

# A Study to Evaluate the Role of Diffusion Weighted Imaging in Detection and Staging of Prostate Cancer and Correlation with Histopathology in and around East Godavari

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## ABSTRACT

### BACKGROUND

Prostate is an associated gland of the male reproductive system. Worldwide, among the men, prostate cancer (PC) is the second most common cancer. PC is the seventh commonest cancers among the Indian male. Studies reported that diffusion weighted imaging (DWI) and dynamic contrast enhanced imaging (DCE-MRI), can offer additional value in localizing cancer. A study was conducted to evaluate and correlate the role of DWI in detection and staging of PC and correlation with histopathology.

### METHODS

A cross-sectional observational study was conducted in the Department of Radiodiagnosis, GSL Medical College, over a period of 18 months. Males with symptoms of nocturia, urinary urgency, frequency, hesitancy and bone pain were included in the study. Trans rectal ultrasound scan (TRUS) biopsy was collected, Gleason's score (GS) was considered for the histopathologic analysis. The evaluation of DWI as a tool for detection of PC was based on comparing the sensitivity and specificity of the results after taking histopathology as the gold standard test chi-square test was used to find the statistical significance and  $P < 0.05$  was considered statistically significant.

### RESULTS

Total, 36 (82 %) were diagnosed to be malignant, maximum number (18; 50 %) were between 61 – 70 years age group. Peripheral zone is the most common (61.2 %; 22) area for the PC followed by transitional (33.3 %) and central zone (5.5 %). In this study, 16.6 % members had GS  $\leq 6$ ; Apparent diffusion coefficient (ADC) was ranged between 0.81 to 0.87 and mean  $\pm$  SD were  $0.85 \pm 0.02$ . Out of the 22.2 % members whose GS was 7, the mean  $\pm$  SD ADC were  $0.74 \pm 0.02$ . For 22 (61 %) members, GS was  $> 8$ ; the mean  $\pm$  SD ADC was  $0.63 \pm 0.08$ ; statistically there was significant difference between the parameters. Magnetic resonance imaging (MRI) revealed that 61.3 % (27) cases as highly suspicious, 25 % (11) as probably malignant and 13.6 % (6) as indeterminate; the sensitivity for MRI was 94.5 % and specificity was 85.7 %.

### CONCLUSIONS

Patients with increased prostate specific antigen (PSA), multi-parametric magnetic resonance imaging (MPMRI) is valuable, non-invasive and a better option to detect PC. Also helps in localizing the exact location.

### KEYWORDS

Cancer, Tumour, Biopsy, Study

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## BACKGROUND

Worldwide, prostate cancer is the second most common and the fifth leading cause of cancer death among men.<sup>1</sup> The global burden is expected to reach 1.7 million new cases and 499000 new deaths by 2030.<sup>2</sup> PC is the seventh commonest cancers among the Indian male.<sup>3</sup>

Prostate is a supplementary gland of male reproductive system. Due to the secretions released from this structure, the quantity of seminal fluid can be increased. It is firm in consistency; the fibro muscular stroma is dense in which glandular elements are embedded. Prostate lies in the true pelvis, below the neck of the urinary bladder, behind the lower part of the pubic symphysis and the upper part of the pubic arch.

The prostate lies in front of rectal ampulla. Prostate resembles an inverted cone, of approx. 4 x 3 x 2 cm size and weighs approx. 8 grams.

PC had become significant health hazard of the globe; the contribution of PC is nearly three fourth of the cases across the world.<sup>3</sup> The incidence of PC is > 25 fold worldwide and it is highest in Australia / New Zealand (104.2/100,000) Western and Northern Europe, North America, largely because the practice of PSA has become widespread in those regions. Although incidence rates of prostate cancer are considered low in Asian and North African countries, ranging from 1 to 9/100,000 persons,<sup>4</sup> demographic and epidemiological transitions in developing countries like India have shown an increasing trend in the burden of various cancer cases including prostate cancer.

