

**Case Report****68Ga-PSMA-11 PET-CT is superior to bone scintigraphy for detection bone metastasis in low and high grade of prostate cancer**Habibollah Dadgar<sup>1\*</sup>**Author Information***1. Razavi Cancer Research Center, Razavi Hospital, Imam Reza International University, Mashhad, Iran*

Submitted: 26.02.2019

Accepted: 24.03.2019

Published : 03.04.2019

**Abstract**

Bone with distant metastasis and morbidity due to skeletal complications is a lesion that encouraged many authors to focus on the new radiotracers for better diagnosis regarding high sensitivity and specificity. However, <sup>99m</sup>Tc-Methylene diphosphonate (MDP) bone scintigraphy (BS) is the current standard imaging due to increase adsorption of the tracer at osteoblastic sites; it shows false-positives in degenerative changes and false-negatives in bone marrow metastasis. Recently, Prostate Specific Membrane Antigen (PSMA) is the promising target in prostate cancer imaging due to the over-expression in cancer cells. <sup>68</sup>Ga-PSMA-11, a small molecule with PSMA enzyme inhibition activity has benefit in bone and lymph-node recurrences and staging. Moreover, as degenerative changes do not have PSMA uptake will have not positive in response to therapy, bone scan has enough quality for degenerative changes. With this consideration, BS is unable to differentiate bone metastasis from degenerative changes. <sup>68</sup>Ga-PSMA-11 could overcome to this limitation from conventional imaging as well. Finally, we concluded that PSMA PET-CT would have better sensitivity and specificity due to unique distinction for detecting metastases.

**Key words:** <sup>68</sup>Ga-PSMA-11 , PET-CT Prostate Cancer, bone metastasis

## Introduction

<sup>99m</sup>Tc-MDP BS is the most common scan for detecting bone metastasis with high sensitivity (range 62-89%) for bone metastasis in PCa [1]. Therefore, guidelines suggest BS to be performed in patients with high risk PCa or those presenting with bone symptoms [2-4]. As bone metastasis firstly commence in bone marrow, hence BS not able to detect bone marrow lesions or early osteoblastic activity. With modern hybrid imaging SPECT-CT (Single Photon Emission Computed Tomography Computed Tomography), MDP BS able to correctly characterized planner imaging equivocal lesions [5]. Despite these limitations, bone scan preferred as standard scan for bone metastasis in clinical diagnosis of prostate cancer. <sup>18</sup>F-Fluoride PET [6] is superior to BS for detection of bone

metastasis due to the prostate cancer but it did not routinely perform in clinical practice. These days prostate-specific membrane antigen (PSMA) has been a promising tracer in low and high grade of PCa. Regarding to its high expression in PCa cells [7], it used as a biomarker like gleason score for evaluation of metastasis and progression [8]. Meanwhile, small molecule inhibitors have been developed to target PSMA; Glu-NH-CO-NH-Lys-(Axe)-[<sup>68</sup>Ga (HBED-CC)] (<sup>68</sup>Ga-PSMA-11) is the most investigated ligand which has high clinical value for lymph node staging [9] and detection of local recurrence [10, 11].

---

## References

1. Daldrup-Link HE, Franzius C, Link TM, Laukamp D, Sciuk J, et al. (2001) Whole-body MR imaging for detection of bone metastases in children and young adults: Comparison with skeletal scintigraphy and FDG PET. *Am J Roentgenol* 177: 229-236.
2. Cook GJ, Azad G, Padhani AR (2016) Bone imaging in prostate cancer: The evolving roles of nuclear medicine and radiology. *Clin Transl Imaging* 4: 439-447.
3. Wollin DA, Makarov DV (2015) Guideline of guidelines: Imaging of localized prostate cancer. *BJU Int* 116: 526-530.
4. Heidenreich A, Bastian PJ, Bellmunt J, Bolla M, Joniau S, et al. (2014) EAU guidelines on prostate cancer. part 1: Screening, diagnosis, and local treatment with curative intent-update 2013. *Eur Urol* 65: 124 -137.
5. Helyar V, Mohan HK, Barwick T, Clarke SE, Fogelman I, et al. (2010) The added value of multislice SPECT/CT in patients with equivocal bony metastasis from carcinoma of the prostate. *Eur J Nucl Med Mol Imaging* 37: 706-713.

PSMA PET is very sensitive for high grade prostate cancer cells as well as low levels but seems to be sensitive for high grades and is controversial for low level of PSA [12, 13]. In short, PSMA-PET has shown higher sensitivity and specificity than BS (90.5% vs. 73.68%, and 97.0% vs. 86%) for bone metastasis of prostate cancer [14].

