GNZ 2024 CME Cases and MCQs

Case: Non-Arteritic Anterior Ischemic Optic Neuropathy (NAION)

Learning outcomes

- To understand the definition and pathophysiology of non-arteritic anterior ischaemic optic neuropathy (NAION)
- To recognise the clinical presentation of NAION
- To identify the risk factors associated with NAION
- To understand the management options for NAION

History

A 49 year-old Caucasian male presents to your practice reporting a 3 week history of right eye reduced vision. He tells you that he woke up 3 weeks ago with blurred vision in his right eye and is worried because it has not improved. He has no other ocular complaints. He denies any eye pain, redness, or discharge. He also denies any headaches, scalp tenderness, or pain on chewing. He has no recent unexplained weight loss.

Previous ocular history: Left eye patching as a child
Previous medical history: High cholesterol, borderline hypertension, concussion in 2011
Current medications: Statin, Fluoxetine
Family history: Nil
Smoking history: Ex-smoker

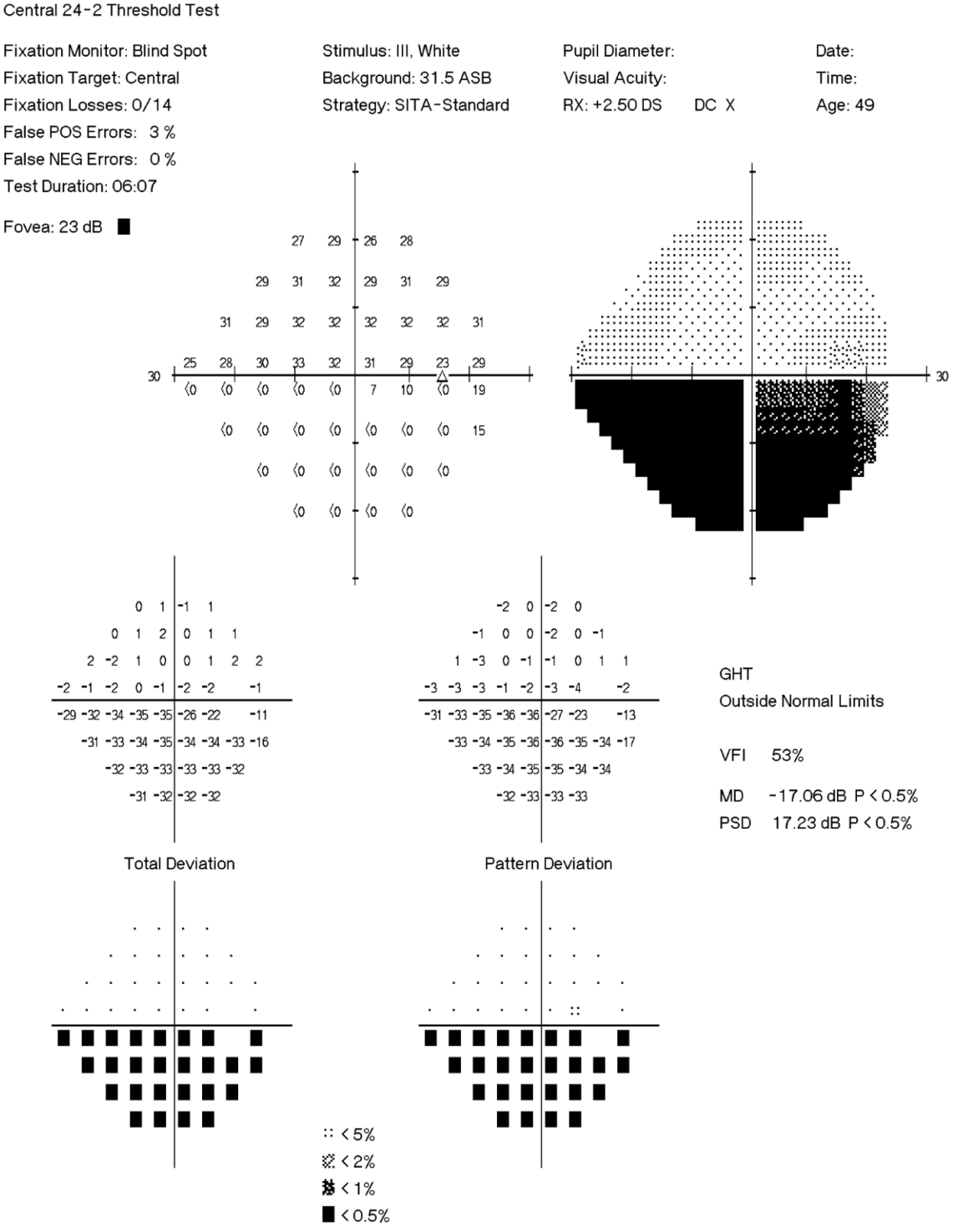
Examination

Examination findings on presentation shown below.

	Right eye	Left eye
Best corrected visual acuity	6/24	6/7.5-2
Subjective refraction	+0.75 / -0.50 x 24	+0.75 / -0.75 x 173
Goldmann tonometry	15 mmHg	14 mmHg
Gonioscopy	Open	Open
Pachymetry	586 µm	597 µm
Extraocular eye movements	Full range No pain, no diplopia	Full range No pain, no diplopia
Ishihara	12/14 (Slow)	14 / 14
Pupils	R RAPD	
Anterior segment	Early lens opacification, otherwise unremarkable	Early lens opacification, otherwise unremarkable
Fundus examination	Swollen optic nerve Macular clear Peripheral retina clear and flat	Small congenitally anomalous optic disc No haemorrhages Macular clear Peripheral retina clear and flat
Visual fields	See visual fields (Figure 1)	
OCT	See RNFL analysis (Figure 2) and GCC scan (Figure 3)	

