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OCT Diagnosis in Glaucoma: Tips & Tricks

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OCT diagnosis in glaucoma: tips & tricks

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Optical coherence tomography in glaucoma is indispensable for documentation, diagnostic assistance and monitoring progression. Critical findings must be considered in conjunction with the patient's clinical condition. This paper uses case studies to illustrate possible applications.

ABBREVIATIONS

AMD	Age-related macular degeneration
APS	Anatomic positioning system
BMO	Bruch's membrane opening
BMO-MRW	Minimum rim width
GCL	Ganglion cell layer
NRR	Neuroretinal rim
OCT	Optical coherence tomography
RNF	Retinal nerve fibre
RNFL	Retinal nerve fibre layer
SD-OCT	Spectral-domain OCT
SS-OCT	Swept-source OCT
TSNIT	temporal-superior-nasal-inferior-temporal

Introduction

The use of optical coherence tomography (OCT), in glaucoma diagnostics, has become standard of care. Spectral-domain OCT (SD-OCT) and swept-source OCT (SS-OCT) acquire high-resolution images with up to 100,000 A-scans per second. Structures of interest, such as the macular ganglion cell layer, the retinal nerve fibre layer, and the optic disc, inclusive of the lamina cribrosa, can be resolved with a digital axial resolution of 3.9 µm. This resolution is comparable to an in vivo histological section and measurable variability does not exceed 1.4 µm [1].

The precision with this level of resolution measures the natural age-related loss of the neuroretinal rim (NRR) and retinal nerve fibre layer (RNFL). Differentiating these from early glaucomatous changes is challenging regardless of the measurement technique. Repeated, precise measurements are essential, since each patient manifests an individual rate of progression [2].

High-resolution OCT has rapidly become widespread in routine care. Glaucoma screening has advanced with the RNFL and BMO-MRW measurement, with high sensitivity in the preperimetric stage of glaucoma. Macular ganglion cell layer (GCL) thickness measurement by SD-OCT discriminates between normal and early glaucoma.

In a literature review of three different OCT devices, Oddone et al. [3] found that RNFL thickness was superior to the macular GCL thickness measurements. The minimum neuroretinal rim width (BMO-MRW) measurement in the optic disc is the latest application. The disc margin is precisely indicated by BMO-MRW, which detects the end of Bruch's membrane and the internal limiting membrane [4]. BMO-MRW is measured at 48 points and extrapolated to sectoral or total values. Initial clinical studies proved BMO-MRW to be almost as meaningful as the RNFL thickness measurement, by OCT, for glaucoma assessment [4–6]. The extrapolated area of the BMO roughly indicates the disc area. It correlates marginally with the disc area as measured by HRT, which is based on the inner margin of the Elschnig scleral ring.

Caveat

BMO and the disc area are not the same.

This paper will answer general questions with respect to assessing OCT images in glaucoma.

How does OCT illustrate measurements relevant to glaucoma?

Retinal nerve fibre layer (RNFL) and minimum rim width (BMO-MRW) measurements are acquired in 360 degrees and displayed in a TSNIT (temporal-superior-nasal-inferior-temporal) X-Y or linear graph. The acquired measurements, as displayed on the TSNIT graph, are compared to the normative database. The twofold standard deviation is shown in each sector and averaged over all sectors. Each measurement for a particular sector will be

color-coded green, yellow (95% percentile or borderline) or red (99% percentile or pathological).

The macular ganglion cell layer thickness of a volume scan is shown in regional absolute values (and as a topography map) or shown colour-coded. Differences from normal thickness values are highlighted in yellow and red and provide a rapid overview of the topography of the macular layers overlaying the ocular fundus image.

▶ **Fig. 1** is an example showing an overview of the right eye.

What indicates glaucoma?

