# Adjunctive Role of Dual Time Point Imaging in Evaluating Bone Lesions with Increased $^{18}$F-PSMA-1007 Uptake

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## ABSTRACT

***Background:***

*Non-specific focal uptake in the skeleton is a diagnostic pitfall on $^{18}$F-PSMA-1007 PET/CT, but adjunctive measures to aid interpretation of these lesions are currently lacking. We present two cases where dual time point imaging provided additional information.*

***Case Presentation:***

*The first patient had a PI-RADS 3 lesion on MRI. No PSMA-avid abnormality was seen on PET, save for focal uptake in the right pubis with no anatomic correlate. Additional imaging showed a decrease in lesion SUV, and this was interpreted as benign. Another patient, diagnosed with prostate cancer, had multiple PSMA-avid pelvic foci. Two suspiciously malignant bone lesions had increasing SUV trend after dual time point imaging despite only faint sclerosis on CT. In contrast, one faint PSMA-avid lesion with no anatomic abnormality was read as benign after a decrease in SUV. A decrease in lesion SUV may point to a benign etiology, while an increase would heighten suspicion for malignancy. One possible molecular explanation is that a true PSMA-overexpressing lesion would bind to the tracer for a longer period than a false positive.*

***Conclusion:***

*Dual time point imaging provides additional information that may be useful in the interpretation of non-specific skeletal lesions with increased $^{18}$F-PSMA-1007 uptake.*

***Keywords:*** *$^{18}$F-PSMA-1007 PET/CT, bone lesions, dual time point imaging*

## INTRODUCTION

Prostate-specific membrane antigen (PSMA) has become a gamechanger in nuclear medicine when it comes to prostate cancer imaging and therapy. Specifically, PSMA positron emission tomography/computed tomography (PET/CT) has become the modality of choice for staging and evaluating biochemical recurrence. When locally available, it is also used to assess eligibility for PSMA radioligand therapy.

Over the past decade, a number of PSMA PET radiopharmaceuticals have been produced for commercial use. In our local setting, $^{18}$F-PSMA-1007 and $^{68}$Ga-PSMA-11 are available. $^{18}$F-PSMA-1007 has a longer half-life than its Ga-68 counterpart, thereby allowing for centralized mass production. Its primary mode of excretion is through the hepatobiliary tree; hence, instances where urinary bladder activity obscures the prostate gland are reduced [1]. Also, $^{18}$F-PSMA-1007 PET/CT is locally offered at a lower price point than $^{68}$Ga-PSMA-11 PET/CT, which is important in places where PET/CT scans are not reimbursed by the national health insurance service.

One potential disadvantage of $^{18}$F-PSMA-1007 PET/CT is the higher reported incidence of PSMA-avid non-specific bone lesions (NSBLs). Otherwise known as unspecific bone uptake (UBU), these are skeletal foci of increased PSMA uptake which are equivocal for metastatic bone disease [1, 2]. A matched-pair comparison showed almost 5 times as many PSMA-avid benign bone lesions in $^{18}$F-PSMA-1007 PET scans relative to $^{68}$Ga-PSMA-11 PET scans [3]. This is supported experientially by the authors, who attest to seeing NSBLs mentioned more frequently in $^{18}$F-PSMA-1007 PET reports than in their

$^{68}$Ga-PSMA counterparts. While these lesions typically do not have morphologic correlates, beginning bone metastasis may present as such. This may lead to either overstaging (interpreting a NSBL as metastatic when it is not) or understaging (calling a truly metastatic NSBL as inflammatory) and may have serious consequences on patient management.

The challenge of interpreting these NSBLs is not lost to those who interpret $^{18}$F-PSMA-1007 PET/CT images on a regular basis. Vollnberg et al. retrospectively analyzed biopsy results of 11 NSBLs from 10 patients, of which only one revealed true metastasis. On review of imaging, 8 of the 11 foci were classified as high-risk for malignancy, and none of these lesions had corresponding CT abnormalities [4]. Arnfield et al. suggests the use of cut-offs on standard uptake values (SUVs). Lesions with a maximum SUV (SUVmax) less than 7.2 are likely benign, while those with SUVmax between 7.2 and 11.1 may be equivocal or metastatic, depending on clinical risk factors, scan appearance, and patient management implications [1].

In our center, dual time point (or delayed) imaging is a common method used to acquire further information on equivocal-looking foci of increased tracer uptake. When deemed necessary, a repeat scan of a section of the patient's body is obtained, usually post-void imaging of the pelvis. It is more commonly employed in $^{18}$F-fluorodeoxyglucose (FDG) and $^{68}$Ga-PSMA-11 PET scans where radioactivity from other organs, commonly in the gastrointestinal tract, may preclude proper evaluation of significant-looking lesions. In a study by Aksu et al., dual time-point imaging with $^{68}$Ga-PSMA-11 PET was shown to aid in differentiating Gleason grade groups [5]. In the context of $^{18}$F-PSMA-1007 PET scans, this technique is usually applied in patients with apparently impaired hepatobiliary excretion where urinary activity may obscure the prostate. This incidentally allows further elucidation of NSBLs in pelvic bones based on appearance and SUV change between the two time points.

