Review Article

Role of OCT in Diagnosis and Progression of Glaucoma

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Optical Coherence Tomography (OCT) has become a common tool in ophthalmic community for imaging of optic nerve head and macula. In glaucoma, it is of utmost importance in early diagnosis and monitoring the progression of the disease. Measurement of peri-papillary RNFL thickness is a common method of diagnosing and monitoring glaucoma. Recently Ganglion Cell Complex (GCC) analysis of macula has also shown to be helpful in identification of early glaucoma and coincides with RNFL damage. OCT can identify the structural damage in eyes before visual field defects occurs. High myopia with large discs, tilting and peri-papillary crescents and occasional hypoplasia of optic disc makes diagnosis of glaucoma difficult. It may be helpful in these patients to map ganglion cell complex (GCC) rather than relying on RNFL thickness. In advanced glaucoma when RNFL thickness level decreases to below 40 – 50 µm, the OCT will be of not much value to record any progression. This is termed as floor effect. OCT has now become commonly available in all parts of the country and is frequently used to determine RNFL and macular thickness in suspected or established cases of glaucoma. It not only helps in diagnosis and progression of the disease but helps us to make the patient being aware of the disease. However, we clinicians should also be aware of various artifacts related to acquisition of scans by our technicians, disease itself and related to the scanner. We must realize the limitation of comparative normative database incorporated in various scanners and that not every RNFL thinning is due to glaucoma.

Key Words: Optical coherence tomography, optic nerve head, macula.

Glaucoma is the leading cause of blindness worldwide[1,2]. In Pakistan, it is third cause of blindness accounting for 7.1% cases[3]. According to Quigly, 58 million people will have primary open angle glaucoma (POAG) by the year 2020, out of which 10% will be bilaterally blind[4].As glaucoma causes irreversible damage to the vision, it is important to detect it at an early stage before significant visual loss occurs. The measurement of intraocular pressure (IOP) is a poor screening tool in the diagnosis of glaucoma as mean IOP in Early Manifest Glaucoma Trial[5] (EMGT) and United Kingdom Glaucoma Treatment Study Group[6] (UK-GTS) was found around 20 mm Hg. The one off measurement of IOP of < 21 mm Hg in our office or clinic does not exclude possibility of glaucoma. In ocular hypertension treatment study[7] (OHTS), most patients who developed glaucoma from ocular hypertension showed changes in the optic disc. In general, structural changes appear earlier than any change in the visual field. The visual field loss occurs after at least 30% - 40% retinal ganglion cells are damaged[8].

Optical Coherence Tomography (OCT) is an optical imaging technique providing high-resolution cross-sectional imaging of retina using near infrared light (840 nm). It uses the principles of low coherence interferometry using light echoes from the scanned structures to determine the thickness of the tissue[9].

OCT detects optic nerve head changes with Retinal Nerve Fiber Layer (RNFL) thinning due to the

loss of ganglion cells at macula. It compares thickness of RNFL between hemispheres of the same eye and between two eyes to determine any asymmetry, which is the hallmark of glaucoma. It measures the thickness of neuro-retinal rim, the inner retinal layer and ganglion cells complex at macula. The thickness of various parameters is then compared to a normative database to determine if the patient falls into abnormal or borderline category. As segmentation algorithms in different scanners are mutually exclusive and are not comparable, so long-term assessment of patients, need to be with the same OCT scanner.

OCT and its use in the measurement of peri-papillary RNFL thickness is a common method of diagnosing and monitoring glaucoma. Recently Ganglion Cell Complex (GCC) analysis of macula has also shown to be helpful in identification of early glaucoma and coincides with RNFL damage[10]. Some studies have evaluated a combined structural index based on peri-papillary RNFL, the macular ganglion cell complex and the optic disc and found it superior and more sensitive in detecting glaucoma, when compared to the individual parameters[11]. OCT can identify the structural damage in eyes before visual field defects occurs. Wollstein and Co-workers determined the RNFL thickness associated with structural changes corresponding with visual field defects. Their study revealed that substantial structural loss of approximately 17% appeared necessary for functional loss to be detectable using the current testing methods on Humphrey Visual Field Analyzer[12].

The recent advent of spectral-domain OCT (SD-OCT) with 40,000 scans per second has reduced scan acquisition time, enhanced resolution and improved layer segmentation. Leung et al[13] found RNFL measurement using SD-OCT with sensitivity of 91.6% and specificity of 87.6% in pre-perimetric glaucoma, while Leite et al[14] found RNFL measurement using SD-OCT in early disease with sensitivity of 82% and specificity of 85%.

High myopia with large discs, tilting and peri-papillary crescents and occasional hypoplasia of optic disc makes diagnosis of glaucoma difficult. It may be helpful in these patients to map ganglion cell complex (GCC) rather than relying on RNFL thickness. Shoji and colleagues[15] analyzed 51 patients with high myopia and associated perimetric glaucoma. They performed ganglion cell complex (GCC) and circumpapillary RNFL analysis using SD – OCT machine. Their conclusion was that GCC measurement offered best parameters for the clinical diagnosis of glaucoma in these patients.

Cvenkel & Kontestabile[16] measured RNFL thickness with SD-OCT in patients with glaucoma to evaluate the correlation between visual field parameters and RNFL thickness & found decreased mean RNFL thickness in eyes with pre-perimetric glaucoma & perimetric glaucoma when compared to healthy control group suggesting the usefulness of the technology.

Koh and Co-workers[17]assessed the repeatability of measuring optic nerve head parameters in relation to the head tilt using Cirrus SD-OCT and found that the optic nerve head parameters maintaining good repeatability despite head tilt to 30 degrees on the either side. The SD-OCT machine has inbuilt software to control for head tilt and eye tracking. In the absence of this software to control head tilt, significant artifacts can occur with even 8 degrees of head tilt[18].

The effect of improper scan alignment on RNFL thickness measurement has been studied and it has been found that the average RNFL thickness is greater when scans are displaced temporally. The para-papillary scan misalignment is characterized by an increase in RNFL thickness in the quadrants in which scan is closer to the disc and significant decrease in RNFL thickness in the quadrant in which scan is displaced further from the disc[19] (Figure A).

