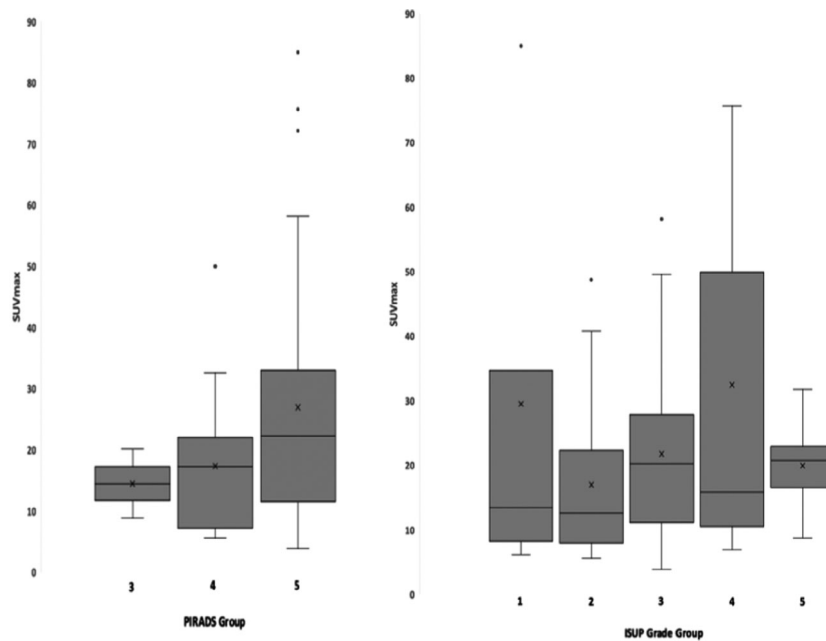


Fig. 1. Box Plots of  $SUV_{max}$  vs. PI-RADS Score and ISUP Group Grade.

PI-RADS grades 3–5 and ISUP grades 1–5 can be seen in Figure 1, with the interquartile range indicated.

### Lesion localisation and pathology grading

Tumours identified through histopathological analysis were located in the right lobe in 36/65 patients (55.4%), left lobe in 26/65 (40.0%) and bilaterally in 3/65 (4.6%). 84.6% (55/65) of tumours was located within the peripheral zone, 13.8% (9/65) in the transition zone and 1.5% (1/65) within the anterior fibromuscular stroma. 93.8% (61/65) of these tumours was classified as clinically significant on pathology (ISUP  $\geq$  2).

### Imaging diagnostic performance

While histopathological analysis of all cases (65/65) was consistent with PCa, 93.8% (61/65) of cases was detected as histologically confirmed csPCa.

$^{18}\text{F}$ -DCFPyL PET/CT detected 96.9% (63/65) of index lesions as suspicious for csPCa, of which 90.8% (59/65) was consistent with histologically confirmed csPCa, providing a sensitivity of 96.7% (95% CI: 88.7%–99.6%). mpMRI detected a similar total with 93.8% (61/65) of index lesions being PI-RADS  $\geq$ 3, of which 87.7% (57/65) harboured csPCa (sensitivity 93.4%, (CI 84.1–98.2%) as demonstrated in Figure S1. No statistical significance was observed between the two imaging modalities ( $P = 0.232$ ). PPV for  $^{18}\text{F}$ -DCFPyL PET/CT was 93.7% (95% CI: 93.4%–93.9%) versus mpMRI 93.4% (95% CI: 93.0%–93.8%). The positive likelihood ratio of  $^{18}\text{F}$ -

DCFPyL PET/CT was 0.97 (95% CI: 0.92–1.01) versus mpMRI 0.93 (95% CI: 0.87–1.0).

### Concordance analysis

MRI and  $^{18}\text{F}$ -DCFPyL PET/CT detected the same csPCa lesion in 90.8% (59/65) of cases. An example is demonstrated in Figure S2.  $^{18}\text{F}$ -DCFPyL PET/CT detected an additional 6.2% (4/65) of csPCa lesions compared with mpMRI, while mpMRI detected an additional 3.1% (2/65) which were occult on  $^{18}\text{F}$ -DCFPyL PET/CT. There were no additional csPCa lesions detected in biopsy and surgical specimens that were not also detected on imaging. Both modalities detected all 4 cases of ISUP grade group 1 disease with these being considered false positives. The free-marginal kappa was calculated at 0.82 (95% CI: 0.67–0.96) indicating almost perfect agreement between reporting of mpMRI and  $^{18}\text{F}$ -DCFPyL PET/CT. There were no true negative cases within the dataset.

