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The Use and Advantage of E-PSMA: The EANM Standardized Reporting Guideline v1.0 in Different Prostate Cancer Patients

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Abstract

Background: Imaging plays an important role in the evaluation of prostate cancer (PC) patients. In recent years, much attention has been focused on 68Ga-PSMA PET-CT in PC patients and has been widely used for staging, especially biochemical relapse-restaging and therapy response for these patients. The aim of this study was to evaluate 68 Ga PSMA PET-CT imaging in initial staging-first line imaging of PC from low to high risk patients based on standard reporting system with E PSMA molecular staging.

Materials & Metods: Twenty patients with low (10 patients), intermediate (5 patients) and high risk (5 patients) newly diagnosed PC referred for initial staging of PC were included in the study. Histopathology and follow-up clinical and radiological information after PET/CT scanning served as the standard of reference.

Results: The study included a total of 20 example of low, intermediate and high risk patients underwent 68 Ga PSMA PET-CT for initial staging with PC final histopathology result. SUVmax in the primary tumor and if any metastases were scored based on E PSMA new scoring system and molecular staging were reported on Ga-68 PSMA PET-CT final reports.

Conclusions: Metastases were detected with a relative high rate in intermediate and high risk group patients as might be expected. Ga-68 PSMA PET-CT imaging in newly diagnosed PC patients even in low risk patients was found to be quite useful in the current study. Ga-68 PSMA imaging should be done in all risk groups as a first-line imaging modality and molecular staging and the use of E PSMA for standardized reporting were found useful in terms of establishing a common language with the clinicians. We received positive feedback from all clinicians. This finding should be supported by other studies with large number of patients.

***Keywords*:** *E-PSMA, PET-CT, prostate cancer, PSMA PET.*

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Introduction

Prostate specific membrane antigen (PSMA) is one of the most successful targets for theranostic applications. It has gained acceptance as a highly sensitive and specific imaging modality for evaluating extent of the disease (1). The initial work-up of high-risk PC patients should include conventional imaging procedures such as pelvic magnetic resonance imaging (MRI), computerized tomography (CT) and bone scintigraphy (BS), according to the 2017 European Association of Urology guidelines (2). Due to the low sensitivity of radiological examinations, used routinely in the clinical imaging of PC, expected success can not be reached in staging and restaging (3). However in several reports 68 Ga PSMA PET-CT was also shown to be superior to conventional imaging for the detection of metastases in initial staging (4-9). Ga-68 PSMA PET/CT has recently gained acceptance as a highly sensitive and specific imaging modality for restaging in the settings of biochemical recurrence. The diagnosis of local-advanced disease or the presence of metastases in PC determines the indication for surgical treatment. The optimal imaging modality is still under debate in initial staging of PC patients. European Association of Nuclear Medicine (EANM) developed a consensus guideline for interpretation of Prostate-Specific Membrane Antigen (PSMA)-Positron Emission Tomography (PET) to provide more consistent reports in clinical practice (10). Herein we report PC patient staging findings on Ga-68 PSMA PET-CT imaging with molecular staging findings according to E-PSMA: The EANM Standardized Reporting Guideline v1.0 in Different PC Patients.

Materials and methods

Patients with newly diagnosed PC were referred for initial staging by Ga-68 PSMA PET/CT. Patients' data diagnosed with biopsy proven newly diagnosed PC and underwent 68Ga PSMA PET-CT were selected. 68Ga PSMA PET-CT scans were performed for initial staging in a total of 20 PC patients were evaluated based on new EANM scoring system and E PSMA molecular staging. Patients with low, intermediate and high risk PC referred for initial staging of PC were included in the current study.

Imaging protocol

After 68 Ga was filtered from the Ge-68/Ga-68 generator system, it was binded with the help of a synthesis unit and quality controls were performed. 68Ga-PSMA-11(Glu-NH-CO-NH-Lys-(Ahx)-[68Ga(HBED-CC)]) was used as the PSMA ligand. 68 Ga PET/CT scans were obtained 60 min (range: 50-100 min) after injection of 185 MBq (5 mCi) 68 Ga PSMA using an integrated scanner (Siemens, Biograph True Point 6 PET/CT, Germany). The patients were instructed to void prior to acquisition. A whole-body CT scan was performed without intravenous contrast administration with 130 kV, 50 mAs, a pitch of 1.5, a section thickness of 5 mm, and a field of view of 70 cm. CT data were used for attenuation correction. A PET scan was performed immediately after an unenhanced CT scan, and acquired from the skull base to the upper thigh with a 2-min acquisition per bed position using a three-dimensional acquisition mode. Maximal standardized uptake values (SUVmax) were obtained for all primary and metastatic lesions. Additionally liver, mediastinal blood pool and parotid gland reference SUVmax values were obtained.