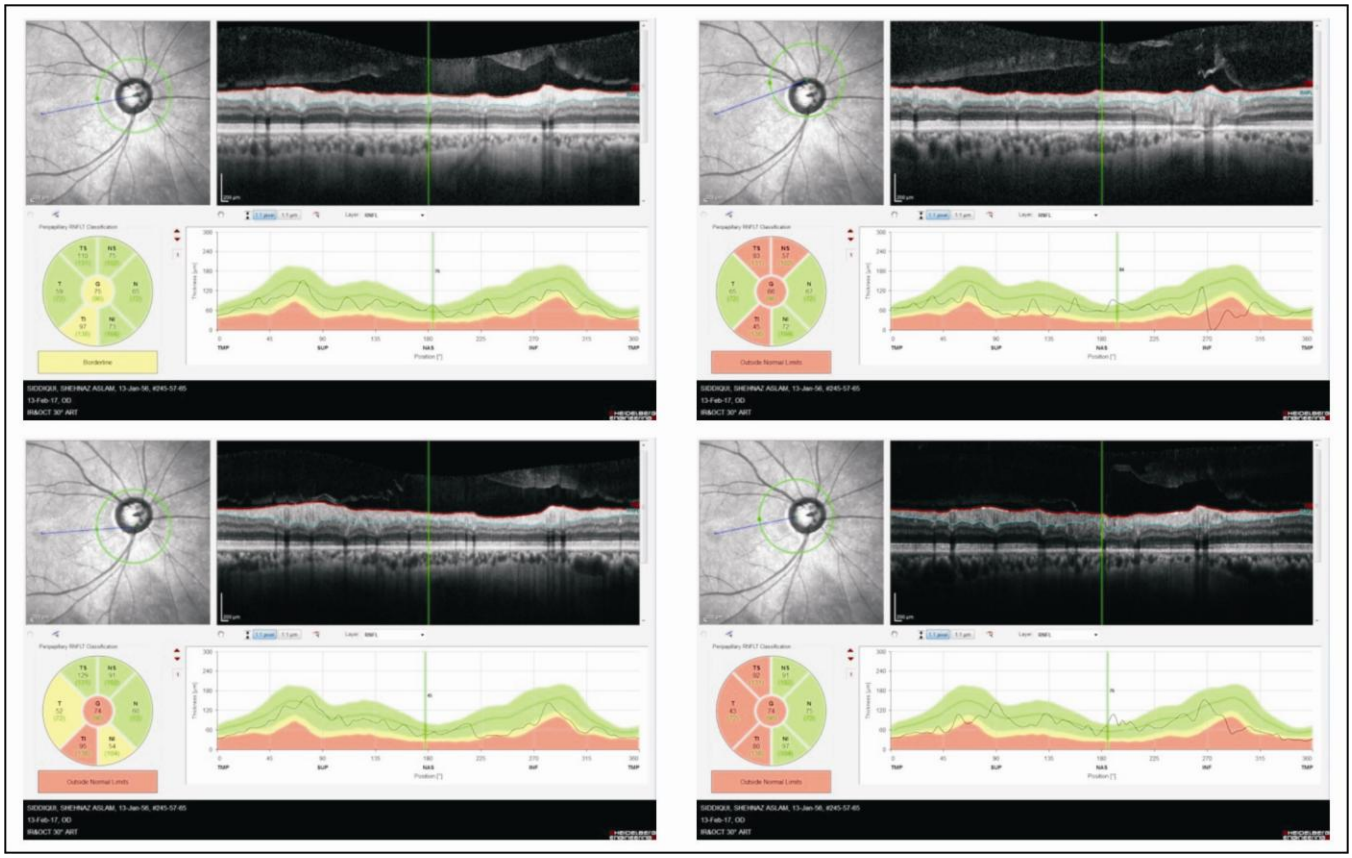

Fig. A: Effect of improper scan alignment on RNFL thickness.

The presence of lens opacities and posterior vitreous detachment (PVD) can cause significant underestimation of RNFL measurement and in some machines, it is important to dilate the pupil[20].

Axial length of the eyeball has shown to influence the OCT measurement of RNFL thickness and optic nerve parameter. The longer the eye the thinner the RNFL measurement[21].

The signal strength should always be noted when assessing the quality of the scan. This is variable in different OCT scanners. For Cirrus scan (Carl Zeiss – Meditec CA), it is reported on scale of 0 – 10 and is defined as the average intensity value of signal pixels in the OCT image. The best quality scan should have signal strength of ≥ 7. For RTVue (Fremont – CA) scanner and Topcon (3D OCT – 100 – Japan), the signal strength range is 0 – 100 and a good quality scan strength should be at least > 40. For Heidelberg (Germany) scanner, the range of signal strength is 0 – 40 with good quality scan at signal strength of > 20. The lower signal strength can occur due to presence of corneal opacity, lens opacity and PVD resulting in artificial thinning of RNFL.

In a series of 277 patients with glaucoma, Asrani found 37 patients (28.2%) had imaging artifacts having macular thickness scan and with RNFL scans, 55 patients (19.9%) had artifacts. The most common cause of artifacts in both types of scans was presence of epi-retinal membrane[22]. The scanner in these cases recognizes the epi-retinal membrane as RNFL and calculates its thickness erroneously. It is important therefore to look at the raw data and recognize the presence of epi-retinal membrane. In new generation of SD-OCT, scanner can deduct the thickness of epi-retinal membrane and can calculate the true RNFL thickness. By looking only at one sheet of RNFL analysis, the observer can misdiagnose the RNFL thickness. For this reason, it is also important to look at macular scan when performing RNFL analysis to exclude disease such as epi-retinal membrane (ERM), Vitreo-macular traction (VMT) and presence of any other macular pathology resulting in scar formation as this will influence the thickness of RNFL (Figure B).

