

# Oligometastatic Lymph Node Recurrence Detected Using $^{18}\text{F}$ -PSMA-1007 PET/CT in a Patient With Castration-resistant Prostate Cancer After Radiation Therapy

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**Abstract.** *Background/Aim:* Prostate cancer (PC) is one of the most common types of cancer in men worldwide. Most patients with metastatic PC are treated with androgen deprivation therapy (ADT) using luteinizing hormone-releasing hormone agonists and antagonists as first-line therapy. The majority of PC patients develop a castration-resistant PC (CRPC), which eventually leads to high mortality with poor prognosis, despite new targeted therapies. However, given that oligometastatic recurrence may enable local therapy in CRPC, accurate detection of metastatic lesions may improve clinical outcomes in patients with CRPC. *Case Report:* We report the case of an 83-year-old man with CRPC.  $^{18}\text{F}$ Fluorine-prostate-specific membrane antigen-1007 positron emission tomography/ computed tomography ( $^{18}\text{F}$ -PSMA-1007 PET/CT) revealed weak physiological PSMA accumulation in the prostate and strong accumulation not only in the internal iliac lymph node but also in the two obturator lymph nodes that could not be detected with conventional CT or magnetic resonance imaging. Prostatic re-biopsy revealed no prostate malignancy. Under the diagnosis of oligometastases in the pelvic lymph

nodes, the patient underwent laparoscopic pelvic lymph node dissection, which revealed lymph node metastases in two obturator lymph nodes and the internal iliac lymph node, corresponding to the PSMA accumulation sites. The patient experienced at least 7 months of recurrence-free duration without additional treatment. *Conclusion:* This study indicates a novel approach to oligometastatic CRPC by means of accurate staging with  $^{18}\text{F}$ -PSMA-1007 PET/CT.

Prostate cancer (PC) is one of the most common types of cancer in men worldwide (1). In 2021, there were 95,400 incidents and 12,900 deaths due to PC in Japan, and the number of patients with PC has continued to rise recently (2). Prostate-specific antigen (PSA) has been found to be a discriminatory screening test for PC and is often used to monitor disease progression, particularly after definitive therapy including radical prostatectomy or radiotherapy (3). Biochemical recurrence (BCR) of PC occurs in 20-30% of patients after radical prostatectomy (4) and in up to 60% of patients after primary external-beam radiotherapy (5). The European Association of Urology guidelines on PC state that the timing and choice of treatment for BCR after definitive therapy remains controversial (6). In clinical practice, conventional imaging modalities, such as computed tomography (CT), magnetic resonance imaging (MRI) and bone scintigraphy are used to identify the site of recurrence or metastasis. However, these imaging tests may not always work for restaging at the BCR of PC after treatment with curative intent. In case of no recurrence or metastasis on conventional imaging, hormone therapy empirically is started as a treatment for BCR of PC after radiotherapy but most patients receiving hormone therapy eventually develop castration-resistant PC (CRPC), whose prognosis is poor despite the development of novel treatments for CRPC.

Recently,  $^{18}\text{F}$ Fluorine-prostate-specific membrane antigen-1007 positron emission tomography/computed tomography ( $^{18}\text{F}$ -

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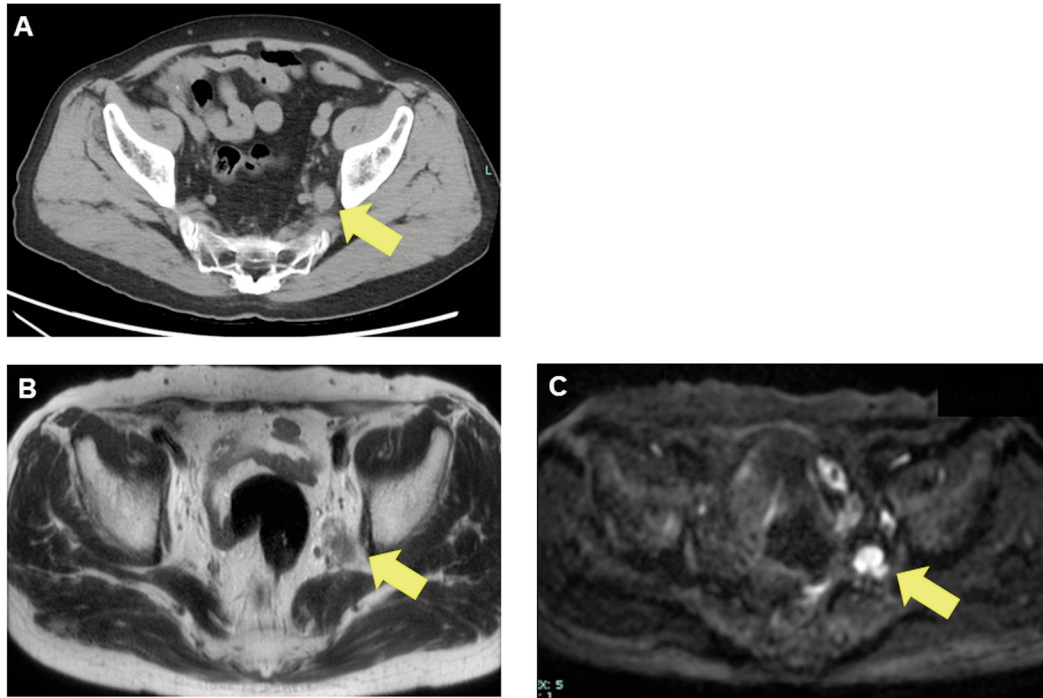


