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The Role of Osteoporosis in Non-Metastatic [^{18}F]PSMA-1007 Bone Uptake — Finding the Missing Piece of the Puzzle

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Short Report

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Abstract

Aim

We investigated the association between surrogate markers of osteoporosis and the occurrence of non-metastatic [^{18}F]PSMA-1007 bone uptake.

Materials and Methods

We retrospectively analysed treatment-naïve patients with a confirmed diagnosis of prostate adenocarcinoma who underwent staging [^{18}F]PSMA-1007 Positron Emission Tomography (PET) and blood count within 3 months. Qualitative image analysis was performed independently by three experienced nuclear medicine physicians. Patients were divided in two groups according to the presence/absence of non-metastatic bone uptake. Clinical information, blood count parameters, Body Mass Index (BMI) and bone density as estimated by Computed Tomography were collected. The Kruskal-Wallis and t-test were used to compare parameters.

Results

We analysed 77 patients: 29 of them had non-metastatic bone uptake at [^{18}F]PSMA-1007 PET, most commonly in the pelvic bones (69%) and ribs (62%). Clinical parameters did not differ in the two groups. In patients with non-metastatic bone uptake, white blood cell and neutrophil counts were significantly higher; in the same group, we observed lower values of BMI and bone density, although not statistically different.

Conclusions

We observed non-metastatic bone uptake on [^{18}F]PSMA-1007 PET in more than 1/3 of patients. We found a significant correlation between blood count parameters and non-metastatic [^{18}F]PSMA-1007 bone uptake. Given the prevalence of the finding and the molecular alterations induced by osteoclastogenic processes, we may speculate that [^{18}F]PSMA-1007 non-metastatic bone uptake could be secondary to underlying osteoporosis. This hypothesis needs to be further investigated in larger populations and exploring more specific markers of osteoporosis.

Introduction

Non-metastatic (i.e., unspecific) bone uptake on PET imaging with [^{18}F]PSMA-1007 has been reported in up to 72% of cases [1]. This phenomenon is a cause for concern as it may lead to misdiagnosis, additional investigations, or delays in treatment. Nonetheless, unspecific bone findings are not unique to

[^{18}F]PSMA-1007 but have also been described, albeit less commonly, with other PSMA-targeting radiopharmaceuticals, including [^{68}Ga]Ga-PSMA-11 [1–6]. Notably, besides bone, unspecific uptake has been reported more frequently with [^{18}F]PSMA-1007 than with [^{68}Ga]Ga-PSMA-11 (approximately three times for lymph nodes and more than five times for ganglia) [4]. This observation suggests that fluorine-18 properties [7–9] and/or injected activity (up to three-fold for [^{18}F]PSMA-1007 compared with [^{68}Ga]Ga-PSMA-11) improve the ability to identify [^{18}F]PSMA-1007-avid foci, ultimately leading to an increased detection rate of false positives. Moreover, evidence does not convincingly support the hypothesis that [^{18}F]PSMA-1007 uptake in the skeleton is secondary to free fluorine-18. Preclinical data in mice showed no significant differences in bone uptake between PSMA-1007 and PSMA-11 [10, 11] and immunochemistry showed that normal bone marrow does not express PSMA [12]. Collectively, although the precise reason for this pitfall is still unknown, underlying benign bone and bone marrow disorders have been suggested as the most rational causes of non-metastatic bone PSMA uptake [2, 13].

Biopsy of focal unspecific bone [^{18}F]PSMA-1007 uptake revealed Paget's disease, hyperplastic bone marrow [13], bland fibroblastic reaction, and 'woven bone", as observed in fibrous dysplasia [2]. These diagnoses might be associated to specific conditions (e.g. aerobic training, chronic anaemia, smoking and obesity) and vary in incidence accordingly [14–17]. However, these benign alterations are much rarer than unspecific findings observed on PSMA imaging, they are generally located in pelvis and legs, and associated with morphological changes evident at radiological imaging or bone scintigraphy. Therefore, non-metastatic bone PSMA uptake in the general population might be related to other, more prevalent conditions. Osteoporosis is the most common metabolic disease, with an overall prevalence in elderly men worldwide of 12.5% (95% confidence interval: 9.3–16.7%) [18]. We aimed to explore the association between surrogate markers of osteoporosis (i.e., blood count parameters [19], BMI [20], and bone Hounsfield Units (HU) values on CT [21]) and the occurrence of non-metastatic bone [^{18}F]PSMA-1007 uptake.

