Analysis of Structural Connectivity on Progression of Alzheimer's Disease using Diffusion Tensor Imaging

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***Abstract* – The occurrence of Alzheimer's disease (AD) in the elderly individuals has been increasing at an alarming rate throughout the world over the past decade. Diffusion Tensor Imaging (DTI) has been widely used to study the white matter tracts in the human brain and for the estimation of structural connectivity parameters through the progression of the disease. Previous studies using fMRI focus on functional decline and adding on to this, DTI helps in analyzing the topological and structural integrity. Histopathological studies of the disease have revealed that major cortical neuronal loss occurred in Corpus Callosum and Cingulate Gyrus regions of the brain. In this work, DTI images of four AD patients for three progressive years have been obtained and the structural connectivity parameters namely: Fractional Anisotropy (FA), Axial Diffusivity, Radial Diffusivity and Mean Diffusivity have been estimated at the onset of the disease and for the three progressive years. Results show that the FA values decreased in the progressive years for all patients whereas the diffusivity parameters increased every year showing abnormalities in the connectivity parameters.**

Keywords - Alzheimer's disease, Diffusion Tensor Imaging, Structural Connectivity, Deterministic Tractography, White Matter tract

I. INTRODUCTION

Dementia refers to the group of diseases which affect the human brain cells leading to sustained and inexorable loss of memory and cognition. Alzheimer's disease has known to be the most common type of dementia, being classified into stages namely: Mild, Moderate and Severe. AD has been reported to advance in the progressive years and affect the thinking ability of patients which eventually leads to complete memory loss and loss of bodily functions [1, 2, 16]. The disease, with no curative found till date has been chronic in nature and its end result has been lethal.

Alzheimer's disease has been diagnosed and studied with the help of various imaging techniques out of which Diffusion Tensor Imaging, in particular has proved to be successful in studying the white matter structure of the human brain [17]. DTI, a type of Magnetic Resonance Imaging technique has been a non-invasive imaging modality which works on the principle of Brownian movement of water molecules that can be used to study characteristics such as magnitude, anisotropy and orientation of the diffused water molecules in tissues [3, 4].

This research work has involved the study of above mentioned structural connectivity parameters namely FA, axial diffusivity, radial diffusivity and mean diffusivity for three progressive years of an AD patient. The parametric values have been obtained every year and their variations in the values for each year has been observed. Previous research work on DTI has elucidated that there has been a change in the structure of white matter in the brain regions, particularly in the regions of frontal lobes, parietal lobes and Corpus callosum as suggested in the available literature [12, 13]. It has also been found that FA values in the above mentioned regions have decreased when compared to the Normal controls. Thus, Corpus callosum (CC) and Cingulate gyrus (CG) have been chosen as Regions of Interest (ROI) for the study. Further, deterministic tractography has been analyzed using Runge-Kutta method to obtain

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connectivity maps, and to estimate structural connectivity parameters present in the white matter tracts which has been proved to be effective than the Euler's method [14]. It uses the diffusion tensor to track fibers along the whole length representing directional anisotropy.

II. METHODOLOGY

A. Data Acquisition

The DTI images of four patients for three progressive years have been obtained from ADNI (Alzheimer's Disease Neuroimaging Initiative) database. The previous work has focused on analysis using fMRI, validating on that, the diffusion tensor images of the same subjects has been used [5]. The demographic details of the patients under study have been tabulated in Table 1.

Table 1 : Demographic Details

Demographic parameters	**Specifications**
Number of subjects	4
Number of progressive years for each subject	3
Gender (M/F)	4/0
Age (years)	60-70

B. Pre-processing of DTI

In diffusion weighted images, the most common artifacts have been observed due to the distortions caused by eddy current and head motion.