Migration of rural population to the urban areas, improved accessibility as well as affordability for diagnostic techniques are the contributory factors for the increased prevalence of PC in India.<sup>4</sup> During the early stage, PC is asymptomatic; digital rectal examination (DRE) and prostate specific antigen (PSA) are two commonly used clinical and biochemical parameters for evaluation of patients suspected of cancer prostate.<sup>5</sup>

Conventional T2 weighted imaging (T2W) used in PC staging but the utility is reported to be minimal due poor morphological difference between cancer tissue and native gland.<sup>6</sup>

Studies reported that diffusion weighted imaging and dynamic contrast enhanced imaging, can offer additional value in localizing cancer.

## Objective

A study was conducted to evaluate and correlate the role of DWI in detection and staging of PC and correlation with histopathology.

## METHODS

It is a cross-sectional observational study, conducted in the Department of Radiodiagnosis, GSL Medical College from January 2018 to June 2019. Study protocol was approved by the Institutional Ethical Committee and informed consent was obtained from all the participants.

All males with symptoms such as nocturia, urinary urgency, frequency, hesitancy and bone pain in case of metastasis and those referred to the department for MRI with clinically suspected PC were included in the study. Individuals with no relevant clinical data, non-co-operative for imaging study and those with contraindication for MRI such as cardiac pacemakers, cochlear implants, tissue expanders, ocular prosthesis, dental implants, neurostimulators and bone growth stimulators were not included.

The MRI scan was performed on MR Philips Ingenia, 16 channel possessing ultra-compact, superconducting, active shielded superconducting magnet with a magnetic field strength of 1.5 Tesla sense coils was used for acquisition of images. Supine position for the MRI sequences and left lateral position for TRUS imaging and biopsy were considered.

Study members were subjected for a TRUS scan using Philips HD7 machine with the rectal probe in the left lateral position. The study members were given one dose of ciprofloxacin 500 mg half an hour before TRUS biopsy and subjected to low rectal enema before the biopsy. No patient developed any untoward complication following the procedure. Complete zonal anatomy of the prostate was studied and systematic sextant biopsies of 8 cores were taken. Each biopsy was labelled explicitly according to the orientation of the biopsy site and sent for histopathological examination.

Gleason's score (GS) was considered for the histopathologic analysis of the TRUS guided biopsy specimens, the tumours were divided into three groups based on the GS; < 6 were low-grade, 7 as intermediate grade and > 7 as high-grade tumours.

## Statistical Analysis

Statistical analysis was done by Statistical Package for Social Sciences (SPSS) software version 20.0. Descriptive data were presented in the form mean, standard deviation (SD) and percentages. Chi-square test was used to find the statistical significance and the P < 0.05 was considered statistically significant.

## RESULTS

Among the 50 study members, the data were analysed using 44 (100 %) participants, the remaining were excluded for various reasons. In this 36 (82 %) were diagnosed to be malignant, maximum number (18; 50 %) were belong to 61 – 70 years age group and the mean age was 68.96 ± 8.6 years. Peripheral zone is the most common (61.2 %; 22) area for the PC followed by transitional (33.3 %; 12) and central zone (2; 5.5 %). The mean ± SD of the serum PSA levels were 53.06 ± 40.32, ranged between 5.5 – 110 ng/ml.

In this study, 16.6 % members had GS ≤6; the mean ± SD for apparent diffusion coefficient (ADC) were 0.85 ± 0.02. Out of the 22.2 % members whose GS was 7, the mean ± SD ADC were 0.74 ± 0.02. For 22 (61 %) members whose GS was ≥8, the mean ± SD ADC were 0.65 ± 0.02.

members, GS was > 8; the mean  $\pm$  SD ADC was  $0.63 \pm 0.08$ ; statistically there was significant difference between the parameters ( $P < 0.001$ ; Table 1).