Material and Methods

We retrospectively analysed treatment-naïve patients with a confirmed diagnosis of prostate adenocarcinoma who underwent [^{18}F]PSMA-1007 PET imaging for staging and blood count within three months. All patients with confirmed metastases, synchronous malignancy, known bone disorders and/or active inflammatory processes were excluded. The patient selection process is summarized in Fig. 1. [^{18}F]PSMA-1007 PET scans were acquired using the SIGNA PET/MR system, PET/CT Discovery-STE or Discovery-690 (GE Healthcare, Waukesha, WI, USA) according to the joint EANM and SNMMI procedure guidelines [22]. Qualitative analysis of [^{18}F]PSMA-1007 PET/CT or PET/MR images was performed independently by three experienced nuclear medicine physicians, and non-specific bone lesions were defined according to specific criteria as described by Arnfield et al [2]. Selected patients were divided in two groups according to the presence/absence of non-metastatic bone uptake. For men with non-metastatic bone [^{18}F]PSMA-1007 uptake, anatomic distribution was recorded. Clinical information (age, Gleason score, iPSA), blood count parameters, and BMI values were collected. Neutrophil to lymphocyte

(NLR), platelet to lymphocyte (PLR) and monocyte to lymphocyte (MLR) ratios were calculated. In all patients who performed PET/CT, bone HU values were measured as previously described drawing a spheric region-of-interest in the central trabecular portion of the L1 vertebral body [21]. Descriptive statistics summarized baseline patients' characteristics and results. The median and mean value of blood count parameters, BMI and bone HU values in the two groups were compared using the Kruskal-Wallis test and the t-test, respectively. P-values < 0.05 were considered statistically significant.

The study was approved by the local Ethics Committee (approval number 81/INT/2022).

Results

A total of 77 patients with a median age of 67 years (range 51–87) who underwent [^{18}F]PSMA-1007 PET/CT (n = 66) or PET/MR (n = 11) between October 2021 and May 2023 were included. The most prevalent Gleason scores were 4 + 3 (29%), 3 + 4 (25%) and 4 + 5 (25%). Median PSA at imaging was 7 ng/mL (IQR 5.4–10). Patient characteristics are summarized in Tables 1 and 2. Forty-eight patients had no bone findings while 29/77 had unspecific bone uptake at [^{18}F]PSMA-1007 PET, most commonly in the pelvic bones (69%), ribs (62%), and vertebrae (17%). Figures 2 and 3 show two examples of patients without and with unspecific [^{18}F]PSMA-1007 bone uptake. No statistically significant difference in clinical parameters between the two groups was found. Median white blood cell and neutrophil counts were significantly higher in patients with non-metastatic bone uptake compared to those without (7100/mm^3 vs 6200/mm^3, p = 0.0337 and 4600/mm^3 vs. 3850/mm^3, p = 0.0452). The same was observed comparing mean counts (7400/mm^3 vs 6400/mm^3, p = 0.0135 and 4650/mm^3 vs 3900/mm^3, p = 0.01). Median MLR was significantly lower in patients with non-metastatic bone uptake (0.27 vs 0.35, p = 0.0369). Other parameters resulted similar in the two groups (Table 3). BMI and median bone HU values were lower in the group of patients with [^{18}F]PSMA-1007 non-metastatic bone uptake, although the difference did not reach statistical significance (24.8 vs. 26, p = 0.17 and 122 vs 134, p = 0.2233, respectively).

Discussion

We found a correlation between blood count parameters and non-metastatic [^{18}F]PSMA-1007 bone uptake. Specifically, patients with unspecific [^{18}F]PSMA-1007-avid foci in the skeleton had significantly higher mean and median white blood cell and neutrophil counts compared to those without unspecific bone findings. These data are consistent with the literature. Recently, Li et al. [19] investigated a large cohort of osteoporotic patients and healthy subjects (more than 1100 people in total) and reported higher white blood cell, neutrophil and monocyte counts in cases than in controls. These results were confirmed even when the analysis was restricted to men (about 6% of this population).

In our cohort, monocyte counts were not significantly different between patients with and without unspecific [^{18}F]PSMA-1007 bone uptake. We also observed a significantly lower median MLR in patients

with non-metastatic [^{18}F]PSMA-1007-avid lesions than in subjects without bone findings; however, data about MLR in osteoporosis are controversial [23, 24].