The majority of lesions were detected in the PZ in both mpMRI (53/61, 86.9%) and PET/CT (52/63, 82.5%). TZ tumours were seen in 7/61 (11.5%) patients in mpMRI and 10/63 (15.9%) patients in PET/CT. One tumour was detected within the anterior fibromuscular stroma on both mpMRI (1/61, 1.6%) and PET/CT (1/63, 1.6%).

### Discordant results

There were 6 lesions (9.2%) with discordance between  $^{18}\text{F}$ -DCFPyL PET/CT and MRI results.

**Table 2.** Characteristics of PIRADS 5 histologically confirmed lesions occult on <sup>18</sup>F-DCFPyL PET/CT

	PSA	PIRADS	ADC	ISUP	Length(mm)	Zone	Type
1	8.8	5	609	5	30*	Peripheral	Biopsy
2	10.1	5	760	2	25	Peripheral	RP

RP: Radical prostatectomy.

\*Size of lesion determined from MRI instead in this case as pathology was derived from biopsy sample.

### <sup>18</sup>F-DCFPyL PET/CT

Two lesions (3.1%) were reported as PIRADS 5 on mpMRI with strong diffusion restriction (ADC 609–760 × 10<sup>-6</sup> cm<sup>3</sup>) and no corresponding PET avidity. Histopathology revealed ISUP 5 and ISUP 2 tumours measuring 30 mm and 25 mm, respectively (Table 2). The median PSA for both these patients was 9.5.

### MRI

An additional four lesions (6.2%) had evidence of uptake on <sup>18</sup>F-DCFPyL PET/CT, suspicious for csPCa (SUV max range 8–12.6, mean SUV 10.3). These were not detected or not considered suspicious on MRI (PIRADS < 3). Two of these lesions were situated within the TZ and two in the PZ. Three lesions were ISUP GG 2, and one was an ISUP GG 5 TZ tumour. Characteristics of these lesions are displayed in Table 3 below. The peripheral zone lesions were reported as PIRADS 2 due to the lack of focal high signal on DWI and corresponding focal low signal on ADC sequences. These lesions correlated with ISUP GG 2 tumours pathologically. The remaining two were not detectable on MR and given a PIRADS 1

grading, including the ISUP GG 5 TZ tumour. They remained undetectable on targeted re-review.

### ISUP GG 1 lesions detected on imaging considered false positive

Of the 4 ISUP GG 1 lesions, MRI scored two as PIRADS 4. These were a 20 mm PZ lesion and 15 mm TZ lesion with SUV<sub>max</sub> of 6.2 and 18, respectively. The former case underwent a radical prostatectomy, while the latter underwent a biopsy.

MRI scored one PZ lesion as PIRADS 3 which measured 9 mm and had an SUV max of 8.9. Subsequently, this case underwent a radical prostatectomy. A further PZ lesion was scored as PIRADS 5, measured 42 mm and had a SUV max of 85. Pathology was derived from a targeted biopsy. These findings are summarised in Table 4.

### Discussion

Management of prostate cancer has traditionally been hindered by the conflicting problems of sampling error related to blind systematic prostate biopsy and

**Table 3.** Characteristics of lesions not detected/characterised as cancer on MRI

	PSA	SUV max	ISUP	Length(mm)	Zone	Specimen	Reason not reported
1	14.4	9.6	2	27	Peripheral	RP	Not detected on ADC. Minor high signal on DWI. Hence, no lesion meeting PIRADS 3 or greater on MR.
2	10	8	2	12	Peripheral	RP	Minor reduced ADC signal. Not detected on DWI. Hence, no lesion meeting PIRADS 3 or greater on MR.
3	4.4	10.8	5	20	Transition	RP	No signal abnormality on MR hence no lesion reported.
4	8.5	12.6	2	20	Transition	RP	No signal abnormality on MR hence no lesion reported.

RP: Radical prostatectomy.

**Table 4.** Characteristics of ISUP GG 1 lesions

Patient	Location	Length(mm)*	Greatest Percentage for biopsy	qADC	PIRADS	SUV	Procedure
1	Peripheral mid	9	NA	1100	3	8.9	Radical Prostatectomy
2	Peripheral base	42	6	590	5	85	Biopsy
3	Peripheral apical	20	70	965	4	6.2	Radical Prostatectomy
4	Transition apical	15	40	500	4	18	Biopsy

\*Length was derived from MRI in these cases.

overdiagnosis of indolent prostate cancer.<sup>14</sup> Introduction of mpMRI prostate prior to prostate biopsy has established itself as the standard of care in recent years to improve detection of csPCa and avoid detection of indolent cancer,<sup>1,15</sup> but retrospective correlation with radical prostatectomy specimens demonstrates up to 7% of csPCa tumours remains occult.<sup>16,17</sup>

