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DIFFUSION TENSOR IMAGING (DTI) EVALUATION IN COMMON PATHOLOGIES OF BRAIN ON 3 TESLA MAGNETIC RESONANCE IMAGING (MRI) SCAN.

Medical Science

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ABSTRACT

Background: Medical and scientific settings are increasingly using Diffusion Tensor Imaging (DTI) for clinical purposes. Advance evaluation of common disorders of the brain that affect the integrity of white matter can be done using Diffusion Tensor Imaging with Fractional Anisotropy (FA), besides routinely used Diffusion Weighted Imaging (DWI) and Apparent Diffusion Coefficient (ADC); so besides routine image interpretation, DTI evaluation gives assessment of integrity of white matter fiber tracts; which are quite necessary for the prognosis in many brain pathologies. **Purpose:** To compare the Fractional Anisotropy (FA) values in white matter on both side of brain in the control group of normal persons and patient group of patients having brain disease/abnormality/lesion by Diffusion Tensor Imaging (DTI) on 3T MRI scan. **Materials and Methods:** Fifty-two patients having normal routine MRI study of brain and another fifty-two patients having brain disease/lesion/abnormality on routine MRI scan of Brain were included in this prospective case control cross-sectional research study. The approval of this research study from Institutional Ethical Committee (IEC) was obtained before the research study was started. The FA values were measured in the pre-defined ten specific regions of white matter on right side and left side of brain using ROI-based measurements. The differences in FA values in white matter in same area on both side of brain were analyzed using mean, standard deviation and paired T test. **Results:** The FA values were observed significantly differ in various regions of the brain in normal group specially in the areas of composed, complex and crossing fibers. The FA values were observed higher in the splenium followed by the genu, body and posterior limb of the internal capsule in both groups. However, on comparison of the FA values at the pre-defined ten specific regions on right side and left side of brain found in the control group and found in the patient group; statistical significance was observed in the FA values measures on right side of centrum semiovale and in the midbrain on both sides. **Conclusion:** The FA values were found to be greater and to vary regionally in different areas of white matter. The control group showed very little differences between right and left side of brain at the same white matter area or at same level of white matter tract; however, these results must be kept in consideration and should be acknowledged when interpreting them in clinical context.

KEYWORDS

Diffusion Tensor Imaging, Fractional Anisotropy, FA values, Brain disorders, White Matter, Brain Stem, Centrum Semiovale

INTRODUCTION:

Once it was demonstrated that the tissue organization affects the signals on diffusion-weighted images in vivo obtained on MRI; Basser PJ, Mattelo J and Lebihan D had introduced the mathematical model of Diffusion Tensor Imaging (DTI) in 1994[(1)]. Their method had described effective diffusion tensor (Deff) within a voxel can be estimated and then, displayed useful quantities about how the phenomenon of anisotropic diffusion of water (or metabolites) in anisotropic tissues can be measured noninvasively by MRI scan. This novel imaging technique gives unique information of white matter (WM) microstructures within the central nervous system (CNS). The DTI measures the directional dependence of water molecule diffusion and generates unique tissue contrasts for studying axonal organization in the CNS; which can be applied in brain and spinal cord for study of axonal connectivity, brain development, and white matter diseases.

Diffusion Tensor MRI imaging nowadays routinely used for clinical and research purposes to assess the integrity of white matter at the cellular and microstructural level. Diffusion Tensor Imaging (DTI) has quantitative metrics of fractional anisotropy (FA) used to measure the direction of diffusion[(2)]. Normal FA values lie between 0-1; but regional variation in FA value has been observed. In various neurological diseases/disorders, this FA value in white matter changes and they can differ from the FA values seen in the same areas of white matter seen in normal brain. There are two methods of determining FA values, one is using voxel-based morphometric measurements and the other is region of interest based measurements. Voxel-wise analysis needs picture smoothing and inter-subject registration, which may result in mistakes in the FA values that are acquired, but it is less operator-dependent and more easily automated than ROI analysis. The ROI-based analysis can be used more easily in a clinical environment [(3,4)]. There are studies that are conducted to find the normal FA values and the regional variation at 1.5 T MRI and 3T MRI scanner [(5-7)]; however, very few studies are published which reflect the differences in FA values between normal white matter and in presence of common diseases or pathologies of brain.

