Original Research Paper

Volume - 11 | Issue - 12 | December - 2021 | PRINT ISSN No. 2249 - 555X | DOI : 10.36106/ijar

Radiology

COMPARISON OF PSMA PET AND MRI FOR STAGING OF PROSTATE CANCER

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ABSTRACT PSMA PET is a recent advance used in the evaluation of prostate cancer and current literature has a paucity of studies comparing it with MRI which is extensively used for clinical evaluation of prostate cancer. The aim of this study was to compare these modalities and understand the agreement between the two for the clinical staging of prostate cancer.Study population included 72 patients referred the Urology and Uro oncology department, Amrita Institute of Medical Sciences, Kochi from June 2018 to 2021 with PSA 7 or more referred for simultaneous PSMA PET MRI. The PSMA PET results were interpreted by a nuclear medicine specialist and the MRI report was interpreted by a radiologist and TNM staging was done for both modalities. Available sextant biopsy data was collected in 43 patients. Quantitative data were expressed as mean ± SD and the qualitative data was expressed as proportions and percentages. Diagnostic measures such as sensitivity, specificity, predictive value positives, negatives and accuracy were also calculated with 95 % confidence interval. A p value of <0.05 was considered to be statistically significant.

There is moderate agreement (kappa value 0.709) between MRI and PSMA PET for T staging of prostate cancer.

There is strong agreement (kappa value 0.8) between MRI and PSMA PET for N staging of prostate cancer.

There is strong agreement (kappa value 0.8) between MRI and PSMA PET for M staging of prostate cancer.

KEYWORDS : PSMA PET,MRI ,Kappa value ,prostate cancer.

INTRODUCTION :

Among all types of cancers in men, the fourth most frequent and the second most prevalent cancer is the Prostate cancer (PCa). It is the world's fifth-largest cause of death [1]. Substantial variation is noticed in worldwide incidence and mortality of prostate cancer. Effectively, 100% 5-year survival rate is observed when the disease is confined to regional area, but in case of metastases to distant regions it drops to 34%. Average survival rate irrespective of the stage is as follows: 90% at 5 years, 92% at 10 years, and 61%at 15 years. [2]

In India, data regarding the true incidence of prostate cancer is restricted partly because it is not a notifiable disease. In India, too, there are very few population-based cancer registries and there are very limited number of community-based prostate cancer studies [3] For optimal treatment planning and to establish the prognosis in prostate PCa patients the role of precise local staging is crucial.

Multiparametric MRI (mpMRI) is the imaging method for local PCa staging and has an increased value in the assessment of pelvic nodal involvement and bone metastasis. MRI provides good diagnostic specificity for extracapsular extension (ECE), invasion of seminal vesicles (SVI), and lymph nodes (LN) metastasis, but sensitivity is still weak. [4]

PSMA PET (Prostate-Specific Membrane Antigen Positron-Emission Tomography) and MRI (Magnetic Resonance Imaging) are new whole-body scan technology, allowing high contrast visualization of Prostate Cancer.

METHODS:

Selection And Discription Os Study Participants:

After obtaining approval from the Thesis Protocol Review Committee (Scientific, Ethical & Financial), Amrita Institute of Medical Sciences, this cross-sectional prospective observational study was carried out.

Study Design: Cross-sectional observational study with diagnostic test evaluation.

Study Duration: 18 months starting from the date of acceptance of protocol of the thesis.

Study Setting: Department of Radio-diagnosis and Imaging, Department of Urology and Uro-oncology, Amrita Institute of Medical Sciences, Kochi.

Study Population

Patients referred from the Urology and Uro oncology department, Amrita Institute of Medical Sciences, Kochi from 2018 to 2019 referred for simultaneous PSMA PET MRI.

Inclusion Criteria

1) Patients with clinical suspicion of prostate cancer referred for simultaneous PSMA PET/MR study.
2) PSA 7 ng/ml or more.

Exclusion Criteria

1) Patients with implants (MRI incompatible) or pacemaker which is a contraindication for MRI.
2) Patients referred for PSMA PET/MR study for evaluation of suspicious recurrent prostate cancer.