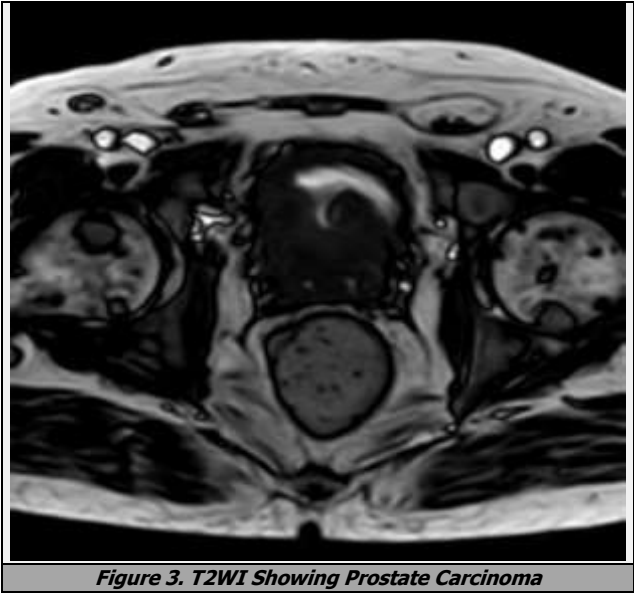
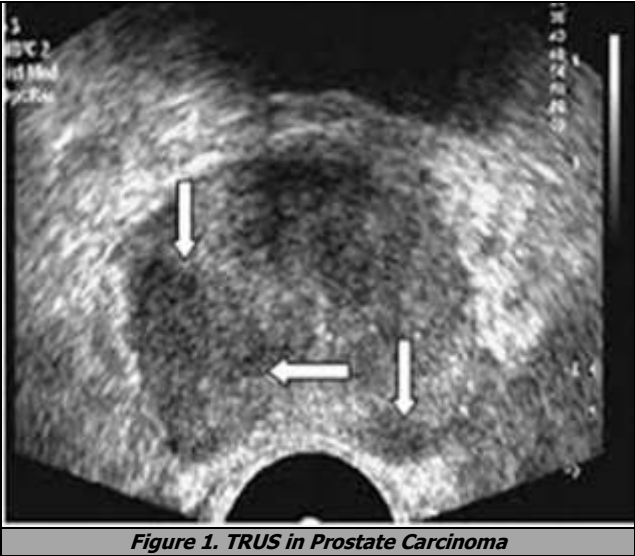
MRI revealed that 61.3 % (27) cases as highly suspicious, 25 % (11) as probably malignant and 13.6 % (6) as indeterminate (Table 2). With these, the sensitivity for MRI was 94.5 % and specificity was 85.7 % in the detection of tumours, compared to histopathology.

GS	Number	Minimum	Maximum	P Value
$\leq 6$	6 (16.6 %)	0.81	0.87	<0.001
7	8 (22.2 %)	0.71	0.77	
> 8	22 (61 %)	0.46	0.74	

**Table 1. Comparison ADC ( $10^{-3} \text{mm}^2/\text{s}$ ) Values and GS among the Study Members**

MRI Finding	Frequency (%)
Highly suspicious malignancy	27 (61.3)
Probably Malignant	11 (25)
Indeterminate / Benign	6 (13.6)
<b>Total</b>	<b>44 (100)</b>

**Table 2. MRI Findings in the Diagnosis of Malignancy among the Study Participants**



**DISCUSSION**

PC is one of the main leading malignancies in the elderly male.<sup>7</sup> Usually, the patients present at late age and by the time the patient presents, the tumour metastasizes to bones, more commonly vertebra. The age of the study members was ranged between 50 to 83 years; mean age was  $68.96 \pm 8.6$  years. Most of the patients present with symptoms of increased frequency, urgency of urine with backache, bone, joint pains, loss of weight and appetite. Some of the patients also had occasional hematuria.<sup>8</sup> In most carcinomas, due to secretion of vascular endothelial growth factors (VEGFs) in relation to the local hypoxia or lack of nutrients, there is an increase in the tumoral vascularity which leads to enhancement patterns with peaks earlier and higher than the healthy surrounding tissue along with early and pronounced contrast wash out. Prostatitis and benign prostatic hypertrophy (BPH) also lead to regional enhancement patterns, therefore it is hard to detect carcinomas using MRI. Carcinoma is characterized by high cellular density and a higher nuclear/cytoplasm ratio than normal healthy tissue with a substitute of glandular parenchyma by tumour cells, which results in a marked reduction in ADC values and increase in diffusion restriction relative to healthy tissues.

MRI is commonly used imaging technique to diagnose and stage the PC.<sup>9</sup> Trans-rectal guided tumour biopsies are invasive and do not accurately classify GS in approximately 38 % of all tumours due to sampling errors.<sup>10</sup> The value of multi-parametric MRI as a non-invasive tool to predict tumour aggressiveness has been under prime focus. The value of multi-parametric MRI as a non-invasive tool to predict tumour aggressiveness has been under prime focus.