Our results showed that patients with unspecific [^{18}F]PSMA-1007 bone uptake had a slightly lower BMI compared with patients with no bone alterations (24.8 vs 26 kg/m^2, p = 0.17). Although obesity is a major cause of several comorbidities, higher BMI levels are associated with increased bone turnover, probably due to increased mechanical stress on the skeletal system. This results in improved bone density and favourable microarchitecture on dual-energy X-ray absorptiometry and quantitative CT [20]. Lee et al. identified a BMI range of 25.0 to 29.9 kg/m^2 as the lowest risk of osteoporosis in men in nationwide Korean population data, and an increase in BMI of 1 kg/m^2 reduces the risk of osteoporosis by 28% [25].

Similarly, even if median bone HU values in our cohort were lower in patients with non-metastatic [^{18}F]PSMA-1007-avid lesions than in those without bone findings (122 vs.134, p = 0.2233), the difference did not reach statistical significance. Vadera et al. [21] recently confirmed bone HU values as surrogate marker of osteoporosis in an adult British population (mean age of 65.8 years) mainly constituted by females (73%). L1 attenuation measurement differed among DEXA-defined normal bone density subjects, osteopenic and osteoporotic patients (178 HU vs. 143 HU, vs. 118 HU, respectively) and they identified a cut-off of 131 HU as the most balanced in terms of sensitivity and specificity (AUC = 0.74, sensitivity = 69%, specificity = 70%). We observed lower values of L1 attenuation measures, but our cohort included older males.

In our cohort, the difference in BMI levels between the two populations might explain the lower HU values in the group with unspecific focal uptake. However, optimal BMI cut-offs for osteoporosis in Western men populations have not been established yet. Moreover, the strong correlation between obesity and diabetes mellitus induces controversial effects on bone health, leading to increased risk of falls and fractures [26].

Considering the significant findings on white blood cell and neutrophils, and trends regarding HU values and BMI, we can speculate that osteoporosis might play a role in non-metastatic [^{18}F]PSMA-1007 bone uptake. Bone is a multi-functional organ that responds to a wide range of different mechanical, hormonal and immune stimuli. Specifically, a close and complex interaction between the immune system and cells involved in bone remodelling has emerged, leading to the genesis of the field of osteoimmunology [27]. Many factors including immune cells, glutamate signalling, mesenchymal stromal cells, and endothelial cells, play a crucial role in bone homeostasis and thus in osteoporosis [19, 28–30]. Non-metastatic [^{18}F]PSMA-1007 bone uptake might be the result of bone remodelling typical of osteoporosis.

The rate of non-metastatic [^{18}F]PSMA-1007 bone uptake observed in our cohort was in line with the literature [2, 5]; moreover, the pelvis and ribs, which are frequently involved in osteoporosis, resulted the most commonly involved sites (69% and 62%, respectively). Age, and in particular the age-related decline in sex hormones (e.g., oestrogen and testosterone), is a major cause of osteoporosis and fractures in men [31]. Rib fractures are associated with the classic risk factors for osteoporosis [32, 33] and are the most common incidental clinical fractures in men. Subjects with diminished bone mineral density suffered rib

fractures and low-energy trauma more frequently than those with normal bone mineral density (74% and 36% vs. 51% and 15%) [33]. Similarly, 64% of all pelvic fractures are osteoporotic and the incidence increases with age, rising to 94% in patients aged > 60 years [34, 35].

Our exploratory analysis has several limitations: first, the small sample size; second, our cohort was retrospective; third, we used blood count parameters, BMI and bone density as estimated on CT, as surrogate biomarkers for osteoporosis in absence of available data on bone mineral density and of bone biomarkers for osteoporosis assessment [36].

It may be true that “if it looks like a duck, swims like a duck and quacks like a duck, then it probably is a duck”: results of our exploratory analyses regarding blood counts, BMI and bone density as estimated on CT, support the hypothesis that non-metastatic [^{18}F]PSMA-1007 bone uptake might be secondary to osteoporotic bone remodelling However, lack of gold standard parameters for diagnosing osteoporosis (e.g., dual-energy X-ray absorptiometry score) prevents further speculations and other conditions altering bone homeostasis cannot be excluded as a cause of this phenomenon.

With PSMA-targeting imaging on the rise and the ever-more-wide use of fluorinated compounds for their many advantages, unravelling the biological phenomena behind non-metastatic bone uptake in [^{18}F]PSMA-1007 is a highly relevant unmet clinical need.

