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Original Research Paper

Radiodiagnosis

DIFFUSIVITY AND BIOCHEMICAL AGE-RELATED CHANGES OF NORMAL PROSTATE

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ABSTRACT

OBJECTIVE: To compare the MR Diffusivity changes in central and peripheral zone of prostate in normal population with respect to age and establishing a nomogram and analyse the age-related biochemical changes of prostate in normal population using Magnetic Resonance Spectroscopy.

BACKGROUND: The internal structures of prostate are constantly changing due to aging. The increased muscle content led to a decreased acinar emptying function as well as aggregated prostatic fluid and consequently, yielding the higher fluid content in peripheral zone (PZ) and the free diffusion of water molecules. In central zone (CZ) it is the fibrous stroma content that chiefly increased with an increase in age. In Magnetic resonance spectroscopy high Citrate and low choline seen in normal prostate.

METHODS: It is a Prospective study. The study population includes outpatients referred for MR imaging, without prostate related pathologies between June 2019 to November 2020. The sample analysed in our study includes 100 males between the age group of 10 to 59 yrs. It divided into 5 groups 10-19 years as one group (19.1 to 19.5 years included in this group),20-29 years as second group (19.6 to 19.9 years included in this group and 29.1 to 29.5 years included in this group),30-39 years as third group (29.6 to 29.9 years included in this group and 39.1 to 39.5 included in this group),40- 49 years as fourth group (39.6 – 39.9 years included in this group and 49.1 to 49.5 years included in this group), 50- 59 years as fifth group (49.6 to 49.9 years included in this group).

RESULTS: Maximum central zone area obtained in the study is 6.8 cm^2 in the age group 50 to 59 years. Maximum peripheral zone area obtained is 7.9 cm^2 in the age group 50 to 59 years. Maximum central zone Apparent Diffusion Coefficient (ADC) value obtained is 1503.2 mm^2/s in the age group 50 to 59 years. Minimum central zone ADC value obtained is 1355.2 mm2/s in 10 to 19yrs age group. Maximum peripheral zone apparent diffusion coefficient (ADC) value obtained is 1839.6 mm^2/s in the age group 50 to 59 years. Minimum peripheral zone ADC value obtained is 1533.7 mm^2/s in 10 to 19 years age group. Maximum Magnetic Resonance Spectroscopy (MRS) ratio obtained in peripheral zone is 0.36 in the age group 50 to 59 years. Minimum MRS ratio obtained peripheral zone is 0.18 in 10 to 19years age group. Maximum Magnetic Resonance Spectroscopy (MRS) ratio obtained in central zone is 0.38 in the age group 50 to 59 years. Minimum MRS ratio obtained central zone is 0.19 in 10 to 19years age group.

CONCLUSION: Both the central and peripheral zone area increases with age, with central zone having more increase in area than peripheral zone. Both the central and peripheral zone ADC value increases with age with peripheral zone having more increase in ADC value than central zone ADC value. MRS ratio increases with increase in age.

KEYWORDS : Diffusion Weighted Imaging, Magnetic Resonance Spectroscopy, Central and Peripheral zone of Prostate.

INTRODUCTION:

The Diffusion imaging is a Magnetic Resonance Imaging (MRI) technique that enables the measurement of the pathological conditions at the cellular and molecular levels[1]. Few studies done in china and European countries[2].

The normal adult Prostate is composed of approximately 70% prostatic gland and 30% mesenchyme tissue which mainly consists of smooth muscle and elastic fibres. Both CZ and PZ were made up of smooth muscle fibres and the concomitant glands. The acinar tissues accounted for an estimated 30% in CZ but occupied about 70% in PZ and thus, the CZ possessed much less water compared with PZ. The smooth muscle fibres organized themselves closely in parallel in CZ and thereby, the water diffusion in CZ was greatly limited and the degree of anisotropic diffusion of water molecules was increased. PZ, on the contrary, had minor restriction on water diffusion due to the loose and cross arrangement of smooth muscle fibres. Therefore, structural difference between CZ and PZ and increased with age[2,3]. A choline plus creatine to citrate ratio (CC/C) used to predict the presence or absence of Prostate cancer, with higher CC/C ratios being suggestive of prostate cancer[4].

In this study, Diffusion and magnetic resonance spectroscopy was applied to investigate the changes in normal prostate in different age groups. Apparent diffusion coefficient (ADC) and Magnetic resonance spectroscopy in normal Prostate Peripheral zone (PZ) and central zone (CZ) were quantified, and their correlations with age were also investigated in an attempt to discern the pathological changes in prostate and thus enable the early detection and diagnosis of prostate diseases.