In this study, 68 % (30) underwent TRUS guided biopsy, remaining were operated for PC and samples were sent for HPE. Of all the cases with a provisional diagnosis of PC by MPMRI, 81 % (36) were proved as PC by fine needle aspiration cytology (FNAC), remaining were

diagnosed to be chronic prostatitis and BPH. The inability of these modalities to diagnose microscopic disease limits the accuracy of almost all the imaging modalities.

However, this limitation had been partially crossed by the utility of MP MRI as it combines multi-modal imaging functions like functional imaging, anatomical imaging, and metabolic imaging. There is lot of literature which reported the uses and drawbacks of the individual components of MPMRI, but studies comparing the efficacy of MP MRI in comparison to Gleason scoring are limited.

Among the PC participants, 2 (5.5 %) of the confirmed PC participants showed recurrence after surgical and radiotherapy treatment, 61 % (22) members showed bony metastasis to the lumbar and sacral vertebra, pelvis, and femur. 17 of them had shown seminal vesicle invasion too. Regional pelvic lymphadenopathy. In multi-parametric prostate study, functional imaging techniques<sup>11</sup> such as diffusion-weighted imaging, dynamic contrast-enhanced imaging and MR spectroscopy were used to detect PC but we were mostly limited to T2WI, T1WI & DWI.

We found that there was a significant decrease in ADC value with increasing GS. This can be explained by an increase in cellular density in high-grade tumours resulting in more restricted diffusion of water molecules as established by Gibbs P et al.<sup>12</sup> In this study, the mean ADC values in the GS were different, which was found to be statistically significant. This may help in differentiation among the tumours, provided if visible on DWI. GS score is ranged between 1, the least to 5, the highest. Some situations, the score can be considered till 10. Scores > 7 were considered to adverse as well as high risk towards PC. Scores of  $\leq 6$  are generally considered to be low risk for malignancy. Score of 7 is considered to be intermediate risk. The severity of PC is directly proportional to GS. Sometimes, the histologic examination may reveal a total score of 7, which is towards the malignant end of the spectrum. Nevertheless, more important is the separate scores of 2 predominant cell patterns. For example, a total score of 7 may be a 4 + 3 type or a 3 + 4 type. In this case, the 4 + 3 type cancer pattern is more aggressive than the 3 + 4 type. Hence, besides the total score, the subcomponent score is also essential.

Yoshimitsu K et al.<sup>13</sup> reported that the mean ADC values could differentiate only the low-risk tumours from high-risk tumours, but there was no statistically significant difference. The authors also concluded that reading T2WI/ADC map was better than reading T2WI in detection and localization of PC. Similar findings were reported by a study by Woodfield CA et al.<sup>6</sup> Yagci AB et al.<sup>14</sup> showed that there was decrease in ADC with increase in tumour grade. Luczynska E et al.<sup>15</sup> showed that DWI may be helpful in differentiating high-grade tumours from intermediate, low-grade and decrease in the mean ADC. Almost similar findings were reported by Anwar SS et al.<sup>16</sup> Yuji Watanabe et al.<sup>17</sup> Woodfield CA et al.<sup>6</sup>

Out of 38 patients studied, 36 patients had a GS of > 6. The rest of the two patients showed GS less than 6 (One showing 3 + 2, another one showing 2 + 2) and proved non-malignant in the biopsy. Six (16.5 %) members had  $GS \leq 6$ , GS was 7 (22 %) for 8 and 7 for 22 (61 %) study

members (Table 2); there was positive linear correlation between MRI findings and GS and statistically it was significant ( $P < 0.001$ ). This indicates that the members who were diagnosed to be PC TRUS biopsy, higher GS, there was higher chance to diagnose as malignancy using MPMRI. Pre-biopsy MRI has an additional advantage, as it may help in targeted biopsy and therapy. This helps in reducing the chance of recurrence and also gives us better guidance for complete surgical clearance.