Figure 1. Imaging tests using conventional computed tomography and magnetic resonance imaging. (A). Abdominal computed tomography examination shows the obturator lymph node with a 15-mm diameter. (B, C) Abdominal magnetic resonance imaging showing signal changes in the obturator lymph node. (B) T2-weighted image, (C) diffusion-weighted image.

PSMA-1007 PET/CT) has been reported to have a high detection efficacy in the BCR of PC for identifying the sites of recurrence or metastasis (7), and the diagnostic accuracy is considered to be superior to conventional imaging (8-11). Fossati *et al.* suggested that accurate detection of oligometastatic recurrence may enable local therapy (12). However, there are no reports on the clinical course after intervention for metastatic sites detected using  $^{18}\text{F}$ -PSMA-1007 PET/CT.

Here, we report a successful case, wherein  $^{18}\text{F}$ -PSMA-1007 PET/CT detected oligometastatic lymph node recurrence in a patient with CRPC after radiation therapy. In this case, the patient experienced no BCR for 7 months after laparoscopic lymph node dissection, highlighting the clinical significance of  $^{18}\text{F}$ -PSMA-1007 PET/CT for the precise detection of recurrence in patients with PC.

### Case Report

An 83-year-old man with no significant medical history presented with an elevated PSA level (11 ng/ml). Transrectal prostate needle biopsy revealed a pathologic diagnosis of adenocarcinoma with a Gleason score of 7 (4+3) in 1 of 12 specimens. Based on the imaging results, the patient was staged as cT1cN0M0. First, the patient received neoadjuvant androgen deprivation therapy (ADT) for 9 months with a

luteinizing hormone-releasing hormone agonist and subsequently underwent three-dimensional conformal radiation therapy (3D-CRT, 72 Gy, 2 Gy/fraction, 5 fractions/week) to the prostatic bed, resulting in a decrease in PSA level to a nadir level (0.06 ng/ml). After 18 months of adjuvant hormonal therapy with ADT, PSA level gradually elevated and reached 0.28 ng/ml, under the castration level of testosterone. Based on a diagnosis of CRPC, the patient was administered bicalutamide. Twenty months after starting combined androgen blockade, bicalutamide was replaced with flutamide. However, the PSA level increased to 4.1 ng/ml, 56 months after initiating ADT, and the patient was referred to our hospital for further treatment. CT and MRI showed lymphadenopathy (size of 15 mm) within the left obturator fossa (Figure 1A-C) with no significant findings on bone scintigraphy.

We further performed  $^{18}\text{F}$ -PSMA-1007 PET/CT to detect possible metastatic lesions other than lymphadenopathy within the left obturator fossa. As a result,  $^{18}\text{F}$ -PSMA-1007 PET/CT showed weak physiological accumulation in the prostate and strong accumulation not only in the internal iliac lymph node but also in the two obturator lymph nodes that could not be detected using CT or MRI (Figure 2A and B). Prostatic re-biopsy revealed no prostate malignancy. Under the diagnosis of oligometastases in the pelvic lymph nodes, the patient underwent laparoscopic pelvic lymph node

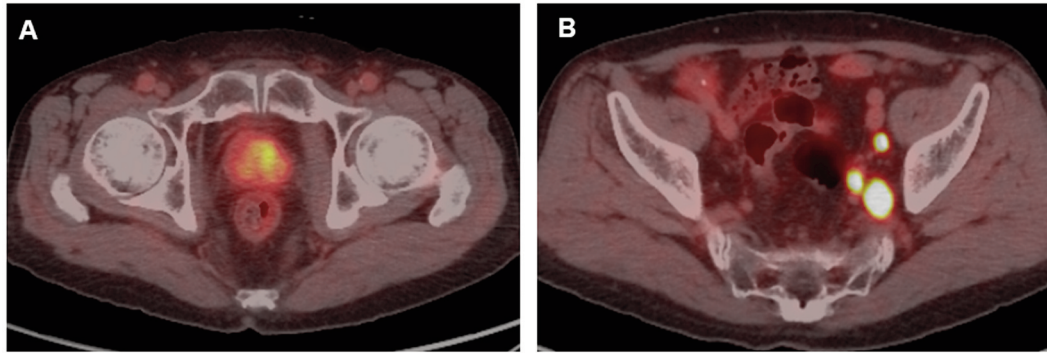


Figure 2. Imaging tests using  $^{18}\text{F}$ Fluorine-prostate-specific membrane antigen (PSMA)-1007-positron emission tomography/computed tomography. (A)  $^{18}\text{F}$ Fluorine-prostate-specific membrane antigen (PSMA)-1007-positron emission tomography/computed tomography showing weak PSMA accumulation in the prostate and (B) strong accumulation in the two obturator lymph nodes and one internal iliac lymph node.