Declarations

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Competing Interests

Prof. Chiti reports personal fees from AAA, Blue Earth Diagnostics and General Electric Healthcare, outside the submitted work. The other authors do not report any conflict of interest.

Author Contributions

M.S. and A.C. conceptualized the study; A.C., F.G., and M.S. designed the study; C.P., F.G, G.N., and S.G. performed patient selection and collected clinical data; A.C., F.G. and L.A. analysed the images; G.N. performed data analysis; A.B., A.C., C.L., F.G., F.M., M.P., M.S. and P.M. critically interpreted the results; C.P.,

F.G., G.N., M.S. and drafted the paper; all authors critically revised the paper and approved the submitted version of the manuscript.

Availability of Data and Material

The manuscript represents valid work, and neither this manuscript nor one with substantially similar content under the same authorship has been published or is being considered for publication elsewhere. Arturo Chiti had full access to all the data in the study and takes responsibility for the data integrity and the accuracy of the data analysis. Raw data are available on specific request to the corresponding author.

Code Availability

Not applicable.

Ethics Approval

The study was performed in accordance with the ethical standards as laid down in the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards. The Ethics Committee of the IRCCS S. Raffaele Hospital approved the study, with the authorization number 81/INT/2022.

Consent to Participate

A specific informed consent was waived because of the observational and retrospective study design.

Consent to Publication

Not applicable.

References

1. Hoberück S, Löck S, Borkowetz A, Sommer U, Winzer R, Zöphel K, et al. Intraindividual comparison of [68 Ga]-Ga-PSMA-11 and [18F]-F-PSMA-1007 in prostate cancer patients: a retrospective single-center analysis. EJNMMI Res. 2021;11.
2. Arnfield EG, Thomas PA, Roberts MJ, Pelecanos AM, Ramsay SC, Lin CY, et al. Clinical insignificance of [18F]PSMA-1007 avid non-specific bone lesions: a retrospective evaluation. Eur J Nucl Med Mol Imaging. Eur J Nucl Med Mol Imaging; 2021;48:4495–507.
3. Pattison DA, Debowski M, Gulhane B, Arnfield EG, Pelecanos AM, Garcia PL, et al. Prospective intra-individual blinded comparison of [18F]PSMA-1007 and [68 Ga]Ga-PSMA-11 PET/CT imaging in patients with confirmed prostate cancer. Eur J Nucl Med Mol Imaging. 2022;49.
4. Rauscher I, Krönke M, König M, Gafita A, Maurer T, Horn T, et al. Matched-Pair Comparison of 68Ga-PSMA-11 PET/CT and 18F-PSMA-1007 PET/CT: Frequency of Pitfalls and Detection Efficacy in

Biochemical Recurrence After Radical Prostatectomy. J Nucl Med. Society of Nuclear Medicine and Molecular Imaging; 2020;61:51.