STUDY DESIGN: It is a prospective study conducted in the Department of Radiodiagnosis at government Stanley

Medical College and Hospital, Chennai.

STUDY DURATION:

The study was conducted for a period of one and half years between June 2019 to November 2020

STUDY POPULATION:

The study population includes outpatients referred for MRI imaging without prostate related pathologies. Written consent was obtained from all the participants before the study. The sample analysed in our study are 100 males between the age group of 10 to 59 yrs.

INCLUSION CRITERIA:

10 - 59 years of age, the volunteers had neither major diseases nor clear signs and symptoms of urinary tract related diseases. The population divided into 5 groups 10-19 years as one group (19.1 to 19.5 years included in this group),20-29 years as second group (19.6 to 19.9 years included in this group and 29.1 to 29.5 years included in this group),30-39 years as third group (29.6 to 29.9 years included in this group and 39.1 to 39.5 included in this group),40- 49 years as fourth group (39.6 – 39.9 years included in this group and 49.1 to 49.5 years included in this group), 50- 59 years as fifth group (49.6 to 49.9 years included in this group)

EXCLUSION CRITERIA:

Patients who are contraindicated for MRI such as Age less than 10 years and more than 60years, Patients with signs and symptoms of urinary system disease, H/O any prostatic surgery, implanted electric and electronic devices, heart pacemakers, Implanted hearing aids, Intracranial metal chips, Metallic bodies in the eye, etc, are excluded, Uncooperative patients and Patients non willing for study.

IMAGING METHOD:

Using 1.5 tesla MAGNETOM AMIRA MRI systems, non-contrast MR Imaging of the prostate was done after emptying of bladder. No medical agents were used during the study.

PATIENT POSITION:

All the patients were subjected for the multi-parametric MRI sequences including T1 and T2 weighted anatomical imaging, functional imaging using diffusion weighted MRI and MR spectroscopy.MR imaging protocol included 2D T2w-MRI, DW-MRI and MRSI. High resolution Axial, Sagittal and coronal T2WI using T2w turbo spin echo sequence was taken in three orthogonal planes. ADC values were calculated by placing ROI in bilateral peripheral zones and central zone. single voxel MR spectroscopy is used to analyse the biochemical changes by measuring peaks obtained in the spectroscopy.

MP-MRI	Routine	Resolution
T2 W	TR: 4000 msTE: 101 ms Slice thickness: 3.0 mm Flip angle: 150°	FOVread:220mm FOVphase:100% Base resolution: 320 Phase resolution: 90%
DWI b values: 50,400,800	TR: 3700 msTE: 68.0 ms Slice thickness: 3.5 mm	FOVread:200mm FOVphase:100% Base resolution: 140 Phase resolution: 100%
MR Spectroscopy	TR: 940 msTE: 145 ms Flip angle: 90°	FOVA >>P:84mm FOV R >>L:84mm FOVF >>H:70mm

MP-MRI	Geometry	Sequence
T2 W	Slices: 20 Matrix: 256 × 256	Band width: 200Hz/Px Echo spacing: 11.2 ms Turbo factor: 25 Echo trains/slice :9
DWI b values: 50,400,800	Slices: 20	Band width: 1190Hz/Px Echo spacing: 0.94 ms EPI factor: 140
MR Spectroscopy	Thickness: 20mm	Band width: 1300Hz/Px Acquisition duration: 393ms Delta frequency: -1.80ppm

IMAGING METHODS:

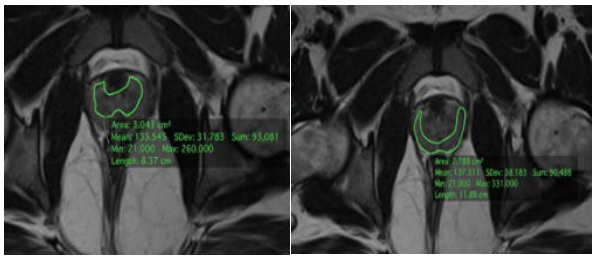


Figure 1: T2 axial weighted image of the prostate showing central and peripheral zone area at the level of mid gland

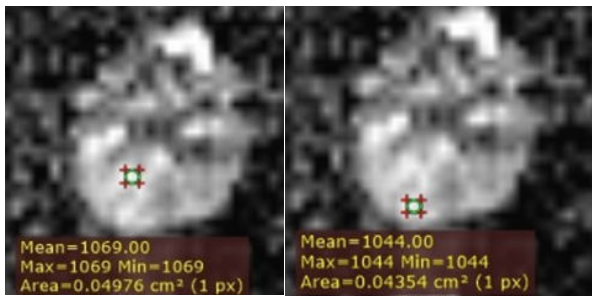


Figure 2: ADC image of the prostate show ROI for obtaining Central and peripheral zone apparent diffusion coefficient value at the level of mid gland.