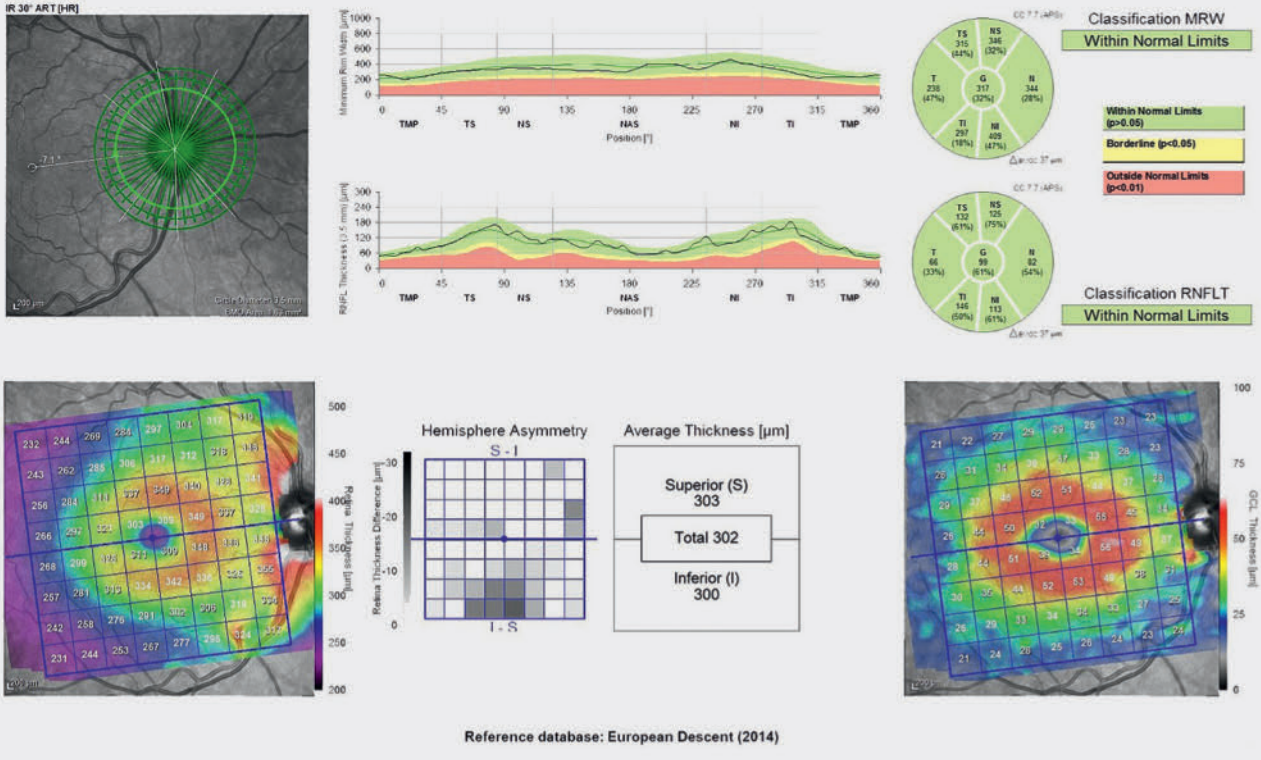
When assessing OCT images, pay attention first to the RNFL (most reliable in early glaucoma [6]), followed by the minimum neuroretinal rim width (BMO-MRW) and ganglion cell layer (GCL) thickness. The RNFL thickness profile and BMO-MRW should display harmonious transitions between peaks and troughs. Abrupt breaks and notches in the thickness profile suggest focal defects in the RNFL or minimum rim width (most commonly temporal superior and temporal inferior).

The thickness profile should lie within the green reference range. Furthermore, the B-scan images and segmentations demand another close look.

The infrared fundus image can provide information about possible optic disc haemorrhages (visible in 50% of cases), the peripapillary atrophy zone and shape of the excavation (light) relative to the NRR shape (dark). Focal RNFL defects can be readily detected (dark on light).

The central macular topography map should show the perifoveolar thickening of the retina as a ring-shaped elevation (doughnut shape). Various manufacturers use colour-coded thickness maps on which differences from the reference can be detected rapidly. Maps depicting differences from the normal population are also offered, which provide information about differences from normal layer thicknesses in green, yellow and red. If the topography shows any abnormalities, the B-scan and segmentation should be re-examined.

The temporal aspect of the GCL ring typically is the first strucutre to show atrophy in glaucoma, corresponding to the superior and inferior temporal RNFL defects. Axons are located in this region, with the raphe, the axis be-