Sample Size

Based on the results of concordance for staging of prostate cancer on PSMA/PET Vs MRI (58.3%) among patients with prostate cancer observed in an earlier publication (Comparison of 68Ga-PSMA PET and multiparametric MRI for staging of high-risk prostate cancer68Ga-PSMA PET and MRI in prostate cancer, Nuclear Medicine Communications.,38(12):1094–1102, DECEMBER 2017) and with 80% power and 95% confidence, the minimum sample size comes to 69.

72 patients were included in the study.

Technical Information:

OBJECTIVES:

Primary:

Comparison of PSMA PET and MRI for concordance in staging of prostate cancer.

Secondary:

Comparison of PSMA PET and DWIBS for concordance in skeletal metastasis.

Technique:

After obtaining informed consent,2.90 mCi of 68Ga-PSMA was injected intravenously. One hour later whole-body simultaneous PET MR Imaging (Head to mid-thigh) was performed on the Siemens BiographmMR (High-definition PET with LSO crystal & 3Tesla MRI) using the latest syngo MR E11 platform. Non contrast CT chest was also acquired. Standardized Uptake Value (SUV) was calculated for body weight and expressed as g/ml. Whole body MR images & MR Prostate images were fused with PET images. Whole body MRI Procedure: Axial STIR T2 weighted images, axial Flash T1 weighted images, axial diffusion weighted images, ADC maps, coronal haste T2 weighted were taken. Postcontrast T1 weighted fat saturated images of the whole body were taken. Dedicated MRI of prostate was done using

multiplanar T2,T1,DW1 and dynamic post contrast sequences.

Statistics:
Statistical analysis was done using IBM SPSS version 20.0 software. Quantitative data were expressed as mean ± SD and the qualitative data was expressed as proportions and percentages. Diagnostic measures such as sensitivity, specificity, predictive value positives, negatives and accuracy were also calculated with 95 % confidence interval. A p value of <0.05 was considered to be statistically significant.

Case Study:
T Staging
In the present study, the table 5.2 depicts the radiologist and nuclear medicine specialist finding for T staging (T0,T2,T3 and T4).

- Out of the cases which were staged as T0 on PSMA PET, MRI agreed with PET in 60% of the cases.
- Out of the cases which were staged as T2 on PSMA PET, MRI agreed with PET in 75 % of the cases.4.5% of the cases were down staged from T3 to T2 on MRI.
- Out of the cases which were staged as T3 on PSMA PET, MRI agreed with PET in 95.5 % of the cases.
- Out of the cases which were staged as T4 on PSMA PET, MRI agreed with PET in 100 % of the cases.

The summary is that MRI seems to have better accuracy for detection of local infiltration of tumour (T0, T2) and PSMA PET has better accuracy for detecting periprostatic extension. This may be due to the fact that seminal vesicle invasion, breech in prostatic capsule may be better detected on PSMA. The results are showing that there is moderate agreement (kappa value 0.709) between MRI (read by Radiologist) and PSMA PET (read by nuclear medicine specialist) for T staging of prostate cancer.

N Staging
The table 5.3 depicts the radiologist and nuclear medicine specialist finding for T staging (N0 and N1). In our study the sentinel nodes were the external iliac nodes and the criterion we followed for involvement of lymph node was increase in short axis diameter of more than 5 mm.

- Out of the cases which were staged as N0 on PSMA PET, MRI agreed with PET in 84.3% of the cases.
- Out of the cases which were staged as N1 on PSMA PET, MRI agreed with PET in 95.2 % of the cases.
- Out of the cases which were staged as N0 on PSMA PET, MRI disagreed with PET in 15.7 % of the cases.
- Out of the cases which were staged as N1 on PSMA PET, MRI disagreed with PET in 4.8 % of the cases.

The summary is that MRI has slightly better accuracy than PSMA PET for detection of nodal metastasis. There is strong agreement (kappa value 0.8) between MRI (read by Radiologist) and PSMA PET (read by nuclear medicine specialist) for N staging of prostate cancer.

M Staging
The table 5.4 depicts the radiologist and nuclear medicine specialist finding for T staging (N0 and N1).