Figure 1: Visual fields

Right eye

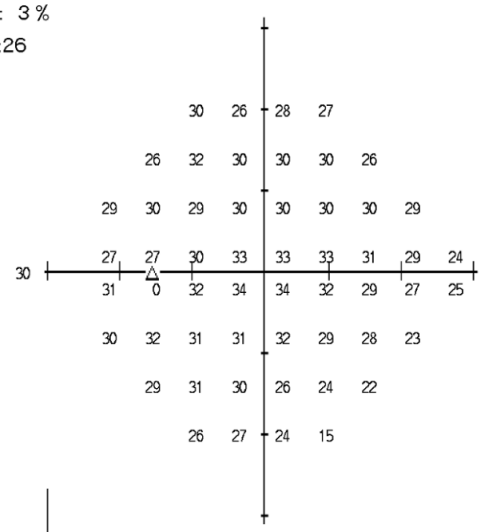


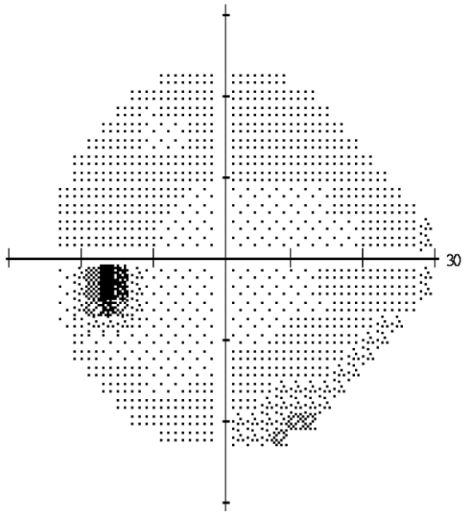
Left eye

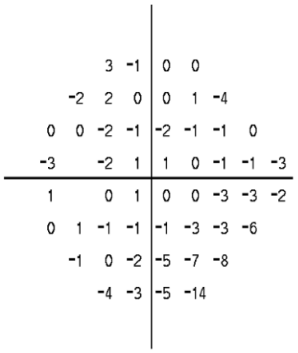
Central 24-2 Threshold Test

Fixation Monitor: Gaze/Blind Spot	Stimulus: III, White	Pupil Diameter:	Date:
Fixation Target: Central	Background: 31.5 ASB	Visual Acuity:	Time:
Fixation Losses: 0/14	Strategy: SITA-Standard	RX: +2.50 DS DC X	Age: 49
False POS Errors: 3 %			
False NEG Errors: 3 %			
Test Duration: 04:26			