5. Seifert R, Telli T, Opitz M, Barbato F, Berliner C, Nader M, et al. Non-specific PSMA-1007 bone uptake evaluated through PSMA-11 PET, bone scan and MRI triple validation in patients with biochemical recurrence of prostate cancer. J Nucl Med. Society of Nuclear Medicine; 2022;jnumed.118.215434.
6. Phelps TE, Harmon SA, Mena E, Lindenberg L, Shih JH, Citrin DE, et al. Predicting Outcomes of Indeterminate Bone Lesions on 18 F-DCFPyL PSMA PET/CT Scans in the Setting of High-Risk Primary or Recurrent Prostate Cancer. J Nucl Med. :2022.
7. Hoffmann MA, von Eyben FE, Fischer N, Rosar F, Müller-Hübenthal J, Buchholz HG, et al. Comparison of [18F]PSMA-1007 with [68Ga]Ga-PSMA-11 PET/CT in Restaging of Prostate Cancer Patients with PSA Relapse. Cancers 2022, Vol 14, Page 1479. Multidisciplinary Digital Publishing Institute; 2022;14:1479.
8. Piron S, Verhoeven J, Vanhove C, De Vos F. Recent advancements in 18F-labeled PSMA targeting PET radiopharmaceuticals. Nucl Med Biol. Elsevier; 2022;106–107:29–51.
9. Maisto C, Aurilio M, Morisco A, de Marino R, Recchimuzzo MJB, Carideo L, et al. Analysis of Pros and Cons in Using [68 Ga]Ga-PSMA-11 and [18 F]PSMA-1007: Production, Costs, and PET/CT Applications in Patients with Prostate Cancer. Molecules. 2022;27.
10. Ioppolo JA, Nezich RA, Richardson KL, Morandeau L, Leedman PJ, Price RI. Direct in vivo comparison of [18F]PSMA-1007 with [68Ga]Ga-PSMA-11 and [18F]AlF-PSMA-11 in mice bearing PSMA-expressing xenografts. Appl Radiat Isot. Pergamon; 2020;161:109164.
11. Piron S, Verhoeven J, Descamps B, Kersemans K, De Man K, Van Laeken N, et al. Intra-individual dynamic comparison of 18F-PSMA-11 and 68Ga-PSMA-11 in LNCaP xenograft bearing mice. Sci Reports 2020 101. Nature Publishing Group; 2020;10:1–11.
12. Silver DA, Pellicer I, Fair WR, Heston WDW, Cordon-Cardo C. Prostate-specific membrane antigen expression in normal and malignant human tissues. Clin Cancer Res. 1997;3.
13. Grünig H, Maurer A, Thali Y, Kovacs Z, Strobel K, Burger IA, et al. Focal unspecific bone uptake on [18F]-PSMA-1007 PET: a multicenter retrospective evaluation of the distribution, frequency, and quantitative parameters of a potential pitfall in prostate cancer imaging. Eur J Nucl Med Mol Imaging. Springer; 2021;48:4483.
14. Shigematsu Y, Hirai T, Kawanaka K, Shiraishi S, Yoshida M, Kitajima M, et al. Distinguishing Imaging Features between Spinal Hyperplastic Hematopoietic Bone Marrow and Bone Metastasis. Am J Neuroradiol. American Journal of Neuroradiology; 2014;35:2013–20.
15. Fibrous Dysplasia - StatPearls - NCBI Bookshelf [Internet]. [cited 2023 May 3]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK532947/#!po=50.0000
16. Appelman-Dijkstra NM, Papapoulos SE. Paget's disease of bone. Best Pract Res Clin Endocrinol Metab. Baillière Tindall; 2018;32:657–68.
17. Shellock FG, Morris E, Deutsch AL, Mink JH, Kerr R, Boden SD. Hematopoietic bone marrow hyperplasia: high prevalence on MR images of the knee in asymptomatic marathon runners. Am J

Roentgenol. American Public Health Association; 1992;158:335–8.

18. Salari N, Darvishi N, Bartina Y, Larti M, Kiaei A, Hemmati M, et al. Global prevalence of osteoporosis among the world older adults: a comprehensive systematic review and meta-analysis. J Orthop Surg Res. BioMed Central Ltd; 2021;16:1–13.
19. Li Y, Hao W, Guan J, Li B, Meng L, Sun S, et al. Relationship between indices of circulating blood cells and bone homeostasis in osteoporosis. Front Endocrinol (Lausanne). Frontiers Media S.A.; 2022;13:2163.
20. Dé Rique Turcotte Id A-F, O'connor S, Morin SN, Gibbs JC, Willie BM, Jean S, et al. Association between obesity and risk of fracture, bone mineral density and bone quality in adults: A systematic review and meta-analysis. 2021;
21. Vadera S, Osborne T, Shah V, Stephenson JA. Opportunistic screening for osteoporosis by abdominal CT in a British population. Insights into Imaging 2023 141. SpringerOpen; 2023;14:1–8.
22. Fendler WP, Eiber M, Beheshti M, Bomanji J, Calais J, Ceci F, et al. PSMA PET/CT: joint EANM procedure guideline/SNMMI procedure standard for prostate cancer imaging 2.0. Eur J Nucl Med Mol Imaging. Springer Berlin Heidelberg; 2023;1466–86.
23. Li H, Zhang X, Zhang Q, Zhang Q, Zhu X, Xie T, et al. The relationship between the monocyte-to-lymphocyte ratio and osteoporosis in postmenopausal females with T2DM: A retrospective study in Chinese population. Front Endocrinol (Lausanne). 2023;14:1–7.
24. Gao K, Zhu W, Liu W, Ma D, Li H, Yu W, et al. The predictive role of monocyte-to-lymphocyte ratio in osteoporosis patient. Med (United States). Lippincott Williams and Wilkins; 2019;98.
25. Lee JH, Kim JH, Hong AR, Kim SW, Shin CS. Optimal body mass index for minimizing the risk for osteoporosis and type 2 diabetes. Korean J Intern Med. 2020;35:1432–42.
26. Schwartz A V. Diabetes Mellitus: Does it Affect Bone? Calcif Tissue Int. Springer; 2003;73:515–9.
27. Takayanagi H. New developments in osteoimmunology. Nat Rev Rheumatol. Nat Rev Rheumatol; 2012;8:684–9.
28. Tuckermann J, Adams RH. Crosstalk between endothelial cells and bone in development, homeostasis and inflammatory disease. Nat Rev Rheumatol. Europe PMC Funders; 2021;17:608.
29. Ganguly P, El-Jawhari JJ, Giannoudis P V., Burska AN, Ponchel F, Jones EA. Age-related Changes in Bone Marrow Mesenchymal Stromal Cells: A Potential Impact on Osteoporosis and Osteoarthritis Development. Cell Transplant. Cell Transplant; 2017;26:1520–9.
30. Morimoto R, Uehara S, Yatsushiro S, Juge N, Hua Z, Senoh S, et al. Secretion of L-glutamate from osteoclasts through transcytosis. EMBO J. EMBO J; 2006;25:4175–86.
31. Riggs BL, Khosla S, Melton LJ. Sex steroids and the construction and conservation of the adult skeleton. Endocr Rev. Endocr Rev; 2002;23:279–302.
32. Barrett-Connor E, Nielson CM, Orwoll E, Bauer DC, Cauley JA. Epidemiology of rib fractures in older men: Osteoporotic Fractures in Men (MrOS) prospective cohort study. BMJ. BMJ Publishing Group; 2010;340:798.

