

Original Research Article

Evaluation of retinal nerve fiber layer thickness in Alzheimer's disease using optical Coherence tomography

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Abstract: 30 diagnosed cases of Alzheimer's disease (AD) were enrolled in this prospective study done from Apr 2015-Mar 2016. The age range of patients was 67-83 years. All subjects underwent detailed ocular examination. Average peripapillary retinal nerve fiber layer (RNFL) thickness of all patients was measured using Spectralis optical coherence tomography (OCT). These were compared with average RNFL thickness of age matched controls. There was a significant difference between RNFL thickness among two groups ($p < 0.05$). The average RNFL thickness was found to be significantly less in patients compared to controls. Alzheimer's disease being a neurodegenerative disorder may affect retinal ganglion cells too, reducing retinal nerve fiber layer thickness. Further, RNFL thickness may be used as a potential biological marker in diagnosis as well as progression of Alzheimer's disease as OCT provides excellent means of keeping track of RNFL thickness.

Keywords: Alzheimer's disease, Retinal nerve fiber layer, Optical coherence tomography

INTRODUCTION:

Alzheimer's disease (AD), a neurodegenerative disorder is the most common cause of dementia in the elderly. Approximately 10% of all patients over the age of 70 have significant memory loss, and in more than half the cause is Alzheimer's disease [1]. It presents with an insidious onset of memory loss followed by a slowly progressive dementia over several years. The cognitive changes in AD follow a characteristic pattern beginning with memory loss and spreading to language and visuospatial deficit. In mild cognitive impairment (MCI) memory loss falls 1.5 standard deviation below normal on standardized memory tests. MCI is now considered as the prodromal stage of AD. The pathogenesis of neurodegeneration revolves around formation of extracellular senile plaques due to amyloid beta deposition ($A\beta$) and formation of intracellular neurofibrillary tangles (NFTs) due to hyper phosphorylation of tau proteins. The neurodegeneration occurs mostly in medial temporal lobe, lateral temporal cortex and nucleus basalis. Visual disturbances in AD have been well documented and attributed to neurodegeneration in the primary and associative visual cortex [1]. Recent studies have shown that neurodegeneration involves retinal ganglion cells

and their axons in optic nerve. [2-4] Histopathological lesions associated with AD like neuronal loss, beta-amyloid proteins, neurofibrillary tangles, and granulo vacuolar degenerations have not only been found in the brain but also in the neuroretina [4].

Alzheimer's disease is characterized by its slow progression, where neurodegeneration starts several years before full blown clinical manifestations. This provides a window period for early diagnosis during the symptom less period and during the prodromal MCI. However, until recently the diagnosis of Alzheimer's has been only possible after symptomatic onset and it has been largely a diagnosis of exclusion. Early diagnosis of Alzheimer's has been a challenge.

So far the diagnosis of Alzheimer's has been on basis of symptoms, neuroimaging studies, CSF evaluation. Neuroimaging studies like CT and MRI show no specific changes especially in the early disease. Functional imaging studies show hypo perfusion or hypo metabolism in the posterior temporo-parietal lobes. The EEG in AD is normal and shows no specific slowing. CSF examination is invasive and shows a

reduced level of A β and increased levels of hyperphosphorylated tau proteins. However, there is considerable overlap of these values with that of normal population, and hence CSF examination too is a non-specific diagnostic tool. A recent tool is blood apo E genotyping, apo E4 allele of apo E gene on chromosome 19 confers increased risk for AD. Despite these diagnostic modalities, only a high probability of AD can be established [1].

Recently, eye has been shown to provide a window of opportunity for early diagnosis. The retina being in continuation with the central nervous system both anatomically and embryologically shows neurodegenerative changes in the ganglion cells and nerve fiber layer which if detected can provide a diagnostic modality for Alzheimer's disease. In the past two decades, several studies have searched for in vivo evidence of retinal involvement in AD. Optical coherence tomography (OCT), is one such sophisticated non-invasive imaging study which can assess morphological changes in retina in AD [5]. The OCT technique for the measurement of peripapillary RNFL has been proven useful for the detection of significant reduced retinal thickness in patients of AD.

AIM OF STUDY:

To evaluate retinal nerve fiber layer (RNFL) thickness in Alzheimer's disease using Spectral is optical coherence tomography (OCT).

MATERIALS AND METHODS:

This is a prospective study which included right eyes of 30 diagnosed cases of AD, meeting the inclusion criteria in the age group of 67-83 years, in the time period of April 2015- March 2016. The diagnosis of AD was made on basis of MRI findings and minimal state examination (MMSE). The control group

consisted of right eyes of 30 patients visiting the outdoor for routine eye examination, mainly for refractive errors.

Inclusion criteria:

- Patients diagnosed with Alzheimer's disease by MRI findings and MMSE.
- Best corrected visual acuity of 20/40 or better.

Exclusion criteria:

- Patients with other known disease affecting the optic nerve like glaucoma, AION, MS etc.
- Patients with unclear media like those with dense cataract.
- Patients with optic disc anomalies.
- Patients with history of IOP elevations.

Both cases and controls underwent detailed ocular examination, including measurement of best corrected visual acuity, slit lamp examination, IOP measurement by applanation tonometry, central corneal thickness and fundoscopy. All subjects underwent OCT scanning using commercially available equipment (Spectralis OCT, Heidelberg Engineering) and an ophthalmic evaluation on the same day. The peripapillary RNFL thickness of all subjects were measured. Only those images with good quality were included.

