Original Research Article

Comparative assessment of multiparametric MRI data with Gleason score in prostatic carcinoma patients

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Abstract

Background: Magnetic resonance imaging (MRI) - targeted biopsy has been widely used in clinical practice. In Gleason score (GS) 7 prostatic cancers, the quantitative analysis of Gleason pattern 4 (GP 4) is a significant prognostic factor and influences treatment decisions. **Aims and Objective:** To investigate the efficacy of MRI-targeted biopsy can diagnose and detect prostate cancer in comparison with greater GP 4 quantitatively. **Materials and Methods:** A total 30 number of patients with paired standard and MRI-targeted biopsies with cancer in either standard or targeted or both were studied, few of whom had a subsequent radical prostatectomy. The biopsy findings, including GS and tumour volume, were correlated with the radical prostatectomy findings. **Results:** All together a total of 30 participants were included in the study. Mean age group and standard deviation were found to be 63.39 ± 9.144 with a range of 50–78 years. In our study, out of 30 patients underwent for TRUS biopsy about 05 patients reported a PIRADS score of 6, 06 patients reported a PIRADS score of 7 and 09 patients reported a PIRADS score of 8 indicating malignancy. **Conclusions:** Magnetic resonance imaging–targeted biopsy can diagnose more aggressive prostate cancers and reduce the risk of Gleason upgrading in radical prostatectomy. Our study highlights the potential role for MRI-targeted biopsy in the workup of prostate cancer and the inclusion of a percentage of GP 4 in prostate biopsy reports.

Key Words: MRI, TRUS, PIRADS, Gleason Score, Prostate cancer

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INTRODUCTION

Prostate cancer is one of the principal causes of cancer-related death among adult men. It is one of the most common cancers among men except the non-cutaneous malignancy[1]. The prevalence of prostate cancer is on the rise, primarily because of the extensive application of diagnostic tests using prostate-specific antigen (PSA) and also partially because of the increase in life expectancy[2]. Most of the prostate cancers are growing at a slow pace and dormant rather than being aggressive, and hence they hardly exhibit any symptoms until the advanced stage. Therefore, timely diagnosis of prostate cancer can lead to improved treatment outcomes besides assisting in the selection of various treatment options available. Routinely, the methods employed include a Prostate-Specific Antigen assay (PSA), Transrectal Ultrasound-guided biopsy (TRUS) and Digital rectal examination (DRE). The final confirmatory diagnosis of prostate cancer can only be made by taking a biopsy which is usually an 8-core TRUS biopsy. However, all these procedures have limitations and disadvantages[3]. PSA assay levels inadequate with sensitivity and specificity while the DRE is a crude technique with a low positive predictive value and high inter-observer variations. Many studies have shown that TRUS biopsy can fail to diagnose up to 20% of prostate cancers because of under-sampling of anterior prostate,

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apex and midline, resulting in high false negativity[4]. About 70% of preliminary biopsies performed in men with increased PSA levels are negative for prostate cancer hence raised the burden of negative biopsies and exorbitant screening costs[4]. Because of these drawbacks of the currently existing techniques, the search for alternative a diagnostic technique which is more sensitive, specific, cost-effective and reliable with good negative and positive predictive values apart from being non-invasive have guided the researchers to consider radiological imaging methods like magnetic resonance imaging (MRI) as a diagnostic technique and more especially multi-parametric MRI (MP-MRI) which has received quite an attention in the current years which depends upon the regular advantages of MRI[5-7]. Multi-parametric MRI (MP-MRI) combines the anatomical imaging in T1 and T2 weighted images with the two functional methods like diffusion-weighted imaging (DWI), dynamic contrast-enhanced imaging (DCE) with or without Magnetic resonance spectroscopy (MR spectroscopy). MP-MRI aids in the pre-biopsy diagnosis of prostate cancer guides biopsy- either real-time or cognitive TRUS guided biopsy or fusion biopsy[8]. It also helps in distinguishing and denoting the extent of the disease involvement, which can aid in minimally-invasive procedures. Moreover, it also helps in predicting the treatment outcomes and selecting amongst the various treatment options available. Furthermore, diffusion-weighted imaging (DWI), dynamic contrast-enhanced imaging (DCE) and Magnetic resonance spectroscopy show promise in better characterization of the lesions and assessment of cancer aggressiveness in correlation with low, intermediate and high Gleason scores. Gleason's grading system is the standard histo-pathological method for estimating the aggressiveness of prostate cancer[6-8]. It is used to describe a tumour as low grade (Gleason's score ≤6), intermediate grade (Gleason's score = 7), or high grade (Gleason's score >7) with respect to tumour aggressiveness. The probability of disease recurrence increases with increasing Gleason's score and increasing percentage core involvement of tumour in biopsy specimens[9]. Hence, accurate scoring is necessary to determinate appropriate therapy, according to risk groups. Active surveillance for low-risk tumours (Gleason's score ≤6), monotherapy for intermediate-risk tumours (Gleason's score = 7) and combination therapy for high-risk tumours (Gleason's score, >7) are the best treatment options. Even today, the confirmatory diagnosis of prostate cancer lies in the histological examination performed on a biopsy specimen and application of Gleason scoring for grading of the two most common patterns of the cells from 1 (lowest) to 5 (highest) and adding them to yield a score with a maximum of 10 and scores above 7 are considered adverse towards prostate cancer[10]. This study was planned to assess the efficacy of multi-parametric MRI in the detection of prostate cancer in correlation with Gleason scores of the biopsies among the men with raised prostate-specific antigen (PSA) levels.