We present two cases where dual time point imaging aided in the interpretation of NSBLs on $^{18}$F-PSMA-1007 PSMA PET/CT. All SUVs reported are SUVmax unless otherwise specified.

# CASE 1

A 76-year-old came to our center with history of lower urinary tract symptoms and benign prostate biopsy findings from three years ago. Surveillance studies from two months prior showed prostatomegaly with a PI-RADS 3 lesion in the left posterolateral to posteromedial peripheral zone and a serum prostate-specific antigen (PSA) value within normal limits at 3.18 ng/mL. PSMA PET/CT imaging was requested by the urologist for further evaluation of possible malignancy. Initial whole-body PET images were acquired 63 minutes after PSMA administration, with delayed imaging of the pelvis done at 84 minutes post-injection.

The PET scan showed diffusely increased PSMA uptake in an enlarged prostate gland (SUV 6.9, Figure 1A). No PSMA abnormality corresponding to the MRI finding was seen. Additionally, a PSMA-avid focus was noted in the right pubic bone (Figure 1B), with no correlate on both diagnostic CT and the prior MRI. Emission images of the pelvis acquired 21 minutes after initial whole-body imaging showed a decrease in lesion SUV from 6.6 to 5.8. Taken together, the findings were signed out as favoring benign prostatic hypertrophy, with the bone lesion being more likely inflammatory or non-specific. Continued monitoring, both biochemically (serum PSA) and through imaging, was advised.

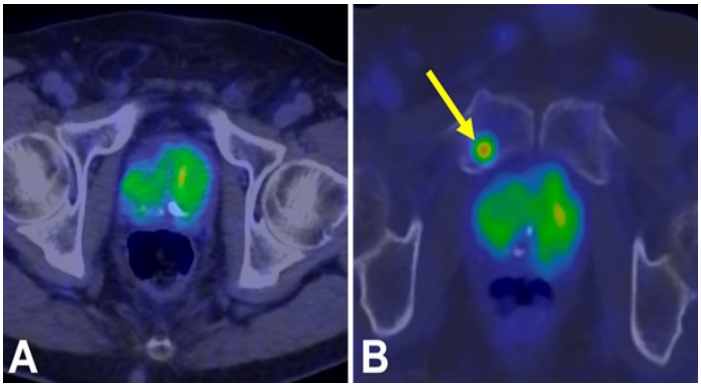


**FIGURE 1.** PSMA PET/CT images of a 76-year-old patient with a suspicious prostate MRI finding. Apart from diffuse PSMA uptake in the prostate (A), a PSMA -positive right pubic bone lesion was also noted (B), which decreased in SUV after delayed imaging

# CASE 2

A 68-year-old with elevated PSA (21.93 ng/mL) and biopsy-proven prostate adenocarcinoma (Gleason score 4+3) was referred to our center. MRI one month prior showed multifocal PI-RADS 4-5 prostatic disease and a suspicious enhancing lesion involving the left superior pubic ramus. PSMA PET/CT was subsequently requested for metastatic work-up. Initial whole-body PET images were acquired 70 minutes after PSMA administration, with delayed imaging of the pelvis done at 103 minutes post-injection.

Apart from multiple PSMA-avid foci in the prostate which coincided with findings in the prior MRI, several pelvic bone lesions with increased PSMA uptake were also seen. These are summarized in Table 1, along with their SUVs on initial and additional emission imaging (done 33 minutes after initial acquisition). The left pubic and left iliac wing lesions with increasing SUV were suspected as beginning bone metastasis, while the faint PSMA-avid lesion near the sacroiliac joint was interpreted as likely degenerative.

# DISCUSSION

A PubMed advanced search using the syntax "PSMA-1007 AND bone" would yield 305 publications at the time of this writing. However, after manually filtering the results, less than 10 actually discussed NSBLs. It can thus be said that based on the current body of knowledge on this topic, there is more than ample room for further research.

**TABLE 1.** PSMA-avid pelvic bone lesions in the PSMA PET/CT of a 68-year-old with prostate carcinoma. PET images were windowed to the same scale to allow visual comparison.

| **Lesion location** | Left superior pubic ramus | Left iliac wing, lateral aspect | Left iliac wing, proximal to |
|---|---|---|---|
| **MRI correlate** | Enhancing lesion (Figure 2) | None | None |
| **CT correlate** | Very faint sclerosis | Faint sclerosis | None |
| **SUV, initial** | 4.0 | 6.1 | 3.8 |
| **SUV, delayed** | 6.5 | 6.5 | 2.9 |
| **Lesion image** | Figure 3A | Figure 3B | Figure 3C |