Diagnostic criteria for metastases

Any lesion inside or outside the prostate gland showing high tumor to background activity compared to surrounding tissue were accepted as pathological site, whereas normal and physiological uptake regions were excluded. Histopathology and follow-up clinical and radiological information after PET/CT scanning served as the standard of reference.

PET/CT images were viewed in the coronal, axial, and sagittal sections. Maximum standard uptake value (SUVmax) of lesions was calculated on PET/CT by using region of interest (ROI) included at least two-thirds of the nodular lesions. Partial volume effect was minimized by this way. The regions were drawn by generating sphere circles. The quantitative uptake values of 68Ga (SUVmax) in the nodules ROIs were semi automatically calculated using workstations (Siemens).

Results

68Ga PSMA PET-CT scans were performed for initial staging in a total of 20 PC patients were evaluated based on new EANM scoring system and E PSMA molecular staging. Patients with low, intermediate and high risk PC referred for initial staging of PC were included in the current study. During the review of the images physiological uptake regions and benign and malignant findings independent of PC were evaluated carefully. Moderate median uptake (SUVmax: > 3) is noted in the spleen, liver and lachrymal glands (11). None of the patients had other malignancies such as renal cell cancer, hepatocellular cancer, breast cancer or lung cancer known to express PSMA. Primary prostate tumor and if any metastases were scored as mentioned as a 4 point scale in the guideline (10). Table 1 demonstrates the 4 point scale and grade of PSMA expression. PSMA uptake in either prostate, prostate bed, or metastases (lymph node, bone, visceral soft tissue) described both qualitative and quantitatively in the final report. According to the experts' recommendation final reports on primary tumor and metastases included TNM classification molecular imaging TM (mi TNM), as proposed by PROMISE criteria (12). Table 2 demonstrates the miTNM classification. Three examples of the patients with low, intermediate and high risk patients are presented as cases and figures.