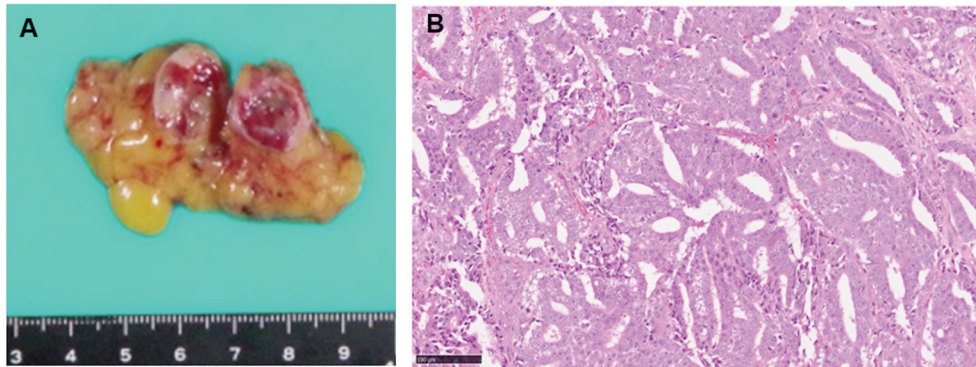


Figure 3. Histopathological findings after laparoscopic pelvic lymph node dissection. (A) Macroscopic finding of the lymph node within the left obturator fossa. (B) Hematoxylin-eosin staining shows typical lymph node metastasis of prostate cancer cells. Scale bar: 100  $\mu\text{m}$ .

dissection as curative treatment. Histopathological findings showed lymph node metastases of prostate cancer in the two obturator lymph nodes and the internal iliac lymph node corresponding to the PSMA accumulation sites (Figure 3A and B). Finally, the patient maintained a low PSA (0.01 ng/ml) for 7 months after the operation.

## Discussion

Restaging PC is essential for determining the most appropriate treatment for BCR after radical therapy. PSMA is a unique membrane-bound glycoprotein, which is an excellent target for imaging and therapy because it is a cell surface protein presenting a large extracellular target and is expressed at levels that are about a thousand-fold greater than the minimal expression seen in other tissues, such as the kidney, proximal small intestine, and salivary gland (13). To date,  $^{68}\text{Ga}$ -PSMA-11, a well-known tracer, has shown high detection rates based on clinical and histological data (14,

15). In contrast,  $^{18}\text{F}$ -PSMA-1007 PET/CT facilitates the detection of local recurrence with decreased activity in the bladder because  $^{18}\text{F}$ -PSMA-1007 offers lower urinary clearance and longer half-life (16). Importantly,  $^{18}\text{F}$ -PSMA-1007 PET/CT has a positive predictive value of 91.3% and a negative predictive value of 97.9% for detecting positive lymph nodes (7), leading to accurate local therapy, including lymph node dissection or salvage radiotherapy to the metastatic lesion (7). However, since its recent introduction, only a few studies using  $^{18}\text{F}$ -PSMA-1007 PET/CT have validated this tracer capacity using histopathology (17).

In this study, we report a patient with CRPC who was diagnosed with lymph node oligometastases in the pelvis by performing  $^{18}\text{F}$ -PSMA-1007 PET/CT, which was not found in other imaging modalities. In previous studies, Sprute *et al.* reported an exceptional specificity of 99.5% for the lymph nodes (7). However, to date, there have been no reports regarding the transition of PSA after lymph node dissection detected using  $^{18}\text{F}$ -PSMA-1007 PET/CT.

Interestingly, the patient experienced at least 7 months of recurrence-free duration without additional treatment after lymph node dissection, which indicates the complete removal of malignant lymph nodes in metastatic CRPC, delaying the initiation of additional drug treatment. Considering that CRPC still has a poor prognosis despite the development of new therapies, our case may indicate a novel approach to oligometastatic CRPC by means of accurate staging with <sup>18</sup>F-PSMA-1007 PET/CT.

In conclusion, we report the diagnostic accuracy of <sup>18</sup>F-PSMA-1007 PET/CT after surgical dissection of oligometastatic lymph nodes. We believe that <sup>18</sup>F-PSMA-1007 PET/CT may detect asymptomatic metastases, which may lead to early diagnosis, treatment, and survival advantage in patients with CRPC.

### Conflicts of Interest

The Authors declare that they have no conflicts of interest.

### Authors' Contributions

S.M conducted the study, data collection and analysis and drafted the manuscript. T.K was responsible for the study conception and design and drafting of the manuscript. T.W, K.H, T.A, S.F, H.K, R.I, M.U, and N.N conducted the study and drafted and reviewed the manuscript. All Authors read and approved the final manuscript for submission.

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