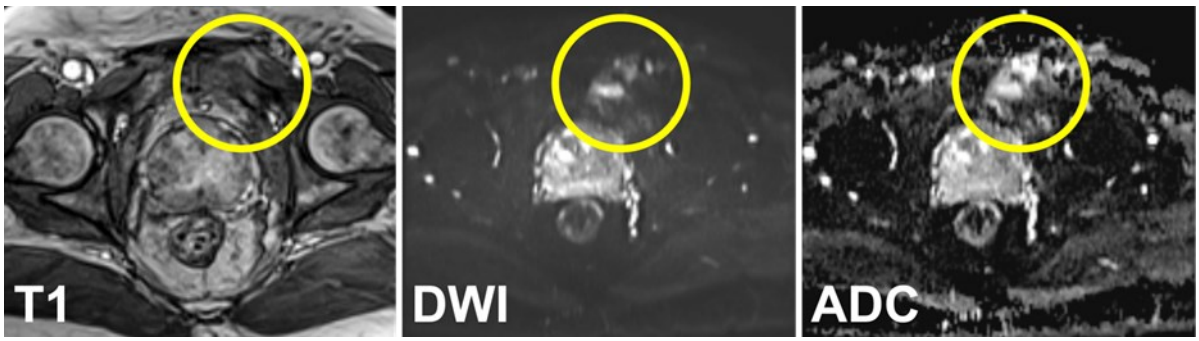


**FIGURE 2.** MRI showed an abnormality in the left superior pubic ramus.

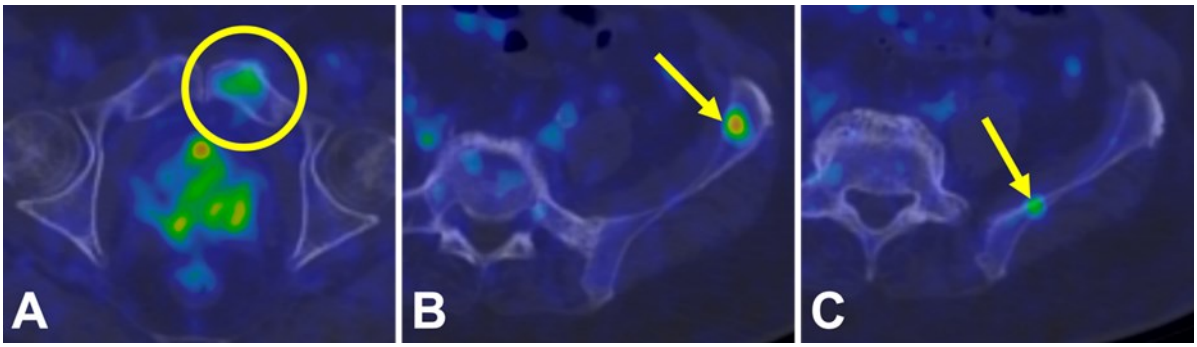


**FIGURE 3.** PSMA PET/CT images of the three PSMA-avid pelvic bone lesions, as described in Table 1

To the knowledge of the authors, this is the first attempt to provide a possible imaging approach in the evaluation of equivocal bone lesions on $^{18}$F-PSMA-1007 PET/CT scans. The two cases both involve pelvic bone lesions and have dual time point images, but their clinical backgrounds and indications for imaging are different.

The first patient had no known malignancy. The clinician was ruling out malignancy given a PI-RADS 3 lesion on a prior MRI, hence PSMA PET/CT evaluation was requested. The MRI lesion had no PET correlate but diffuse prostatic PSMA avidity was seen. Using the recently published PRIMARY scoring system for patients clinically suspected with prostate cancer, this lesion would have a score of 1, thus decreasing the probability of metastasis should other PSMA-avid findings be encountered [6]. Additionally, a PSMA-avid bone focus was seen in the right pubis. The tracer washout manifested by an SUV decrease on dual time point imaging, on top of the lack of a distinct CT correlate, supports a benign interpretation of this finding.

In contrast, the second patient was already diagnosed with prostate cancer, and PSMA PET/CT was performed for staging. Two PSMA-avid bony foci had faint sclerosis on CT, with one of them also having an MRI correlate. In both cases, an increase in SUV was noted on dual time point imaging, which increased reader confidence in interpreting these lesions as beginning metastasis. A third lesion was seen which was fainter than the previous two, had no CT correlate, and showed a decreasing SUV trend. Based on this, as well as its proximity to the sacroiliac joint, the lesion was interpreted as degenerative.

All the mentioned bone lesions in both cases had SUVmax values below the previously described threshold of 7.2 [1]. Using this cut-off without anatomic correlates, some of the abovementioned skeletal foci would have been labeled as benign. SUV change on dual time point imaging thus provides additional information in discriminating between possibly benign and possibly malignant bone lesions. A molecular-level explanation for this phenomenon still needs to be elucidated. However, it can be postulated that true PSMA-overexpressing lesions would have more favorable receptor binding kinetics toward the tracer compared to false positives where tracer washout is seen. Bone lesion biopsy remains to be the best means of confirming such hypothesis, but financial and ethical hurdles in the local setting are dissuasive for independent research.

This case report highlights the potential adjunctive value of dual time point imaging in the interpretation of NSBLs with increased $^{18}$F-PSMA-1007 UBU. Further studies are recommended to establish the utility of dual time point imaging under such context on a larger scale. This includes prospective follow-up to confirm the benign or malignant nature of the bone lesions, as well as possible integration in future imaging protocols and guidelines, such as the optimal interval time of second scan imaging.

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