On the other hand, the mean ADC value of tumours decreased progressively with increasing GS, the correlation coefficient was  $-0.912$ . The correlation between multi-parametric MRI based diagnosis and GS had a sensitivity of around 68.9 % and a specificity of 85.4 %. The specificity of multi-parametric MRI is also on the higher side, indicating its potential in eliminating the patients who would otherwise undergo TRUS biopsy for a negative result. Therefore, unwanted and unnecessary biopsies can be avoided using multi-parametric MRI and hence reducing the patient discomfort and unnecessary burden on the health system. These study findings are similar to Delongchamps NB et al.<sup>18</sup> where the tumour size was correctly estimated in 77 % of cases, and about 80 % of the bilateral cancers were detected, and also MPMRI can be used to rule out bilateral involvement and also of very good prognostic value. On DWI, the restricted diffusion areas show a hyper intense signal. Based on diffusion-weighted images, the ADC was calculated, which provides quantitative information that is inversely proportional to the degree of restricted diffusion. Low ADC values are hypo intense and represent areas with restricted diffusion.

A healthy prostate in the peripheral zone shows unrestricted diffusion of water molecules, manifests low signal intensity on DWI, and high ADC values. Usually, the peripheral zone is easily discerned from the central zone due to homogeneously higher ADC values.<sup>18</sup> With aging, both central and peripheral zones show an increase in ADC values due to atrophic changes causing a decrease in cell volume and enlarged ducts. BPH also shows areas of low ADC values intermixed with areas of high values. In prostatitis, ADC values are lower than healthy tissue and significantly higher than low and high-grade prostate carcinoma. However, in granulomatous prostatitis, ADC values are lower than carcinoma ADC values.<sup>19</sup>

Similar findings were observed by de other investigators,<sup>10</sup> in a meta-analysis of studies for the accuracy of MPMRI, which showed a specificity of 88 % and a sensitivity of 74 % for MPMRI in prostate cancer detection. Moreover, the negative predictive value was in ranged from 66 % to 81 % in the above stated study. The sensitivity and specificity of MPMRI observed in this study was higher than that of Citak E et al.<sup>19</sup> report. Using a standard principal component analysis before GS, the sensitivity was 51.19 % and 64.37 % with specificities of 72.7 % and 39.9 % for LDA and SVM, respectively. They concluded that the SVM classifier resulted in a slightly higher sensitivity but low specificity than LDA.

Based on these study findings, it can be safely declared that MPMRI has positive correlation with GS and ADC has negative correlation with GS with high sensitivity and

specificity with better predictive values and hence pre-biopsy MPMRI can serve as not only as a screening tool but also a valuable diagnostic investigation. L M vu et al.<sup>17</sup> conducted a study on MPMRI and reported that in recurrent PC stated that following radical prostatectomy, postoperative fibrosis may mimic recurrent tumours, particularly if the fibrosis has a nodular morphology.

Rosenkrantz et al.<sup>20</sup> mentioned that around 30 % of PC arise from transition zone, similar results were showed by Oto et al.<sup>21</sup> Hoeks et al.<sup>22</sup> whereas peripheral zone is the most common in this report. In the present study, 61.2 % of the patients, that is, 22 patients showed carcinoma in the peripheral zone. In 12 patients, that is in approx. 33.3 % transitional zone is involved. In the rest of the 5.5 % (2 patients) central zone is involved.

## CONCLUSIONS

Based on our study findings, among the patients with raised PSA, MPMRI is valuable, non-invasive and a better option to detect PC. It also helps patients, by localizing the exact location of the PC and which support for targeted biopsy and also in characterizing the extent and aggressiveness of the tumour.

Data sharing statement provided by the authors is available with the full text of this article at jebmh.com.

Financial or other competing interests: None.

Disclosure forms provided by the authors are available with the full text of this article at jebmh.com.