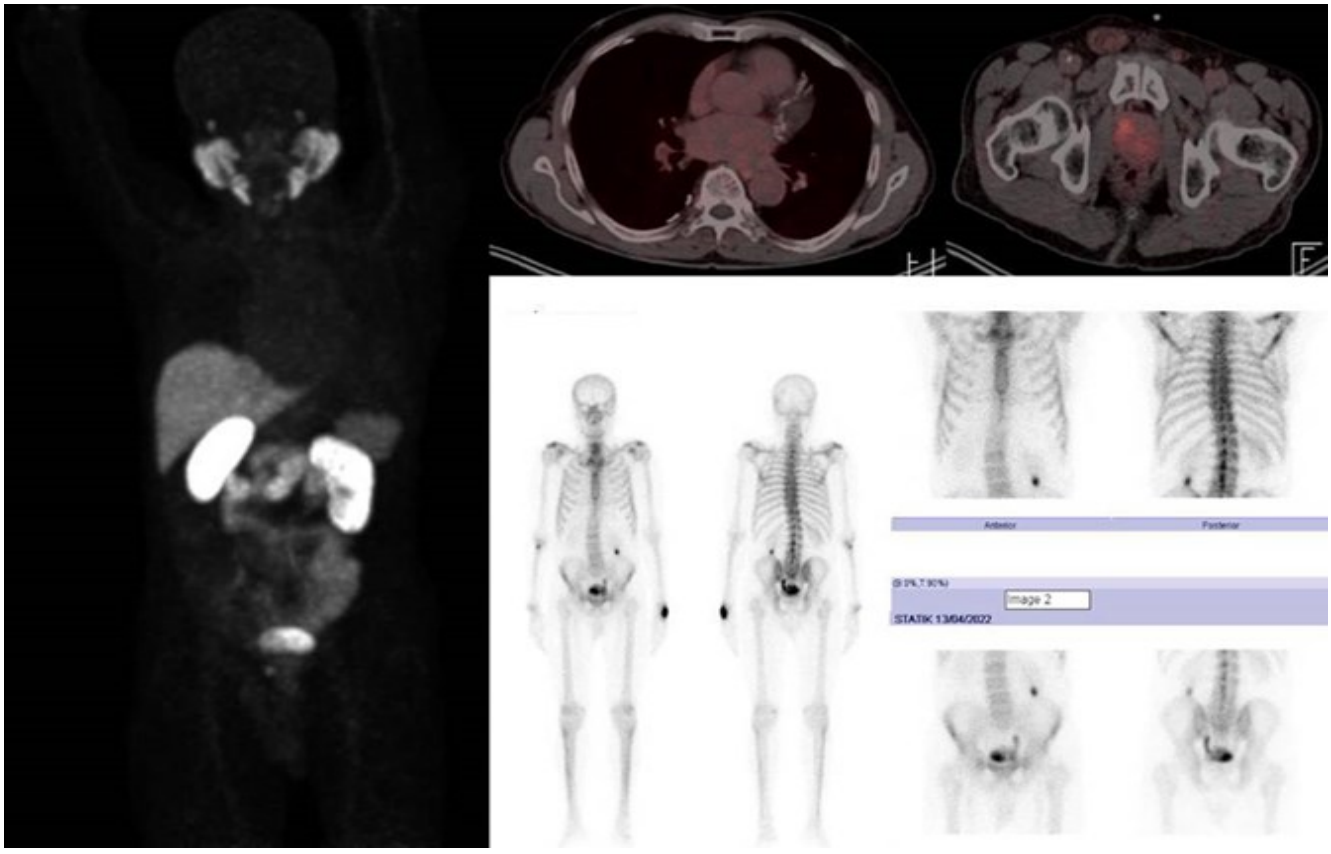

Fig.1: Seventy-one years old PC patient with Gleason score: 6 (3+3) was referred to our department for Ga-68 PSMA PET-CT and bone scan imaging for evaluation of suspicious metastases and initial staging. Bone scan of the patient was normal. On PET-CT imaging multifocal PC was detected on left posterior wall and right anterior wall of prostate with SUVmax values 8.38 and 5.37 respectively. According to EANM consensus guideline primary lesions were score: 1. No additional loco regional or distant metastasis were found in the patient. Molecular staging of the patient was reported as **miT2.**