AIMS AND OBJECTIVES:

This research study was aimed to measure and compare the Fractional Anisotropy (FA) values on Diffusion Tensor Imaging (DTI) in the white matter areas and white matter tracts on both sides of brain in the control group of persons with normal brain on routine MRI scan and as well as in the white matter areas and tracts on both sides of brain (ipsilateral and contralateral white matter of brain abnormality/ disease) in the group of patients having brain disease / lesion / abnormality on routine MRI scan; which were done on 3T MRI scanner.

MATERIAL AND METHODS:

The prospective case control cross-sectional research study was carried out on Siemens Spectra 3 Tesla MRI scanner between April 2020 and November 2022 in the Department of Radiodiagnosis, Shree Krishna Hospital, Pramukhswami Medical College, Bhaikaka University, Karamsad. The proposal of this research study was submitted to the Institutional Ethical Committee (EC) and clearance from IEC was obtained as the participants had to undergo additional 9 minutes, 58 seconds in routine MRI scan of brain, specially for this DTI study, for which informed consent were taken. This research study was done on 3 Tesla Siemens Spectra MRI scanner [Menu.: Siemens Healthineers, H.Q.: Erlangen, Bavaria, Germany].

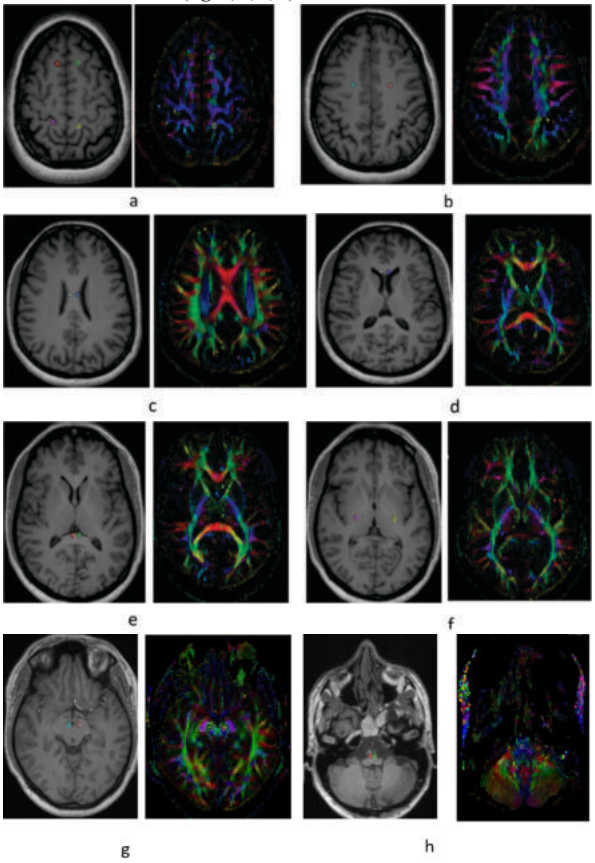
First, the routine MRI scan of Brain was done for any clinical indication. This routine MRI scan was performed by taking 4 mm thick Spin Echo T1 Weighted (SE T1W) images, Turbo Spin Echo T2 Weighted (TSE T2W), T2 Weighted Fluid Attenuated Inversion Recovery (FLAIR), Susceptibility Weighted (SWI) & Diffusion Weighted (DW) with Apparent Diffusion Coefficient (ADC) axial sequences; 5 mm thick T2 Weighted Fluid Attenuated Inversion Recovery (FLAIR) & Gradient Recalled (GRE T2*) coronal sequences and 4 mm thick SE T1W sagittal images. The contrast enhanced study, if indicated, was performed after taking Diffusion Tensor imaging (DTI) acquisition; in which, after intravenous contrast administration of Gadolinium contrast medium; 4 mm thick T1W with

Magnetization transfer Contrast (MTC) axial and sagittal images and 5 mm thick T1W with fat saturation coronal images of brain were obtained.