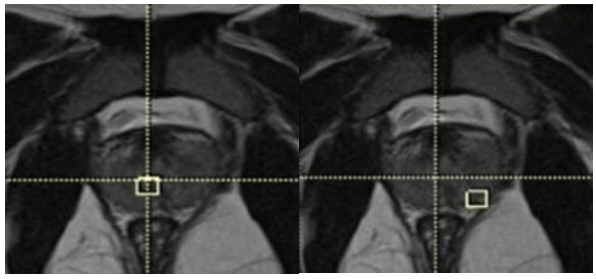


Figure 3: Central and Peripheral zone of single voxel Magnetic Resonance Spectroscopy

STATISTICAL ANALYSIS:

All continuous variables will be expressed as mean and standard deviation. All categorical variables will be expressed as percentages and proportions. Chi square test will be considered as test of significance. The test will be considered significant if $p < 0.05$ at 95% confidence interval.

Table 1: Age distribution in study groups

Age distribution		
	Frequency	Percent
10 - 19 years	21	21.0
20 - 29 years	19	19.0
30 - 39 years	16	16.0
40 - 49 years	21	21.0
50 -59years	23	23.0
Total	100	100.0
Highly Statistically Significant at $p < 0.01$ & No Statistically Significant at $p > 0.05$		

Age distribution (Table- 1) were 21.0% is 10-19 years, 19.0% is 20-29 years, 16.0% is 30- 39 years, 21.0% is 40-49 years, 23.0% is 50-59 years. p value >0.05, statistically no significant in age distribution

Table 2: Central and Peripheral zone areas in Different Age Groups

AGE GROUP	Number	Central zone (cm^2)	Central zone Comparison with other age groups		Peripheral zone (cm^2)	Peripheral zone Comparison with other age groups		P value of central and peripheral zone area using unpaired T test
			Age group	Post HOC test p value		Age group	Post HOC test p value	
10 - 19 years	21	3.1	20-29	0.013 *	2.9	20-29	0.041 *	0.001**
			30-39	0.0005 **		30-39	0.001 **	
			40-49	0.0005 **		40-49	0.0005 **	
			50-59	0.0005 **		50-59	0.0005 **	
20 - 29 years	19	3.5	30-39	0.001 **	3.3	30-39	0.708 #	0.015**
			40-49	0.0005 **		40-49	0.0005 **	
			50-59	0.0005 **		50-59	0.0005 **	
30 - 39 years	16	4.2	40-49	0.0005 **	3.5	40-49	0.0005 **	0.0007**
			50-59	0.0005 **			0.0005 **	
						50-59	0.006 #	
40 - 49 years	21	5.3	50-59	0.0005*	4.2	50-59	0.041 *	< 0.0001**
50 -59 years	23	6.8			4.7			< 0.0001**
** Highly Statistically Significant at p < 0.01 & * Statistically Significant at p < 0.05 # No Statistically Significant at p > 0.05								

Central zone Area with Age Groups (Table -2) by One-way ANOVA were F-value=228.855, p=0.0005<0.01 which shows highly statistically significant difference between Central zone Area and Age Groups. Peripheral zone Area with Age Groups by One-way ANOVA were F- value=53.258, p=0.0005<0.01 which shows highly statistically significant difference between PZ Area and Age Groups. Comparison of central and peripheral zone area by unpaired t test were p value < 0.0005 which shows highly statistically significant difference between central and peripheral zone area

Table 3: Central and peripheral zone ADC value in Different Age Groups

AGE GROUP	Number	Central zone 10^{-6} mm^2/s	Comparison with other age groups		Peripheral zone 10^{-6} mm^2/s	Comparison with other age groups		P value of central and peripheral zone ADC value using unpaired t test
			Age group	Post HOC test P value		Age group	Post HOC test P value	
10 - 19 years	21	1355.2	20-29	0.950 #	1533.7	20-29	0.0005 **	0.00009**
			30-39	0.982 #		30-39	0.0005 **	
			40-49	0.042 #		40-49	0.0005 **	
			50-59	0.0005 **		50-59	0.0005 **	
20 - 29 years	19	1377.3	30-39	0.001**	1625.2	30-39	0.015 *	<0.0005**
						40-49	0.0005 **	
			40-49	0.001 **			0.0005 **	
						50-59	0.018 *	
			50-59	0.001 **			0.0005 **	
30 - 39 years	16	1372.6	40-49	0.001 **	1694.4	40-49	0.001 **	<0.0005**
			50-59	0.001 **		50-59	0.0005 **	
40 - 49 years	21	1440.0	50-59	0.001 **	1760.8	50-59	0.0005 **	<0.0005**
50 -59 years	23	1503.2			1839.6			<0.0005**
** Highly Statistically Significant at p < 0.01 & * Statistically Significant at p < 0.05 # No Statistically Significant at p > 0.05								