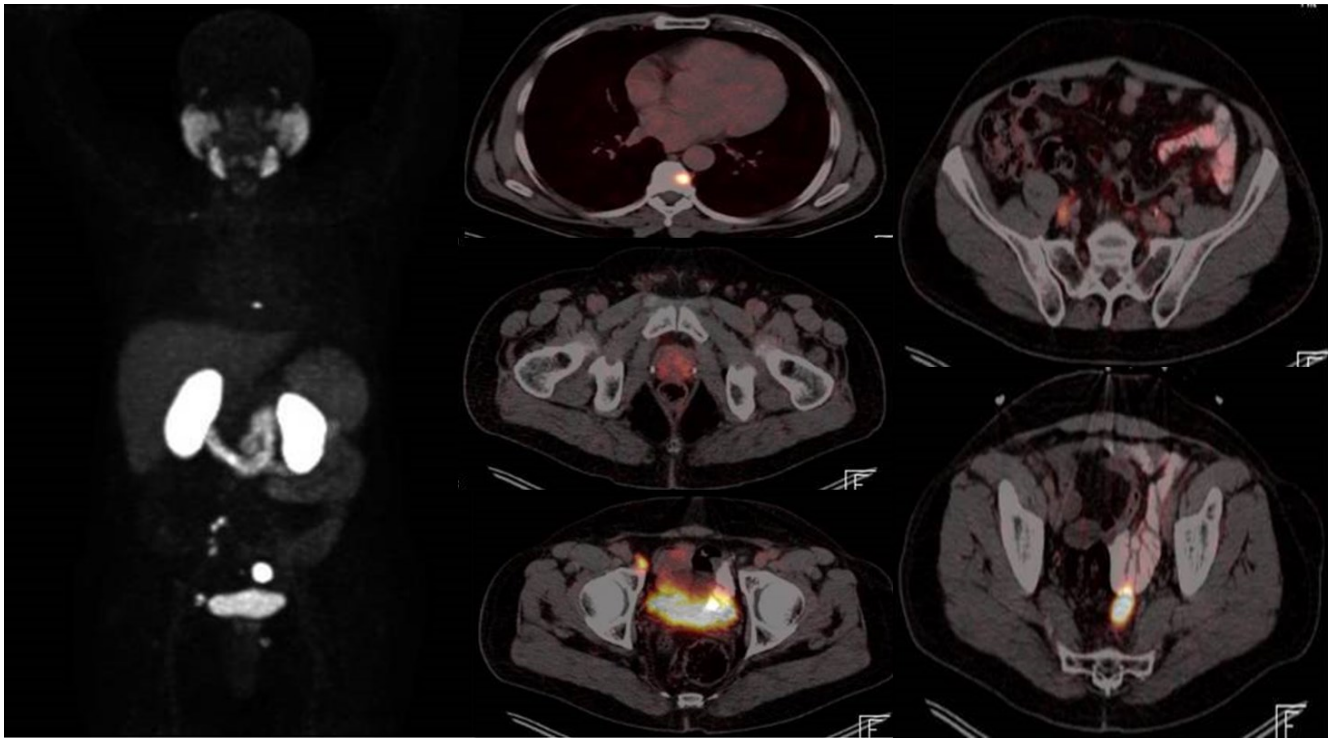

Fig.2: A sixty two years old PC patient was referred to our department for Ga-68 PSMA PET-CT imaging for evaluation of suspicious metastases and initial staging. On PET-CT imaging, prostate gland size was larger than normal. Hypermetabolic thickening and mass appearance consistent with primary malignancy were observed in all walls of the prostate gland (SUVmax: 59 & score:3). It was noted that the mass compatible with primary malignancy in the prostate gland invaded bilateral seminal vesicles. Millimetric-sized metastatic hypermetabolic lymphadenopathies were observed in the bilateral pelvic chain and pararectal area (SUVmax: 28 & score: 3). No additional loco regional or distant metastasis were found in the patient. Molecular staging of the patient was reported as **miT3bN1.**