Once the routine MRI scan of brain was done; the MR images were quickly assessed on MRI console or in Picture Archiving and Communication System (PACS) [Manu.: Meddif Technology Pvt. Ltd., Bangaluru, Karnataka, India] by a qualified consultant radiologist. Then, depending on the MRI findings seen in the MRI scan of brain; the participants were assigned to control group (participants having normal MRI appearance of brain) or patient group (participants having common pathologies of brain such as cerebral atrophy, chronic ischemic diseases, demyelinating diseases, tumor, infarct, brain damage due to various etiology etc.).

The DTI study was performed on Siemens Spectra 3T MRI scanner using the 16 channel head & neck coil (used for brain MRI scan) after routine non-contrast MRI scan of brain. For anatomical guidance and to ensure that there were no unexpected aberrant findings, 3D T1 weighted (T1W) sagittal sequence T1_mprage_sag_p2_iso was taken first. Then, A Single Shot Spin Echo, echo-planar DTI sequence with the parameters Ep2d_diff_mddw_20p2_dti with TR = 7500ms, TE = 103ms, FOV = 220 mm, Number of Averages = 5, Acquisition Time = 9 minutes, and bipolar gradients applied in 12 directions (max b factor = 800s/mm^2) was used to perform diffusion tensor MR imaging. Then, this acquisition of DTI sequence is post-processed by using specific software - Neuro 3D Card.

On the colour coded Diffusion Tensor image with T1W axial image for reference; Free hand Region of Interest (ROI) was drawn in ten regions in brain on both sides (10 x 2 = total 20 regions); which included anterior part of Frontal Lobe, posterior part of Frontal Lobe, Centrum Semiovale, Body of the Corpus Callosum (CC), Genu of Corpus Callosum, Splenium of Corpus Callosum, Posterior Limb of Internal Capsule (PLIC), Midbrain, Pons and Medulla Oblongata **(fig. 1 (a-i))**. These ROIs were kept the same for all these regions and drawn in DTI images of brain in all the participants of control group (having normal appearance of brain on routine MRI scan) and in DTI images of brain of patient group (having brain disease/lesion/abnormality on routine MRI scan). The ROP for FA values were also put in few additional white matter region/s in MR lesion/abnormality in patient's group for their DTI evaluation. (**fig. 2, 3, 4, 5**).



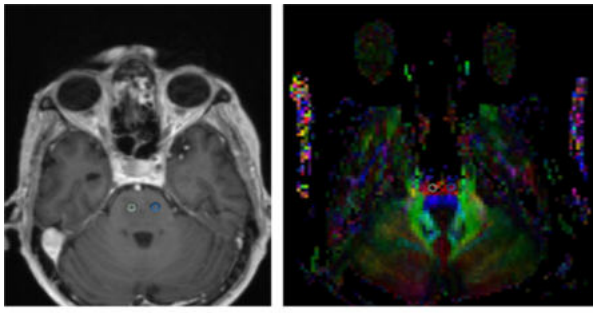


Figure 1: a.- i. MRI Diffusion tensor post-processed colour coded images with ROI drawn on different regions of white matter (WM) to measure FA values of white matter at different predefined regions. This participant has normal routine non-contrast MRI scan of brain.

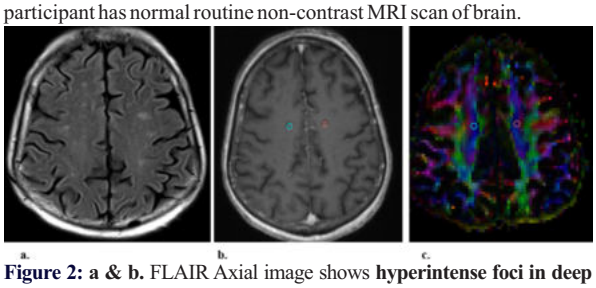


Figure 2: a & b. FLAIR Axial image shows **hyperintense foci in deep white matter including bilateral centrum semiovale, b. T1W hypointense foci in the frontal lobes, with small lacunar infarcts [at other level - not seen in these images] and cerebral atrophy**. **c.** DTI axial image with ROIs on the anterior and posterior side parts of frontal lobe.