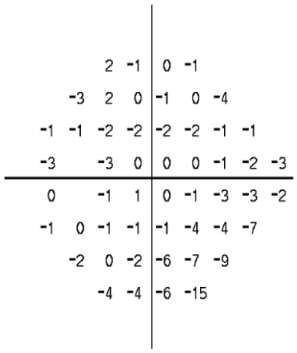
Fovea: 36 dB







Total Deviation



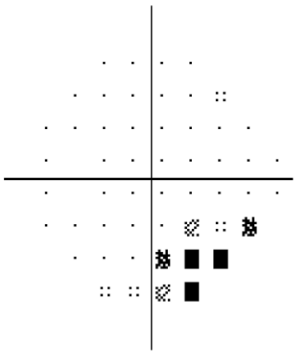
Pattern Deviation

GHT
Outside Normal Limits

VFI 97%

MD -1.68 dB P < 10%

PSD 2.89 dB P < 2%



:: < 5%
▨ < 2%
▩ < 1%
■ < 0.5%

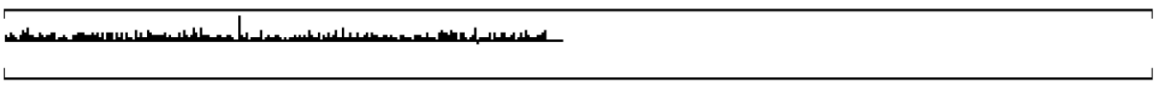


Figure 2: RNFL thickness analysis

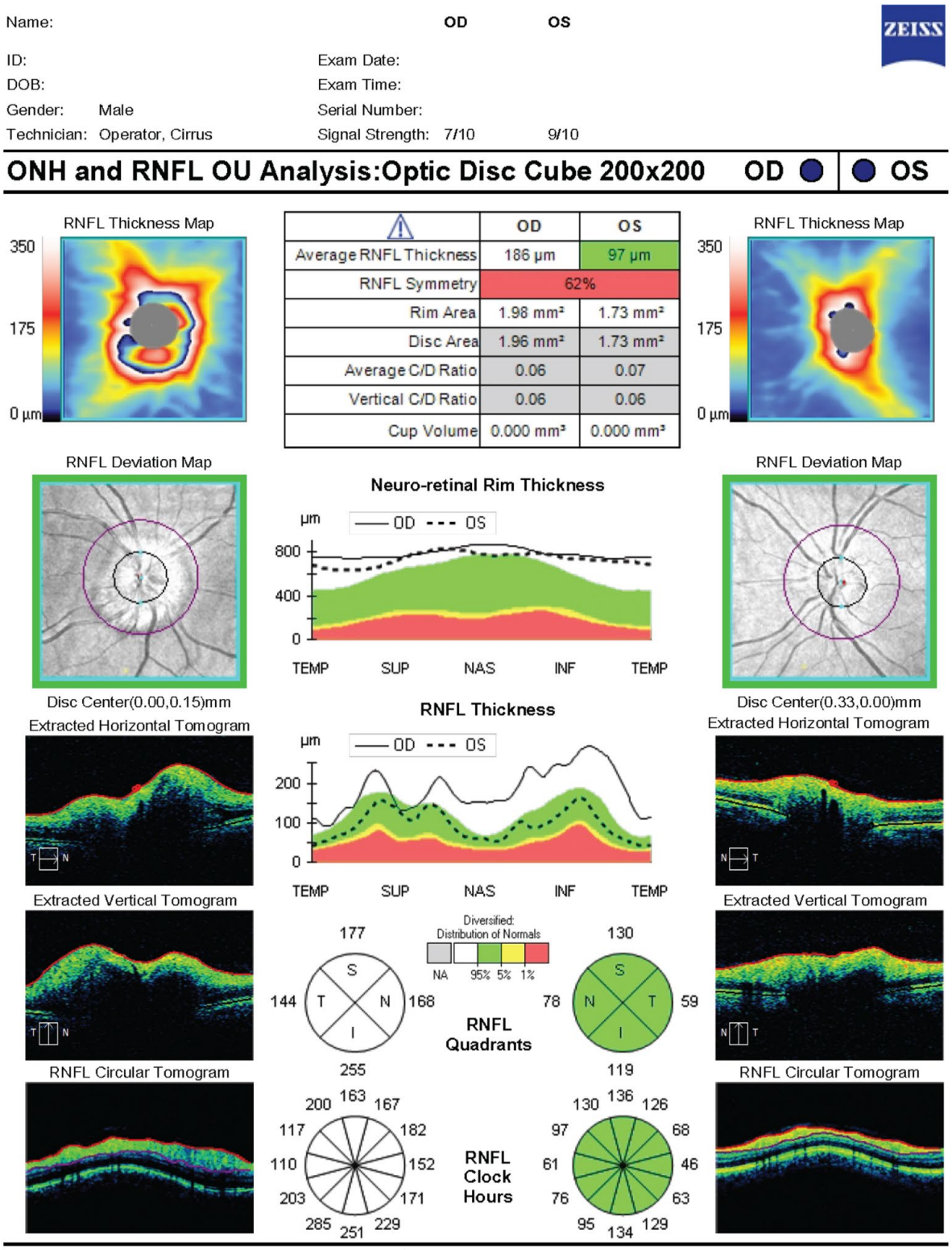
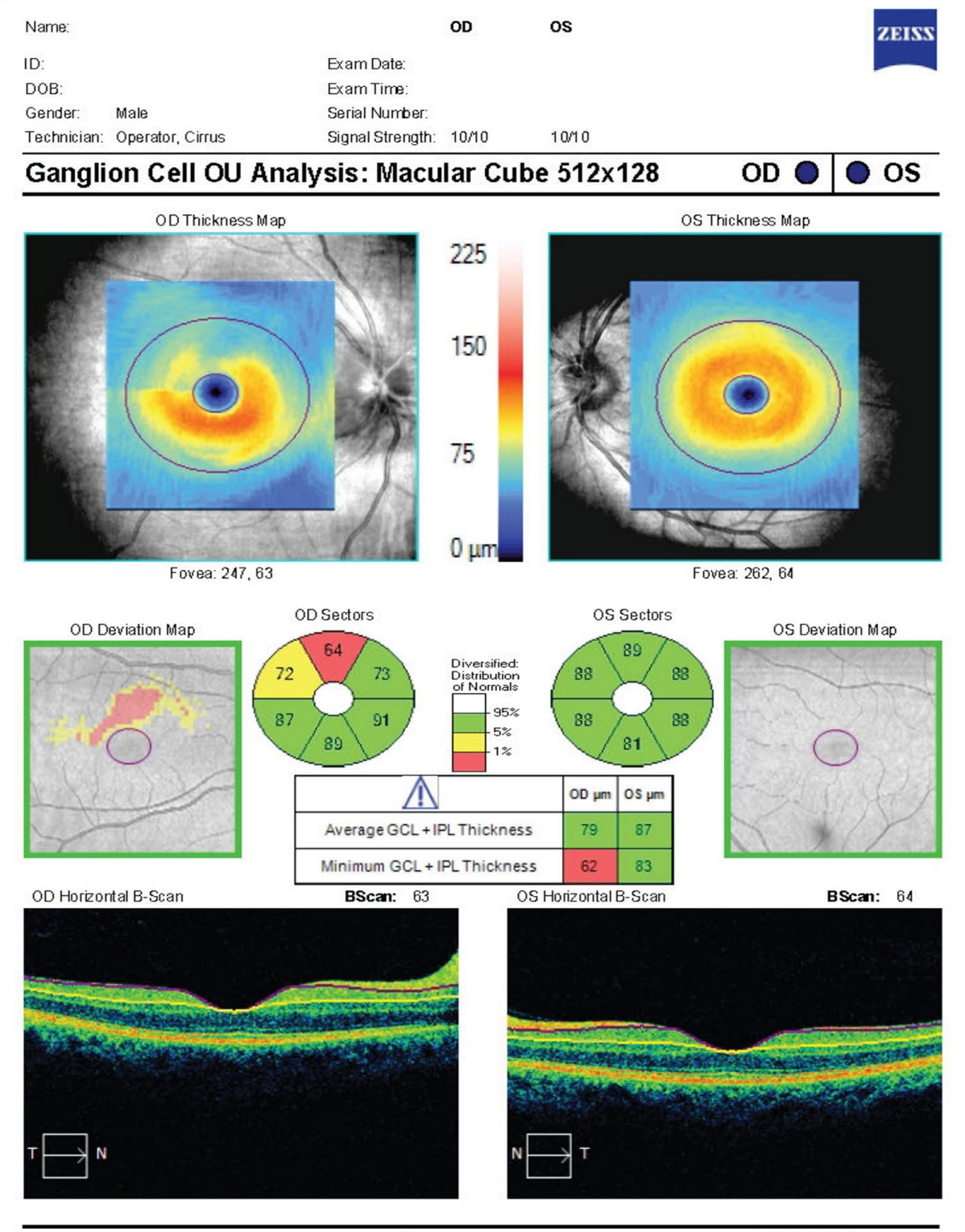


Figure 3: GCC thickness analysis



Question 1

How do you distinguish a true disc pallor from a glaucomatous disc appearance?

Answer
Glaucomatous optic neuropathy is associated with disc cupping and focal thinning of the neuroretinal rim. Cupping typically starts in the superior and inferior regions, leading to vertical enlargement of the cup. Other glaucomatous features include posterior bowing of the lamina cribosa, visible laminar pores (laminar dot sign), bayoneting and nasal shifting of the retinal vessels, disc haemorrhages and increasing peripapillary atrophy. The main feature that distinguishes glaucomatous discs from disc pallor due to atrophy is the well-perfused neuroretinal rim in glaucomatous discs.

Answer ends

Question 2

What is your assessment of the visual fields?

Answer
This is a HVF 24-2 visual field for the right and left eye. There is an inferior hemi-field defect that respects the midline in the right eye and inferior quadrant visual field defect in the left eye. The inferior hemi-field defect in the right eye is also referred to as an altitudinal defect.