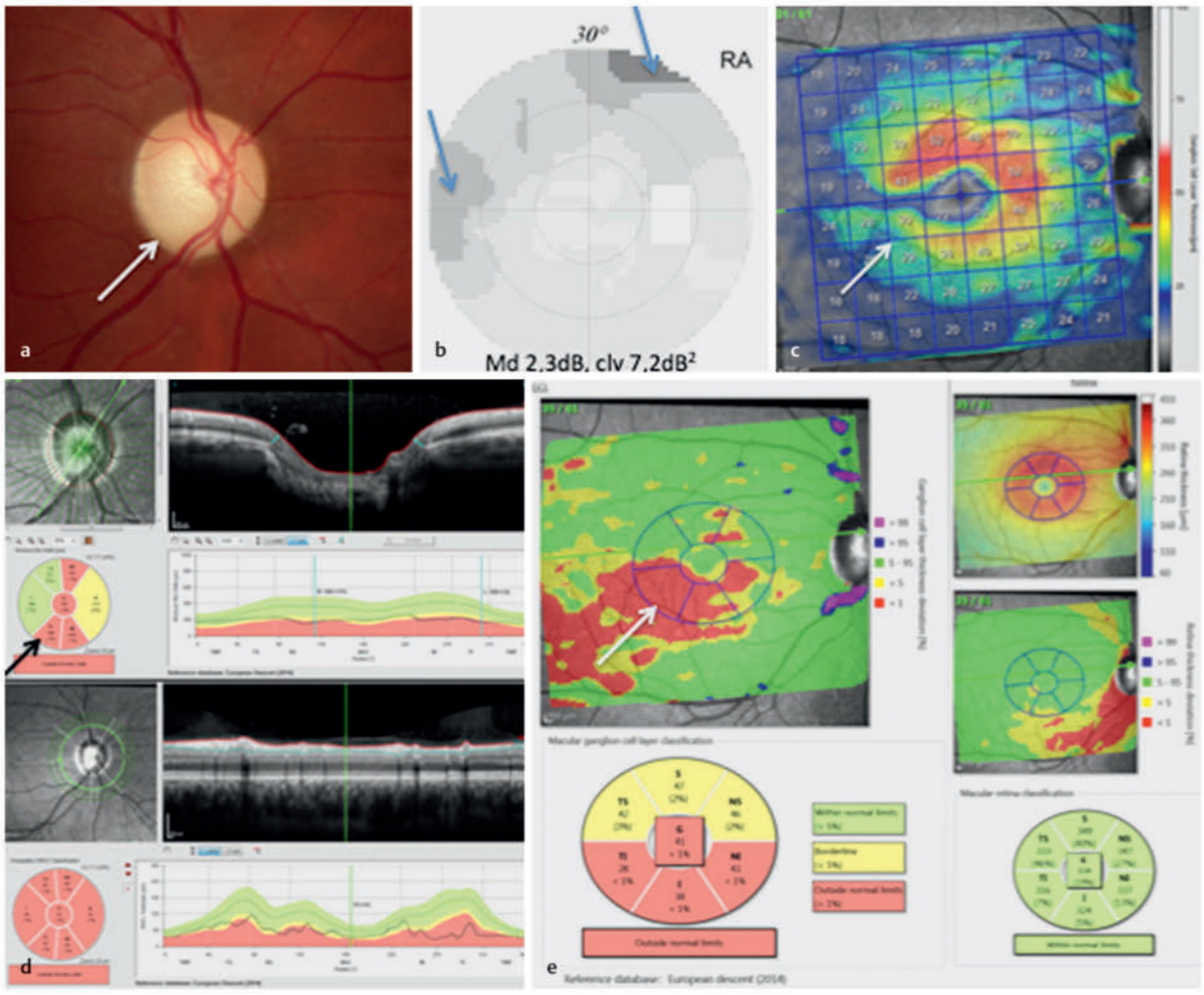


▶ **Fig. 1** An example showing an overview of a right eye with the TSNIT (temporal-superior-nasal-inferior-temporal) graphs for minimum rim width (BMO-MRW), retinal nerve fibre layer (RNFL) (top) and the retina and ganglion cell layer (GCL) thickness (bottom). Between the graphs at the bottom there is an image showing macular hemisphere symmetry (the degree of deviation is coded grey).

CASE STUDY 1

Right eye of a 32-year old female patient. Familial juvenile open-angle glaucoma with extremely high intraocular pressure greater than 40 mmHg at the time of diagnosis. Intraocular pressure now controlled, 9–20 mmHg. Distant vision is 1.0 bilaterally, and the central corneal thickness is 542 µm on R, 536 µm on L. The disc is slightly excavated (**a**, white arrow), pale; probably because of the initial high pressure, there is also simple atrophy. There is early glaucomatous change in the visual field (**b**, blue arrows).

The thickness of the retinal nerve fibre layer (RNFL) is significantly reduced because of the simple optic atrophy component (**d**, bottom), and the minimum neuroretinal rim width (BMO area 2.56 mm^2) is atrophied especially in the inferior region of the disc (**d** top, black arrow). The topography of the macular ganglion cell layer is reduced inferiorly and temporally (**c**, cold colours, white arrows), and in the deviation map the thinning beyond the 99% percentile is shown in red (**e**, white arrow).



▸ **Fig. 2** Familial juvenile open-angle glaucoma.

tween the fovea and the centre of the disc, as dividing line. Advanced glaucoma often presents with diffuse thinning of the retinal nerve fibre layer (RNF), minimum rim width (BMO-MRW) and ganglion cell layer (GCL) in OCT images.

Asymmetry between right and left eye is also an important marker in unilateral glaucoma. OCT devices offer asymmetry analysis for this purpose. Asymmetry within the GCL is meaningful since atrophy is more pronounced here either superiorly or inferiorly.

If in doubt about whether glaucoma is the cause, follow-up observation provides good information. The average peripapillary nerve fibre layer thickness (normal, mean RNFL) is approximately 100 µm. If a reduction in thickness is greater (RNFL loss > 1.2 µm/year) than age-related loss (RNFL about 0.6 µm/year), this may also be interpreted as progressive atrophy. Graphic illustration of this as an event or trend provides clarity.