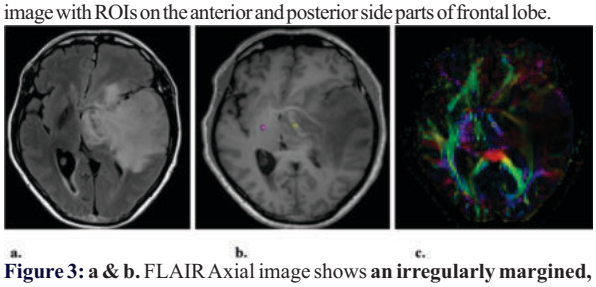


Figure 3: a & b. FLAIR Axial image shows **an irregularly margined, intra-axial, FLAIR hyperintense area and T1W hypointense area in the left perisylvian white matter and white matter of left temporal lobe, representing vasogenic edema around a tumour**. **c.** DTI axial image with ROIs on the posterior limb of internal capsule.

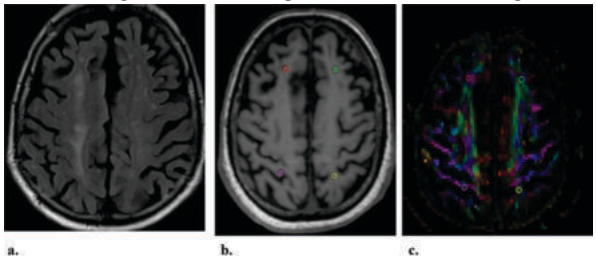


Figure 4. **a.** FLAIR axial image shows **multiple, very small to early confluent, hyperintense areas in bilateral centrum semiovale** *associated with* similar hyperintense areas in bilateral fronto-parietal subcortical white matter, bilateral periventricular white matter and bilateral corona radiata [images not shown]. These suggest **chronic white matter ischemic areas possibly due to small vessel disease (Fazekas grade II)**. **b.** T1W axial image of bilateral centrum semiovale with ROI on both sides. **c.** DTI axial image with ROIs in bilateral central semiovale at same level.

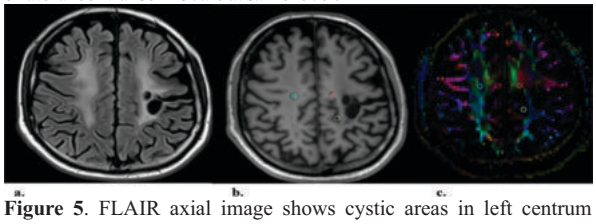


Figure 5. FLAIR axial image shows cystic areas in left centrum

semiovale (brain damage) as well as hyperintense areas in bilateral centrum semiovale. These suggest **small cystic encephalomalacias with surrounding gliotic area in left centrum semiovale and chronic ischemic areas in bilateral centrum semiovale**. **b.** T1W image shows cystic areas in left centrum semiovale and mildly hypointense areas in bilateral centrum semiovale. **c.** DTI image with ROIs in central semiovale on both sides.

Statistical Analysis :
The mean and standard deviation (SD) of FA values in all pre-defined white matter regions were calculated for the control group and the patient group with few additional white matter region/s in patient's group using Statistical Pacakage for Social Scienecs (SPPS) analysis software version 22.0. The mean and standard deviation of bilateral white matter areas and tracts were compared using the independent paired T test.

RESULTS:
A healthy 52 participants having normal MRI of brain were included in the study as control group. Other 52 patients having brain disease/ lesion/abnormality on routine MRI scan were included in this study as patient group. These patient group participants were included in the study after confirming the significant abnormalities on conventional routine MRI scan; which was diagnosed by a qualified consultant radiologist. This patients group participants have common pathologies of brain such as cerebral atrophy, chronic ischemic diseases, tumors, demyelinating diseases, infarcts or brain damage due to previous brain trauma, cerebro-vascular stroke or surgery etc.