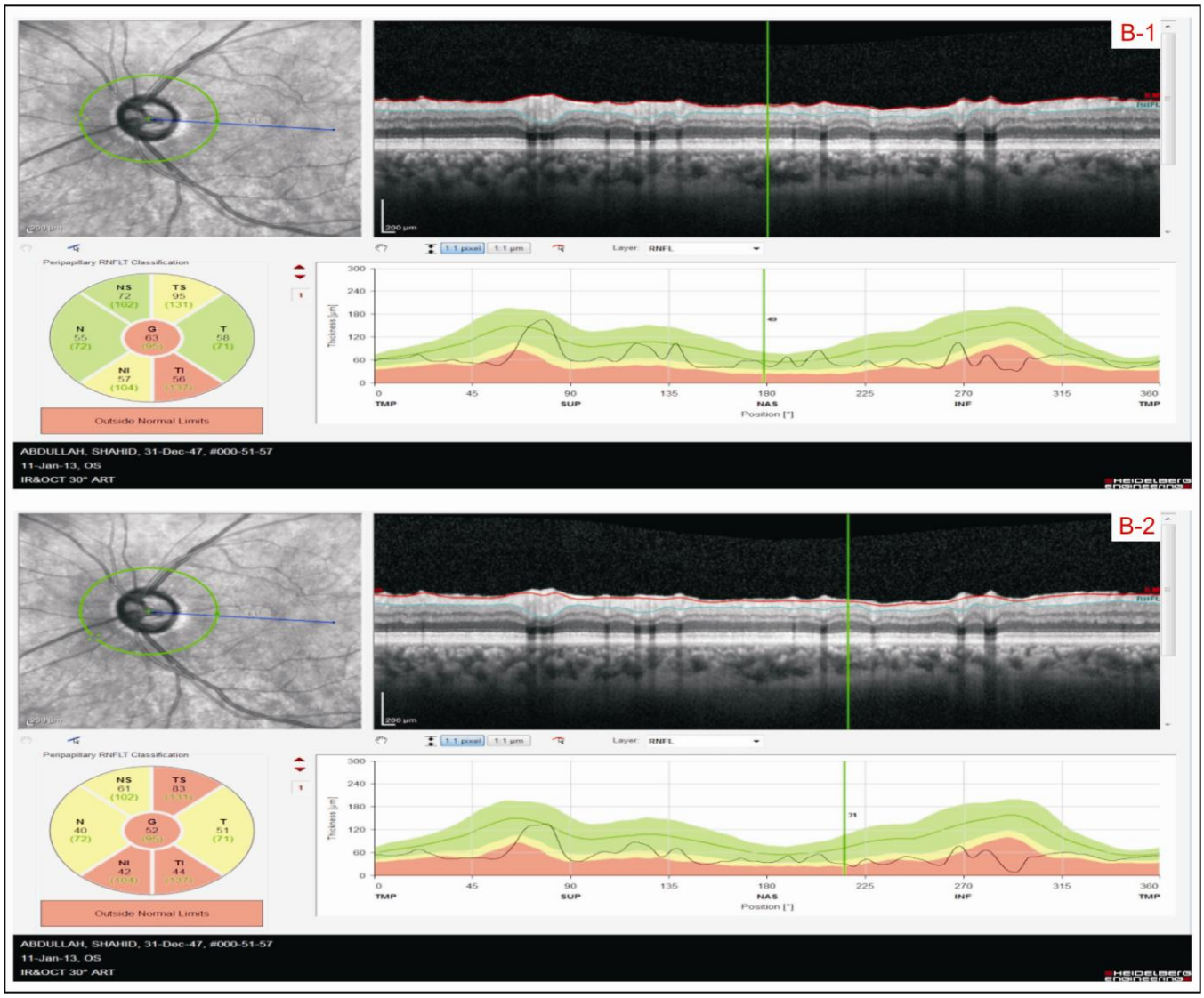

Fig. B1: RNFL Left eye with Epiretinal membrane.
B2: RNFL Left eye with Epiretinal membrane adjusted.

Ghazi and Much studied a series of 13 eyes in whom repeated attempts at OCT imaging failed to yield a good quality scan despite the absence of significant media opacity and inadequate pupil dilatation. Corneal lubricants achieved a significant improvement in OCT image quality from 4.35 to 6.2 on Cirrus machine[23].

In advanced glaucoma when RNFL thickness level decreases to below 40 – 50 µm, the OCT will be of not much value to record any progression. This is termed as floor effect.

The normative database in most scanners is based on 300 – 400 patients with average age of 15 – 78 years and they do not necessarily have patients with extreme refractive errors, young children and people from different races. Due to relatively small normative database, RNFL measurement may be flagged in patients who are not represented in the database. One common example is the patient of glaucoma with high myopic error as high myopes are not included in the normative database. As myopic eyes have already thin RNFL, this can be interpreted as having RNFL thinning due to the disease process. The limitation of normative database can affect the utility of OCT scanner in diagnosing glaucoma in certain cases. It is therefore advised to take serial OCT scans in these cases to judge glaucomatous progression by setting a