Trend analysis shows poorer local resolution than the event analysis but gives the examiner slightly more certainty in assessing progression through a statistical statement (loss of how many µm per year, with what statistical significance). The patient should be seen more often than just once a year, e.g., every three or six months, so that short-term changes are more likely to be noted. Since statistical significance is shown in trend analysis after the 5th measurement, the patient can, for example, be examined again 3 months after the baseline examination and then 4 more times in the first 2 years.

The causes of artefacts and incorrect measurements lie firstly in the scanning technique and secondly in the individual pathology of the examined eye. The latter includes anatomical peculiarities such as vitreoretinal traction, cystoid oedema (such as widening of the inner macular nuclear layer), soft drusen, areas of myopic stretching, and, on the other hand, optic nerve pathology not associated with glaucoma such as drusen or simple optic atrophy of ascending and descending origin. For this reason, it is essential to carefully examine the anterior and posterior chamber of the eye before evaluating the OCT scan. The same applies for evaluating the OCT B-scans for segmentation errors, anatomical features (optic disc haemorrhage) and scan quality.

TIP

One must be aware of numerous factors (segmentation errors, sector classification) in order not to be deceived by “green disease” or “red disease” when comparing thickness measurements to the reference database.

Caveat

An OCT scan does not provide an automatic diagnosis comparable to a black box. This topic will become even more important in future with increasing use of artificial intelligence.

What to pay attention to during scan acquisition?

Correctly position the patient’s head to avoid tilting. Head tilting has great influence on follow-up examinations as these cannot be completely corrected by the device. Different degrees of tilting to the left or right subsequently leads to different positions in the x,y axes of the fundus image. Consequently, rotational artefacts are introduced, especially with peripapillary circular scans. One option to correct this in a follow-up examination is to align the centre of the optic disc on the fovea (FoDi, Heidelberg Engineering) for proper alignment of the subsequent peripapillary circular scans.

CASE STUDY 2

Male patient, 67 years old, normal-tension glaucoma. In the left eye, there is an NRR notch in the disc at 5 o’clock (**a**, white arrow), and the retinal nerve fibre layer (RNFL) shows marked temporal thinning in the OCT (**b**, black arrow) (▶ **Fig. 3**).

The retinal thickness (**c**, black arrow) is superiorly and inferiorly symmetrical although a clear curved RNFL loss inferiorly (**f**, white arrow) is visible on the infrared image (**d**, white arrow). In this area (**d**, green line), the inner nuclear layer shows obvious cystoid distension (**e, h**, white arrow), but the ganglion cell layer (GCL) is thinned (**g**, white arrow). Therefore, there is no thinning of overall retinal thickness.

On the deviation map shown below (**i**), significantly more pronounced atrophy (middle, red) can be seen in red in the GCL thickness map than in the retinal thickness map (right, top).

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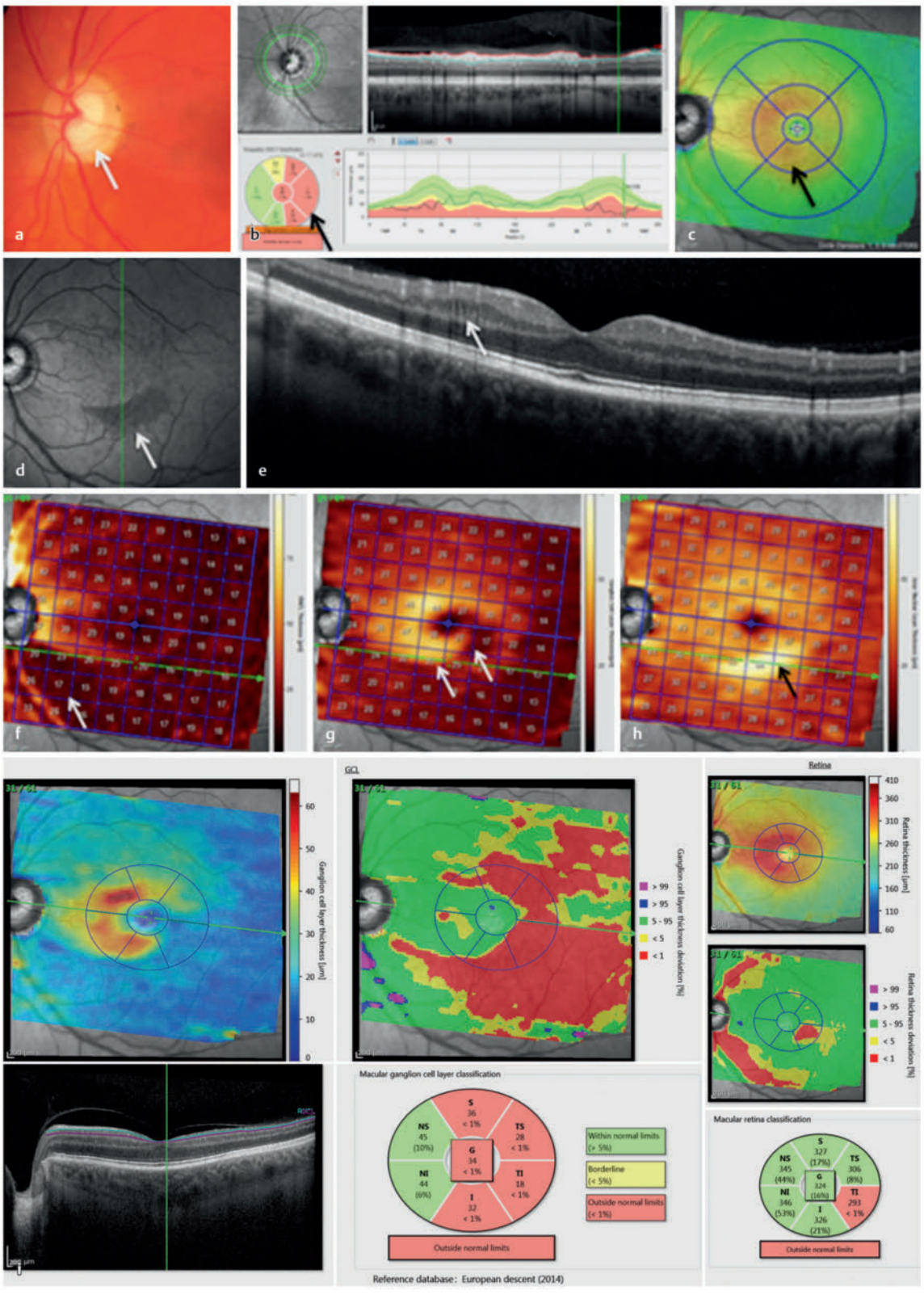
CASE STUDY 2