A total of 52 patients brain FA values data from each group – control group and patient group were included in this research study. The mean age of the control group was 48.93 years ± 18.32 (Mean + SD) and for the patient group was 51.31 Years ± 18.77 (Mean + SD) respectively.

Table 1: Personal Demographic Data Of Participants In Control Group.

Total No. Of Participants	Age in years (mean ± SD)	Gender	
		Male	Female
52	48.93 years ± 18.32	18	34

Table 2: Patient Demographic Data Of Various disease/ abnormality/ lesion In Patient Group.

Total No of patients	Age in years (mean ± SD)	Gender		Brain Disease / Lesion / Abnormality
		Male	Female	
52	51.31 Years ± 18.77	20	32	Chronic ischemic diseases = 15 Cerebral atrophy = 10 Demyelinating diseases = 04 Brain damage = 06 Tumor = 05 Acute infarct = 05 Miscellaneous = 08

The mean for FA values in control group range from 0.435 to 0.294; while in patient group, mean FA values varies from 0.400 to 0.269.

Table 3: Comparison Of FA Values Of Same Side Of Same Region Of Brain Between Control Group And Research Group.

Anatomic regions of brain	No of control group (N_c)	No of patient group (N_p)	Mean ± SD (N_c)	Mean ± SD (N_p)	Value P value
Frontal lobe anterior right side	52	52	0.435±0.144	0.400±0.124	0.092
Frontal lobe anterior left side	52	52	0.403±0.168	0.399±0.139	0.451
Frontal lobe posterior right side	52	52	0.502±0.133	0.454±0.148	2.09
Frontal lobe posterior left side	52	52	0.45±0.153	0.450±0.138	0.497
Centrum semiovale right side	52	52	0.440±0.09	0.404±0.150	0.052
Centrum Semiovale left side	52	52	0.446±0.09	0.402±0.126	0.434
Body of CC right side	52	52	0.632±0.185	0.617±0.193	0.341
Body of CC left side	52	52	0.622±0.200	0.616±0.181	0.490
Genu of CC right side	52	52	0.616±0.181	0.666±0.200	0.321
Genu of the CC of left side	52	52	0.758±0.134	0.773±0.152	0.259
Splenium of CC right side	52	52	0.825±0.138	0.800±0.194	0.240
Splenium of CC left side	52	52	0.839±0.121	0.813±0.179	0.259
PLIC of right side	52	52	0.729±0.120	0.746±0.056	0.170
PLIC of the left side	52	52	0.713±0.125	0.710±0.125	0.452
Right side of the middle brain right side	52	52	0.441±0.124	0.399±0.083	0.026
Left side of the midbrain	52	52	0.432±0.123	0.371±0.094	0.001
Pons right side	52	52	0.498±0.119	0.472±0.135	0.107
Pons left side	52	52	0.512±0.108	7.257±48.66	0.162
Medulla oblongata right side	52	52	0.256±0.074	0.272±0.101	0.192
Medulla oblongata left side	52	52	0.294±0.113	0.269±0.086	0.451

N_c : No. of control group, **Np :** No of patients, **CC:** Corpus Callosum, **PLIC:** Posterior limb of the internal capsule.

Level of Significance was considered ≤ 0.005 at 95 percent Confidence interval.

The mean FA values of the control group and the patient group were analyzed using an independent T-test and a *p* value of < 0.05 was considered significant. A *p* value of 0.05 was observed in the right side of the centrum semiovale between the control group and the patient group (significant difference); followed by *p* value of 0.026 in the right side of the midbrain and 0.001 in the left side of the midbrain (significant difference); while the FA values in other regions of white matter were found to be statistically non-significant.

DISCUSSION:
The normative data of Fractional Anisotropy (FA) values of DTI evaluation of brain varies at different magnetic field strength like 1.5 Tesla and 3.0 Tesla [6, 7]. The FA value also have variation on different MRI scanner made by various manufacturer companies.