## REFERENCES

- [1] Bray F, Ferlay J, Soerjomataram I, et al. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin* 2018;68(6):394–424.
- [2] Ferlay J. GLOBOCAN 2008: cancer incidence and mortality worldwide: IARC Cancer Base No. 10. <http://globocan.iarc.fr> 2010.
- [3] Hariharan K, Padmanabha V. Demography and disease characteristics of prostate cancer in India. *Indian J Urol* 2016;32(2):103–108.
- [4] Jain S, Saxena S, Kumar A. Epidemiology of prostate cancer in India. *Meta Gene* 2014;2:596–605.
- [5] Ingle SP, Ramona I, Sukesh. The efficiency of the serum prostate specific antigen levels in diagnosing prostatic enlargements. *J Clin Diagn Res* 2013;7(1):82–84.
- [6] Woodfield CA, Tung GA, Grand DJ, et al. Diffusion-weighted MRI of peripheral zone prostate cancer: comparison of tumor apparent diffusion coefficient with Gleason score and percentage of tumor on core biopsy. *Am J Roentgenol* 2010;194(4):W316–22.
- [7] Stangelberger A, Waldert M, Djavan B. Prostate cancer in elderly men. *Rev Urol* 2008;10(2):111–119.
- [8] Hamilton W, Sharp DJ, Peters TJ, et al. Clinical features of prostate cancer before diagnosis: a population-based, case-control study. *Br J Gen Pract* 2006;56(531):756–62.
- [9] Rouvière O, Puech P, Renard-Penna R, et al. Use of prostate systematic and targeted biopsy on the basis of multiparametric MRI in biopsy-naïve patients (MRI-FIRST): a prospective, multicentre, paired diagnostic study. *The Lancet Oncol* 2019;20(1):100–109.
- [10] Bjurlin MA, Taneja SS. Standards for prostate biopsy. *Curr Opin Urol* 2014;24(2):155–61.
- [11] Langer DL, van der Kwast TH, Evans AJ, et al. Prostate cancer detection with multi-parametric MRI: Logistic regression analysis of quantitative T2, diffusion-weighted imaging, and dynamic contrast-enhanced MRI. *J Magn Reson Imaging* 2009;30(2):327–34.
- [12] Gibbs P, Liney GP, Pickles MD, et al. Correlation of ADC and T2 measurements with cell density in prostate cancer at 3.0 Tesla. *Invest Radiol* 2009;44(9):572–576.
- [13] Yoshimitsu K, Kiyoshima K, Irie H, et al. Usefulness of apparent diffusion coefficient map in diagnosing prostate carcinoma: correlation with stepwise histopathology. *J Mag Reson Imaging* 2008;27(1):132–139.
- [14] Yagci AB, Ozari N, Aybek Z, et al. The value of diffusion-weighted MRI for prostate cancer detection and localization. *Diagn Inter Radiol* 2011;17(2):130–134.
- [15] Luczyńska E, Heinze-Paluchowska S, Domalik A, et al. The utility of diffusion weighted imaging using apparent diffusion coefficient values in discriminating between prostate cancer and normal tissue. *Pol J Radiol* 2014;79:450–455.
- [16] Anwar SS, Khan ZA, Hamid RS, et al. Assessment of apparent diffusion coefficient values as predictor of aggressiveness in peripheral zone prostate cancer: comparison with Gleason score. *ISRN Radiology* 2014;2014:263417.
- [17] Watanabe Y, Nagayama M, Araki T, et al. Targeted biopsy based on ADC map in the detection and localization of prostate cancer: a feasibility study. *J Magn Reson Imaging* 2013;37(5):1168–1177.
- [18] Delongchamps NB, Beuvon F, Eiss D, et al. Multiparametric MRI is helpful to predict tumor focality, stage, and size in patients diagnosed with unilateral low-risk prostate cancer. *J Prostate Cancer and Prostatic Dis* 2011;14(3):232–237.
- [19] De Rooij M, Hamoen EH, Fütterer JJ, et al. Accuracy of multiparametric MRI for prostate cancer detection: a meta-analysis. *Am J Roentgenol* 2014;202(2):343–351.
- [20] Rosenkrantz AB, Ream JM, Nolan P, et al. Prostate cancer: utility of whole-lesion apparent diffusion coefficient metrics for prediction of biochemical recurrence after radical prostatectomy. *Am J Roentgenol* 2015;205(6):1208–1214.
- [21] Oto A, Kayhan A, Jiang Y, et al. Prostate cancer: differentiation of central gland cancer from benign prostatic hyperplasia by using diffusion-weighted and

dynamic contrast-enhanced MR imaging. Radiology 2010;257(3):715–723.

[22]Hoeks CMA, Hambrock T, Yakar D, et al. Transition zone prostate cancer: detection and localization with

3-T multiparametric MR imaging. Radiology 2013;266(1):207-217.