▶ **Fig. 3** Normal-tension glaucoma.

Three-dimensional scans in particular require multiple, well aligned B-scans without image shift (e.g., by using an anatomic positioning system [APS]). Involuntary eye movements are the main reason for motion artefacts, which have a negative effect on scan quality. Tremor, slow deviation and microsaccades must be corrected. The manufacturers attempt to compensate for this with various hardware and software solutions (e.g., TruTrack, Heidelberg Engineering; V^{Trac} Active Tracking, Optovue; FastTrac, Zeiss; SmartTrac, Topcon).

The same applies for selecting the correct distance between the eye and the lens, which affects the quality and position of the scan (sensitivity roll-off in spectral-domain OCT).

A dry eye with pathological tear film is managed with artificial tears before the examination. A prolonged examination can lead to drying of the corneal surface sometimes resulting in a considerable reduction in scan quality. The tear film and corneal epithelium are the first interface between air and solid medium and thus influence refraction of the laser beam. This can be counteracted by administering artificial tears prior to the scan.

Fixation, whether internal or external, in poor or functionally monocular vision can be challenging.

It is essential to obtain correct illumination of the infrared fundus image without shadows at the margin and clear focus on the structure being examined.

Correct positioning and centring of the peripapillary circular scans and centring the macular volume on the foveola are crucial for reference database comparison.

Severe astigmatism and long axial lengths can be managed with the following measures:

- Wearing contact lenses/glasses
- Attachment of astigmatic lenses
- Correct device setting:
  - Normal
  - Myopic
  - Highly myopic

TAKE HOME MESSAGE

Scan quality must be in the normal range in order to draw conclusions from the examination.

What factors in OCT measurements are associated with glaucoma?

In focal defects of the RNFL, cystoid expansion of the underlying inner nuclear layer can occur as a result of focal loss of the corresponding ganglion cell layer. Expansion of the inner nuclear layer and thinning of the overlying ganglion cell layer (GCL) can lead to total retinal thickness that appears normal although pronounced damage is already present. In other words, it is pseudo-normal. The cystoid expansion may indicate glaucoma progression. This change is clearly recognizable in B-scans of the macular volume and is a marker for disease severity in multiple sclerosis and other types of optic atrophy.

Progression is no longer to be expected in a mean RNFL thickness of about 50 µm [7]. At this stage, macular GCL thickness and a reduction in capillary density in OCT angiography appear to be more conclusive [8].

Optic disc haemorrhage extending to the periphery can lead to artificial thickening of the layer, with subsequent thinning of the RNFL.

In order to assess glaucoma-associated anatomical changes, the high-resolution B-scans should be considered as histological sections.

What anatomical factors in OCT measurements are not associated with glaucoma?