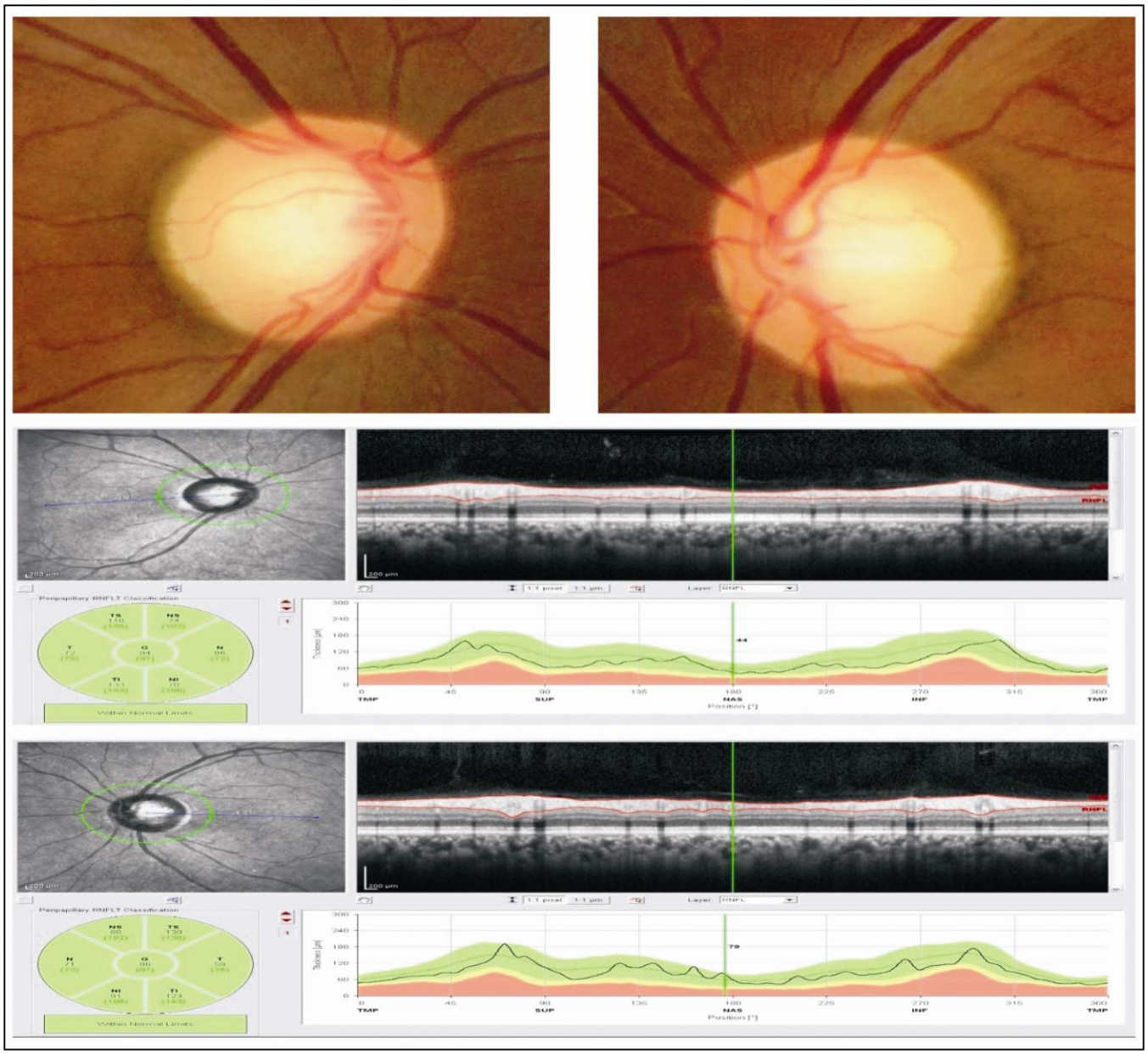

Fig. 1: Optic disc showing cup disc ratio of 0.5 – 0.6 in both eyes. RNFL analysis is within normal limits.

baseline scan against which subsequent scans can be compared for RNFL thinning. Thus, each patient can act as his or her own normative database to diagnosis glaucoma and its progression. In this situation the clinician should be aware that RNFL thickness decreases with age which is estimated to be about 0.52 – 1.35 µm per year[24].

Clinical interpretation errors also include failure to recognize Compressive optic neuropathies (pituitary tumors) ischemic optic neuropathies, retinal vein occlusions & toxic optic neuropathies (methanol poisoning)[25] which can damage the optic nerve and show changes in RNFL analysis and macular scan.

Chen and Kardon have advised a systematic approach for acquisition and interpretation of OCT[26]. Some tips for better acquisition are, reducing room light in case of undilated pupil, the forehead of the patient has to be in constant touch with the headband and reminding patients to blink before scan is taken. Confirm the name and age of the patient, check the signal strength, check refractive error and if available axial eye length. Compare the fundus image and