33. Prins JTH, Van Lieshout EMM, Reijnders MRL, Verhofstad MHJ, Wijffels MME. Rib fractures after blunt thoracic trauma in patients with normal versus diminished bone mineral density: a retrospective cohort study. Osteoporos. Int. 2020.
34. Krappinger D, Kammerlander C, Hak DJ, Blauth M. Low-energy osteoporotic pelvic fractures. Arch. Orthop. Trauma Surg. 2010.
35. Kannus P, Palvanen M, Niemi S, Parkkari J, Järvinen M. Epidemiology of osteoporotic pelvic fractures in elderly people in Finland: Sharp increase in 1970-1997 and alarming projections for the new millennium. Osteoporos Int. 2000;11.
36. Kuo TR, Chen CH. Bone biomarker for the clinical assessment of osteoporosis: Recent developments and future perspectives. Biomark. Res. 2017.

Tables

Tables 1 to 3 are available in the Supplementary Files section.

Figures

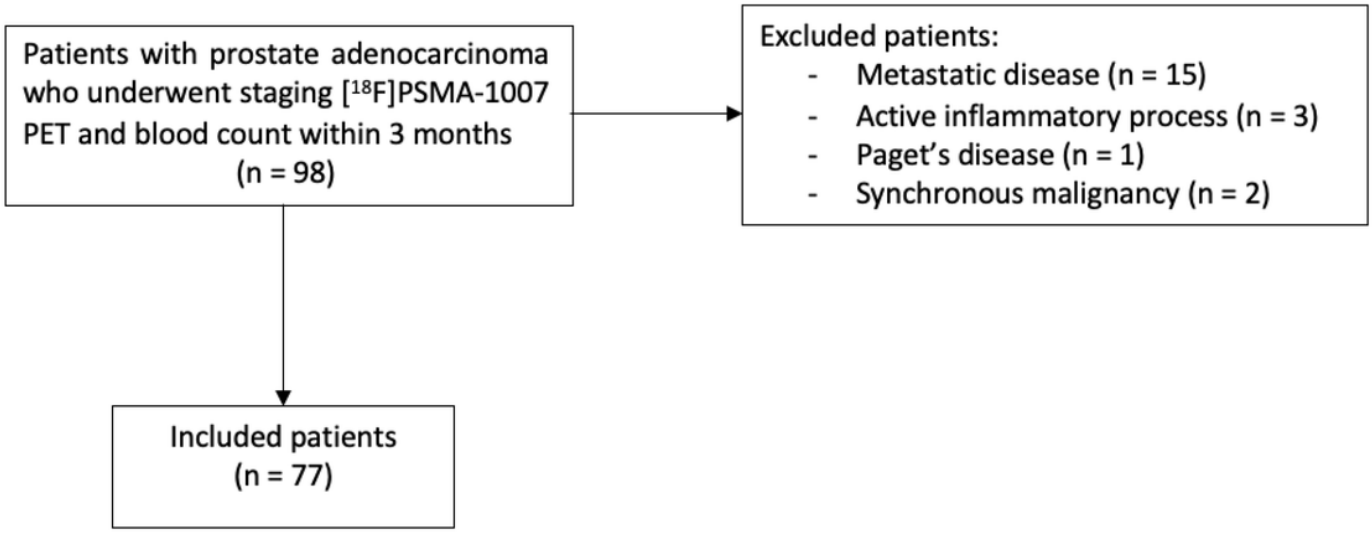

Figure 1

Summary of the patient selection process

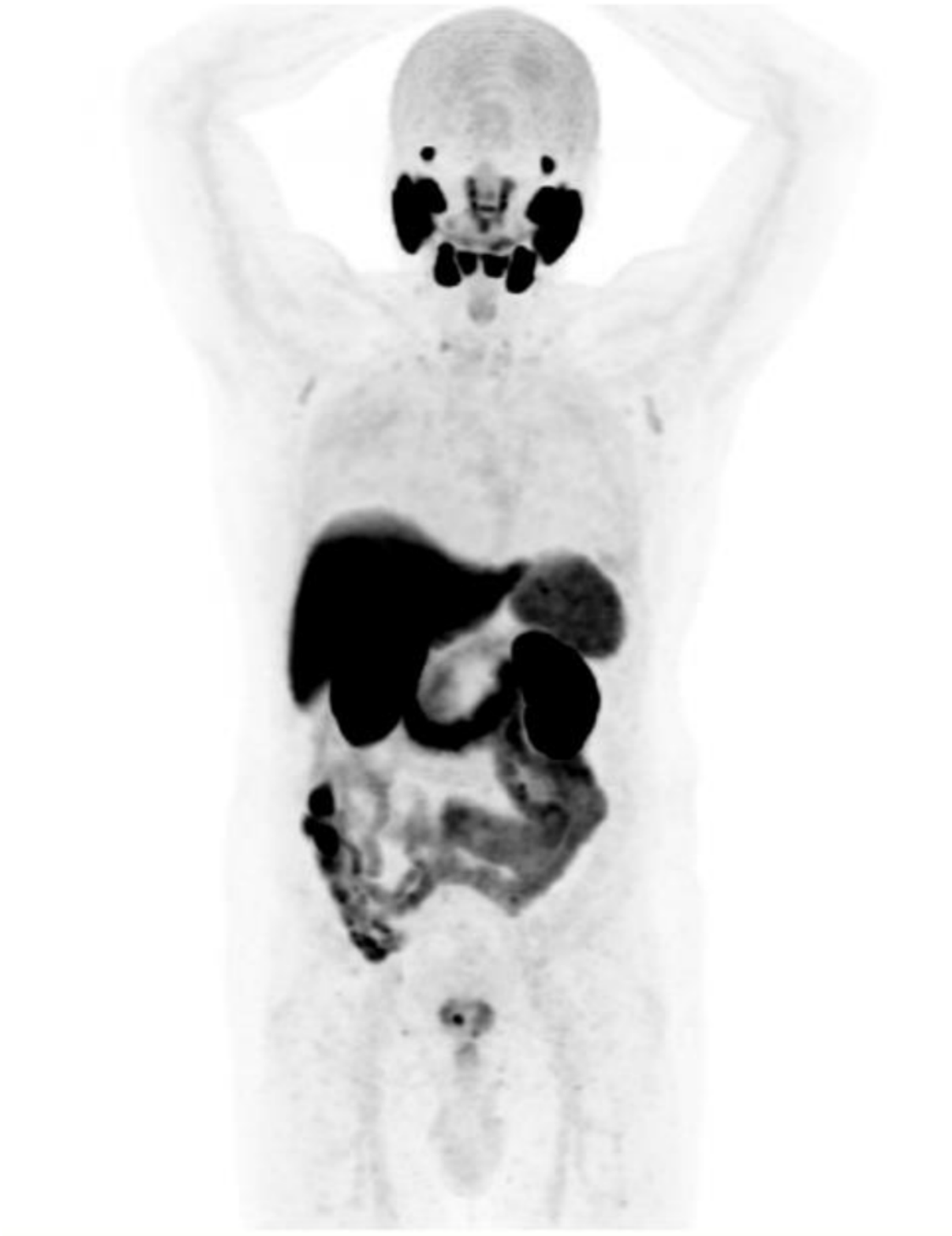

Figure 2

Maximum intensity projection image of a 68-year-old patient without unspecific bone uptake at [18F]PSMA-1007 PET presenting with a prostate adenocarcinoma Gleason score 4+3 and iPSA = 5,8 ng/mL. Focal [18F]PSMA-1007 uptake is visible at the level of the prostate gland