- Out of the cases which were staged as M0 on PSMA PET, MRI agreed with PET in 95% of the cases.
- Out of the cases which were staged as M1 on PSMA PET, MRI agreed with PET in 90 % of the cases.
- Out of the cases which were staged as M0 on PSMA PET, MRI disagreed with PET (was staged as M1)in 4.9% of the cases.

The summary is that MRI is more sensitive and PSMA PET is more specific in M staging of prostate cancer. This could be due to the fact that sclerotic metastasis, bone oedema can show signal changes on MRI but may not show uptake on PSMA PET. There is strong agreement (kappa value 0.8) between MRI (read by Radiologist) and PSMA PET (read by nuclear medicine specialist) for M staging of prostate cancer.

MRI(DWI) vs PSMA PET for skeletal metastasis:
The table 5.5 depicts the radiologist and nuclear medicine specialist finding for detection of skeletal metastasis in prostate cancer.

- Out of the cases which were skeletal metastasis were present on PSMA PET, DWI agreed with PET in 95.3% of the cases.
- Out of the cases in which were skeletal metastasis were absent on PSMA PET, DWI disagreed with PET in 27% of the cases.
- Out of the cases which were staged as M0 on PSMA PET, MRI disagreed with PET in 4.9% of the cases.

The summary is that there was no failure of MRI for detection of skeletal metastasis. This could be due to the fact that sclerotic metastasis, bone oedema can show signal changes on MRI but would not show uptake on PSMA PET. There is strong agreement (kappa value 0.810) between DWI MRI (read by Radiologist) and PSMA PET (read by nuclear medicine specialist) for identification of bone metastasis.

In our study out of 72 cases 43 patients underwent sextant biopsy.IN our study PIRADS 4 and PIRADS 5 lesions were considered malignant.

Central Zone Lesions
MRI vs SEXTANT BIOPSY

- Out of the cases which were reported as malignant lesion on sextant biopsy, only 34.6% cases were reported as malignant on MRI (underreporting in MRI).
- Out of the cases which were reported as benign lesion on sextant biopsy, in 94.1% the lesion was detected as benign on MRI.

The summary is that MRI has misidentified many malignant lesion in central zone as benign, hence not a reliable modality for detection of central zone lesion.

There is no statistically significant difference between the MRI (read by RADIOLOGIST A) and sextant biopsy p- value 0.070) for the detection lesion in central zone with sensitivity of 34.62% specificity 94.12%, PPV90.00%,NPV48.48%and accuracy 58.14% with sextant biopsy as the gold standard

Central Zone Lesions
PSMA PET vs SEXTANT BIOPSY

- Out of the cases which were reported as malignant lesion on sextant biopsy, only 37.5% cases were reported as malignant on PSMA PET (marginally more underreporting in PSMA PET than in MRI).
- Out of the cases which were reported as benign lesion on sextant biopsy, 73.7% were reported as benign PSMA PET.

The summary is that PSMA PET has misidentified many malignant lesions in central zone as benign, hence not a reliable modality for detection of central zone lesion.

There is no statistically significant difference between the PSMA PET (read by nuclear medicine specialist) and sextant biopsy (p- value 0.437) for the detection lesion in central zone with sensitivity of 62.50%,specificity 26.32%,PPV51.72%,NPV35.71% and accuracy 46.51% with sextant biopsy as the gold standard.

Transitional Zone Lesions
MRI vs SEXTANT BIOPSY

- Out of the cases which were reported as malignant lesion on sextant biopsy, only 46.2 % cases were reported as malignant on MRI (under reporting in MRI).
- Out of the lesions that were reported as malignant lesion on sextant biopsy, 53.8 % cases were reported as benign on MRI
- Out of the cases which were reported as benign lesion on sextant biopsy, in 82.4% the lesion was detected as benign on MRI.

The summary is that MRI has misidentified many malignant lesion in central zone as benign, hence not a reliable modality for detection of transitional zone lesion.

There is no statistically significant difference between the MRI (read by RADIOLOGIST A) and sextant biopsy (p- value 0.112) for the detection lesion in transitional zone with sensitivity of 46.15%, specificity 82.35%, PPV80.00%, NPV50.00% and accuracy 60.47% with sextant biopsy as the gold standard.