MATERIALS AND METHODS

Our study was in a prospective observational category study. This study was approved by the institutional scientific and ethical committee review board. Recruitment of Patients: This study was conducted during October 2018 To September 2019. Male patients who were showing the symptoms of obstructive in the lower urinary tract, difficulty in passing urine etc. reported to OPD of Mamata Academy of Medical Sciences, Bachupally, Telangana. A total number of 30 Patients were selected from the age group of 50-78 years, who also have elevated Prostate-Specific Antigen (PSA) levels. And those who have willingly signed self-declaration related to he/she does not suffer from any other metabolic disorders, and the informed consent form for this study were considered for this study. Patients with urinary tract infections, bleeding disorders, claustrophobia, patients with implants were excluded from the study.

Patient preparation: In terms of prior precautionary measures, antibiotic in the form of Tab. Ciprofloxacin 500mg 30 minutes before the procedure and rectal enema were given. Viral serological tests were done, and all the patients were explained about the indications, risks of the methods and signed informed consent was obtained from all the participants.

Patient position: Supine position for the MRI sequences and left lateral position for TRUS imaging and biopsy.

Imaging examination: All the 30 patients were subjected for the multi-parametric MRI sequences, including T1 and T2 weighted anatomical imaging, functional imaging using diffusion-weighted MRI and DCE along with MR spectroscopy. The machine used in this study is SIEMENS 1.5 Tesla. Multi-parametric MR imaging protocol included 2D T2w-MRI, DW-MRI, DCE-MRI and MRSI. High-resolution Axial, Sagittal and coronal T2WI using T2w turbo spin-echo sequence were taken in three orthogonal planes. TRUS scan and TRUS guided biopsy: All the thirty patients were subjected for TRUS scan with 7 MHz Aloka machine with the rectal probe in left lateral position. Complete zonal anatomy of the prostate was studied, and systematic sextant biopsies of 8 cores were taken. Each biopsy specimen was labelled explicitly according to the orientation of the biopsy site and sent for histopathological examination. All the patients were given one dose of ciprofloxacin 500 mg half an hour before TRUS biopsy. All the patients were given a low rectal enema before biopsy. No patient developed any untoward complication following the procedure.

Histopathological analysis: Gleason's score was obtained by histopathological analysis of the TRUS guided biopsy specimens. The tumours were then divided into three groups based on Gleason's score. Tumours with Gleason's score <6 was categorised as low-grade tumours, a score equal to 7 as intermediate-grade tumours and those with score >7 as high-grade tumours.

Statistical analysis: The consolidated and compiled data were analysed with SPSS statistics software. To explain the descriptive data statistics, frequency analysis, percentage analysis was used for categorical variables and the mean and S.D was used for continuous variables. To find the agreement between PI-RADS and Gleason's score, the Inter rate reliability Cohen's Kappa was used. The sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of DWI were computed for low grade (GS <6), intermediate grade (GS =7) and high grade (GS >7) tumours. Kappa value was also calculated for individual tumour grades which measure inter-rater agreement for the categorical variable.

Ethical approval was taken from Institutional ethical committee.

RESULTS

A total of 30 participants were included in the study. Mean age group and the standard deviation were found to be 63.39 ± 9.144 with a range of 50–78 years.

Table 1: Classification and distribution of multiparametric – MRI PIRADS score

PIRADS Score	Frequency	Percentage
Highly Suspicious Malignancy	15	50
Probably Malignant	09	30
Indeterminate	06	20
Total	**30**	**100**

In this study, 30 patients subjected for TRUS biopsy about 05 patients reported a PIRADS score of 6, 06 patients reported a PIRADS score of 7 and 09 patients reported a PIRADS score of 8 indicating malignancy as shown in Table 2.

Table 2: Distribution of Gleason Score of the malignancies in TRUS biopsy

Gleason sum Score	Frequency	Percentage
9	10	33.33
8	09	30
7	06	20
6	05	16.67
Total	**30**	**100**

Out of the 30 patients subjected for TRUS biopsy about 05 patients reported a Gleason score of 6, 06 patients reported a Gleason score of 7 and 19 patients reported a Gleason score of 8 and above indicating in favour of Malignancy as shown in Table 3.

Table 3: Patient's histopathological data used in this study (n = 30)

Grade	Gleason's score	Frequency	Percentage
High	> 7	4	13.33
	8 (4+4)	3	10
	8 (5+3)	3	10
	9 (5+4)	5	16.67
Intermediate	= 7	3	10
	7 (3+4)	2	6.67
	7 (4+3)	4	13.33
Low	≤ 6 (3+3)	6	20
Total		**30**	**100**

Our study also showed that the mean ADC value of tumours with Gleason's score <6 was significantly different from the tumours with Gleason's score =7 and Gleason's score >7. The difference in mean ADC value of tumours with Gleason's score =7 and Gleason's score >7 was also found to be statistically significant.

Table 4: Summary of sensitivity, specificity, positive predictive value, negative predictive value and kappa value for PI-RADS Vs Gleason's sum score

PI-RADS Score	Gleason's score	Sensitivity %	Specificity %	PPV %	NPV %	Kappa value	P-value
5	> 7	81.8	85.7	81.8	85.7	0.68	0.001 **
4	7	75	70.6	54.5	85.7	0.42	0.032 *
3	< = 6	50	100	100	86.4	0.60	0.001 **
Overall accuracy		**68.9**	**85.4**	**78.8**	**85.9**	**0.56**	

** Highly Sig. at P < 0.01 level and * Sig. at P < 0.05 level

This suggests that mean ADC value could differentiate between low risk (GS <6), intermediate-risk (GS =7) and high-risk tumours (GS >7), provided the tumour is visible on DWI.

Table 5: Correlation of prognostic factors and elevated Prostate-Imaging Reporting and Data Scoring System

Prognostic Factors	Estimate	Standard Error	Wald	df	p-value
Total Gleason score	1.052	0.198	17.317	1	<0.01
Surgical margin positivity	0.597	0.411	2.979	1	0.029
Extracapsular extension	1.431	0.578	20.177	1	<0.05
Seminal vesicle invasion	1.956	0.689	8.266	1	0.005

In our study, mean ADC for tumours with Gleason's score of <6 was $0.85 \pm 0.02 \times 10^{-3}$ mm^2/s, Gleason's score of 7 was $0.74 \pm 0.02 \times 10^{-3}$ mm^2/s and Gleason's score >7 was $0.63 \pm 0.08 \times 10^{-3}$ mm^2/s. In contrast, previous studies estimating the significance of differences in mean ADC values between the three groups had shown variable results.

DISCUSSION

Magnetic resonance imaging (MRI) is a routinely used imaging technique to diagnose and stage prostate cancer. The introduction of more conservative treatment options and an increasing number of dormant tumours has increased the need for better characterization of tumour aggressiveness to choose the appropriate treatment. This study found that conventional and MRI-guided target biopsies had similar cancer detection and diagnosis rates and failed to detect a similar proportion of prostate cancers (10.7% versus 10.3%). This is consistent with the earlier research findings that MRI-targeted biopsy has a similar cancer detection rate compared with standard sextant biopsy. However, a targeted biopsy can detect more clinically significant prostatic carcinomas. We have shown in this study that prostatic carcinomas detected and diagnosed by using targeted biopsy has more likely to have GS 7 or higher (grade group >2) than standard biopsy (81.9% versus 64.2%) [11, 12]. Since trans-rectal guided tumours biopsies are invasive and do not accurately classify Gleason's score in approximately 38% of all tumours[13] due to sampling errors, the value of multiparametric MRI as a non-invasive tool to predict tumour aggressiveness has been under investigation. In the multiparametric prostate study, functional imaging techniques such as diffusion-weighted imaging, dynamic contrast-enhanced imaging and MR spectroscopy are used to detect prostate cancer. Diffusion-weighted imaging is the only functional imaging technique that can assess the diffusion of proton molecules in vivo and provides information about the biological properties of tissue. Diffusion-weighted imaging has numerous advantages over other MR techniques such as short acquisition time, less subjective signal interpretation as compared to T2 weighted and dynamic contrast-enhanced imaging[14] and less partial volume effects than MR spectroscopy. Parallel imaging technique further improves the quality of DWI by reducing the sampling time, reducing motion artefacts, decreasing the number of gradient echoes and reducing magnetic susceptibility artefacts. Neoplastic tissues are characterized by increased cell density with decreased extracellular space, thereby reducing the diffusion of free water molecules resulting in restricted diffusion. In evaluating the relationship between ADC value and tumour aggressiveness, we found that there is a significant decrease in ADC value with increasing Gleason's score as reported by previous studies[15, 16]. This finding suggests an inverse relationship between ADC value and tumour aggressiveness with reference to biopsy Gleason's score. This can be explained by an increase in cellular density in high-grade tumours resulting in more restricted diffusion of water molecules as established[17]. Earlier studies by Yoshimitsu K *et al.*.[13] on peripheral zone prostatic cancers showed that mean ADC values could differentiate only the low-risk tumours from high-risk tumours. No statistically significant difference in mean ADC value between low risk and intermediate-risk tumours and between intermediate-risk and high-risk tumours were observed. Other techniques and tests, including multiparametric MRI and molecular and genetic markers, are increasingly used to supplement Gleason grade for risk stratification. Executing magnetic resonance imaging and targeted

biopsy, typically, improves detection of high-risk prostatic carcinomas and provides better characterization of prostatic carcinomas pathology in the prostate gland.[18, 19] Molecular and genetic tests designed to interrogate the critical pathways involved in prostatic carcinomas development and progression may aid in the identification of morphologic low-grade but biologically aggressive tumours for early intervention[19, 20].

In conclusion, MRI-targeted biopsy is considered to outshine standard biopsy in the detection of histologically more aggressive prostatic carcinomas, including more prostate cancers with GS 7 or higher (grade group >2) and a greater quantity of GP 4. Moreover, MRI-targeted biopsies decrease the risk of Gleason upgrading in radical prostatectomy. Our study highlights the potential role for MRI and targeted biopsy in the workup of prostatic carcinomas.

LIMITATIONS

There are a few limitations in this study. First, sextant based TRUS biopsy was used as the reference standard for comparing ADC values with Gleason's score rather than step section histopathology of radical prostatectomy specimens. Gleason's score derived from histopathological analysis of radical prostatectomy specimens may differ from TRUS guided biopsy derived Gleason's score, and there may be 20-30% upstaging of Gleason's score from core biopsy to radical prostatectomy specimens85. TRUS guided biopsies could miss small tumour focus visible on MR imaging, making it less accurate for diagnosis. The false-negative rate of standard sextant biopsy is around 39%86. Simple sextant matching of the prostate on TRUS guided biopsy and MRI is subjective and is prone to errors. Second, the ADC values are influenced by the degree of diffusion sensitization (b-value) used in the study. In our study, we used b values of 50, 400 and 800 s/mm2 and the mean ADC values for tumours with GS <6, GS =7 and GS >7 obtained in our study may not be similar like it has been observed in other studies with different values.

REFERENCES

1. Amin A, Partin A, Epstein JI. Gleason score 7 prostate cancer on needle biopsy: relation of primary pattern 3 or 4 to pathological stage and progression after radical prostatectomy. J Urol. 2011;186(4):1286–1290.
2. Berg KD, Roder MA, Brasso K, Vainer B, Iversen P. Primary Gleason pattern in biopsy Gleason score 7 is predictive of adverse histopathological features and biochemical failure following radical prostatectomy. Scand J Urol. 2014; 48(2): 168–176.
3. Chan TY, Partin AW, Walsh PC, Epstein JI. Prognostic significance of Gleason score 3þ4 versus Gleason score 4þ3 tumor at radical prostatectomy. Urology. 2000; 56(5):823–827.
4. Khoddami SM, Shariat SF, Lotan Y, *et al...* Predictive value of primary Gleason pattern 4 in patients with Gleason score 7 tumours treated with radical prostatectomy. BJU Int. 2004; 94(1):42–46.
5. Burdick MJ, Reddy CA, Ulchaker J, *et al...* Comparison of biochemical relapse-free survival between primary Gleason score 3 and primary Gleason score 4 for biopsy Gleason score 7 prostate cancer. Int J Radiat Oncol Biol Phys. 2009; 73(5):1439–1445.
6. Stamey TA, McNeal JE, Yemoto CM, *et al...* Biological determinants of cancer progression in men with prostate cancer. JAMA. 1999; 281(15):1395–1400.
7. Reese AC, Cowan JE, Brajtbord JS, *et al...* The quantitative Gleason score improves prostate cancer risk assessment. Cancer. 2012; 118(24):6046–6054.
8. Vis AN, Roemeling S, Kranse R, Schr¨oder FH, *et al...* Should we replace the Gleason score with the amount of high-grade prostate cancer? Eur Urol. 2007; 51(4):931–939.
9. Deng FM, Donin NM, Pe Benito R, *et al...* Size-adjusted quantitative Gleason score as a predictor of biochemical recurrence after radical prostatectomy. Eur Urol. 2016; 70(2):248–253.
10. Cole AI, Morgan TM, Spratt DE, *et al...* Prognostic value of percent Gleason grade 4 at prostate biopsy in predicting prostatectomy pathology and recurrence. J Urol. 2016; 196(2):405–411.
11. Nagayama M, Watanabe Y, Terai A, Araki T, Notohara K, Okumura A, *et al...* Determination of the cutoff level of apparent diffusion coefficient values for detection of prostate cancer. Jpn J Radiol. 2011 Aug; 29(7):488-94.
12. Hambrock T, Somford DM, Huisman HJ, van Oort IM, Witjes JA, Hulsbergen-van de Kaa CA, *et al...* Relationship between apparent diffusion coefficients at 3.0-T MR imaging and Gleason grade in peripheral zone prostate cancer. Radiology. 2011 May;259(2):453-61
13. Yoshimitsu K, Kiyoshima K, Irie H, Tajima T, Asayama Y, Hirakawa M, *et al...* Usefulness of apparent diffusion coefficient map in diagnosing prostate carcinoma: correlation with stepwise histopathology. J Magn Reson Imaging. 2008 Jan; 27(1):132-9.
14. Verma S, Rajesh A, Morales H, Lemen L, Bills G, Delworth M, *et al...* Assessment of aggressiveness of prostate cancer: correlation of apparent diffusion coefficient with histologic grade after radical prostatectomy. AJR Am J Roentgenol. 2011 Feb; 196(2):374-81.
15. Woodfield CA, Tung GA, Grand DJ, Pezzullo JA, Machan JT, Renzulli JF 2nd. Diffusion-weighted MRI of peripheral zone prostate cancer: comparison of tumor apparent diffusion coefficient with Gleason score and percentage of tumor on core biopsy. AJR Am J Roentgenol. 2010 Apr; 194(4):W316-22.
16. Yağci AB, Ozari N, Aybek Z, Düzcan E. The value of diffusionweighted MRI for prostate cancer detection and localization. Diagn Interv Radiol. 2011 Jun; 17(2):130-4.
17. Choy B, Pearce SM, Anderson BB, *et al...* Prognostic significance of percentage and architectural types of contemporary Gleason pattern 4 prostate cancer in radical prostatectomy. Am J Surg Pathol. 2016; 40(10):1400–1406.

18. Keefe DT, Schieda N, El Hallani S, *et al*... Cribriform morphology predicts upstaging after radical prostatectomy in patients with Gleason score 3 þ 4 ¼ 7 prostate cancer at transrectal ultrasound (TRUS)-guided needle biopsy. Virchows Arch. 2015; 467(4):437–442.
19. McGrath S, Christidis D, Perera M, *et al*... Prostate cancer biomarkers: are we hitting the mark? Prostate Int. 2016; 4(4):130–135.
20. Chua MLK, Lo W, Pintilie M, *et al*... A prostate cancer ‘‘nimbosus’’: genomic instability and SChLAP1 dysregulation underpin aggression of intraductal and cribriform subpathologies. Eur Urol. 2017; 72(5):665–674.

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