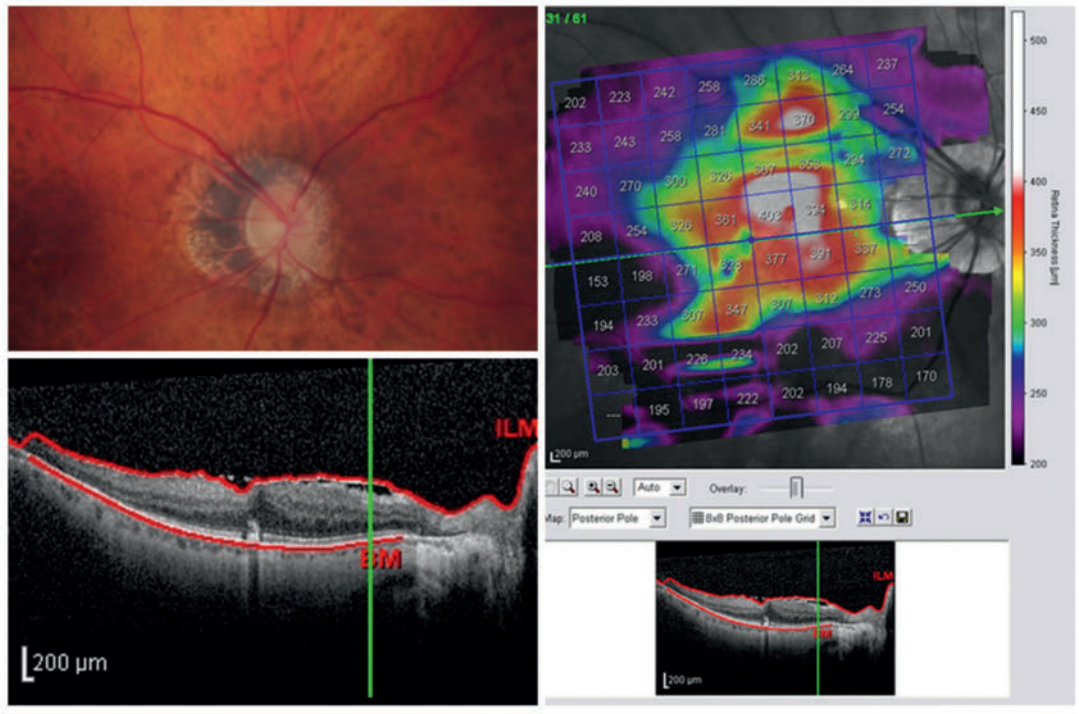
Changes independent from glaucoma can influence the anatomy and thereby thickness measurements of the retinal nerve fibre layer (RNFL), the ganglion cell layer (GCL) and the minimum rim width (BMO-MRW). These changes often affect the vitreoretinal interface, such as epiretinal membranes and tractions, that lead to fraying of the already diseased RNFL. Macular tractions can also lead to incorrect segmentation of the volume scan.

Intraretinally, cystoid oedema due to neovascular age-related macular degeneration (AMD), diabetic retinopathy and retinal vascular occlusion can lead to incorrect segmentation of the retinal layers or cause excessively high values. Furthermore, age-related macular degeneration with soft confluent drusen and elevations of the retinal pigment epithelium can impair RNFL segmentation in OCT, resulting in altered values of layer thickness.

CASE STUDY 3

52-year-old female patient with suspected glaucoma and oblique, vital, myopic disc (image top left) (▶ **Fig. 4**). The macular OCT (right) shows irregular retinal thickness topography due to segmentation of the epiretinal membrane (B-scan, below), which also leads to thickening of the central retina.

This examination is therefore not conclusive.



▶ **Fig. 4** Suspected glaucoma.

Artificial measurements of retinal vessels or shadowing effects, vitreous opacities at the internal limiting membrane or an atypical end of Bruch's membrane are problematic. The latter are found in the periphery of the temporal sector of shallow myopic discs and lead to inaccurate thickness values of the outer retinal layers. Therefore all measurement points in the B-scan must be checked by the examiner and corrected if necessary.

Highly myopic eyes with a long axial length and posterior staphyloma display a different distribution of the retinal nerve fibres (RNF) in the fundus and thus in the scan circle as well. The RNFL peaks tend to shift temporally and therefore fall outside the normal TSNIT graph. The OCT devices attempt to compensate this artefact by taking the corneal curvature and refraction into account. However, these are not always entered in practice, so the defaulted values are used by the software. A long axial length, in highly myopic eyes, leads to the scan circle being imaged too far from the optic disc. Due to the curved course of the RNF to the disc, the RNF maxima are shifted too far temporally.

Posterior staphyloma and oblique optic nerve entry sometimes make useful segmentation of the RNF impossible. The SPECTRALIS-OCT (Heidelberg Engineering, Heidelberg) offers scan circles with a diameter greater than 3.5 mm to allow RNFL measurements in regions outside the staphyloma (4.1 and 4.7 mm). Alternatively, the macular ganglion cell layer thickness can also be used as a glaucoma marker. If this is unsuccessful, other parameters relevant to glaucoma, such as disc morphology and focal RNF defects can be considered.

The shape and size of the optic disc can affect the analysis of the minimum neuroretinal rim width in OCT. Exceedingly small discs show minimum neuroretinal rim width (BMO-MRW) values in the upper percentile range due to the small diameter of the scleral canal. In contrast, due to

the NRR distribution along a larger scleral canal, large discs show values in the lower percentile range.