Transitional Zone Lesions
PSMA PET vs SEXTANT BIOPSY

- Out of the cases which were reported as malignant lesion on sextant biopsy, only 37.5% cases were reported as malignant on PSMA PET (more underreporting in PSMA PET than in MRI).
- Out of the lesions that were reported as malignant lesion on sextant biopsy, 62.5 % cases were reported as benign on PSMA PET
- Out of the cases which were reported as benign lesion on sextant biopsy, in 78.9% the lesion was detected as benign on PSMA PET.

The summary is that PSMA PET has misidentified many malignant lesions in central zone as benign, hence not a reliable modality for detection of transitional zone lesion. There is no statistically significant difference between the PSMA PET (read by nuclear medicine specialist) and sextant biopsy (p- value 0.244) for the detection lesion in transitional zone with sensitivity of 62.50%,specificity 21.05%,PPV50.00%,NPV30.77% and accuracy 44.19% with sextant biopsy as the gold standard.

Peripheral zone lesions Mri vs sextant biopsy

- Out of the cases which were reported as malignant lesion on sextant biopsy, only 75%cases were reported as malignant on MRI (under reporting in MRI).
- Out of the cases which were reported as benign lesion on sextant biopsy, in 84.2% the lesion was detected as benign on MRI.

The summary is that MRI is considerably accurate for detection of peripheral zone lesions. There is statistically significant difference between the MRI (read by RADIOLOGIST A) and sextant biopsy (p-value 0.00) for the detection lesion in peripheral zone with sensitivity of 75.00%, specificity 84.21%, PPV85.71%, NPV 72.73% and accuracy 79.07% with sextant biopsy as the gold standard.

Peripheral Zone Lesions

MRI vs SEXTANT BIOPSY

- Out of the cases which were reported as malignant lesion on sextant biopsy, only 66.7%cases were reported as malignant on MRI (under reporting in MRI).
- Out of the cases which were reported as benign lesion on sextant biopsy, in 68.4 % the lesion was detected as benign on MRI.

The summary is that PSMA PET is considerably accurate for detection of peripheral zone lesions. However, MRI is better than PSMA PET for detection of peripheral zone lesion. There is statistically significant difference between the PSMA PET (read by nuclear medicine specialist) and sextant biopsy (p- value 0.022) for the detection lesion in transitional zone with sensitivity of 33.33%, specificity 31.58%, PPV38.10%, NPV 27.27% and accuracy 32.56% with sextant biopsy as the gold standard

Limitations: Few limitations were present in our study:

1. In our study as the patient population was not followed up, so the staging according to final gross pathology following surgery could not be commented upon.
2. In our study as the patient population was not followed up till the patient underwent radical prostatectomy therefore we could not compare PSMA PET and MRI with regards to periprostatic infiltration.
3. Only 43 patients out of 72 patients underwent sextant biopsy, this limits the result interpretation for presence of central, peripheral and transitional zone lesions.

CONCLUSION:

- **T Staging**

MRI seems to have better accuracy for detection of local infiltration of tumor (T0-T2) and PSMA PET has better accuracy for detecting periprostatic extension. This may be due to the fact that seminal vesicle invasion, breech in prostatic capsule may be better detected on PSMA and it is difficult to distinguish fibrosis from tumor infiltration on MRI.This finding was found to be statistically significant.

- **N STAGING**

MRI has slightly better accuracy than PSMA PET for detection of nodal metastasis. This finding was found to be statistically significant.

- **M Staging**

MRI is more sensitive and PSMA PET is more specific in M staging of prostate cancer. This could be due to the fact that sclerotic metastasis bone oedema can show signal changes on MRI but would not show uptake on PSMA PET if there is no active disease. This finding was found to be statistically significant.

- **MRI(DWI) vs PSMA PET for skeletal metastasis:**

There was no failure of MRI for detection of skeletal metastasis. This could be due to the fact that sclerotic metastasis, bone oedema can show signal changes on MRI but would not show uptake on PSMA PET. This finding was found to be statistically significant.

