The ABCs of OCT 3:
glaucoma diagnosis and management
COPE Course ID: 60760-PD

Derek MacDonald, OD, FAAO

WOVS CE 2019
June 14 2019

UW School of Optometry and Vision Science
Financial Disclosures

Honoraria:  Alcon
           Allergan
           Carl Zeiss Meditec
           Eye Recommend

The content and format of this course is presented without commercial bias and does not claim superiority of any commercial product or service.
Course objectives

MAKE GLAUCOMA GREAT AGAIN
The traditional paradigm

Conventional diagnostic testing for glaucoma historically included clinical assessment of the optic nerve head and retinal nerve fiber layer (structure), and 24- or 30-2 visual field analysis (function)
An evolving paradigm

Optical coherence tomography (OCT) has revolutionized the way we care for patients with a number of ophthalmic diseases, including (arguably most significantly) glaucoma.

OCT initially allowed objective analysis of the ONH and RNFL.
An evolving paradigm

The evolution of OCT now allows accurate segmentation of macular retinal ganglion cell/inner plexiform layer thickness
1991
OCT developed at MIT\(^1\)

2001
Time-domain: TD-OCT
• 400 A-scans/sec
• axial resolution: 10μm

2004
Spectral-domain: SD-OCT
• up to 40,000 A-scans/sec
• axial resolution: 5μm

2012 and beyond ...
Swept-source: SS-OCT
• up to 300,000 A-scans/sec
• axial resolution: 3μm

OCT Angiography
• non-invasive assessment of blood flow

---

The evolution of OCT: improving resolution

2001: TD-OCT

2004: SD-OCT

2012: SS-OCT
The evolution of OCT: improving resolution
## Objective imaging: caveats

| **Objective imaging complements but does not replace systematic clinical assessment and sound clinical judgment**
|---|
| “... the clinical disc examination remains the most important screening test for detecting the optic neuropathy of glaucoma ...”
| **With increasing reliance on imaging, the clinical exam is increasingly in danger of being relegated to afterthought, or even worse, as a means of confirming imaging results ... a thorough clinical examination combined with a healthy dose of common sense is superior to imaging technology ...”**

---

Objective imaging: caveats

“The thought that these devices can diagnose glaucoma in the absence of corroborating clinical evidence is ... the most common (and potentially dangerous) misunderstanding. The limited normative databases against which scans are compared can never cover the remarkably varied appearance and structure of the optic nerve we encounter in normal individuals.”

OCT: accuracy and reliability

However, objective imaging has become invaluable in:

• the diagnosis of pre-perimetric glaucoma (PPG)\(^1\)
• quantifying disease progression post-diagnosis

SD-OCT provides accurate and consistent measurement of RNFL thickness, ONH parameters, and macular RGC thickness\(^2-4\)

• 4 to 5μm axial resolution
• ≤3% intra- and inter-visit variability (better for GCIPL)
• versus up to 28% variability for AVF analysis\(^5\)

Unfortunately, segmentation algorithms differ between instruments, making direct comparison all but impossible\(^6\)

---

OCT: reference database limitations

Comparison to a (small and healthy) reference database:
- **yellow**: found in <5% of an age-matched population
- **red**: found in <1%¹

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Normal Range*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average RNFL Thickness</td>
<td>75.0 - 107.2</td>
</tr>
<tr>
<td>RNFL Symmetry</td>
<td>76% - 95%</td>
</tr>
<tr>
<td>Rim Area</td>
<td>1.03 - 1.69</td>
</tr>
<tr>
<td>Average C/D Ratio</td>
<td>0.64 - 0.21</td>
</tr>
<tr>
<td>Vertical C/D Ratio</td>
<td>0.62 - 0.21</td>
</tr>
<tr>
<td>Cup Volume</td>
<td>0.01 - 0.035</td>
</tr>
</tbody>
</table>

Note that 30% RNFL loss can still fall in the “normal” range: *some of us are more normal than others...*

The Cirrus RNFL reference database includes only 284 individuals:
- no ocular or systemic disease (unrealistically healthy)
- predominantly Caucasian
- all between +8.00 and -12.00
- only 31 over the age of 70 (and only 3 over the age of 80)²

---

Glaucoma is a clinical, not a statistical diagnosis: beware of red disease and note that green is not always good\textsuperscript{1,2}