Especially in myopic eyes, the disc area and BMO area correlate positively with axial length [9]. This can lead to incorrect estimation of the BMO-MRW. Large and small Bruch's membrane openings influence the degree of deviation from the normal population [6]. In small discs with early glaucoma, the values of the BMO-MRW can show greater deviation from the reference database than those of the RNFL. The opposite tends to be true in large discs.

TAKE HOME MESSAGE
All pathological anatomical changes of the fundus can influence OCT measurements.

How do I distinguish other forms of ganglion cell and optic atrophy in the differential diagnosis of glaucoma with OCT?

Even when the scan and segmentation of the neuroretinal rim (NRR), the retinal nerve fibre layer (RNFL) and the ganglion cell layer (GCL) are error-free, there can still be pathological findings not associated with glaucoma. All causes of optic atrophy, whether it is ascending (from the inner retinal layers to the lamina cribrosa) or descending (from the lamina cribrosa to the geniculate ganglion), affect OCT thickness measurements and can be considered pathological.

Caveat
If glaucoma damage is indeterminate, the disc must be examined by ophthalmoscopy and simple optic atrophy must be excluded. This is supported by visual field examination.

Certain combinations of OCT measurements can also indicate non-glaucomatous optic atrophy.

Note
In glaucoma, thinning of the retinal nerve fibre layer (RNFL) and minimum neuroretinal rim width (BMO-MRW) with an arcuate shape most commonly appear in the superior and inferior temporal regions. In the temporal sector, thinning appears at a later stage.

Deviations from this pattern with a normal disc shape and normal position of the retinal vascular tree (mainly superior nasal) and with predominant temporal RNFL thinning may indicate, for instance, postneuritic atrophy. A segmental RNFL thinning, primarily in horizontal orientation, can be associated with a hemispheric retinal vascular occlusion or non-arteritic disc atrophy. With simple optic atrophy there is flattening of the neuroretinal rim (preservation of astroglia and loss of axons) with slightly increased excavation. Therefore, the NRR thickness is less likely abnormal or reduced.

Macular ganglion cell layer loss in glaucoma follows the curved focal RNFL defect with atrophy of the ganglion cell bodies. The thickness map is thus pathological in the superior or inferior temporal sector at the start of the disease (shape of a bitten doughnut or nautilus shell). With complete simple optic atrophy, the GCL thickness is reduced diffusely and resembles advanced glaucomatous optic atrophy. Concurrently, the RNFL thickness is diffusely pathological. In contrast to these findings, the BMO-MRW thickness is usually only slightly thinned in OCT.

TIP
If the macular thickness of the ganglion cell layer and retinal nerve fibre layer are reduced in OCT and the minimum rim width is nearly normal, a degenerative neurological condition such as Alzheimer's disease should be considered. Astonishingly, initial pathological OCT changes are quite often found in the thickness of the ganglion cell layer.

Homonymous or binasal vertical alignment of ganglion cell layer thinning indicates descending atrophy of the optic nerve due to cerebral midline disorders. This may indicate a pituitary adenoma causing compression, or left- or right-sided cerebral disease with transsynaptic degeneration. The OCT scan should then be followed by visual field examination because homonymous or bitemporal defects congruent with the OCT result are often apparent.

Caveat
The differential diagnosis of glaucomatous disc damage can be vitally important for the patient.