Altitudinal defects can be associated with several conditions including:

1. Ischaemic optic neuropathy
2. Optic neuritis
3. Compressive lesions including tumours, aneurysms, and other space-occupying lesions within the visual pathway
4. Hemibranch artery or vein occlusion
5. Advanced glaucoma

Answer ends

Question 3

Describe the patient's OCT retinal nerve fibre layer (RNFL) and ganglion cell layer (GCL) analysis

Answer
The RNFL OCT scans are of good quality and adequate signal strength (6/10) in both eyes. They show marked asymmetry between the two eyes. The affected right eye shows increased thickness of the RNFL globally. The OCT of the unaffected left eye shows RNFL thickness within normal limits.

The GCC OCT scans were of good quality and excellent signal strength (10/10) in both eyes. The affected right eye showed two abnormal sectors superiorly - one superotemporally measuring below the fifth percentile and one superiorly measuring below the first percentile. The left eye GCC measurements were all within normal limits. No macular pathology was identified in either eye.

Answer ends

Question 4

What is the likely diagnosis?

Answer

This patient most likely has non-arteritic anterior ischaemic optic neuropathy. However, as this is a diagnosis of exclusion, other conditions need to be ruled out first. The differential diagnosis includes

- Other optic neuropathies, including anterior optic neuritis (idiopathic, demyelinating, sarcoid-related, etc)
- Anterior compressive optic neuropathy (from anterior orbital lesions)
- Infiltrative optic neuropathy
- Advanced glaucoma

Relevant blood tests and neuroimaging should be arranged to exclude the other differential diagnoses.

Non-arteritic anterior ischaemic optic neuropathy (NAION) is the most common acute optic neuropathy in patients over 50 years of age, with an estimated annual incidence in the United States of 2.3-10.3 per 100,000 population. The disease affects Caucasians more than African-American or Hispanics.

Patients typically present with persistent sudden, painless, unilateral loss of vision and visual field defects. Visual acuity in patients with NAION varies considerably from 6/6 to no perception of light.

Clinical features of NAION include relative afferent pupillary defect (RAPD), diffuse or segmental optic disc swelling in the affected eye, which may be associated with flame peripapillary haemorrhages; and a contralateral crowded ‘disc at risk’. Soft exudates are unusual. The swelling typically resolves within 4-6 weeks and is replaced by sectoral or diffuse pallor, as seen in our patient.

An important differential includes arteritic anterior ischaemic optic neuropathy (AAION), caused by occult giant cell arteritis (GCA). As such, an urgent full blood count, ESR and CRP should be requested to rule out GCA. Occult GCA manifests as acute blindness with minimal systemic symptoms. In both conditions, the optic nerve head is swollen with flame-shaped haemorrhages, however only AAION is associated with pallor of the swollen nerve (due to severe infarction). AAION is more likely to be present in the older population.

Answer ends

You suspect that the patient has non-arteritic anterior ischaemic optic neuropathy (NAION).

Question 5

Discuss the pathophysiology of NAION, including the risk factors.

Answer
The pathophysiology of NAION is controversial with no one mechanism definitively demonstrated. It is presumed to result from circulatory insufficiency within the optic nerve head. Blood flow through the short posterior ciliary arteries (SPCAs) is reduced in patients with NAION. One proposed mechanism is that the acute ischaemia at the optic nerve head impairs orthograde axonal transport and results in axonal oedema. This then creates a compartment syndrome in predisposed eyes (e.g. those with crowded discs).

Risk factors associated with the development of NAION include hypotension (especially nocturnal), systemic arterial hypertension, diabetes mellitus, hyperlipidaemia, anaemia, obstructive sleep apnoea syndrome, hyperhomocysteinemia, various coagulopathies, migraine, smoking, optic disc drusen, and uncomplicated cataract extraction (Miller and Arnold 2015).

Answer ends

Question 6

Discuss the management options for NAION.

Answer
There is as yet no medical or surgical intervention that has shown conclusive benefit in the treatment or prevention of NAION. The Ischaemic Optic Neuropathy Decompression Trial (IONDT) is a randomised, single-blind study, which investigated the effectiveness of optic nerve sheath fenestration (a surgical technique to create openings within the optic nerve sheath to reduce the hydrostatic pressure within the subarachnoid space of the optic nerve). This trial demonstrated no benefit of optic nerve sheath fenestration in acute NAION. Optic nerve sheath fenestration is therefore no longer offered as a treatment option.

Similarly, systemic corticosteroids and intravitreal injection of anti-VEGF antibodies have both been tested in clinical trials, but neither treatment significantly altered the course of NAION.

Referral to a physician for the management of cardiovascular risk factors is the mainstay of treatment. The goal of treatment is to reduce the chance of fellow eye involvement. Aspirin may be considered if there are no contraindications.

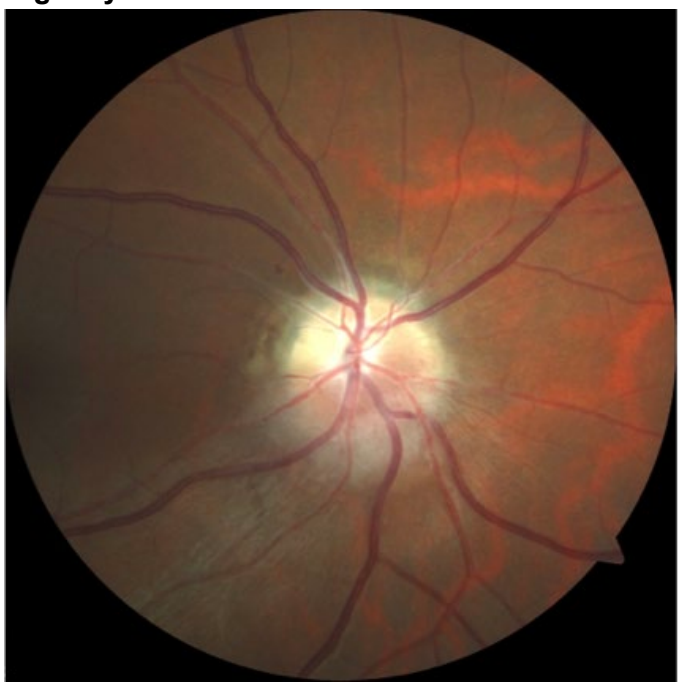
Answer ends

The patient returns 2 months later for his follow up appointment. Examination findings from that appointment are shown below.

	Right eye	**Left eye**
Best corrected visual acuity	6/19	6/9.5-1
Goldmann tonometry	16 mmHg	14 mmHg
Gonioscopy	Open	Open
Pachymetry	586 µm	597 µm
Extraocular eye movements	Full range No pain, no diplopia	Full range No pain, no diplopia
Ishihara	14/14	14 / 14
Pupils	R RAPD	
Anterior segment	Early lens opacification, otherwise unremarkable	Early lens opacification, otherwise unremarkable
Fundus examination	See disc photos (Figure 4) Macular clear Peripheral retina clear and flat	See disc photos (Figure 4) Macular clear Peripheral retina clear and flat
Visual fields	See visual fields (Figure 5)	
OCT	See RNFL analysis (Figure 6) and GCC scan (Figure 7)	

Figure 4: Colour photos

Right eye



Left eye

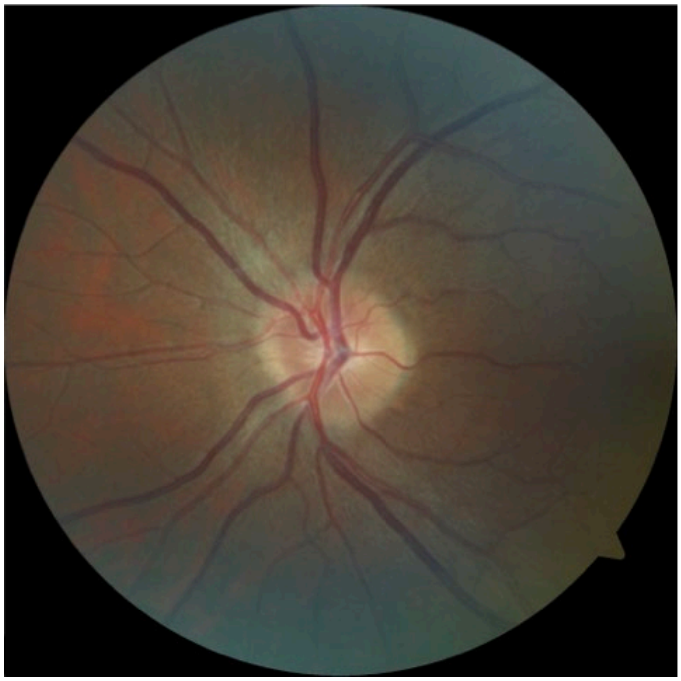
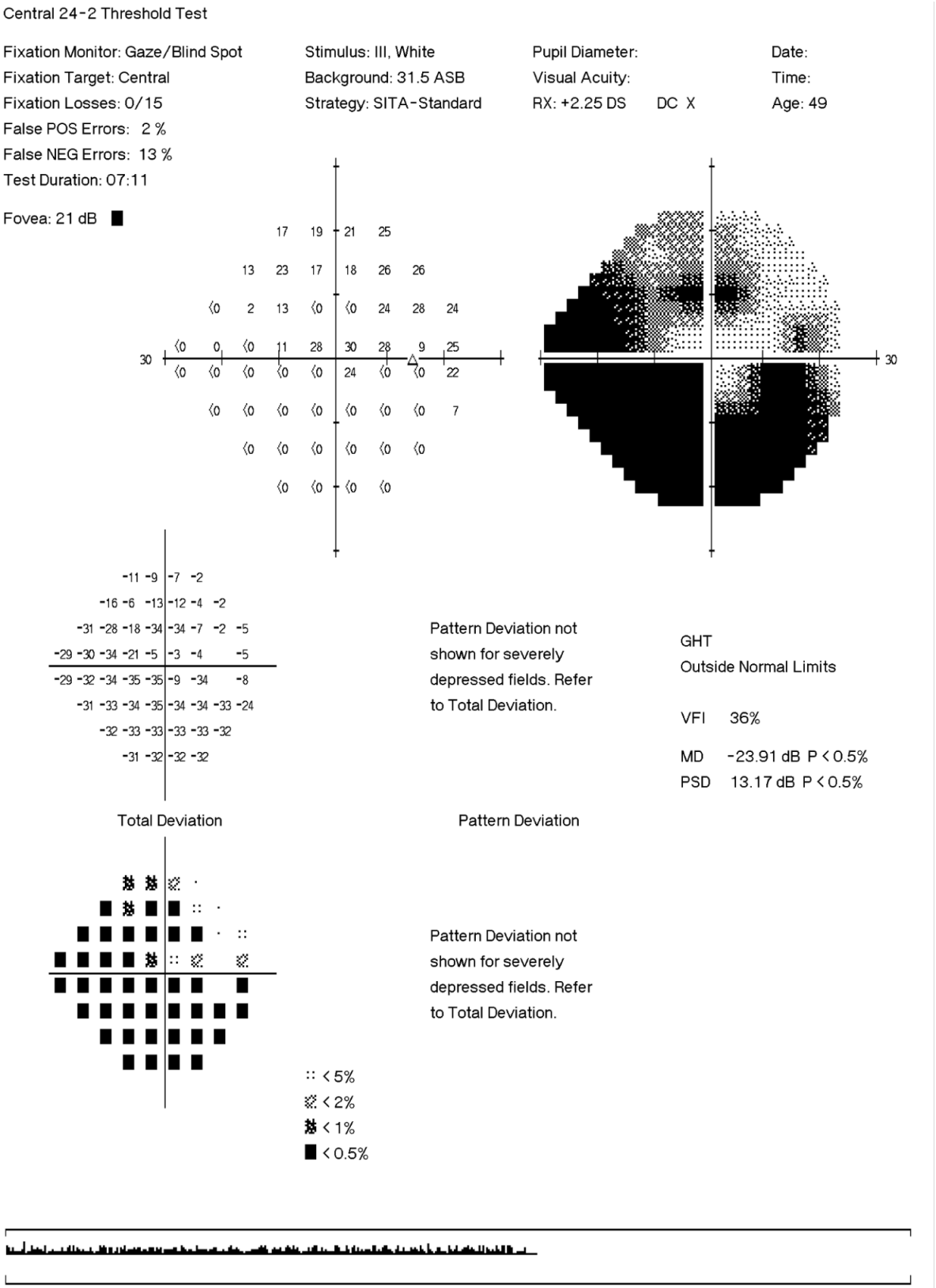


Figure 5: Visual fields - 2 months

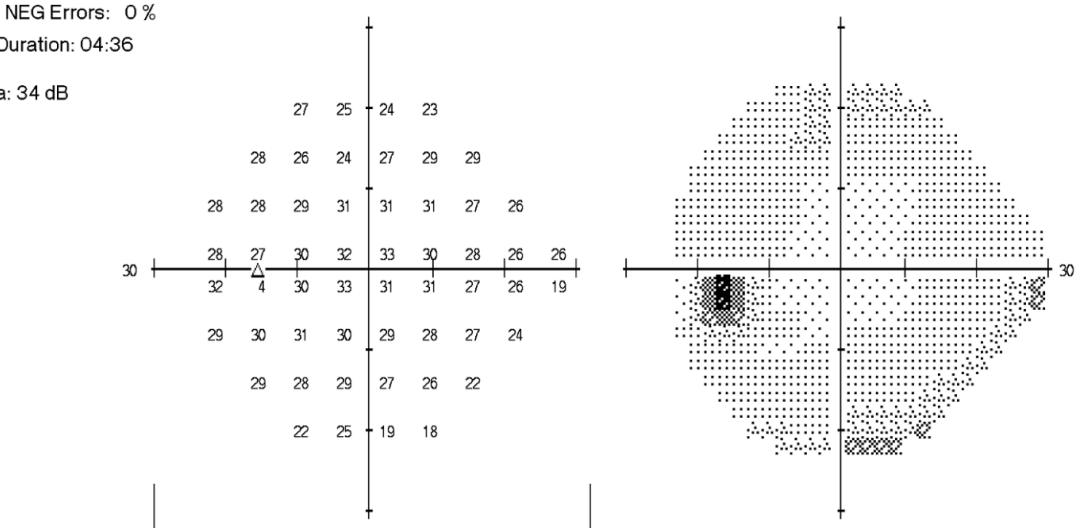
Right eye

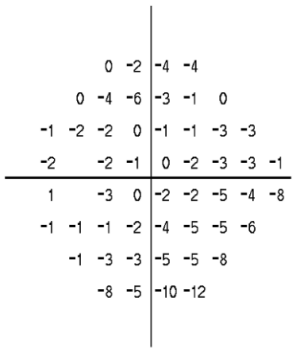


Left eye

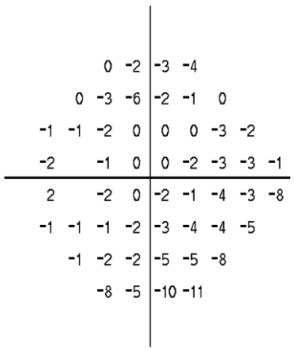
Central 24-2 Threshold Test

Fixation Monitor: Gaze/Blind Spot	Stimulus: III, White	Pupil Diameter:	Date:
Fixation Target: Central	Background: 31.5 ASB	Visual Acuity:	Time:
Fixation Losses: 0/14	Strategy: SITA-Standard	RX: +2.50 DS DC X	Age: 49
False POS Errors: 1 %			
False NEG Errors: 0 %			
Test Duration: 04:36			
Fovea: 34 dB			