## Case report

### References

6. Even-Sapir E, Metser U, Mishani E, Lerman H, Lievssitz G, et al. (2006). The detection of bone metastases in patients with high-risk prostate cancer: 99mTc-MDP Planar bone scintigraphy, single- and multi-field-of-view SPECT, 18F-fluoride PET, and 18F-fluoride PET/CT. *J Nucl Med* 47:287-97.
7. Silver DA, Pellicer I, Fair WR, Heston WD, Cordon-Cardo C (1997) Prostate-specific membrane antigen expression in normal and malignant human tissues. *Clin Cancer Res* 3: 81-5.
8. Chang SS (2004) Overview of prostate-specific membrane antigen. *Rev Urol* 6: S13-S18.
9. Gupta M, Choudhury PS, Hazarika D, Rawal S (2017) A Comparative study of 68Gallium-prostate Specific membrane antigen positron emission tomography-computed tomography and magnetic resonance imaging for lymph node staging in high risk prostate cancer patients: An initial experience. *World J Nucl Med* 16: 186-191.
10. Eiber M, Maurer T, Souvatzoglou M, Beer AJ, Wester HJ, et al.(2015) Evaluation of Hybrid 68Ga-PSMA Ligand PET/CT in 248 Patients with Biochemical Recurrence After Radical Prostatectomy. *J Nucl Med* 56:668-674.
11. Perera M, Papa N, Christidis D, Hofman MS, Bolton D, et al. (2016) Sensitivity, specificity, and predictors of positive 68Ga-prostate-specific membrane antigen positron emission tomography in advanced prostate cancer: A systematic review and meta-analysis. *Eur Urol* 70: 926-937.
12. Pyka T, Okamoto S, Dahlbender M, Heck M, Eiber M, et al. (2016) Comparison of bone scintigraphy and 68Ga-PSMA PET for skeletal staging in prostate cancer. *Eur J Nucl Med Mol Imaging* 43: 2114-2121.
13. Schreiter V, Gericke M, Heimann U, Steffen I, Hamm B, et al. (2016) Comparison of [68Ga]Ga-PSMA-HBED-CC PET versus whole-body bone scintigraphy for the detection of bone metastases in patients with prostate cancer. *J Nucl Med Radiat Ther* 7: 302.
14. Lengana T, Modiselle M, Lawal I, Ebenhan T, Vorster M, et al. (2017) 68Ga-PSMA-PET/CT and bone scintigraphy imaging for staging of high- risk prostate cancer. *J Nucl Med* 58: 757.

The scan showed abnormally increased throughout spleen, small intestine and urinary inhomogeneous uptake in lumbar spine. No other bladder. Intense PSMA uptake at prostate gland abnormal uptake was noted in the rest of the with SUVmax 27.20 was seen. Numerous skeleton. In short, bony lesion with osteoblastic Osteoblastic bone metastasis throughout the axial reaction of lumbar vertebrae is involved. and appendicular skeleton including spine, ribs Moreover, SPECT imaging was performed from bilaterally sternum, scapulae, clavicle, humera, thoracolumbar spine and reconstruction was pelvic and proximal both femura. performed in the transverse, coronal and sagittal Regarding patient's history, PSMA activity at axes. The SPECT slices showed abnormal uptake prostate gland as a primary tumor, multiple para- in body of lumbar vertebrae. For more assessment aortic and pelvic chain lymph nodes metastasis, MRI correlation for ruling out of metastasis and liver metastasis and wide spread bone metastasis degenerative change was recommended. as mentioned above.

After bone SPECT, the patient refers to the  $^{68}\text{Ga}$ -PSMA PET-CT for better diagnosis. In this reason, therefore, 4.4 mCi of  $^{68}\text{Ga}$ -PSMA-11 was administered intravenously via the vein in the dorsum of the left hand. To allow for distribution and uptake of radiotracer, the patient was allowed to rest quietly for 60 minutes in a shielded room. Imaging was performed on an integrated 6-slice PET/CT scanner, with scanning from the skull top to the mid thigh. CT scanning was performed without oral or intravenous contrast material. There are PSMA uptakes in the peri-vascular, sub carina and right hilar lymph node with SUVmax up to 17.71. There are numerous nodal abnormal uptakes in the para-aortic and pelvic chains with SUVmax up to 40.16. In addition the scan showed PSMA uptake in the peripheral of the liver. Moreover, Physiologic tracer uptake was seen

### Result and Conclusion

For the current patient, as discussed above, bone scan and  $^{68}\text{Ga}$ -PSMA PET were performed between one week distances. Bone scan showed one lesion in lumbar spine while PET scan revealed multiple bone metastases Therefore, in this case disseminated and/or refractory to treatment, RIT with  $^{177}\text{Lu}$ -PSMA is recommended. While  $^{99\text{mTc}}$ -MDP BS is the current standard imaging for bone metastasis of prostate cancer but it seems that PSMA PET is superior to BS for metastatic work up in high risk prostate cancer [Figures 1-3 section A, B].