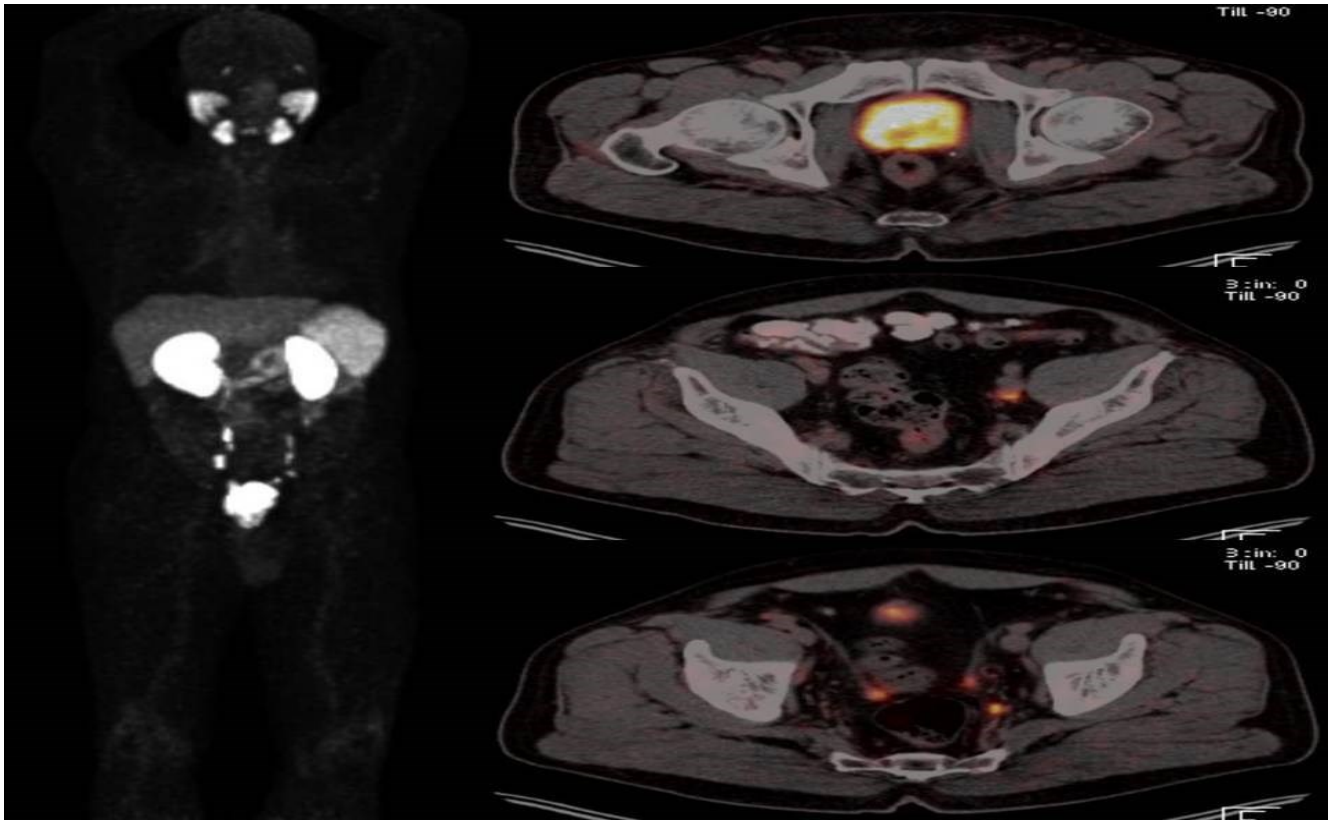

Fig.3: A sixty four years old PC patient was referred to our department for Ga-68 PSMA PET-CT imaging for evaluation of suspicious metastases and initial staging. There was heterogeneous increased metabolic activity in the prostate gland (SUVmax: 9 & score: 2). Metastatic lymphadenopathies were observed in the left (SUVmax: 102 & score: 3) and right (SUVmax: 13 & score: 2) presacral areas and right deep inguinal (SUVmax: 44 & score: 3) region. Additionally, on PET-CT imaging, prominent in left ischium anterior (SUVmax: 16 & score: 2), right iliac crest anterior, T8 vertebra corpus left anterior (SUVmax: 43 & score: 3), right 2nd rib (SUVmax: 12 & score: 2) metastatic bone lesions were detected in several sclerotic areas in the ribs, vertebrae, and pelvic bones. No additional loco regional or distant metastasis was found in the patient. Molecular staging of the patient was reported as **miM4b.**

All of the 20 patients were staged as the example case patients and molecular staging results were reported in the final report.

Discussion

PC is one of the most commonly diagnosed cancers in men and one of the leading cause of cancer death. Accurate staging for effective therapeutic options is critical for patient management. Staging of patients with PC using conventional imaging methods such as MRI, CT and bone scintigraphy is limited because of low sensitivity for metastatic disease, especially in low PSA levels. Ga-68 PSMA PET/CT is a new, very sensitive and non-invasive imaging method in PC patients targeting transmembrane protein called PSMA. Ga-68 PSMA (Prostate specific membrane antigen) as an initial staging-first line imaging modality, is limited. PSMA (glutamate carboxypeptidase II) is a cell surface glycoprotein. The specific presence of this enzyme in the

prostate gland, has made it an ideal theranostic target in the diagnosis and treatment of PC (13). The results of studies with 68 Ga PSMA are exceptionally good compared to other imaging methods. The development of consensus guidelines for interpretation of PSMA PET is needed to provide more consistent reports in clinical reports. The E-PSMA standardized reporting guidelines, a document supported by the the European Association of Nuclear Medicine (EANM), provided consensus statements among a panel of experts in PSMA-PET imaging, to develop a structured report for PSMA-PET in PC. The standardization of PSMA-PET interpretation also contributes to increasing the data reproducibility within clinical trials. In the current study, 68Ga PSMA PET-CT scans were performed for initial staging in a total of 20 PC patients who were evaluated based on new EANM scoring system and E PSMA molecular staging. Additionally, according to the experts' recommendation final reports on primary tumor and metastases included TNM classification molecular imaging TM (mi TNM), as proposed by PROMISE criteria. Final reports of the patients included both 4 point scale table and regional miTNM classification of PSMA PET-CT in order to familiarize clinicians. We received positive feedback from all clinicians. This finding should be supported by other studies with large number of patients.

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Authorship Contributions

Concept: ,**Design:**., **Supervision:** , **Data Collection and/or Processing:**, **Analysis and/or Interpretation:**., **Literature Review: Writer:**

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