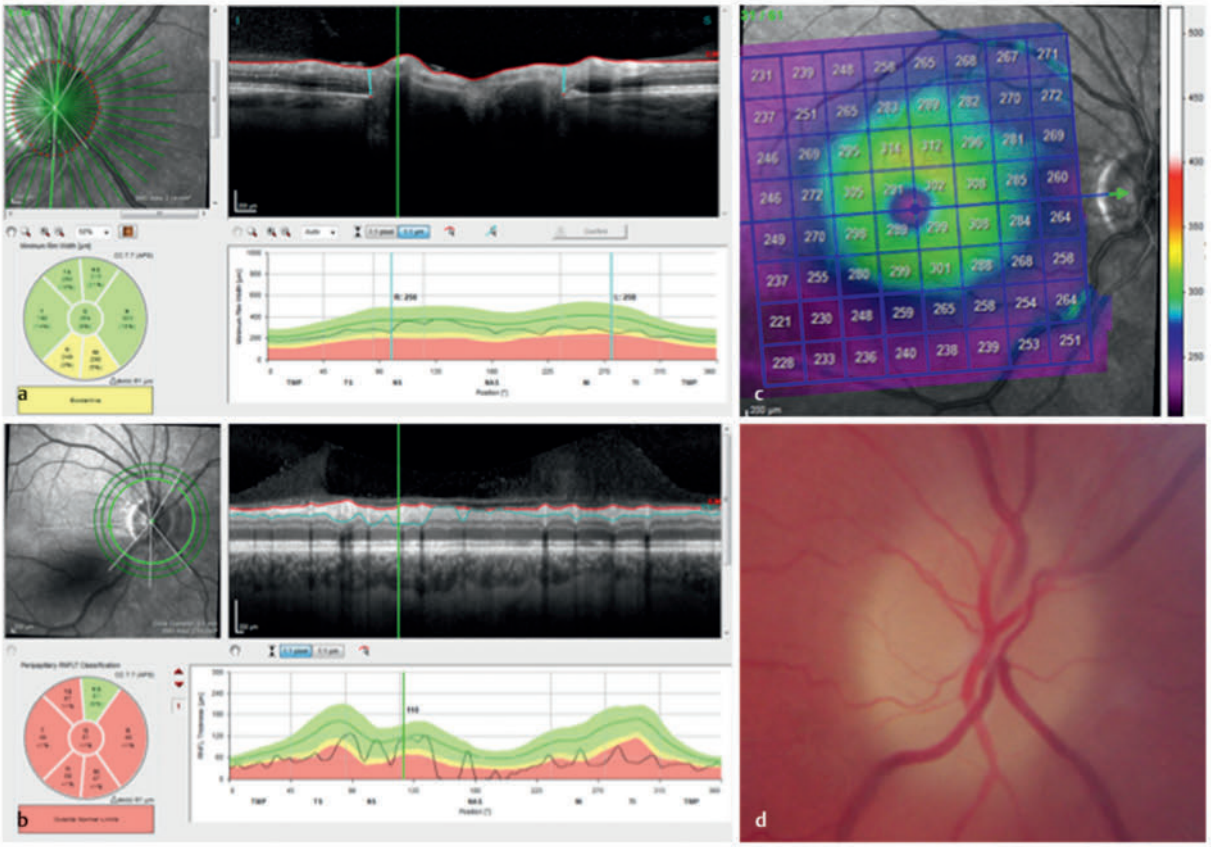
What to do in case of disc drusen, papilloedema or papilla leporina?

Optic disc drusen and papilloedema increase thickness measurements of the minimum rim width. However, with edema, the retinal nerve fibre layer (RNFL) appears even thicker. This is due to congestion, inflammation and ischemia, and tends to form folds with congestion (Paton's lines). Shadowing due to retinal vessels, oedema and drusen can make it more difficult to identify the end of Bruch's membrane and thus complicate segmentation.

CASE STUDY 4

42-year old male patient. Right eye vision reduced to 0.15 within the last few days; afferent pupil defect positive. The patient was referred with suspected glaucoma due to visual field defects.

When looking at the OCT scan only, the examiner will note a borderline minimum rim width (BMO-MRW; **a**) with markedly reduced retinal nerve fibre layer (RNFL) thickness (**b**) and retinal atrophy (**c**) (▶ **Fig. 5**). Ophthalmoscopy explains the discrepancy: This is not glaucoma but rather simple descending optic atrophy with temporal pallor (**d**) following optic neuritis.



▶ **Fig. 5** Differential diagnosis in suspected glaucoma.

Retinal nerve fibre layer (RNFL) thickness is an alternative measurement to assess atrophy. RNFL thinning occurs both with drusen and after a neuritic or ischaemic event. Measuring ganglion cell layer (GCL) thinning is also a good marker for assessing simple atrophy occurring after the ischemic event.

Complex disc atrophy, caused by an increase of astroglia with simultaneous loss of axons (e.g., after arteritic disc apoplexy) leads to a pale, blurred disc. This is reflected by RNFL thinning in the OCT scan with above-normal minimum neuroretinal rim width (BMO-MRW). Here, too, assessment of the thinned out GCL is helpful for diagnosis.

Myelination of the retinal nerve fibres, in papilla leporina, leads to artificial thickening of the BMO-MRW and RNFL. Both make it more difficult to assess glaucomatous damage. It is advisable here, too, to assess the GCL thickness.

KEY MESSAGES

- High-resolution OCT allows imaging and measurement of the retinal ganglion cell layer (GCL) and nerve fibre layer with high resolution similar to a histological section.
- OCT measurement of structures in the ocular fundus relevant in glaucoma facilitates diagnosis of and follow-up in early disease states.
- The colour-coded visualisation of differences from the normal population provides the examiner with a rapid overview of pathological measurements.
- The image quality of OCT scans is crucial for the reliability of the measurements.
- It is the task of the reporting physician to identify artefacts and incorrect measurements so as to avoid misinterpretations.
- Artefacts can be caused both by glaucoma-associated pathology and by non-glaucomatous changes in the posterior pole of the eye.
- Myopic discs with thinned retinal layers and oblique optic nerve entry also present a challenge for OCT scanning.
- It is important in differential diagnosis to identify neurological diseases and the changes they produce in the retinal ganglion cell and nerve fibre layers.

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Conflict of Interest

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Scientifically responsible according to certification rules

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