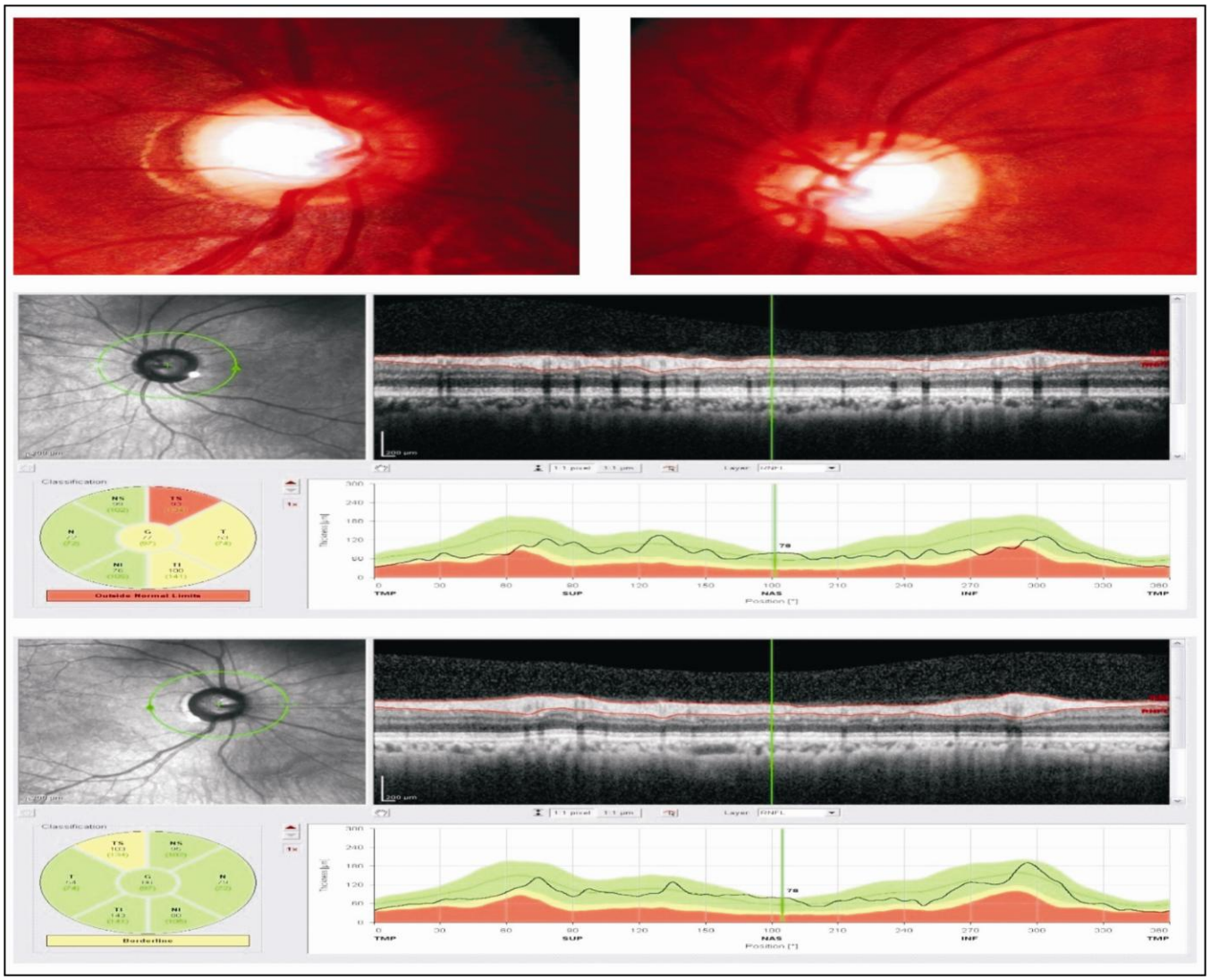

Fig. 2: Optic disc on left side shows couple of splinter hemorrhages superiorly with corresponding RNFL thinning.

thickness map to check that the border and cup identification by OCT corresponds to clinical estimation. Examine TSNIT RNFL plot to ensure its peak corresponds to the peak from the normative database.

CLINICAL CASES

Patient 1: (Figure 1)

A 39 year old male was referred for evaluation of his glaucoma. He had been using topical Latanoprost with the diagnosis of POAG. His best-corrected vision was 6/6 in both eyes. His central corneal thickness was 537 and 536 µm in either eye with IOP of 14 mmHg in both eyes. His fundi showed cup to disc ratio of 0.5 – 0.6 with good neuro retinal rim thickness. His OCT (figure 1) showed normal RNFL thickness chart and full visual fields. Patient's Latanoprost was discontinued and his IOPs were checked after 4 weeks (washout period of Latanoprost) and were still found at 13 mmHg in both eyes (Mean at 9 am & 4 pm). He has been followed up for last couple of years with no further change in his IOPs and RNFL thickness.

Patient 2: (Figure 2)

A 40 years old female was referred for painless decrease in vision in her left eye. She did not have any co-morbids. Her best-corrected visual acuity was 6/6 in right eye (unaided) and 6/9 (- 0.75/-1.50 × 140) in

his left eye. Her anterior segments were unremarkable. The IOP was 12 mm Hg in right eye and 14 mm Hg in left eye (at 10:00 am). Her CCT were on thin side measuring 486 µm in right eye and 492 µm in the left eye. The angles were open on Gonioscopy. The fundus showed cup to disc ratio of 0.6 – 0.7 in both eyes but there was some splinter hemorrhages seen near the disc margin superiorly in the left eye. Her IOPs were phased and they increased to 25 mm Hg in her either eye at 5:00 pm. The RNFL on OCT in right eye was normal but left eye showed thinning in superior-temporal quadrants. Her visual fields were full on Humphrey's field analyzer. Due to her thin corneas, her adjusted IOP would have been + 4 mmHg and as her IOP were recorded at 25 mmHg in afternoon, she was diagnosed has having pre-perimetirc glaucoma.

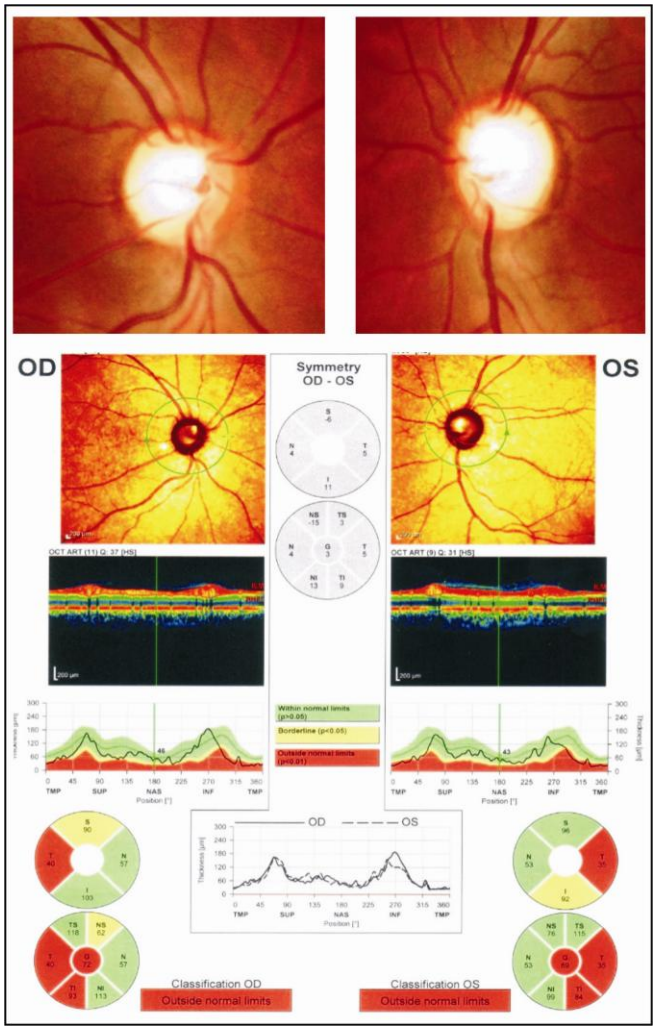

Fig. 3: Neuroretinal rim thinning in both eyes with corresponding changes on RNFL analysis.

Patient 3: (Figure 3)

A 26 years old female with family history of glaucoma was reviewed for glaucoma evaluation. Her best corrected visual acuity was 6/6 (unaided) in both eyes. The IOPs were recorded 10 mm Hg in morning and remained same throughout the day on phasing. Her CCT were 519 µm in both both eyes. The anterior chamber angles were wide open and fundus examination showed optic disc cupping in both eyes with thin neuro-rims. The RNFL analysis on OCT showed thinning in her both eyes though her fields of vision were normal. She was diagnosed with normal tension glaucoma. She had carotid Doppler and MRI scan of brain, which were within the normal limits.

Patient 4: (Figure 4 A & B)

A 44 years old woman with positive family history of glaucoma came for regular eye examination. Her visual acuity was 6/7.5 in either eye. Her IOPs were 25 mm Hg in right eye and 26 mm Hg in left eye. She was already on full anti-glaucoma medical treatment comprising of Latanoprost at night, Dorzolamide/ Timolol combination and Brimonidine eye drops, both twice a day in her each eye. Her fundi showed 0.6 – 0.7 cup-disc ratio. OCT revealed RNFL thinning throughout her follow-up with her fields of vision staying within normal limits. This case elegantly illustrates the role of OCT in progression of early glaucoma.

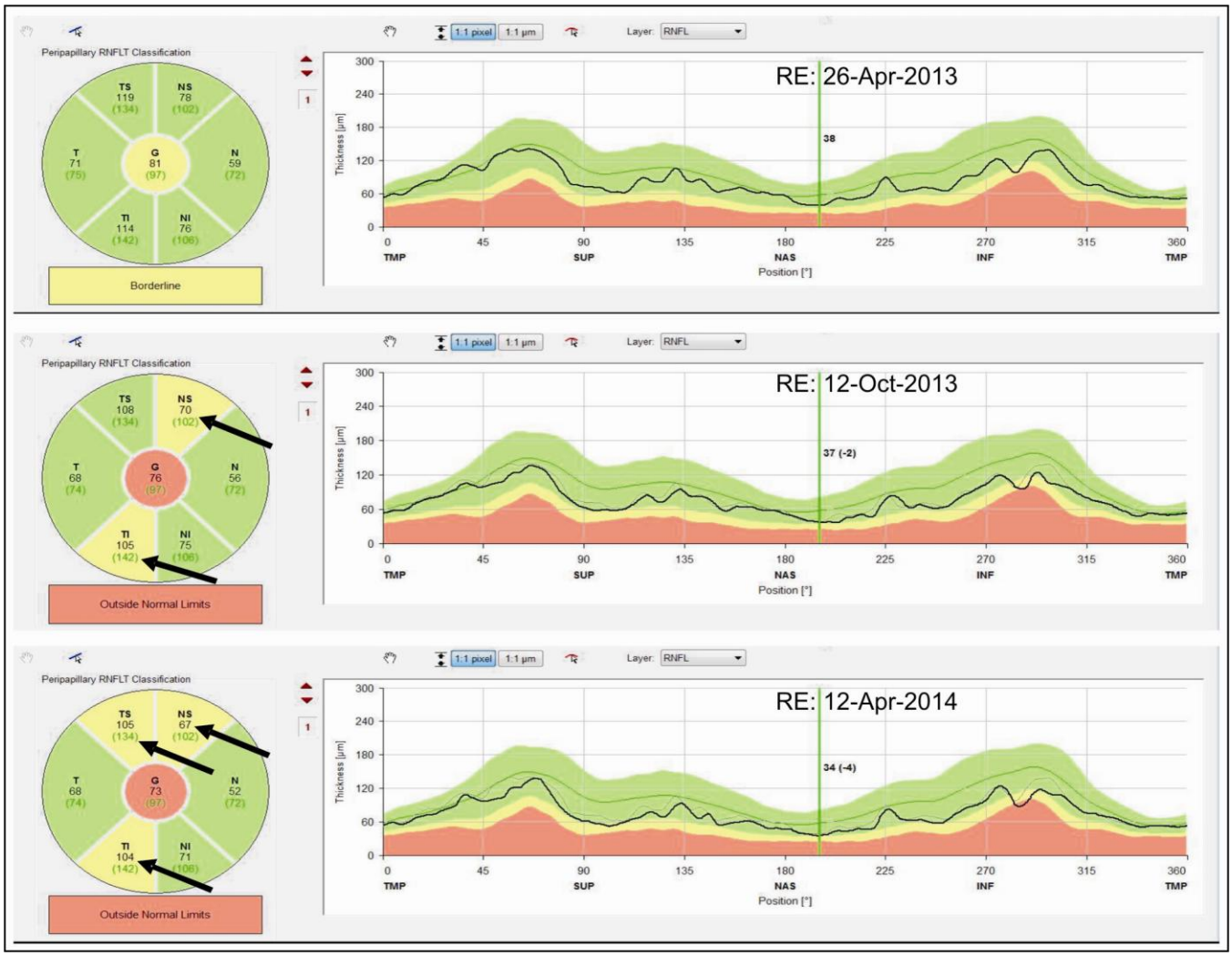

Fig. 4A: Progression of RNFL thinning in right eye.

Fig. 4B: Progression of RNFL thinning in left eye.

Next two cases demonstrate that not every RNFL thinning on OCT examination is because of glaucoma

Patient 5:(Figure 5 A & B)

A 27 years old physician complained of inability to appreciate the inferior part of his visual field in his left eye for last couple of years. He had MRI brain to rule out any space occupying lesion and was found within normal limits. He did not have any other significant medical and surgical history. He was diagnosed somewhere else as having glaucoma and was using combined Dorzolamide/Timolol drops in his left eye. His visual acuity was 6/6 with – 2.00 DS in his both eyes. IOPs measured 16 mm Hg in either eye with anterior chamber angles open and CCT of 550 µm in both eyes. The fundus examination showed his right optic disc with cup disc ratio of 0.1 while the left optic disc had no visible cup with blurred margins. The RNFL analysis was normal in right eye while showed severe thinning in the left eye. His visual field was normal/full on right side but showed arcuate type of scotoma inferiorly on the left side. His clinical diagnosis was apparent to us that he had optic nerve drusen on left side responsible for RNFL thinning and changes in the visual field. The treating physician only looked at patient's OCT and visual field and made the diagnosis of glaucoma without considering the appearance of his left optic disc.

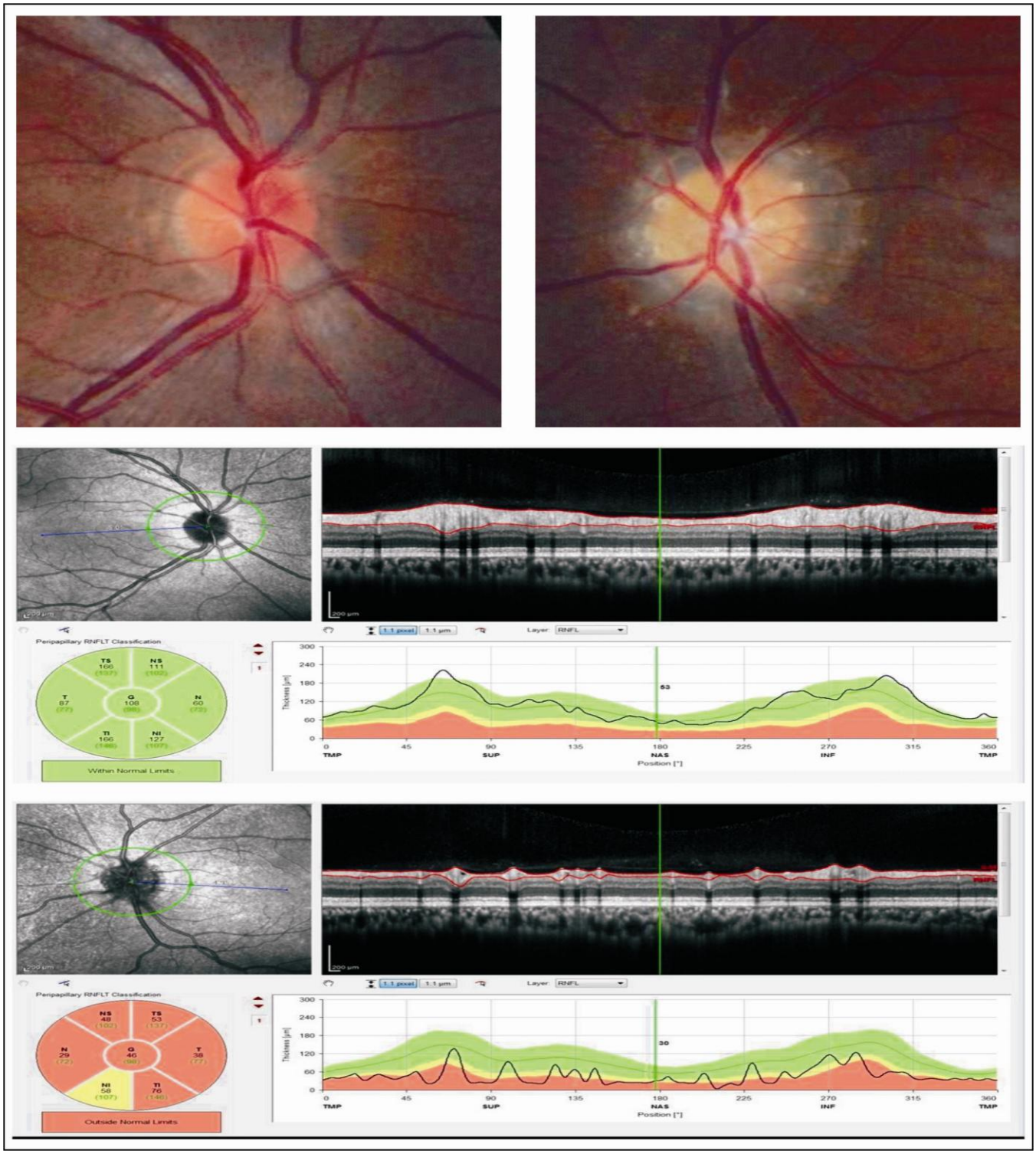

Fig. 5A: Left optic disc drusen with thinning of RNFL in left eye.