PSMA-PET/CT has primarily been investigated for its role in initial staging of prostate cancer and assessing biochemical recurrence. Its role in primary diagnosis is yet to be fully investigated. Our study demonstrates that <sup>18</sup>F-DCFPyL PET/CT has an excellent sensitivity (97%) for detecting csPCa. It showed 91% concordance with MRI and high inter-reader agreement. Although <sup>18</sup>F-DCFPyL PET/CT detected more csPCa lesions than MRI, this was not statistically significant and both modalities demonstrated high sensitivity. PET, however, does have a radiation burden and is more expensive than MRI. Hence, these factors need to be considered when determining its place in the diagnostic algorithm of primary diagnosis. The majority of the lesions (84.6%) in our study were located within the peripheral zone. This is greater than the percentage expected based upon the literature and subsequently is a limitation of our study. The detection of small tumours in large glands, especially those containing multiple stromal hypertrophic nodules, is challenging on MRI, and further studies are required to define the patient population that will benefit most from adding <sup>18</sup>F-DCFPyL PET/CT to the diagnostic armamentarium.

Few studies have been published comparing PSMA-PET/CT and mpMRI for primary diagnosis. Most have been retrospective and utilised <sup>68</sup>Ga tracers. Zamboglou *et al.* found that <sup>68</sup>Ga-PSMA-PET/CT and MRI detected all tumours with histology obtained from radical prostatectomy used as a reference. However, the study included only 7 patients.<sup>18</sup> In an ongoing prospective study by Bauman *et al.* including only 6 patients at time of publication, all had index lesions detected by both MRI and <sup>18</sup>F-DCFPyL PET/CT. However, it is uncertain if the modalities were read in conjunction or blinded to each other.<sup>19</sup> A more recent study, Lopci *et al.*, looked at the diagnostic performance of <sup>68</sup>Ga-PSMA-PET/CT in patients who either had a negative MRI or positive MRI but a previous negative biopsy. They found that PET/CT had a higher sensitivity for detecting csPCa than MRI (60% *versus* 38%) when they used a cut-off of  $\geq$  PIRADS 4 for positivity. However, the MRI sensitivity increased to 81%, which was closer to that of ours, 93%, when the cut-off for positivity was lowered to  $\geq$  PIRADS 3 such as in our study.<sup>20</sup>

A recent multicentre prospective Australian study of 291 men, PRIMARY by Emmett *et al.*, largest to date, assessed the ability of MRI and a targeted pelvic <sup>68</sup>Ga-PSMA-PET/CT in identifying csPCa.<sup>21</sup> Combined PET and MRI showed a significant increase in NPV for detecting csPCa compared with MRI alone (91% *vs.* 72%). PET was positive in 90% of PIRADS 2 and 3 prostates with

csPCa, which is similar to our study where PET was positive in 100% of PIRADS  $<$ 3 glands. This could allow the concurrent use of PET in primary diagnosis and reduce unnecessary intervention. Similar to our study, PET had a non-significant increase in sensitivity compared with MRI.

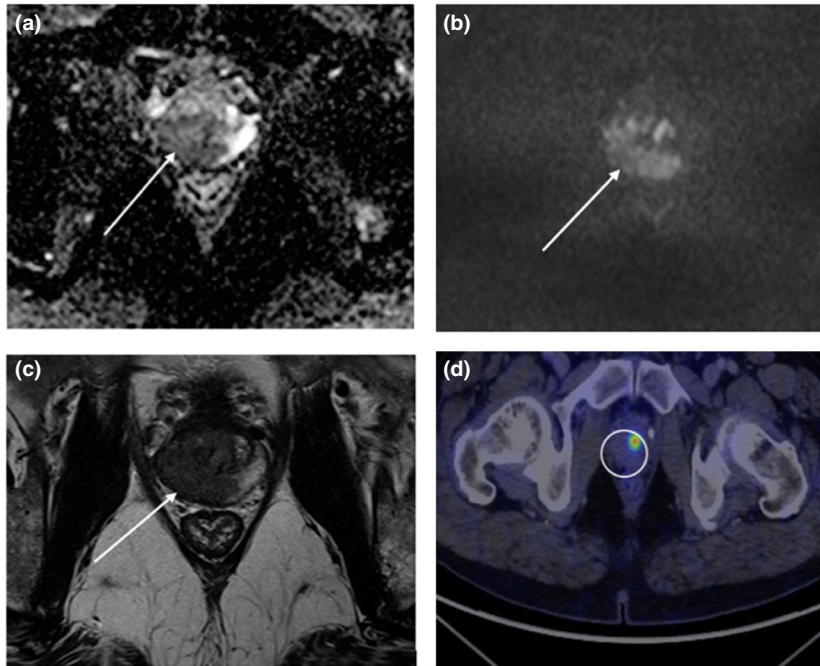
Another large retrospective study involving 205 patients by Kalapara *et al.*,<sup>22</sup> again using <sup>68</sup>Ga PSMA-PET/CT, found that a focal lesion corresponding to tumour at prostatectomy was identified in 94% of PET/CTs and 95% of MRI's. In this study, 5.9% of index tumours was not avid on PET/CT with histology ranging from ISUP GG 2–5. On mpMRI, 5.4% of index lesions was occult and these comprised of ISUP GG 2, 3 and 5 tumours. Only one lesion (0.4 cc) representing 0.5% of the cohort was occult on both MRI and PET CT showing the complementary nature of these two modalities.