**FIG1.** a) After IV injection of 20mci of  $^{99m}\text{Tc}$ -MDP scanning was performed 3 hours later in multiple spot views. The scan showed abnormally increased inhomogeneous uptake in lumbar spine. No other abnormal uptake was noted in the rest of the skeleton. b) SPECT imaging was performed from thoracolumbar spine and reconstruction was performed in the transverse, coronal and sagittal axes. The SPECT slices showed abnormal uptake in body of lumbar vertebrae.

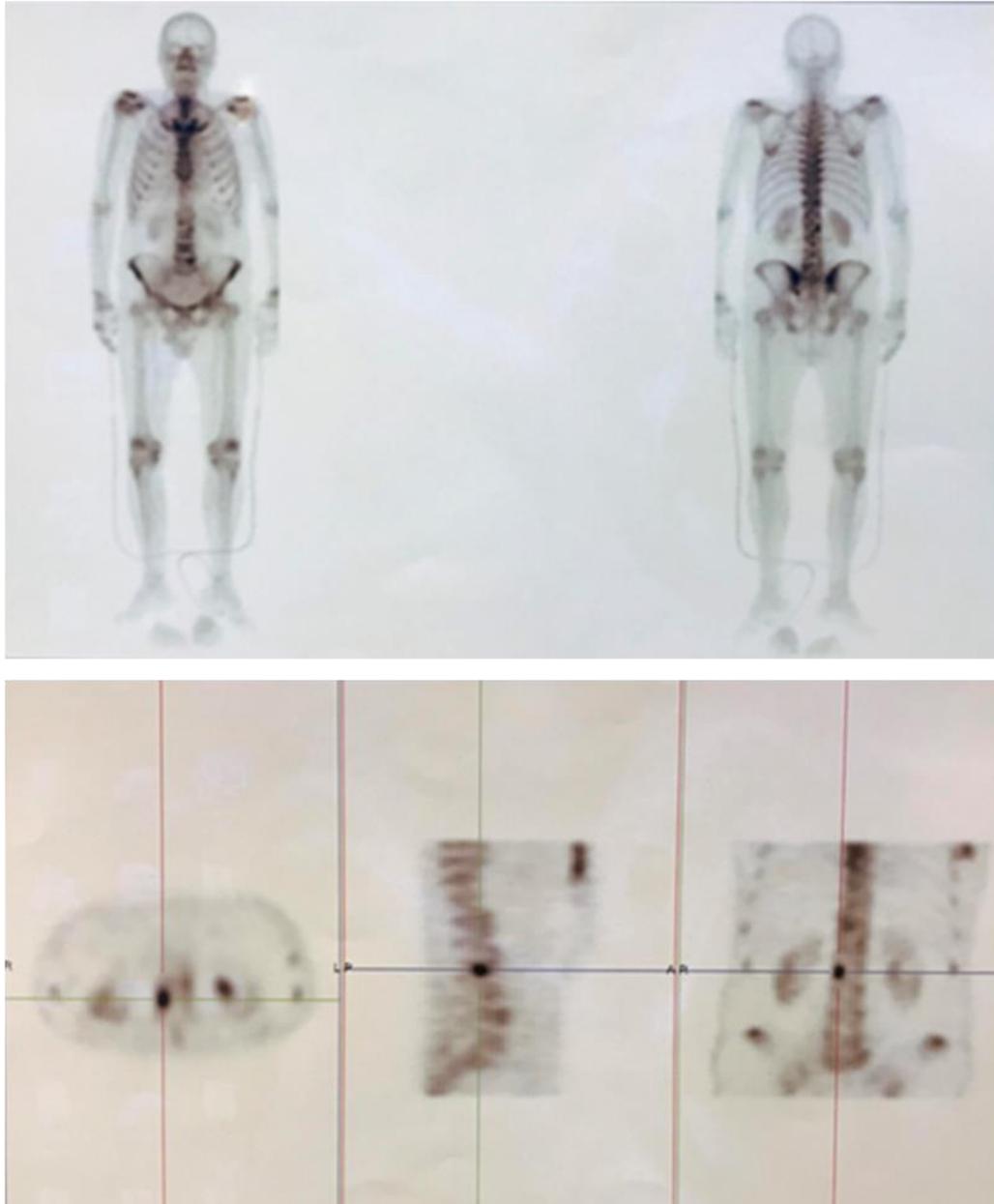