- **Peripheral Zone Lesions**

MRI and PSMA vs SEXTANT BIOPSY

MRI and PSMA PET are considerably accurate for detection of peripheral zone lesions. However, MRI is slightly better than PSMA PET for detection of peripheral zone lesion. There is a statistically significant difference for detection of peripheral zone lesion between the MRI (read by RADIOLOGIST A) and sextant biopsy (p- value 0.00). There is statistically significant difference between the PSMA PET (read by nuclear medicine specialist) and sextant biopsy (p- value 0.022) for detection of peripheral zone lesion.

Tables And Figures:

Table 1: Radiologist and Nuclear medicine specialist findings for T staging (T0-T2, T3 and T4)

MRI T STAGING	PSMA T staging				Kappa value (95%CI)	P value
	PSMA T0	PSMA T2	PSMA T3	PSMA T4		
MRI T0	60.0%	5.0%	0.0%	0.0%	0.709	<0.001
MRI T2	20.0%	75.0%	4.5%	0.0%		
MRI T3	20.0%	17.5%	95.5%	0.0%		
MRI T4	0.0%	2.5%	0.0%	100%		

In our study there is moderate agreement **(kappa value 0.709)** between MRI (read by Radiologist) and PSMA PET (read by nuclear medicine specialist) for T staging of prostate cancer.

Table 2: Radiologist and Nuclear medicine specialist findings for N staging (N0 and N1)

	PSMA N STAGING		Kappa value (95%CI)	P value
MRI N STAGING	PSMA N0	PSMA N1	0.84	<0.001
MRI N0	84.30%	4.80%		
MRI N1	15.70%	95.20%		

In our study there is a strong agreement **(kappa value 0.84)** between MRI (read by Radiologist) and PSMA PET (read by nuclear medicine specialist) for N staging of prostate cancer.

Table 3: Radiologist and Nuclear medicine specialist findings for M staging (M0 and M1)

MRI M STAGING	PSMA M STAGING		Kappa value (95%CI)	P value
	PSMA M0	PSMA M1		
MRI M0	95.10%	9.10%	0.8	<0.001
MRI M1	4.90%	90.90%		

In our study there is strong agreement **(kappa value 0.8)** between MRI (read by Radiologist) and PSMA PET (read by nuclear medicine specialist) for M staging of prostate cancer.

Table 4: Radiologist (using DWI) and nuclear medicine specialist findings for presence of skeletal metastasis

MRI Bone metastasis	PSMA Bone metastasis		Kappa value (95%CI)	P value
	Absent	Present		
Absent	95.3%	0.0%	0.819	<0.001
Present	27.30%	72.7%		

In our study there is strong agreement **(kappa value 0.819)** between DWI MRI (read by Radiologist) and PSMA PET (read by nuclear medicine specialist) for identification of bone metastasis.

Table 5:Table showing sensitivity, specificity, PPV, NPV and accuracy for detection of peripheral zone lesion (MRI Vs Sextant biopsy)

Statistic	Sensitivity	Specificity	Positive Predictive Value (*)	Negative Predictive Value (*)	Accuracy (*)
Value	75.00%	84.21%	85.71%	72.73%	79.07%

There is statistically significant difference between the MRI (read by RADIOLOGIST A) and sextant biopsy (p- value 0.00) for the detection lesion in peripheral zone with sensitivity of 75.00%, specificity 84.21%, PPV85.71%, NPV 72.73% and accuracy 79.07% with sextant biopsy as the gold standard.

Table 6:Table showing sensitivity, specificity, PPV, NPV and accuracy for detection of peripheral zone lesion (PSMA Vs Sextant biopsy)

Statistic	Sensitivity	Specificity	Positive Predictive Value (*)	Negative Predictive Value (*)	Accuracy (*)
Value	33.33%	31.58%	38.10%	27.27%	32.56%

There is statistically significant difference between the PSMA PET (read by nuclear medicine specialist) and sextant biopsy (p- value 0.022) for the detection lesion in transitional zone with sensitivity of 33.33%,specificity 31.58%,PPV38.10%,NPV 27.27%and accuracy 32.56% with sextant biopsy as the gold standard.