In our cohort, 2 (3.1%) index PZ lesions were PET occult and these were detected as csPCa on histopathology. This correlates well with the study by Kalapara *et al.*<sup>22</sup> An example of a PET occult lesion in our study is shown in Figure 2.

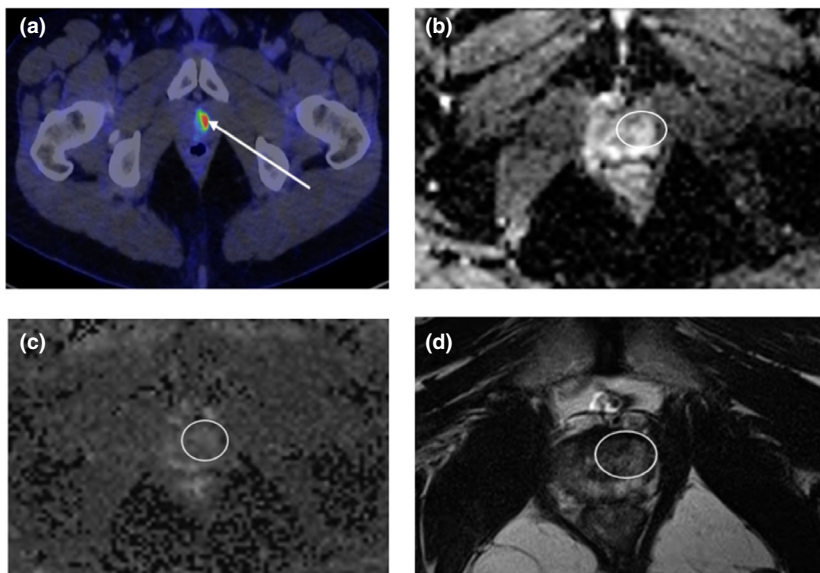
We encountered 4 PET positive index lesions (6.2%) returning csPCA, which on MRI were either undetectable or given a PIRADS score of less than 3. An example is demonstrated in Figure 3. This is again concordant with the MRI occult rate of 5.4% in Kalapara *et al.*'s study.<sup>22</sup> However, Lopci *et al.*<sup>20</sup> found that 25% of patients with csPCa had lesions not identified on MRI. The higher percentage compared with our study could be attributed to varying sample size. Furthermore, the study used negative MRI as an inclusion criteria, which would have artificially reduced the sensitivity of this modality. 50% of our 4 PET positive lesions was located within the TZ. Although this result is derived from a small sample size, it is still important to note as TZ tumours account for approximately 30% of all prostate cancer cases and have a known lower detection rate than that of peripheral tumours.<sup>23,24</sup> The addition of DWI/ADC is also challenging in the TZ as TZ ISUP GG1 lesions have a lower ADC than compared with their PZ counterparts.<sup>25,26</sup> The TZ can also be more difficult to sample *via* TRUS biopsy due to the relatively anterior location and may require a transperineal approach or in-bore MRI biopsy. PSMA-PET may then prove to be useful in this setting to complement MRI in detecting TZ cancers.

Of note, a recent Australian study (SAMURAI) looked at the role of <sup>68</sup>Ga-PSMA-PET/MRI in 20 patients in the detection and localisation of primary prostate cancer. PET/MRI demonstrated superior diagnostic accuracy and sensitivity compared with mpMRI and PET/CT, respectively, and can potentially be used as a single modality for primary diagnosis and staging. However, larger studies are required to further validate this with PET/MRI access and cost being limitations.<sup>27</sup>

Our cohort also had 4 (6.2%) false-positive cases, ISUP GG 1 lesions, detected on both MRI and PET/CT.