RESULTS:

The age difference between two groups was not statistically significant ($p=0.74$). The average RNFL thickness in Alzheimer's disease patients was found to be $111.9 \pm 8.25 \mu\text{m}$ while it was 117.97 ± 9.29 in control group. Using unpaired, Student's t-test, the average RNFL thickness in AD patients was found to be significantly less than in controls ($p < 0.01$).

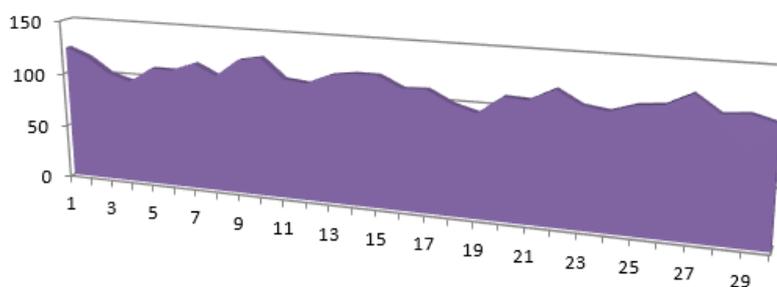


Fig-1: Avg. RNFL thickness (μm) in patients with AD

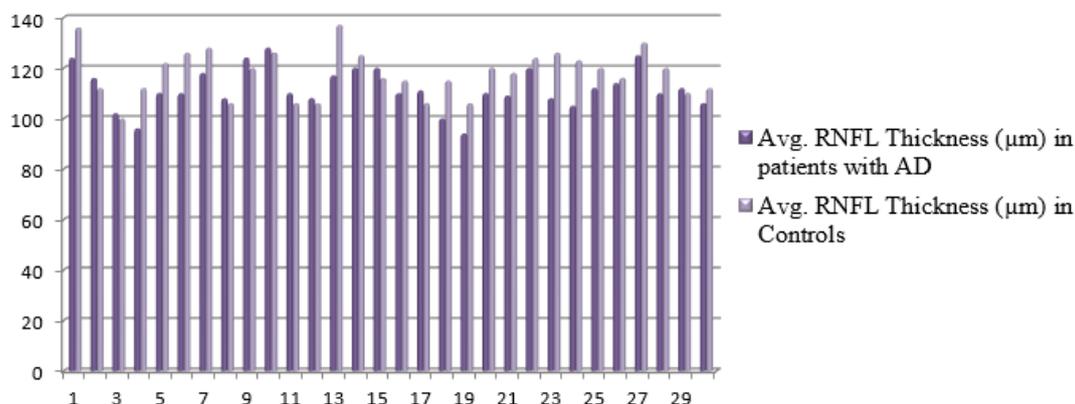


Fig-2: Comparison of average RNFL thickness in two groups

DISCUSSION:

In this study, RNFL thickness in a group of 30 Alzheimer's disease patients was evaluated using Spectral is OCT and compared with age matched controls. The average RNFL thickness in Alzheimer's disease patients was found to be significantly less than that of the control group ($p < 0.01$). Coppola *et al.*; [3] in their meta-analysis report have supported the important role of OCT for RNFL analysis in monitoring the progression of AD. Cunha *et al.*; [2] reported decreased peripapillary RNFL thickness measurements, suggesting that a diffuse axonal degeneration occurs in AD patients. Salobar-Garcia *et al.*; [6] reported peripapillary RNFL thickness did not statistically differ in comparison to control eyes, the increase in peripapillary thickness in mild-AD patients.

CONCLUSION:

The average RNFL thickness was found to be significantly less in patients of Alzheimer's disease compared to controls and hence RNFL measurement by OCT can be used as an early and important tool to aid the diagnosis of Alzheimer's disease. Additionally, RNFL thickness changes can be used to monitor progression of Alzheimer's disease.

REFERENCES:

1. Seeley W, Miller BL. Alzheimer's disease and other dementias. In: Kasper DL, Braunwald E, Fauci AS, et al., eds. Harrison's Principles of Internal Medicine. 19th Ed. New York: McGraw-Hill; April 2015.
2. Cunha LP, Lopes LC, Costa-Cunha LV, Costa CF, Pires LA, Almeida AL, Monteiro ML. Macular Thickness Measurements with Frequency Domain-OCT for Quantification of Retinal Neural Loss and its Correlation with Cognitive Impairment in

- Alzheimer's Disease. PloS one. 2016 Apr 22; 11(4):e0153830.
3. Coppola G, Renzo AD, Ziccardi L, Martelli F, Fadda A, Manni G, Parisi V. Optical coherence tomography in Alzheimer's disease: A meta-analysis. PLoS One, 2015; 10(8)
4. Jones-Odeh E, Hammond CJ. How strong is the relationship between glaucoma, the retinal nerve fibre layer, and neurodegenerative diseases such as Alzheimer's disease and multiple sclerosis? Eye. 2015 Sep 4.
5. Kanamori AK, Escano MF, Eno A, Nakamura M, Maeda H, Seya R, Ishibashi K, Negi A. Evaluation of the effect of aging on retinal nerve fiber layer thickness measured by optical coherence tomography. Ophthalmologica. 2003 Jun 17; 217(4):273-8.
6. Salobar-Garcia E, Hoyas I, Leal M, de Hoz R, Rojas B, Ramirez AI, Salazar JJ, Yubero R, Gil P, Triviño A, Ramirez JM. Analysis of retinal peripapillary segmentation in early Alzheimer's disease patients. Biomed research international. 2015 Oct 18; 2015.