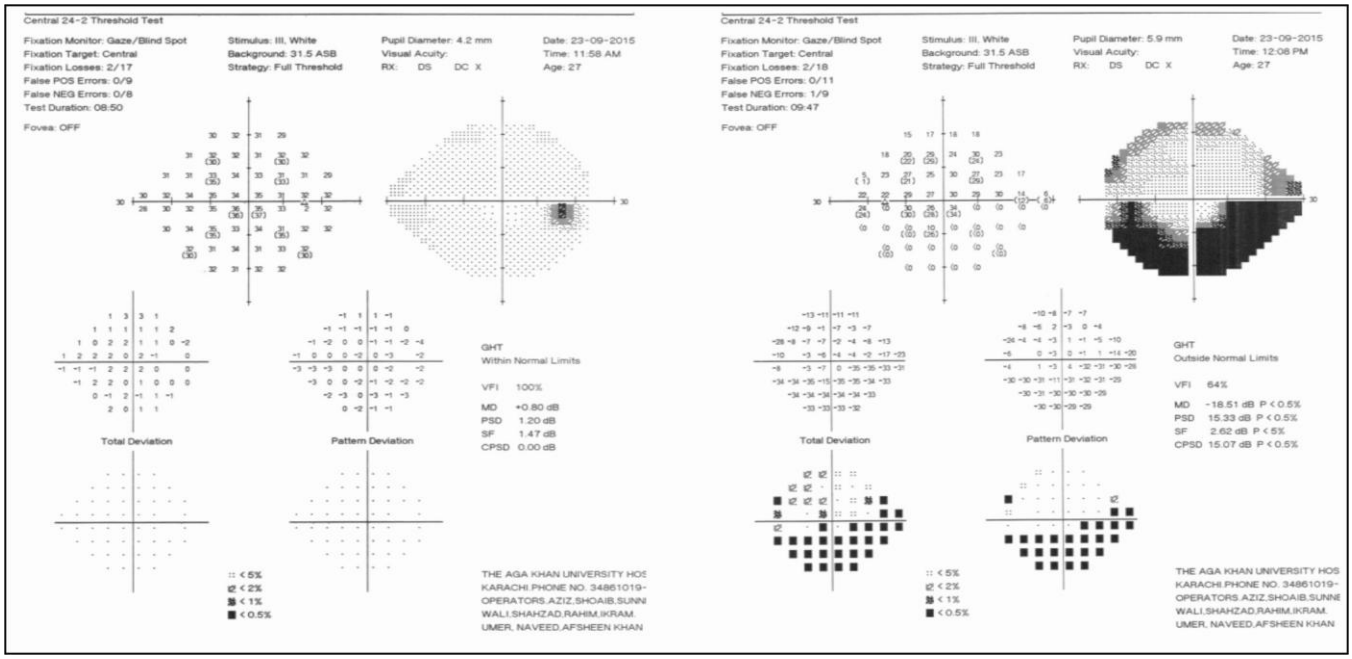

Fig. 5B: Left visual field demonstrating inferior arcuate scotoma.

Patient 6: (Figure 6)

A 43 years old female was referred for assessment of her glaucoma. She had been using Timolol/ Dorzolamide eye drops and Latanoprost in her both eyes for last 1 year. Her best corrected vision was 6/6 in her both eyes with small correction. Her IOPs were 13 mm Hg in her both eyes with angles open and central corneal thickness of 500 µm in right eye and 495 µm in the left eye. Her cup to disc ratio were 0.4 in either eyes with healthy looking neuroretinal rim. Her OCT showed RNFL thinning in both eyes temporally with visual fields demonstrating temporal defects. MRI revealed presence of pituitary macroadenoma. Her glaucoma drops were discontinued and she was referred for neuro-surgical opinion.

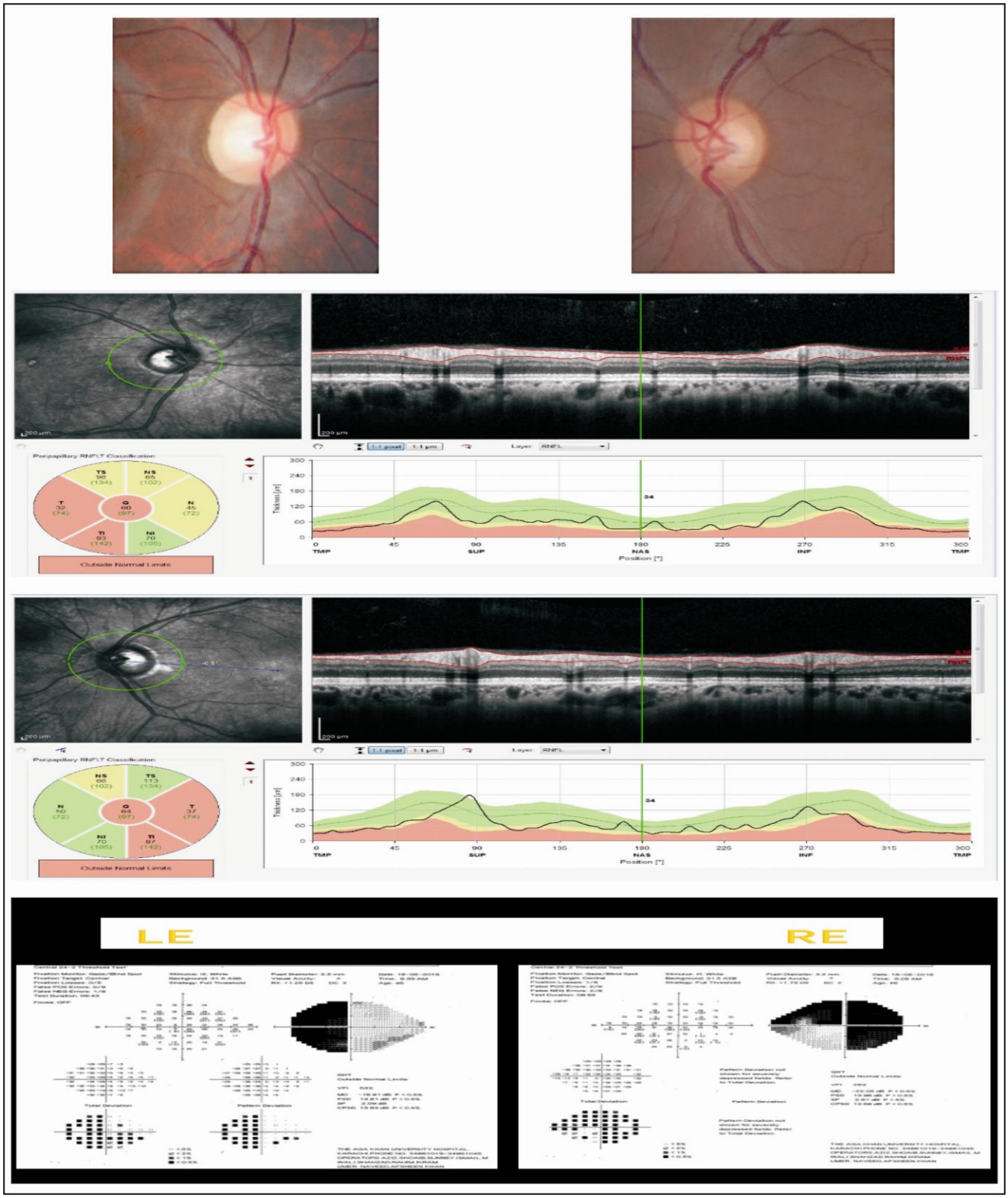

Fig. 6: Patient with bitemporal hemianopia with corresponding changes on RNFL analysis. MRI confirmed presence of pituitary macroadenoma

CONCLUSION

OCT has now become commonly available in all parts of the country and is frequently used to determine RNFL and macular thickness in suspected or established cases of glaucoma. It not only helps in diagnosis and progression of the disease but helps us to make the patient being aware of the disease. However, we clinicians should also be aware of various artifacts related to acquisition of scans by our technicians, disease itself and related to the scanner. We must realize the limitation of comparative normative database incorporated in various scanners and that not every RNFL thinning is due to glaucoma.

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