Figure 1: Radiologist And Nuclear Medicine Specialist Findings For T Staging In Graph (t0-t2,t3 And T4)

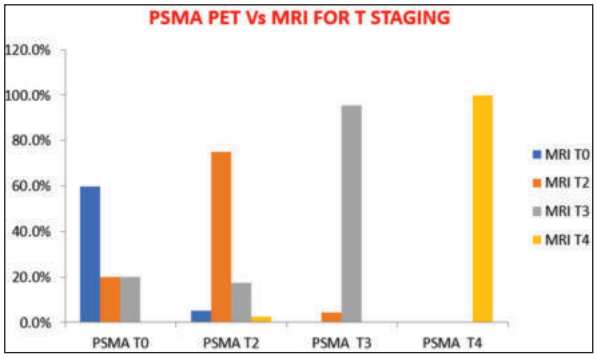

Figure 2: Pi-rads 5 Lesion In The Peripheral Zone Extending Into The Transition Zone (a)axial T2wi Showing Well Defined T2 Hypointense Lesion In The Pz Involving The Right Base, Midgland And Apex (b) Coronal T2wi Showing Lesion In Pz; (c) Axial Dwi Showing Diffusion Restriction(d) Adc Image Showing Marked Hypointense Lesion

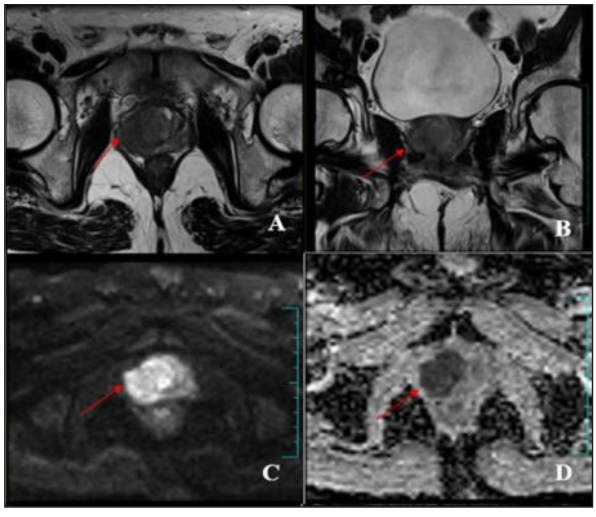

Figure 3: Image showing PSMA uptake in prostate gland

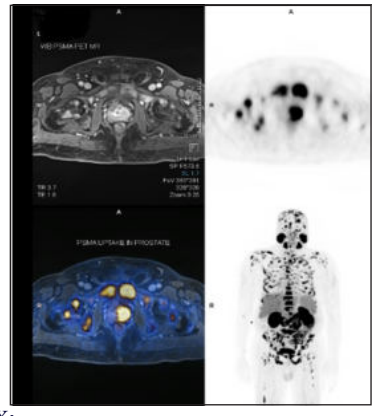

Table 1: TNM staging of prostate cancer.(5)

CLASSIFICATION	DEFINITION
TUMOR	
Tx	Tumor cannot be evaluated (due to lack of information)
T0	No evidence of a primary tumor
T1*	Tumor was not detected during a digital rectal exam (DRE) and cannot be seen on imaging studies (tumor may be discoverd during surgery for a reason other cancer)*
T2 T2a T2b T2c	Tumor can be detected during a DRE but is present in the prostate only Tumor is in half or less than one side (lobe) of the prostate Tumor is in more than half of one prostate lobe, but has not yet invaded the other lobe Tumor is in both prostate lobes
T3 T3a T3b	Tumor extends outside of the prostate Tumor extends outside the prostate on one or both sides Tumor has spread to the seminal vesicles (the glands on each side of the bladder)
T4	Tumor has spread to tissues near the prostate other than the seminal vesicles, such as the bladder or wall of the plevis
Nearby (regional) lymph nodes (N)	
Nx	Nearby lymph nodes are not evaluated
N0	No cancer cells are found in nearby lymph nodes
N1	Cancer cells are found in nearby lymph nodes
Distant Metastasis (M)	
M0 M1 M1a M1b M1c	Cancer has not spread beyond the prostate Cancer has spread beyond the prostate Cancer has spread to distant lymph nodes Cancer has spread to bone Cancer has spread to another organ or site, with or without bone disease

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APPENDIX: