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Original Research Article

Role of Diffusion Weighted MRI in Prostatic Lesions

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Abstract: Prostate cancer is 2nd most common cancer in adult Indian males and is a potentially curable disease when diagnosed in early stages. Multiparametric MRI is a competitive and comprehensive modality for assessing the morphology and functional characteristics of the prostate in cases of diffuse and focal prostatic disease. 50 patients with Lower urinary tract symptoms and abnormal USG underwent non-contrast MRI. T1w, T2w and Diffusion weighted images were taken and ADC values were calculated using ADC maps. When a cut off ADC value of 1.4 x 10-3 mm^2/s is applied to prostatic lesions, and the results obtained are added to the anatomical details obtained from T1WI & T2WI, there is a considerable increase in the Specificity, Sensitivity, PPV and NPV. Due to the very high accuracy, non-contrast MRI with the help of diffusion weighted imaging and the corresponding ADC values can obviate the need for multiple diagnostic procedures and can act as a one stop shop for diagnosing all the prostatic lesions, both for its identification and characterization.
Keywords: Prostate Carcinoma, Diffusion weighted MRI Prostate, Multiparametric MRI.

INTRODUCTION

Prostate cancer is a major public health problem and is the 2nd most common cancer after oral cancer in adult Indian males. The exploration of non-invasive imaging methods that have the potential to improve specificity, while maintaining high sensitivity is still critically needed.

Prostate cancer is a potentially curable disease and combined effects of early detection and therapeutic intervention are likely the key elements that explain the observed reduction in cancer mortality. Prostatic lesions present with LUTS (lower urinary tract symptoms) but none of the symptoms are specific. Current methods for detection include digital rectal examination (DRE), serum PSA testing and 24 core TRUS guided biopsy. DRE is anatomically limited to the posterior and lateral aspects of the gland. Stratification of PSA levels is currently the most often used index for prediction of malignancy.

The Role of Imaging

Ultrasonography offers direct visualization of prostatic pathologies.But its operator dependence, lack of specificity and poor characterisation and localization of lesions are its main drawbacks. Over 30% appear isoechoic on US and have a high chances on been missed on sonography. TRUS also has low sensitivity as biopsy from smaller lesions is often inadequate.

Multidetector Computed Tomography (MDCT) studies showing the value in demonstrating enlarged gland size and abscess cavity, but it cannot differentiate benign from malignant lesions on the basis of size alone.

Multiparametric MRI is a competitive and comprehensive modality for assessing the morphology and functional characteristics of the prostate in cases of diffuse and focal prostatic disease.

Diffusion weighted imaging (DWI) is a type of MR sequencefor developing image contrast and relies on changes in the Brownian Movement of water molecules in tissues. The use of DWI in abdomen and pelvis is relatively new, but very promising for the detection and differentiation of benign and malignant lesions, imaging for dissemination (i.e. staging) in oncological patients, before treatment and for follow up after treatment of prostatic tumors.

The main aim of the present study is to measure the ADC values of benign and malignant mass lesions of the prostate using diffusion weighted MRI and to determine their contribution to differential diagnosis and also to propose a cut off ADC value for differentiating benign from malignant prostate lesions.

MATERIALS AND METHOD

Ours was a prospective study done in the Department of Radio diagnosis & SRL diagnostic centre of Mahatma Gandhi Memorial Medical College & M. Y. Hospital, Indore, Madhya Pradesh, Indiafrom November 2013 to October 2014. A total of 50 patients who were referred to our department with strong clinical suspicion of lower urinary tract symptoms and those diagnosed by ultrasonography underwent noncontrast Magnetic Resonance Imaging evaluation of abdomen using 1.5 T 8 channel MRI scanner after getting approval by ISRB (Institutional Scientific Review Board).

Patients with lower urinary tract symptoms like increased frequency of micturition, hesitancy, urgency with /without prostatic enlargement on USG & DRE were included while those Post Hormonal/ Radiotherapy, hemorrhagic area(on imaging) in prostate, with mass lesions infiltrating the prostate from outside and with general contraindication to MRI such as those with pace makers, cochlear implants and other electromagnetic implants in body were excluded.

PULSE SEQUENCES & IMAGING PLANES

A three plane localizer is obtained for planning of the various sequences.T2W(axial,coronal and sagittal), T1W axial, DWI transverse and STIR sequences were taken.

- T2W fast spin-echo with TR/TE of 4900/97 ms and flip angle of 150º with 5 mm slice thickness is obtained. A FOV of 220 mm is used with a 232x256 matrix in the axial plane.T2W fast spin-echo with TR/TE of 4910/97 ms and flip angle of 150º with 5 mm slice thickness is obtained. A FOV of 230 mm is used with a 256x256 matrix in the coronal plane.T2W fast spin-echo with TR/TE of 4000/97 ms and flip angle of 150º with 4 mm slice thickness is obtained. A FOV of 230 mm is used with a 256x256 matrix in the sagittal plane.
- This is followed by DWI obtained through a multisection spin-echo singleshot echoplanar sequence in the transverse plane, using b values of 0, 500 and 800 sec/mm^2. A TR/TE of 8000/94 ms, flip angle of 150º and slice thickness of 5 mm is used.
- A T1W fast spin-echo with TR/TE of 402/10 ms and flip angle of 150º with 5 mm slice thickness is obtained. A FOV of 350 mm is used with a 256x512 matrix in the axial plane.
- STIR sequence is obtained in the axial plane using TR/TE of 7090/80 & TI of 130 ms. 5mm slice thickness is used.
- Analysis of ADC is an automated process, available as an application on our scanner. Calculation of ADC is made for each voxel of an image and is displayed as a parametric (ADC) map. ADC measurements are then recorded for a given region by drawing regions of interest (ROIs) on the ADC map.

The prostate was viewed in T1W, T2W and DWI sequences with calculation of ADC values using the ADC maps and any abnormality was identified. When multiple lesions are noted, the most representative lesion or the largest of the lesions was taken into consideration. The following characteristics of the lesions were noted.

MR IMAGING APPEARANCE OF NORMAL PROSTATE ANATOMY

T1-weighted MR images- the normal prostate gland demonstrates homogeneous intermediate to low signal intensity and is best for visualization of prostatic anatomy.

T2-weighted MR images-The zonal anatomy of the prostate gland is best depicted on high-resolution T2-weighted images. The central and transitional zones cannot be distinguished and are collectively called the central gland. Differentiation between the two cannot be made by imaging appearances but is based primarily on anatomic location, which is separated from the peripheral zone by a thin pseudocapsule[1]. On T2W images the peripheral zone shows high signal intensity, which is either equal to or more than that of the fat in the vicinity [2]. The high signal intensity is attributed to the fluid filled ductal and acinar components, with agerelated increase in the signal intensity [3].

Compared with the peripheral zone, the central gland displays a low or heterogeneous T2 signal intensity since it contains fewer glandular structures and smooth muscles. The true capsule, seen as a lowintensity rim, is best appreciated on the posterior and poster lateral aspects of the gland.

DIFFUSION WEIGHTED MR IMAGING of PROSTATE

DWI relies on measuring diffusion of water molecules in the tissue by MRI.DWI is sensitive to very small scale motion of water molecules at a microscopic level. The sensitivity of a DWI sequence is characterized by its b-value, expressed in s/mm^2. The higher the b-value, the more sensitive the sequence is to diffusion effects. DWI is performed with at least two b-values. ADC measurements are then recorded for a given region by drawing regions of interest (ROIs) on the ADC map. Low ADC values mean restricted diffusion, thus in tissues which are highly cellular. High ADC values are seen in areas with relative free diffusion, thus in tissues with low cellularity.

In normal prostate tissue, the ADC is significantly higher in the peripheral zone , which has abundant glandular tissue , compared to the transitional or central zones due to the fact that prostate tissue in the transitional and central zones have more compact stroma and more longitudinally arranged smooth muscle than in the peripheral zone tissue. non-cancerous tissue of the prostate has various diffusion properties according to its various tissue composition types. A benign prostatic hyperplasia (BPH) gives rise to inhomogeneous diffusion patterns as it changes the distribution of cellular density. Whereas, BPH-related increased cellular density decreases the diffusion of the central gland, which is usually less predominant than prostate cancer but may mimic prostate cancer[4, 5]. Moreover, SI on DWI and the ADC may change with increasing age due to atrophy in the prostate, which leads to reduced cell volume and enlarged glandular ducts [6].

High lesion conspicuity on DWI and ADC maps can help the introduction of an image-guided biopsy in patients with previous negative biopsy results and elevated serum prostate-specific antigen (PSA) levels[7]. DWI and T2WI showed a better diagnostic performance than T2WI alone for predicting seminal vesicle invasion.

OBSERVATION

The prostate was viewed in T1W, T2W and DWI sequences with calculation of ADC values using the ADC maps and any abnormality was identified. When multiple lesions are noted the most representative lesion or the largest of the lesions was taken into consideration. When different types of lesions were identified in the same person representative lesions of each type was considered. The following characteristics of the lesions were noted.

A cut off ADC value of 1.4 x 10-3 mm^2/s is considered for differentiating benign from malignant lesions.

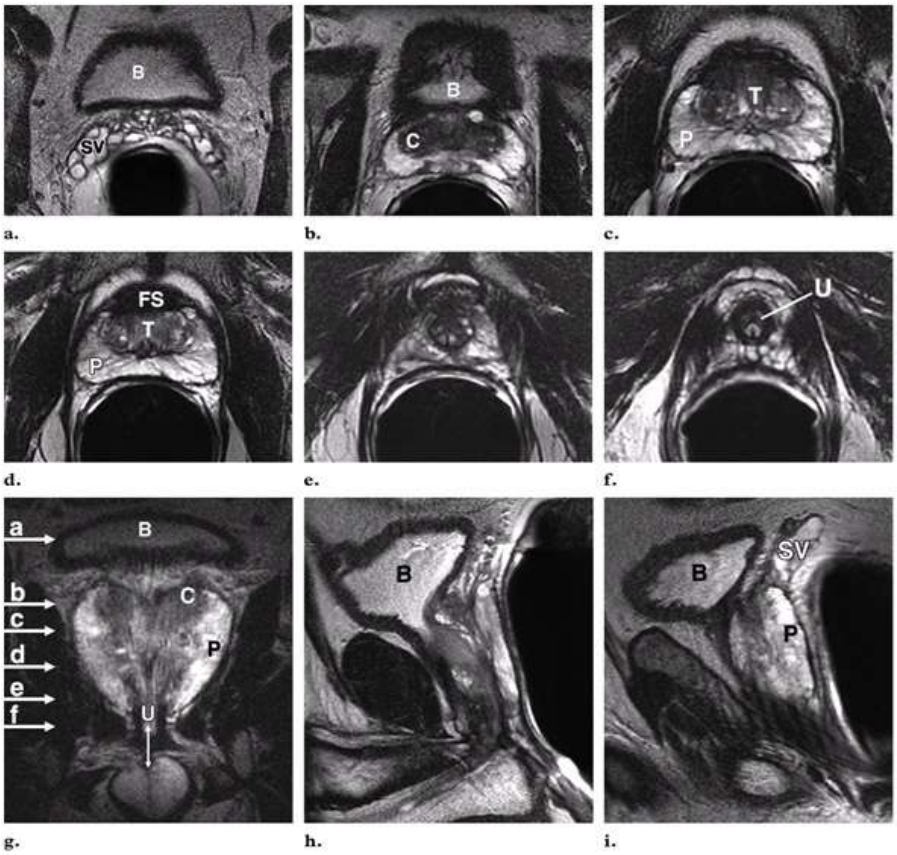
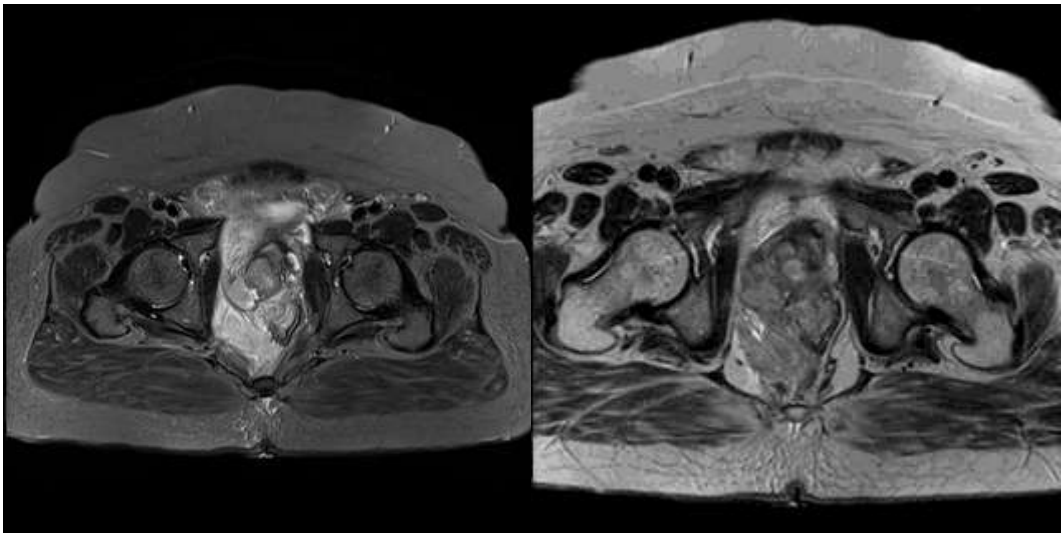
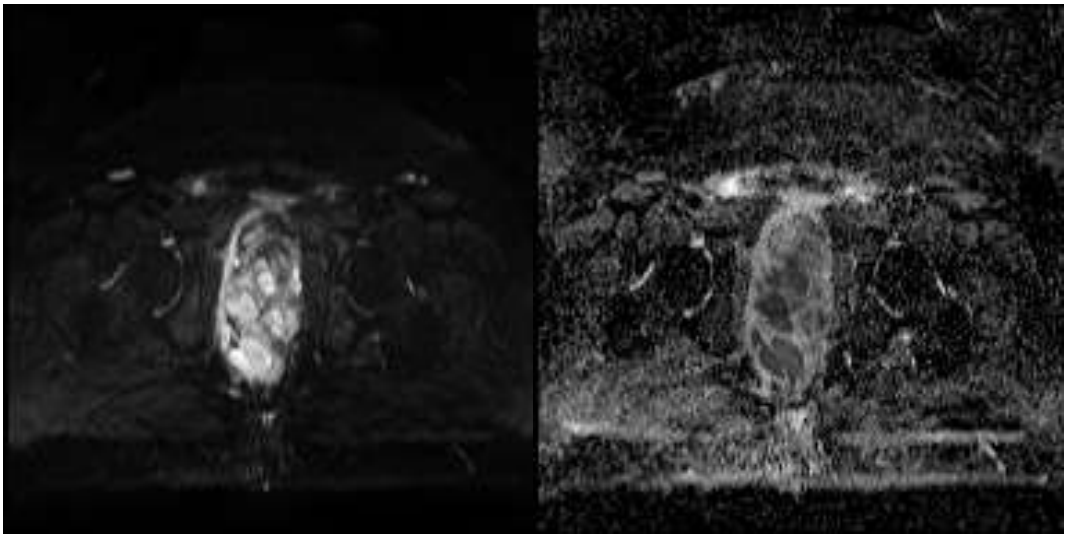


Fig .1 T2-weighted axial MR images obtained at the level of the seminal vesicles (a), the base of the prostate (b), the mid-gland (c, d), the apex (e), and the membranous urethra (f), as well as coronal (g), midsagittal(h), and parasagittal (i) MR images. The letters in g correspond to the anatomic levels used for images a–f. The vertical line in g indicates the membranous urethral length. B - urinary bladder, C - central zone, FS - anterior fibromuscularstroma, P - peripheral zone, SV – seminal vesicles, T - transition zone, U - urethra.

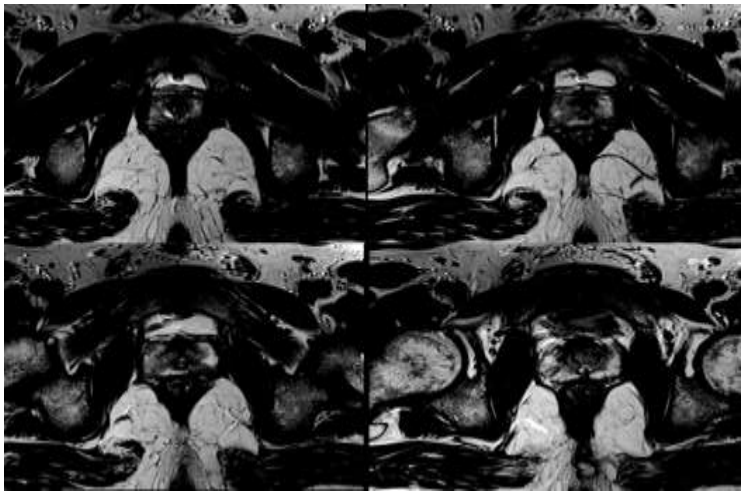


A. STIR AXIAL **B. T2 WI AXIAL**

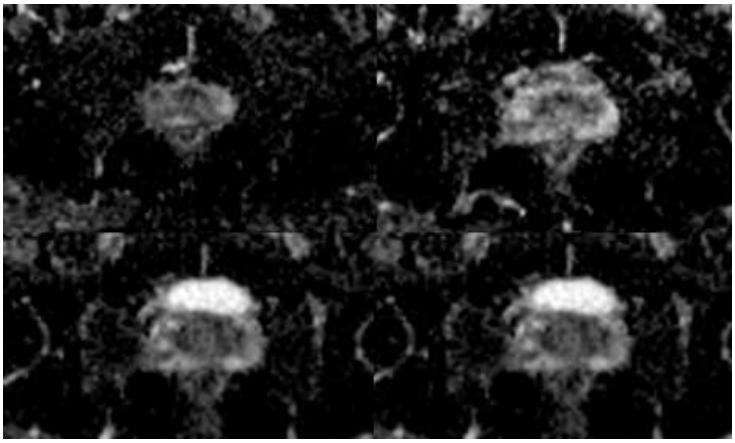


C. DWI AXIAL **D. ADC AXIAL**

Fig-2: Prostatic Abscess(Irregular well defined multiloculated cystic lesion appearing high signal intensity on T2WI seen in prostatic parenchyma with surrounding inflammatory fat stranding which is giving restricted diffusion on DWI.)

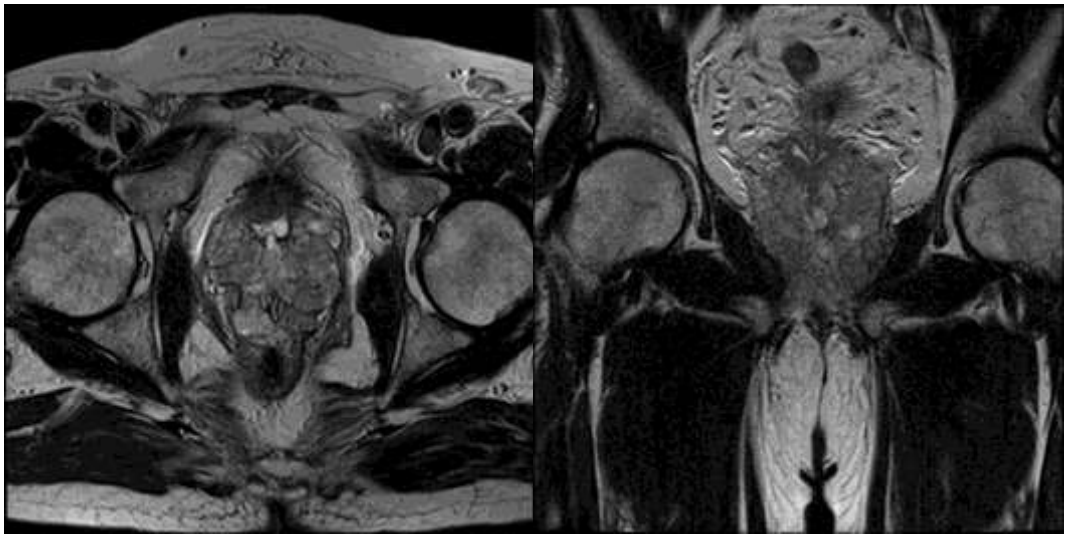


A.T2WI AXIAL

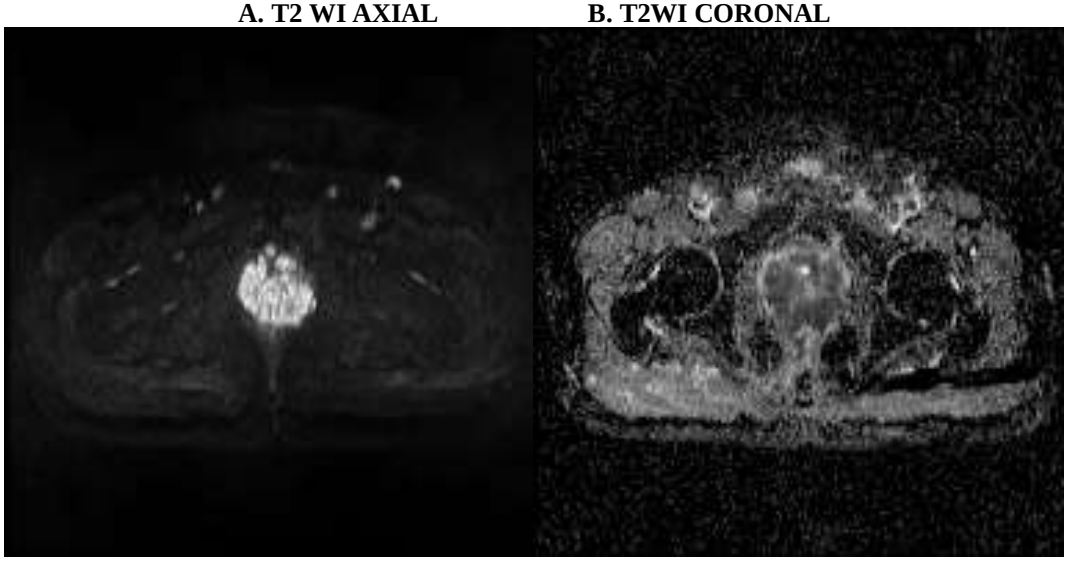


B.ADC AXIAL

Fig: 3: Chronic Prostatitis (Linear, wedge shaped ill defined T2 hypointensity in right peripheral zone with restricted diffusion- PIRADS 3)



A. T2 WI AXIAL **B. T2WI CORONAL**



C. DWI AXIAL **D. ADC AXIAL**

Fig 4: Carcinoma Involving Peripheral Zone & Central Gland (Diffuse infiltrating ill defined mass lesion involving both central gland as well as peripheral zone which is reaching & invading anterior wall of rectum with restricted diffusion – PIRADS 5)

Table-1:Classification of patients at Initial Scans & at Follow Up

S. No.	TYPE OF LESION	ADCVALUE	T2+ ADC	FOLLOW-UP
1	Inflammatory	1	2	3
2	Benign	27	28	29
3	Malignant	22	20	17
	TOTAL	50	50	49

On initial scan 2 patients were diagnosed with Inflammatory lesion, 1 each with prostatic abscess and chronic prostatitis, 28 were diagnosed with benign lesions, 2 patient had prostatic cyst,8 patients had stromal hyperplasia and 18(36%) glandular hyperplasia. Out of the 20 patients diagnosed with malignant lesion, 15 were distributed in the peripheral zone, 3 in the Transitional zone and 2 diffusely involving both zones.

On follow up, 3 patients who were initially labelled as malignant showed benign characteristics, 1 was diagnosed as chronic prostatitis and 2 as Benign prostatic hyperplasia.1 Patient initially diagnosed with prostatic cyst was lost to Follow up.

Table-2: Average ADC values of prostate lesions

S. No.	TYPE OF LESION	No. OF LESIONS	MEAN ADC VALUE
1	Abscess	1	0.6.
2	Chronic Prostatitis	1	1.49
3	Simple Cyst	1	2.55
4	Stromal Hyperplasia	8	1.4
5	Glandular Hyperplasia	19	1.73
6	TZ Ca	3	0.94
7	PZ Ca	15	0.9

Table-3: Morphoogical Features, ADC values and MRI features with ADC in predicting malignancy

MORPHOLOGY T1/ T2	FOLLOW UP		
	MALIGNANCY	BENIGN	
MALIGNANCY	14 (TP)	6 (FP)	20
BENIGN	3(FN)	26 (TN)	29
	17	32	49
ADC	FOLLOW UP		
	MALIGNANCY	BENIGN	
MALIGNANCY	13 (TP)	9 (FP)	22
BENIGN	4(FN)	23 (TN)	27
	17	32	49
ADC + MORPHOLOGY	FOLLOW UP		
	MALIGNANCY	BENIGN	
MALIGNANCY	15 (TP)	5 (FP)	20
BENIGN	2(FN)	27 (TN)	29
	17	32	49

Table- 4: Accuracy of ADC values & MRI in predicting malignancy

S. No.	STATISTICS	ADC VALUE	T1W + T2W	ADC+T1W+T2W
1	SENSITIVITY	77%	82%	88%
2	SPECIFICITY	72%	81%	85%
3	PPV	60%	70%	75%
4	NPV	85%	89%	93%

DISCUSSION

Focal masses are diagnosed using ultrasonography (USG) and if needed TRUS guided biopsy. Additionally, magnetic resonance imaging (MRI) is preferred when further characterization of these masses is needed. MRI has many advantages (e.g., high contrast resolution, the ability to obtain images in any plane, lack of ionizing radiation, and the safety of

using particulate contrast media rather than those containing iodine) that make it a favoured modality. Lesion morphology, signal intensity, and contrast enhancement pattern are taken into consideration when characterizing masses with MRI; however, even if the data are evaluated together, there can still be difficulties in the differentiation of benign and malignant lesions.

In the present study,50% of cases were in the seventh decade(60-69 years), most common presenting complaint was increased urinary frequency, present in 36% of the study. These observations are in concordance with various previous studies by Hambrock et al[8] and D J Chadwick et al[9].

On ultrasonography, out of 50 lesions, 35 lesions (70%) were there in transitional zone,13(26%)in the peripheral zone and 2(4%) were in both zones.2 (4%) lesions were diagnosed as inflammatory lesions. There were also 66% benign lesions and 30% malignant lesions in our study. The less number of inflammatory lesions in our study can primarily be attributed to the fact that very few diagnosed in ultrasonography warranted further evaluation by MRI examination. USG findings are similar to the observations made by Sheila Seth et al[10], Matthew D Rifkin et al[11].

Estimation of ADC is done by measuring the amount of signal loss between images obtained using different b-values. Calculation of the ADC (reported in units of x 10-3 mm^2/sec) requires a minimum of 2 b-values. Using more than 2 b-values will improve the accuracy of the calculation, but requires a longer scan time. In this study, we used 3 b values (50, 100 & 800), with gradients applied in all the three directions. These are the same sequence parameters that were used by Katahira K et al[12], Yoshimitsu et al[13], Boonsirikamchai P et al[14].

Out of the 50 lesions identified in the MRI examination, 62% lesions were found to be located in the transitional zone of prostate. The peripheral zone consisted of only 34% prostate lesions, whereas 4% lesions were found to involve both zones. Among the lesions that were identified in our study, 36% of the lesions gland volumes were between 31-40 ml. On MRI, 96% of the lesions that were identified were solid, with the remaining were cystic lesions.These findings are in concordance with the studies by S SDesilva et al[15], OzgurKiliclesmez et al[16] and BarisTurkbey et al[17].

On MRI evaluation, based on T1WI, T2WI and DWI, there were 4% lesions that were classified as inflammatory. 56% lesions turned out to be benign lesions and the remaining 40% focal lesions were classified as malignant lesions. Inflammatory lesions of prostate accounted for only 4% of the total lesions primarily because of the fact that they were seldom referred for further MRI evaluation.

The focal lesions are identified with the T1W and T2W images and their morphological characteristics assessed. On MRI, prostatic abscess show hyperintensity on T2-weighted images, with the abscess cavity showing even more marked hyperintensity. The walls are well defined and irregular and show a significant surrounding edema. The abscess cavity consists of thick proteineceous viscous contents with cell debris. Septations are also frequently encountered. Abscess show significant restriction of diffusion that appears bright on DWI and appears hypointense on ADC maps. This was also seen in the study by Paramjeet singh et al[18] and Oliveira et al[19]. The mean ADC value for the abscess was $0.6\pm0.22\times10^{-3}$ mm^2/s.

Acute prostatitis appears as aymmetrically enlarged gland appears hypointense on T1WI & hyperintense on T2WI with stranding of adjacent fat with disruption of true capsule. In Chronic prostatitis lesser inflammatory changes, ill-defined hypointense on T1WI &iso to hypointense on T2WI seen. There is a significant overlap, ADC values of prostatitis are lower than normal prostate & significantly higher than low and high grade prostatic carcinomas. However, due to a very high cell density, granulomatous prostatitis can present itself by ADC values lower than the ADC values of prostatic carcinomas. The mean ADC value for the chronic prostatitis was $1.49 \pm 0.22\times10^{-3}$ mm^2/s.

The MRI features of an uncomplicated prostatic cyst are a well defined intraprostatic mass of water signal intensity (Hyper-intense on T2WI & Hypo-intense on T1WI), round or oval shape with smooth thin walls and absence of internal structures. It is hypointense on DWI and Hyperintense on ADC map suggesting facilitated diffusion with high ADC values. The mean ADC value for simple cystic lesions was $2.55\pm0.26\times 10^{-3}$ mm^2/s ,which was observed by also Yi Haun*et al*. [20].

BPH is low in signal intensity on T1WI & homogenous/heterogenous on T2WI in appearance, ranging from medium to high in signal intensity. Compression of the adjacent peripheral zone results in a low - signal - intensity band referred to as the surgical pseudocapsule .Interstitial/Stromal Hyperplasia result in homogenous low signal intensity of the enlarged gland on T2 – weighted images .In Glandular Hyperplasia diffuse heterogenous low signal in enlarged central gland. Focal alterations in signal intensity may result from infarction or cystic changes within nodules of glandular BPH .DWI-Heterogenity also manifested as foci of low ADC values interspersed with high ADC

values.Mean ADC value for glandular hyperplasia was $1.73\pm0.21\times10^{-3}$ mm^2/s & for stromal hyperplasia was $1.4\pm0.21\times10^{-3}$ mm^2/s.