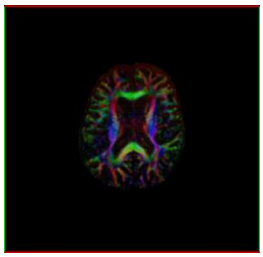

Fig 1a: Raw data

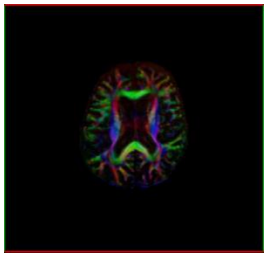

Fig 1b: Pre-processed image

Two scan parameters have been extracted to determine the tensor information: B- Value (.bval) - the amount of diffusion weighting and Diffusion Gradient Table (.bvec) - the gradient directions. Using these, the images have been corrected by removing distortions with the tool implemented in available literature [11, 15]. Eddy current induced distortions have been corrected by affine registration and the motion artifacts have been corrected by rigid body transformations with respect to the b0 image. The raw image and the pre-processed image of a representative subject have been shown in Figures 1a and 1b respectively.

C. Extraction of ROI

Corpus Callosum, the largest nerve fiber in the nervous system connecting the left and right hemispheres of the brain forming a biological network and Cingulate gyrus, an arched convolution that lies next to the Corpus callosum have been two of the severely affected regions in AD. Corpus callosum has been divided into 9 segments which have been predefined in the atlas - sri24_tzo116plus and Cingulate gyrus has been divided into left and right regions which have been defined in atlas - JHU White Matter Label as shown in Figures 2 and 3. During the onset of Alzheimer's disease, the changes in the shape of CC and reduction in the metabolic activities have been observed in the posterior CG [9, 10].

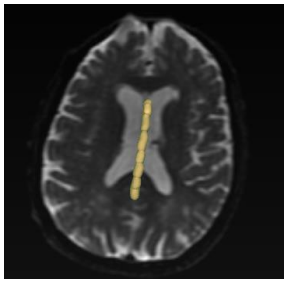

Fig 2

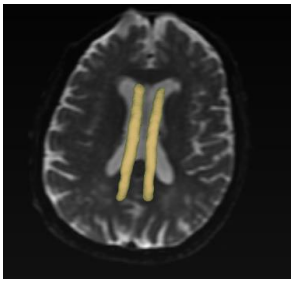

Fig 3

Axial view of (2) Corpus callosum (3) Cingulate gyrus

Keeping these two regions as the ROI, fiber tractography procedure has been performed to estimate the structural connectivity parameters at the onset of the disease and the variations of these parameters for three progressive years have been analyzed.

D. Fiber Tractography

DTI has been an efficient imaging modality which has availed the process of fiber assignment by continuous tracking (FACT), giving an output of

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three dimensional trajectories that has followed the white matter tracts. In addition to tract analysis, they have helped in determining the diffusion measures (FA, MD, RD and AD).

Tractography has been performed using Runge-Kutta method, a deterministic fiber tracking algorithm. Euler's method takes into account only the first order derivative and has been sensitive to noise resulting in propagation of errors, thus leading to erroneous estimation of tracts trajectories. Hence a more reliable solution has been adopted implementing Runge-Kutta method which uses higher order derivatives.

Three Eigen values (e1,e2,e3) and the corresponding Eigen vectors (λ_1, λ_2, λ_3) have made up the diffusion vector, where e1 and λ_1 have been considered to be the largest Eigen value and Eigen vector. Axial diffusivity has given an estimate on the direction of the fastest diffusivity and it lies parallel to the direction of white matter tracts. The Eigen values λ_2 and λ_3, refers to the medium and small Eigen values which have been assumed to be perpendicular to the white matter tracts , referring to radial diffusivity, RD = (λ_2+ λ_3)/2. Mean diffusivity refers to the average of the above mentioned Eigen values [7]. Diffusion Anisotropy refers to the variation of the diffusion properties with respect to the direction. Fractional Anisotropy (FA) has been the most common measurement of diffusion anisotropy. FA can be calculated by normalizing the Eigen value and standard deviation of the diffusion tensor [8].