Lots of normative data of FA values of DTI study of brain done on 1.5 T MRI scanner were published [7]. However, few normative data of FA values of DTI evaluation of brain done on 3 Tesla MRI scanner were published [5, 8]. There are even less research publications to find the changes in FA values of DTI evaluation of brain in various brain diseases, lesions and abnormalities; which were done on 3 Tesla MRI scanner.

We looked for variation in FA values in ipsilateral regions of the brain white matter between the control group and the patient group. It is very important to know the differences while using DTI in research settings, which could be applicable in clinical conditions to better evaluate various brain diseases/abnormalities. Although FA value does not reflect any unique specific tissue attribute, it is affected by tissue hydration, myelination, cell packing density, fiber diameter, and directional coherence. The FA is widely employed as a measure of the integrity of white matter tissues [9, 10]. Few research studies had done the DTI evaluation and their FA values on both 1.5T and 3.0T MRI scanners and also compared these data [7, 11].

In a study using 3T MRI scanner by Lee et al. [5] of 31 healthy people had revealed FA values that varied regionally from 0.121 for the deep grey matter of the putamen to 0.806 for the genu of corpus callosum. White matter regions with the most uniform fiber orientation and densely packed fibers are always observed to have high FA values. The corpus callosum, a dense mass of fibers with a medio-lateral orientation (transverse orientation) that connects the cerebral hemispheres, has consistently been found to have the highest regional

FA values [12], which were also found to be highest in the present study, FA values were seen to be highest bilaterally in all three parts of corpus callosum, but no significant ipsilateral differences were found between these control and patient groups. In present study, FA values were seen higher in splenium on both sides in both these groups and our findings are aligned with the study reflected that in general, the FA values for the splenium and the posterior white matter, have been higher than those for the anterior part of white matter [13]. In our study, FA values in control group are found to be higher in various white matter region of the brain on both sides due to the presence of complex and crossing fibers than those found the same region on same side of brain in the patient group. In patient group comprising of general brain pathologies; the FA values were found to be low with significance of 0.05 in right centrum semiovale; which are similar to the result of the research study conducted by Sinha S et al[13] in order find out the FA value and Diffusion Weighted images (DW) in normal patients and patients with tumours, where FA values were seen higher in the white matter of normal group. Other than this finding; the FA values were found to be low in the tumors having non-enhancing tumor core and the variation between the DW and FA values in the enhancing tumour margin, edematous brain and ipsilateral white matter in seven patients in whom the ipsilateral centrum semiovale looked to be normal was significant statistically [13,14]. In our study; a significance of 0.026 and 0.001 was observed in the midbrain in right half and left half between the control group and patient group. However, in other white matter regions in white FA value were taken; the differences with respect to mean were very low and within one standard deviation (Mean + 1 SD). Our study findings suggested that FA values decreases in common pathologies of brain and could be a bio-marker for the prognosis of common brain pathologies [15,16]. The FA values in different brain diseases and abnormalities decreases in bigger lesions or big area of abnormality in white matter; while in case of subtle changes or very small abnormality, the FA values does not change significantly and remain in normal range.

It must be noted that regional FA values also depend on the size of ROI, region of measurement, magnetic field strength and model of MRI scanner.

This research study has few limitation; which are small sample size, inability to classify FA values for each sub-groups of different pathology/abnormality/lesion, because there were fewer cases in each of this sub-group. We were unable to follow up with each of the participant for longitudinal evaluation of these brain diseases/lesions; because of no need of follow up study, patient lost in follow up or choose to go other center and in some cases, cost constraint. Despite this, this study can be used as a baseline in the future to conduct DTI studies in common brain diseases and abnormalities.

CONCLUSION

We have measured and comparatively evaluated the Fractional Anistropy (FA) values in various white matter areas and white matter tracts in the brain at predefined site in the control group and patient group in DTI evaluation on 3T MRI scanner. The FA values in different brain diseases and abnormalities decreases in bigger lesions or big area of abnormality, which may need to be tracked or observed for a prognosis. In case of subtle changes or changes or very small abnormality, the FA values may remain within normal range or may not have statistically significant difference.

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