Peripheral zone carcinoma appears as discrete homogenous low signal focus/mass on T2& T1WI.Due to the increased cell density, malignancy typically show restricted diffusion with very low ADC values on the diffusion weighted images. The normal prostatic parenchyma had a mean ADC value of $1.839 \pm 0.223 \times 10^{-3}$ mm^2/s in peripheral zone & $1.469\pm 0.239\times 10^{-3}$ mm^2/s in central gland, whereas the malignant peripheral zone parenchyma had a mean ADC value of $0.9\pm0.20\times10^{-3}$ mm^2/s & malignant transitional zone parenchyma had a mean ADC value of $0.94 \pm 0.20 \times 10^{-3}$ mm^2/s.The same values were also obtained by various previous studies by Peter Gibs et al[21] and Kim JK et al[22].

From our study, we found that, non-contrast MRI with diffusion weighted imaging and its corresponding ADC values have very high sensitivity, specificity and overall accuracy in the identification and characterization of the lesions in prostate. Good correlation existed between the study findings and the findings obtained in follow-up. Due to the very high accuracy, non-contrast MRI with the help of diffusion weighted imaging and the corresponding ADC values can obviate the need for multiple diagnostic procedures and can act as a one stop shop for diagnosing all the prostatic lesions, both for its identification and characterization. There were 34% lesions that turned out to be malignant lesions on follow-up histopathological evaluation, among which 28% were peripheral zone adenocarcinoma, 4% were transitional zone adenocarcinoma & 2% were including both zones. MRI had identified all the lesions that were identified on following up these cases.

The true positive and false negative for ADC alone to predict malignant prostatic lesion were 13 and 4. The false positives and true negatives were 9 and 23 respectively. The sensitivity and NPV of the ADC values in predicting malignancy turned out to be an impressive 77% and 85% respectively. The specificity and PPV were 72% and 60% respectively.This was similar to the study conducted by AhmetBakiYagci et al[23], Gibbs P.[24], Kim CK[25] and deSouza NM et al[26]. 3 lesions were wrongly diagnosed as malignant in the MRI, out of which 2 lesions turned out to be benign prostatic hyperplasia & 1 lesion turned out to be chronic prostatitis.

From our study, we found that, non-contrast MRI with diffusion weighted imaging and its corresponding ADC values have very high sensitivity, specificity and overall accuracy in the identification and characterization of the lesions in prostate. Good correlation existed between the study findings and the findings obtained in follow-up. Due to the very high accuracy, non-contrast MRI with the help of diffusion weighted imaging and the corresponding ADC values can obviate the need for multiple diagnostic procedures and can act as a one stop shop for diagnosing all the prostatic lesions, both for its identification and characterization.

CONCLUSION

From our study we conclude that the drop in specificity (72%) and PPV (60%) of ADC values alone is mainly due to the overlapping ADC values of prostatitis with Prostate carcinoma.So, ADC values alone should not be criteria to label prostatic lesions as malignant and benign. When T1WI &T2WI findings are combined with ADC sensitivity, specificity, PPV & NPV increased to 88 %, 85%, 75% & 93% respectively. So we conclude DWI should always be used in conjunction to conventional MRI since there is considerable overlap between ADC values of benign and malignant lesions.

The ADC values of the normal Prostate peripheral gland and central gland is - 1.839 x 10-3 mm^2/s & 1.469 x 10-3 mm^2/s respectively.

The mean ADC values of the various prostatic lesions encountered in our study were,

- Abscess - 0.6 x 10-3 mm^2/s
- Chronic prostatitis – 1.49 x 10-3 mm^2/s
- Simple cyst - 2.55 x 10-3 mm^2/s
- Stromal hyperplasia –1.4 x 10-3 mm^2/s
- Glandular hyperplasia - 1.73 x 10-3 mm^2/s
- Peripheral zone carcinoma - 0.9 x 10-3 mm^2/s
- Transitional zone carcinoma – 0.94 x 10-3 mm^2/s

- The ADC value of malignant prostatic parenchyma is less than that of the normal prostatic parenchyma.
- Benign lesions generally have an ADC value of >1.6 x 10-3 mm^2/s.
- Malignant lesions generally have an ADC value of <1 x 10-3 mm^2/s.

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