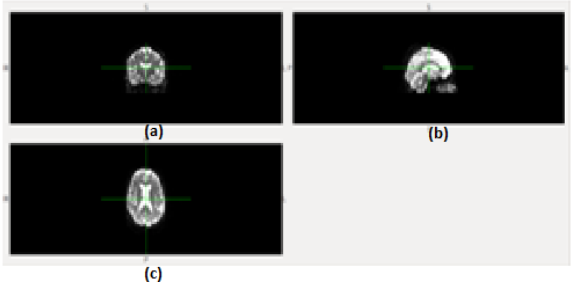

Fig 4: Post processed data with skull surface in (a) coronal

(b) sagittal and (c) axial view

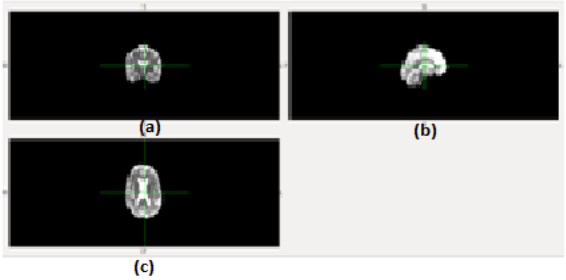

Fig 5: Post processed data without skull surface in (a) coronal

(b) sagittal and (c) axial view

extracted brain region excluding dura matter and outer cerebrospinal fluid , where (a), (b) and (c) are the coronal, sagittal and the axial views respectively.

Fractional anisotropy has helped in measuring the micro structural integrity of fibers and they have been highly sensitive towards tissue structural changes and neuronal degeneration [12]. Diffusivity parameters have traced the structural changes of white matter, membrane density and axonal diameter. FA and other parameters have been obtained from the Eigen values of the diffusion tensor,

λ_1 = longitudinal (axial) diffusivity [AD] (1)

$(\lambda_2 + \lambda_3)/2$ = radial diffusivity [RD] (2)

$(\lambda_1 + \lambda_2 + \lambda_3)/3$ = mean diffusivity [MD] (3)

$$\sqrt{\frac{1}{2}} \frac{\sqrt{(\lambda_1 - \lambda_2)^2 + (\lambda_1 - \lambda_3)^2 + (\lambda_2 - \lambda_3)^2}}{\sqrt{(\lambda_1^2 + \lambda_2^2 + \lambda_3^2)}} = \text{FA} \quad (4)$$

III. RESULTS AND DISCUSSION

The diffusion measures of the progressive stages for four subjects have been calculated, analyzed and the results obtained for a representative subject has been tabulated as shown in Table 2. The same trend in parameters has been observed for all the subjects. It has been observed that FA values have declined with the proliferation of the disease. FA has been sensitive to the micro structural changes and hence declining as a result of neuronal degeneration. In contrast to FA, the diffusivity parameters such as AD, RD, and MD have increased along the line as an effect of free diffusion with the deterioration of the fibers.

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Table 2: Quantification of the decline in FA and increase in diffusivity for a representative subject

Diffusivity parameters (mean)	Stage I	Stage II	Stage III
FA	0.966	0.582	0.545
MD	0.010	1.769	1.765
AD	0.025	2.830	2.910
RD	0.002	1.198	1.233

The variation in connectivity parameters has represented the declined connectivity of white matter in AD patients.

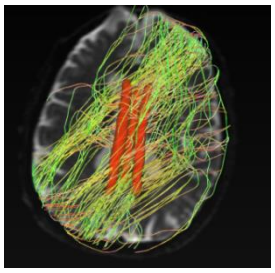

Fig 6: Axial view of tracts along the ROI in brain

Fig 7a Fig 7b

Tracts passing through ROI in (a) sagittal view (b) axial view

V. CONCLUSION

In this work, the WM tracts have been obtained from the images using deterministic tractography. Since the overall representation of the tracts have not been effective in analyzing the structural abnormalities of the progression of disease, fractional anisotropy (FA) and diffusivity parameters have been estimated to assess the decline in the structural connectivity. The results obtained have supported the consequent deterioration in the structural connectivity, implying cognitive impairment. Thus the overall study has suggested that these parameters would serve as an efficient biomarker in quantifying the progression of the disease.

REFERENCES

[1] Ranjan Piyush, Ramakrishnan S., "Variations of White Matter Tract Length in Regions of Emotional Regulation as Assessed in Alzheimer Diffusion Tensor Images ", IEEE Xplore, June 2015

[2] Tinu Varghese, Sheela Kumari R., Mathuranath P.S., " Evaluation of different stages of Alzheimer's disease using unsupervised clustering techniques and voxel based morphometry" 2012 World Congress on Information and Communication Technologies, 953-958

[3] Le Bihan D., Mangin J.F., Poupon C., Clark C.A., Pappata S.,Molko N., Chabriat H., 2001. Diffusion tensor imaging: concepts and applications. J. Magn. Reson. Imaging 13, 534–546.