Central zone ADC with Age Groups (Table – 3) by One-way ANOVA were F-value=8.696, p=0.0005<0.01 which shows highly statistically significant difference between Central zone ADC and Age Groups. Peripheral zone ADC with Age Groups by One-way ANOVA were F-value=74.814, p=0.0005<0.01 which shows highly statistically significant difference between PZ ADC and Age Groups. Comparison of central and peripheral zone ADC by unpaired t test were p value < 0.0005 which shows highly statistically significant difference between central and peripheral zone ADC value.

Table 4: Central and Peripheral zone MRS ratio (choline add with creatine divided by citrate) in different Age Groups

AGE GROUP	Num	Mean CZ MRS ratio	CZ Comparison with other age group- post HOC test – p value	Mean PZ MRS ratio	PZ Comparison with other age group post HOC test – P value	P value of central and peripheral zone MRS ratio using Unpaired t test		
10 - 19 years	21	0.20	20-29	0.169 #	0.18	20-29	0.157 #	0.28 #
			30-39	0.0005 **		30-39	0.0005 **	
			40-49	0.0005 **		40-49	0.0005 **	
			50-59	0.0005 **		50-59	0.0005 **	
20 - 29 years	19	0.24	30-39	0.089 #	0.22	30-39	0.076 #	0.38#
			40-49	0.0005 **		40-49	0.0005 **	
			50-59	0.0005 **		50-59	0.0005 **	
30 - 39 years	16	0.29	40-49	0.564 #	0.27	40-49	0.678 #	0.57#
			50-59	0.0005 **		50-59	0.0005 **	
40 - 49 years	21	0.32	50-59	0.005 **	0.30	50-59	0.005 **	0.12#

50 -59years	23	0.38			0.36			0.10#

** Highly Statistical Significant at $p < 0.01$ & * Statistical Significant at $p < 0.05$
# No Statistical Significant at $p > 0.05$

MRS ratio with Age Groups (Table -4) by One-way ANOVA were F-value=32.230, p=0.0005<0.01(Table-4) which shows highly statistically significant difference between MRS ratio and Age Groups. MRS ratio of central and peripheral zone by unpaired t test P value >0.01 which shows statistically no significant difference of central and peripheral zone MRS ratio.

RESULTS:

In our study, there were 100 participants between the age group of 10 to 59 years They were split into 5 groups based on their age.21 % of study population belongs to 10to 19 years age group,19% of study population belongs to 20 to 29 years age group .16% belongs to 30 to 39 years age group.21% of study population belongs to 40 to 49yrs age ,23% of population belongs to 50 to 59 years of age .The mean area of peripheral zone of prostate in our study population are 2.9 cm2 in 10 to 19yrs age group ,3.3 cm2 in 20 to 29yrs age group, 3.5 cm2 in 30 to 39yrs age group. ,4.2 cm2 in 40 to 49 years age group and 4.7 cm2 in 50 to 59yrs age group. Maximum peripheral zone area obtained in our study is 7.9 cm2 in the age group 50 to 59 years. Minimum peripheral zone area obtained in our study is 3.6 cm2 in 10 to 19yrs age group the mean ADC value of peripheral zone of prostate in our study population are 1533.7 mm2/s in 10 to 19years age group ,1625.2 mm2/s in 20 to 29yrs age group, 1694.4mm2/s in 30 to 39yrs age group ,1760.8 mm2/s in 40 to 49 years age group and 1839.6mm2/s in 50 to 59yrs age group. Maximum peripheral zone area obtained in our study is 1839.6 mm2/s in the age group 50 to 59 years. Minimum peripheral zone area obtained in our study is 1533.7 mm2/s in 10 to 19 years age group. The mean MRS ratio of prostate in our study population are 0.18 in 10 to 19years age group ,0.22 in 20 to 29years age group, 0.27 in 30 to 39years age group. ,0.30 in 40to 49 years age group and 0.36 in 50 to 59years age group. Maximum MRS ratio obtained in peripheral zone is 0.36 in the age group 50 to 59 years. Minimum MRS ratio obtained in peripheral zone is 0.18 in 10 to 19years age group. Maximum MRS ratio obtained in central zone is 0.38 in the age group 50 to 59 years. Minimum MRS ratio obtained in peripheral zone is 0.19 in 10 to 19years age group.