**Fig. 2.** (a) Markedly reduced signal on corresponding ADC map(arrow). (b) Axial DWI B value 1500 shows markedly increased signal( arrow) in association with right apex peripheral zone(PZpl and PZpm) ISUP 5 tumour. (c) Axial T2 sequence demonstrates that the region of diffusion restriction corresponds to a 30mm non circumscribed low T2 right peripheral lesion(PZpl and PZpm) (arrow). (d) Axial fused  $^{18}\text{F}$ -DCFPyL PET/CT through the prostate gland apex in the same patient, demonstrates no significant avidity (circle) to correlate with pathologically described tumour. Central uptake is secondary to urine within the prostatic urethra.



**Fig. 3.** (a) Axial fused  $^{18}\text{F}$ -DCFPyL PET/CT through the prostate gland apex demonstrates significant avidity in location of pathologically proven 20 mm ISUP 5 left transition zone tumour(SUV max 10.8) (arrow). (b, c) Axial DWI B value 2000 and corresponding ADC map demonstrate no abnormal restricted diffusion within the region of PET avidity(circle). (d) Axial T2 through prostatic apex demonstrates no suspicious signal characteristics at site of the pathologically proven ISUP 5 transition zone tumour(circle).

This could be due to sampling error rather than false-positive studies in 2 out of 4 cases who had pathological correlation from biopsy rather than RP. For example, 1

lesion was reported to have a SUV of 85 and greatest percentage of tumour on biopsy as 6%; hence, this case could potentially relate to sampling error. One of the

index lesions which underwent biopsy was situated within the apical segments. Hence, this may have limited sampling as this is a well-recognised site of false-negative biopsy. At the time of writing, these patients have not undergone further follow-up.

## Limitations

Limitations of this study include its retrospective nature and selection bias given the current indications for  $^{18}\text{F}$ -DCFPyL PET/CT. Hence, we had a substantially higher incidence of csPCa in our cohort than background. This is likely to artificially increase the specificity and sensitivity of both modalities with a high pretest probability of csPCa. However, the strong concordance between MRI and  $^{18}\text{F}$ -DCFPyL PET/CT is reassuring. The relatively small numbers in our study also increased selection bias; however, the numbers were kept low due to our stringent inclusion criteria and requirement of histopathologic correlation. Our numbers are also similar to several published studies assessing  $^{68}\text{Ga}$ . The retrospective nature of the review meant that detected lesions could not be sampled if the review detected additional disease to the original report. This supports the requirement for future prospective studies as discussed above. Ideally, studies would include radical prostatectomy on all patients as a gold standard reference; however, this is not ethically achievable. The reliance upon biopsy does introduce the potential for undersampling and missed csPCa. This may also explain 2 of the 4 ISUP GG1 lesions that were detected on both modalities.

In conclusion, within the limits of a small select group of patients, both mpMRI and  $^{18}\text{F}$ -DCFPyL PET/CT demonstrate high concordance in the detection of csPCa with no statistical difference between the two modalities. Although not every patient had RP, there were no synchronous csPCa lesions detected on biopsy and surgical specimens that were not also detected on imaging. PET/CT has strong correlation with pathologically proven cancers and may also assist in cancer detection within larger glands and within the TZ. Hence, we believe both modalities could potentially complement each other in the primary diagnosis of prostate cancer. However, larger prospective studies are required to validate these findings in a cohort of patients clinically suspected of having prostate carcinoma and this is currently being undertaken at our institutions. Further studies will be required to identify the group of patients that should undergo either both examinations or be primarily investigated with  $^{18}\text{F}$ -DCFPyL PET/CT.

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## Data availability statement

Availability of Data and Material: The datasets analysed during the current study are available from the corresponding author on request.

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## Supporting Information

Additional Supporting Information may be found in the online version of this article at the publisher's web-site:

**Fig S1.** Index lesion positivity compared with csPCa as identified via PSMA or mpMRI

**Fig S2.** (a) Corresponding low signal within the left peripheral zone (PZpl) on corresponding ADC map (Red arrow). (b) Axial DWI B value 2000 (a) demonstrates 8mm focus of high signal within the left mid gland peripheral zone (PZpl) (Red arrow). (c) Axial T2 sequence demonstrates corresponding well defined hypointense T2 lesion within the left peripheral zone (PZpl) (Red arrow). (d) Axial fused 18F- DCFPyL PET/CT through the prostate demonstrates corresponding increased PSMA expression, SUV 23.5. This lesion correlates with an ISUP 3 tumour on histopathology.