Total Deviation



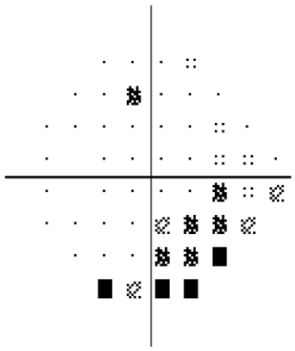
Pattern Deviation

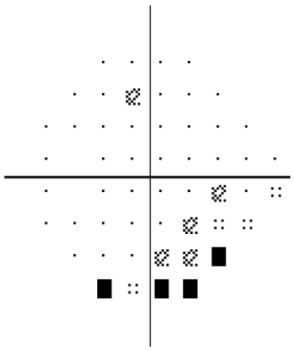
GHT
Outside Normal Limits

VFI 96%

MD -3.00 dB P < 2%

PSD 2.73 dB P < 2%





:: < 5%
▨ < 2%
▩ < 1%
■ < 0.5%

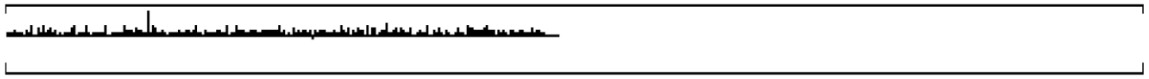


Figure 6: RNFL thickness analysis - 2 months

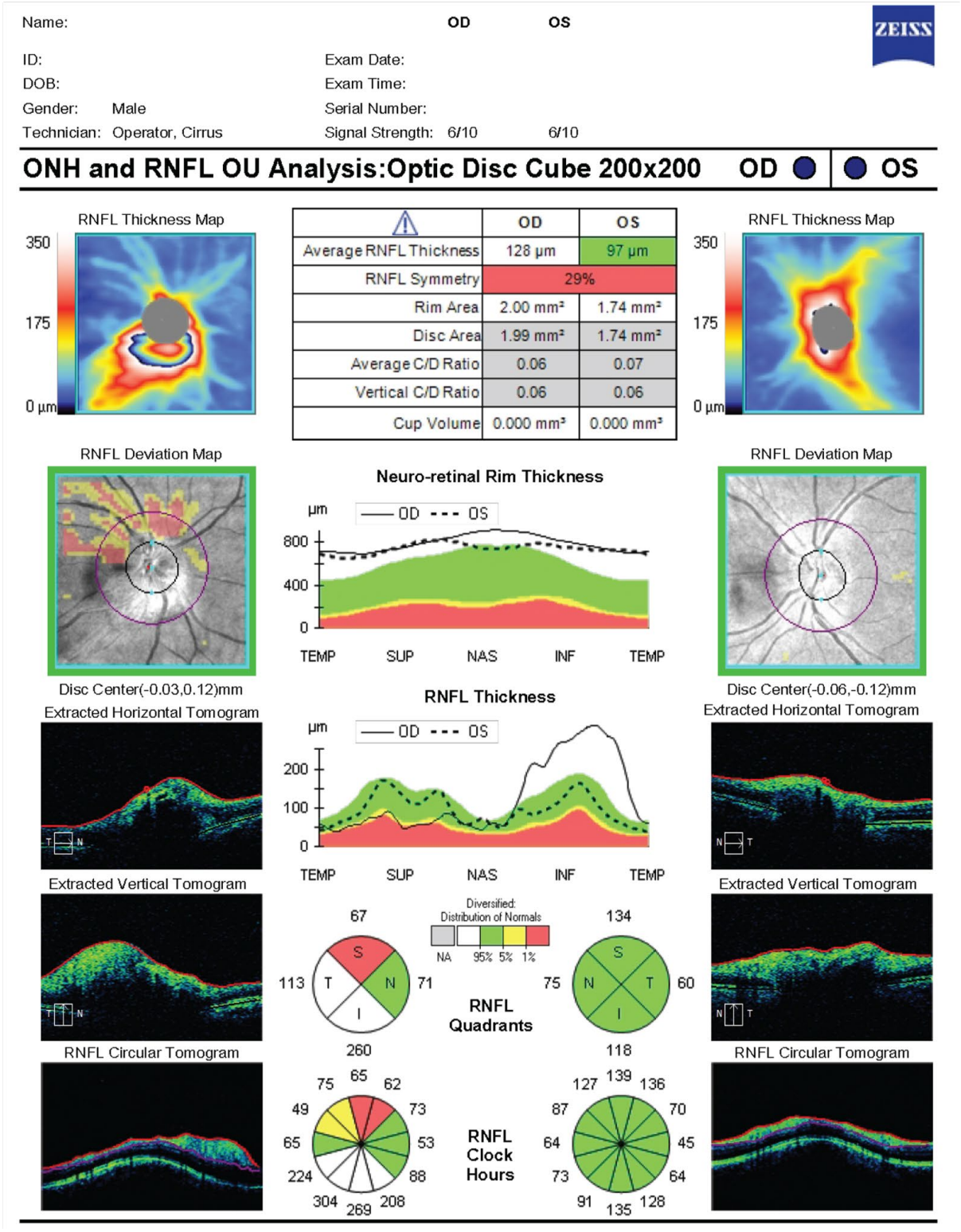
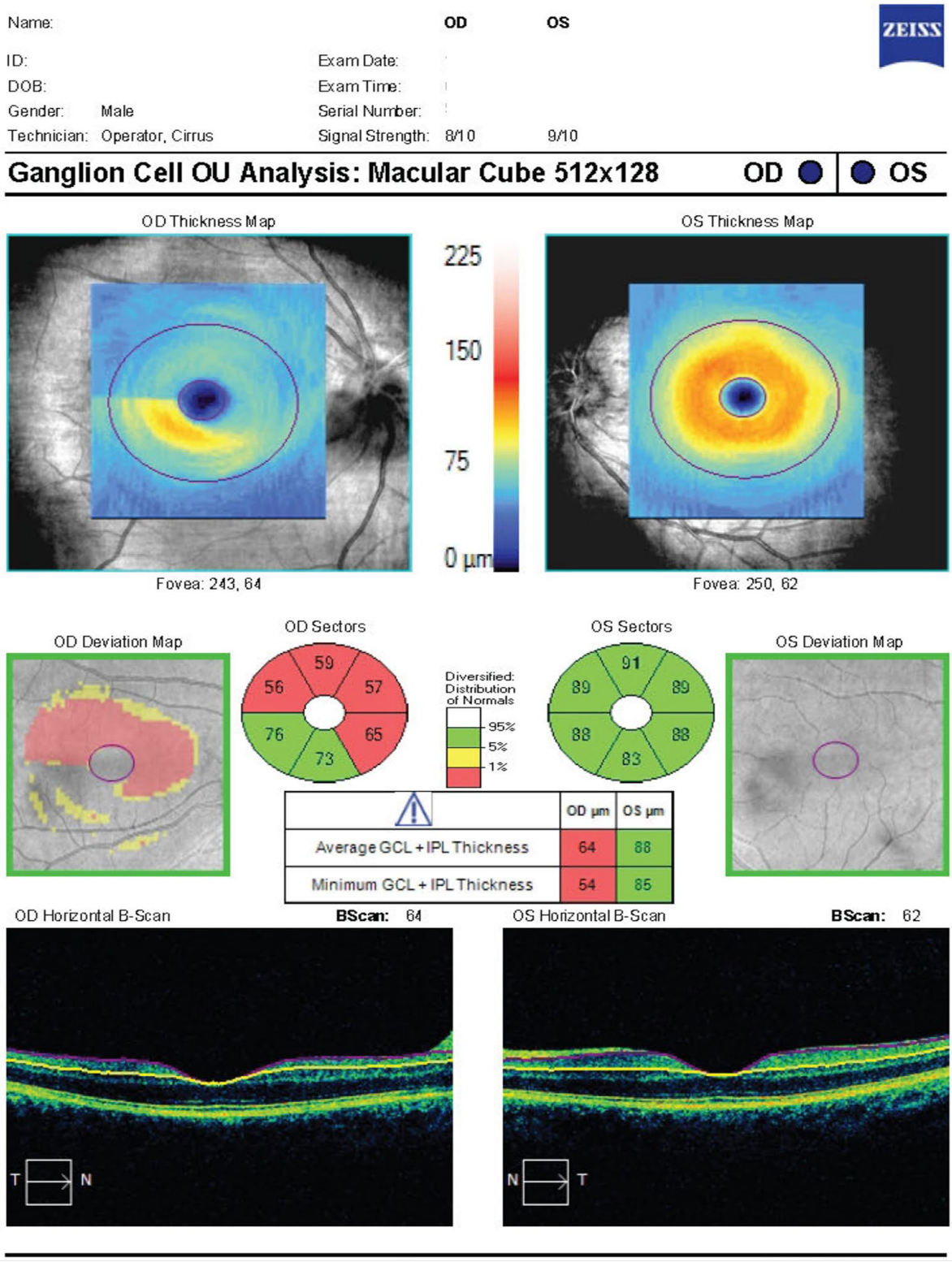