FIG2. B) <sup>68</sup>Ga-PSMA-11 PET-CT scan

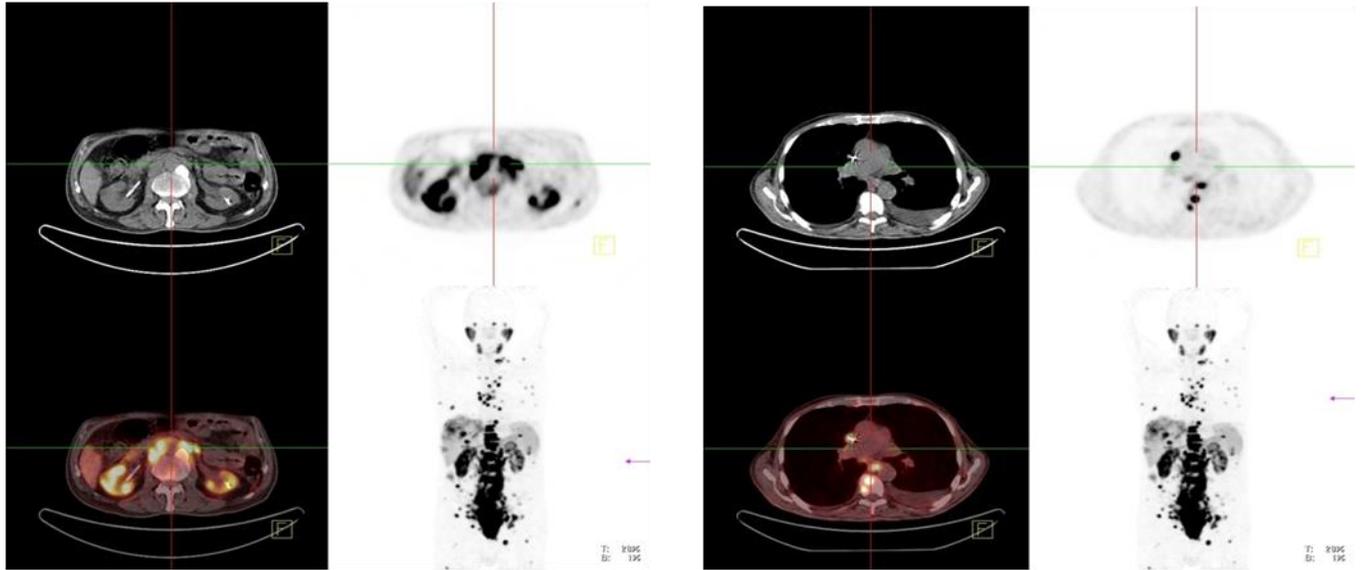
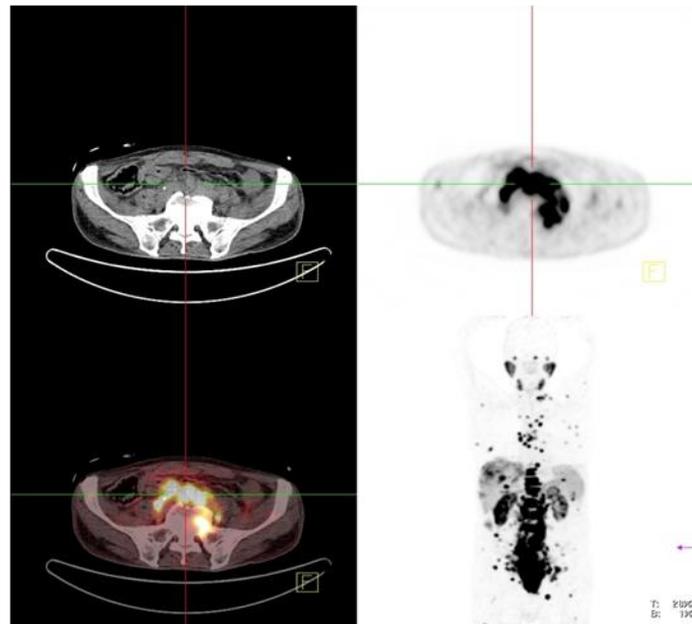


FIG3. <sup>68</sup>Ga-PSMA PET/CT scan, Skull top to Mid-Thigh



Moreover, as degenerative changes do not have PSMA uptake will have not positive in response to therapy, bone scan has enough quality for degenerative changes. With this consideration, BS is unable to differentiate bone metastasis from degenerative changes. In addition, we believe that PSMA PET will have upper hand in degenerative changes versus bone scan.

---