[4] Melhem E.R., Mori S., Mukundan G., Kraut M.A., Pomper M.G.,van Zijl, P.C., 2002. Diffusion tensor MR imaging of the brain and white matter tractography. AJR Am. J. Roentgenol. 178, 3–16.

[5] Bhuvaneshwari B., Kavitha A., "Assessment of Brain Connectivity Patterns in Progression of Alzheimer's Disease" 2nd International Conference on Biomedical System, Signals and Images, Feb 2016.

[6] Hao Hong, Li Yao, Xiaojie Zhao, "A study of human brain structural connectivity based on diffusion tensor imaging in Alzheimer's disease", Proceedings of 2009 ICME, 1-4.

[7] Xiaoyan K; Shanshan Hong; Tianyu Tang; Qinghai Huang; Bing Zou; Huiguo Li; Yueyue Hang; Zuhong Lu "An Analysis Method of the Fiber Tractography of Corpus Callosum Autism Based on Diffusion Tensor Imaging Data", Proceedings of 2008 ference on Bioinformatics and Biomedical Engineering, IEEE publications, 2409-2413.

[8] Pierpaoli C., Basser P.J., : Towards a quantitative assessment of diffusion anisotropy. Magn Reson Med1996, 36(6):893-906.

[9] Hampel H., Teipel S.J., "Corpus Callosum Atrophy is a Possible indicator of region and Cell Type-Specific Neuronal Degeneration in Alzheimer's Disease ", Arch Neurol. 1998 Feb;55(2):193-8.

[10] Jones BF1, Barnes J et al " Differential Regional Atrophy of the Cingulate Gyrus in Alzheimer Disease: A Volumetric MRI Study", Cereb Cortex. 2006 Dec;16(12):1701-8.

[11] Leemans A1, Jones D.K.., " The B-matrix must be rotated when correcting for subject motion in DTI data ", Magn Reson Med. 2009 Jun;61(6):1336-49.

[12] Djyldyz Sydykova, Robert Stahl, Olaf Dietrich, Michael Ewers,Maximilian F. Reiser, Stefan O. Schoenberg, Hans-Jürgen Möller, Harald Hampel and Stefan J. Teipel. Fiber Connections between the Cerebral Cortex and the Corpus Callosum in Alzheimer's Disease: A Diffusion Tensor Imaging and Voxel-Based Morphometry Study. Cerebral Cortex 2007 17(10):2276-2282

[13] Takahashi S., Yonezawa H., Takahashi J et al, 2002. Selective reduction of diffusion anisotropy in white matter of Alzheimer disease brains measured by 3.0 Tesla magnetic resonance imaging. Neurosci Lett 332(1):45–48

[14] Descoteaux, Deriche R., Knosche T.R., and Anwande A., "Deterministic and probabilistic tractography based on complex fibre orientation distributions," Medical Imaging, IEEE Transactions on, vol. 28(2), 2009, pp. 269-286.

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[15] Leemans A., Jeurissen B., Sijbers J., and Jones D.K., "ExploreDTI: a graphical toolbox for processing, analyzing, and visualizing diffusion MR data" In: 17th Annual Meeting of Intl Soc Mag Reson Med, Hawaii, USA, 2009, pp. 3537.

[16] Braak and Braak E., "Frequency of stages of Alzheimer-related lesions in different age categories," Neurobiol Aging, vol. 18, 1997, pp. 351–357.

[17] Basser P.J., Pajevic S., Pierpaoli C., Duda J., Aldroubi A., 2000. In vivo fiber tractography using DT-MRI data. Magn Reson Med 44, 625-632.

[18] Wedeen V.J., Wang R.P., Schmahmann J.D., Benner T., Tseng W.Y., Dai G., Pandya D.N., Hagmann P., D'Arceuil H., de Crespigny A.J., 2008. Diffusion spectrum magnetic resonance imaging (DSI) tractography of crossing fibers. Neuroimage 41, 1267-1277.

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