DISCUSSION:

Diffusion weighted imaging of prostate 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 and less partial volume effects than MR spectroscopy[5].

All functional MR imaging techniques diffusion weighted imaging (DWI) is the most practical and simple in its use. It has the advantages of not requiring IV contrast material and of being simple to process. Moreover, DWI requires less time to acquire than proton MR spectroscopy and less technologist training to perform. However, it has the disadvantages of being susceptible to motion and to magnetic field in homogeneities.

In young men, the transition and central zone are usually indistinguishable from each other, being usually referred together as the 'central or internal gland'. With increasing age, the prostate zonal anatomy changes. In young men, the central gland is composed mainly of the central zone.

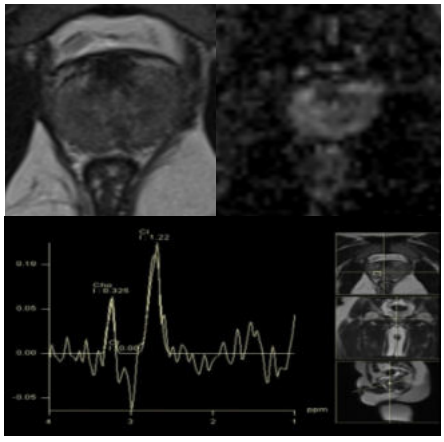
In older men the central gland is composed mainly of the transition zone, due to the development of benign prostatic hyperplasia. Benign prostate hyperplasia (BPH) leads to the formation of adenomatous nodules in the transition zone. Mostly, the central zone becomes compressed and will be displaced towards the prostatic base, making it a difficult task to accurately define the zonal anatomy of the central gland by MR imaging. As for the peripheral zone, it is generally not affected by BPH and retains its histological features.

Both the central and peripheral zone area increases with age, with central zone having more increase in area than peripheral zone. Similar results were obtained in study conducted by KS Allen[6]. Both central and peripheral zonal area shows high statistical significance with age in all the age groups in our study population. ($p < 0.05$) Table 2,3. The central has more statistical significance with age than peripheral zone. Similar results were obtained in many other studies. Both the central and peripheral zone ADC value increases with age with peripheral zone having more increase in ADC value than central zone. similar results were obtained in study conducted by Zi chang et al[7]. Both central and peripheral zonal ADC value shows high statistical significance with age in all the age groups in our study population. ($p < 0.05$) Table 3. The peripheral zonal ADC value has more statistical significance with age than central zone ADC value. Similar results were obtained in many other studies. High statistically significant difference between the MRS ratio and age groups. MRS ratio increased with increased age groups.

The internal structures of prostate were constantly changing due to aging and alterations in sex hormone. The prostate starts to develop and the lumen of the gland appears to be acinar shape from the beginning of adolescence. The lumen increases with age and tends to be vesicular-shaped. Meanwhile the secretion, synthesis, and storage of prostate fluid are also increased. The lumen continuously expanding and eventually form glandular epithelial cyst as age increased. Moreover, the increased muscle content led to a decreased acinar emptying function as well as aggregated prostatic fluid and consequently, yielding the higher fluid content in PZ and the free diffusion of water molecular. Unlike PZ, in CZ it is the fibrous stroma content that chiefly increased with an increase in age. Mean area of central zone grossly increased that is increased difference in first age group (10 – 19 years) compared to last age group (50 -59 years)[8,9].

CONCLUSION:

The central and peripheral zone area increases with age, with central zone having more increase in area than peripheral zone. The central and peripheral zone ADC value increases with age with peripheral zone having more increase in ADC value than central zone ADC value. Central and peripheral zone MRS ratio increases with increase in age. Central zone slightly increases in MRS ratio than peripheral zone.



A 37 years old male shows T2 WI, Diffusion ADC and MR spectroscopy shows central zonal area 3.6 cm2, Peripheral zonal area 3.9cm2, Central zone ADC value is 1389 x 10 -6 mm2/sec, Peripheral zone ADC value is 1690 x 10 -6 mm2/sec and MRS ratio is 0.17 in peripheral zone.

Abbreviation: ADC- Apparent Diffusion Co-efficient, DW MRI- Diffusion Weighted Magnetic Resonance Imaging, MRI - Magnetic Resonance Imaging, MRSI Magnetic resonance spectroscopy imaging, CZ – central zone, PZ – Peripheral zone, ANOVA Analysis of Variance, TE- Time to Echo, TR- Time to Relax, ROI- Region of Interest

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