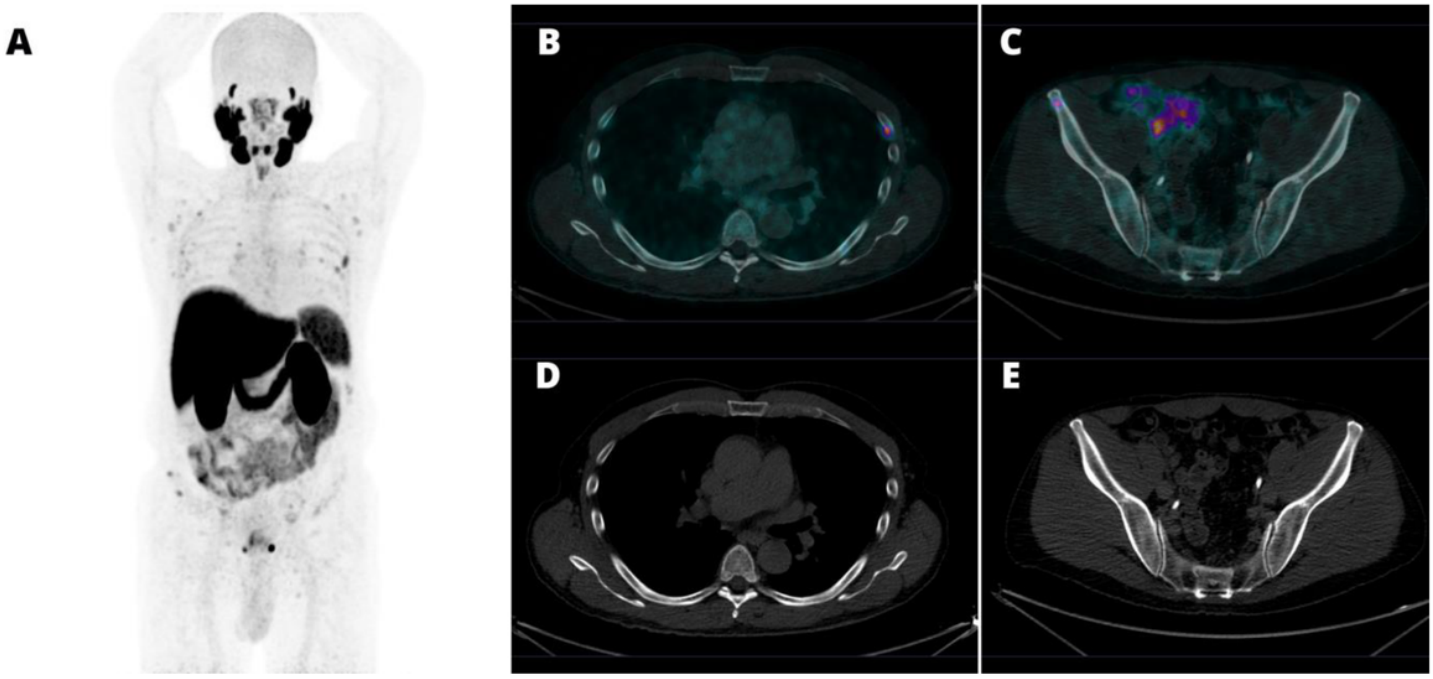

Figure 3

Example of a 65-year-old patients with non-metastatic [18F]PSMA-1007 bone uptake presenting with a prostate adenocarcinoma Gleason score 4+3 and iPSA = 5 ng/mL. Maximum intensity projection image (A) demonstrates intense [18F]PSMA-1007 bifocal uptake at the level of the prostate gland and multiple areas of bone uptake in the ribs and pelvic bones. Axial fused PET/CT images showing uptake in the antero-lateral tract of the left IV rib (B) and in the right anterior superior iliac spine (C) and corresponding axial bone window CT scan (D, E) are displayed

Supplementary Files

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