Figure 7: GCL thickness analysis - 2 months



Question 7

Describe the patient's OCT retinal nerve fibre layer (RNFL) and ganglion cell layer (GCL) analysis

Answer
The OCT scans are of good quality and show ongoing asymmetry between the two eyes. The swelling in the affected right eye has improved with increased RNFL thickness seen inferiorly now. The left eye RNFL thickness is within normal limits.

The GCC scans in the right eye have worsened compared to the initial presentation. In the right eye the average GCL + IPL thickness is below the first percentile. The left eye remains unremarkable.

In NAION, the peripapillary RNFL may initially become thick while the disc is swollen. A retrospective observational case series of 14 eyes in 13 patients (Dotan et al 2013) reported RNFL thinning on average 6 months following the onset of NAION and no statistically significant difference at 13 months.

A prospective study of eyes with acute NAION showed that GCL thinning developed within 1 to 2 months of onset, which is prior to RNFL swelling resolution.(Kupersmith et al. 2016) Kupersmith et al reported that average GCC plus inner plexiform layer thinning below the fifth percentile of normal eyes occurred while the OCT still showed RNFL thickening.

Answer ends

Question 8

Is the patient's fellow unaffected eye at risk of developing NAION? Why or why not?

Answer
The risk of developing NAION in the contralateral eye has been reported in 15-19% of patients within 5 years of initial eye involvement.(Miller and Arnold 2015) Occurrence in the second eye produces the clinical appearance of a 'pseudo-Foster Kennedy syndrome,' in which the previously affected disc is pale and the currently affected disc is swollen.

The IONDT Follow-Up Study reported that a history of diabetes and baseline visual acuity of 20/200 (6/60) or worse in the affected study eye were significantly associated with new NAION in the fellow eye; but not age, sex, aspirin use, or smoking. Furthermore, final fellow eye visual acuity was significantly worse in those patients with new fellow eye NAION whose baseline study eye visual acuity was 20/200 (6/60) or worse.

Answer end

You have seen previous similar patients where the ophthalmologist started them on topical Brimonidine tartrate twice a day in the affected eye.

Question 9

Why would you use Brimonidine tartrate in NAION?

Answer

There is no proven treatment for NAION. However, the use of Brimonidine tartrate in eyes with NAION is based on animal studies suggesting a potential neuroprotective effect on retinal ganglion cells in cases of NAION. The BRAION study did not indicate any harmful effect of Brimonidine in patients suffering from NAION. However, a statistically significant advantage for patients receiving brimonidine tartrate could not be shown.(The BRAION study group, 2006)

Answer ends

You have another patient with a similar history. This second patient reveals that he is taking sildenafil, a phosphodiesterase-5 inhibitor.

Question 10

What is the relevance of taking sildenafil in this case?

Answer
Phosphodiesterase-5 inhibitors, such as sildenafil (Viagra), tadalafil (Cialis), and vardenafil (Levitra), are commonly used for erectile dysfunction and have been associated with the development of spontaneous NAION in men with predisposed crowded discs. This association is somewhat controversial. It is believed that the therapeutic dose of these drugs may lower systemic blood pressure and potentially reduce perfusion to the optic nerve head, thereby increasing the risk of NAION.(Miller and Arnold 2015)

Other medications, including interferon-alpha and amiodarone, have also been associated with the development of spontaneous NAION.

Answer ends

References and recommended reading

Required reading

Miller, N., Arnold, A. Current concepts in the diagnosis, pathogenesis and management of nonarteritic anterior ischaemic optic neuropathy. Eye 29, 65–79 (2015). https://doi.org/10.1038/eye.2014.144

Recommended reading

Martin-Gutierrez MP, Petzold A, Saihan Z. NAION or not NAION? A literature review of pathogenesis and differential diagnosis of anterior ischaemic optic neuropathies. Eye (Lond). 2023 Sep 28. doi: 10.1038/s41433-023-02716-4. Epub ahead of print. PMID: 37770527.

Kupersmith MJ, Garvin MK, Wang JK, Durbin M, Kardon R. Retinal Ganglion Cell Layer Thinning Within One Month of Presentation for Non-Arteritic Anterior Ischemic Optic Neuropathy. Invest Ophthalmol Vis Sci. 2016 Jul 1;57(8):3588-93. doi: 10.1167/iovs.15-18736. PMID: 27388052; PMCID: PMC5996873.

Newman NJ, Scherer R, Langenberg P, Kelman S, Feldon S, Kaufman D, Dickersin K; Ischemic Optic Neuropathy Decompression Trial Research Group. The fellow eye in NAION: report from the ischemic optic neuropathy decompression trial follow-up study. Am J Ophthalmol. 2002 Sep;134(3):317-28. doi: 10.1016/s0002-9394(02)01639-2. PMID: 12208242.

The BRAION study group., Wilhelm, B., Lüdtke, H. et al. Efficacy and tolerability of 0.2% brimonidine tartrate for the treatment of acute non-arteritic anterior ischemic optic neuropathy (NAION): a 3-month, double-masked, randomised, placebo-controlled trial. Graefe's Arch Clin Exp Ophthalmo 244, 551–558 (2006). https://doi.org/10.1007/s00417-005-0102-8

Gad Dotan, Michaella Goldstein, Anat Kesler & Barry Skarf (2013) Long-term retinal nerve fiber layer changes following nonarteritic anterior ischemic optic neuropathy, Clinical Ophthalmology, 7:, 735-740, DOI: 10.2147/OPTH.S42522