However, be cognizant that OCT may detect glaucomatous RNFL thinning up to 6 years before VF loss is detected\textsuperscript{3}

Scan quality and imaging artifacts

Quality scans are essential for accurate interpretation

However:

• imaging artifacts are common (approximately one in every three scans), and can dramatically impact the ability to detect disease or its progression
• concurrent disease is also common
  • non-glaucomatous changes to the ONH, RNFL, and GCIPL can simulate or mask glaucomatous change

Don’t blindly trust the numbers or fall in love with the colors:

• systematically and qualitatively scrutinize each and every scan to ensure quality and accuracy

Red disease: poor signal strength

Poor signal strength:
• weak scans can dramatically underestimate RNFL thickness\(^1,2\)
  • note: a 25% reduction in superior quadrant RNFL thickness with a decrease in signal strength from 10 to 6

![Images of scan quality with different signal strengths](image)

Accurate segmentation depends upon adequate signal strength

Dilation **may** improve scan quality, whereas a thin artificial tear **invariably** improves scan quality\(^3\)

Red disease: segmentation errors

Segmentation errors are common, particularly with poor signal strength, concurrent disease, and high myopia (see below)

- watch for atypical results (dramatic sector differences)
- carefully inspect each scan for segmentation accuracy

Red disease: opacities

Cataract, corneal scarring, dry eye, and vitreous opacities can interfere with OCT scans\(^1,2\)

- particularly when superior- or inferior-temporal near ONH
- blink or eye movement before the scan may be helpful

Red disease: blink or motion artifacts

Motion artifacts
• discontinuity in the blood vessels seen in the *en face* image indicates eye movement during scan acquisition\(^1\)
  • particularly important within the ONH or RNFL scan circle

Blink artifacts
• horizontal or vertical bars are blinks during the scan

---

Red disease: cropping/truncation

Alignment and centration

- due to improper alignment along the z-axis (anterior-posterior) or greater than 2mm of axial depth difference (staphyloma)\textsuperscript{1,2}
- crops/truncates the image and results in missing data
- <optimize> and manually center in acquisition window

The RNFL floor is \textasciitilde 50\textmu m: anything lower should raise suspicion\textsuperscript{3}

Red disease: high myopia

High myopia can mimic glaucomatous structural change, and confound the reference database\(^1\)

A posterior staphyloma can make it difficult to simultaneously capture the base of the cup and the peripapillary retina in the 2mm deep acquisition window, leading to image truncation.

The RNFL bundles may be shifted temporally, decentering the peaks
- the scan circle is imaged farther from the ONH: thinner RNFL

Macular scans may be more helpful in highly myopic eyes\(^2\)

---

Red disease: atypical anatomy/concurrent disease

Atypical anatomy and concurrent non-glaucomatous disease can mask change or confound the reference database

Split RNFL bundle:
- the deviation map shows a pseudo-defect due to the superior-temporal RNFL bundle being split rather than single (note thickness map)
  - ~7% of eyes: red disease, not real disease

Epiretinal membrane (ERM):
- the most common confounding disease for both RNFL and macular scans
  - look for “spoke-like” irregularity on the GCIPL thickness map

A systematic approach to evaluating OCT scans

Systematically and critically obtain and evaluate each scan\textsuperscript{1,2}

1. Confirm patient: don’t get a great scan on the wrong eye
2. Confirm age: comparison to age-matched controls
3. Confirm signal strength: instrument-specific minimums
4. Note refractive error: particularly high myopia
5. Recognize concurrent disease: ERM/AMD/DME
6. Qualitatively assess the scan for accuracy and artifacts:
   • segmentation errors
   • cropping/truncation
   • blink and/or motion and/or media opacities
7. Reconcile and topographically compare imaging with clinical exam and functional (AVF) analysis:
   • do these results make sense?

\textsuperscript{1} Hood DC, Raza AS. On improving the use of OCT imaging for detecting glaucomatous damage. \textit{Br J Ophthalmol} 2014;98:ii1-ii9.
# OCT: glaucoma diagnosis

## Optic nerve head (ONH) parameters
- OCT analysis of the ONH can accurately identify GON
- progressive NRR loss is predictive of future VF loss
  - less helpful with anomalous ONHs or advanced disease

### Be suspicious of:
- NRR area $<1\text{mm}^2$
- statistically abnormal vertical C/D ratio

### Remember: OCT cannot detect DH or NRR pallor

---

Retinal nerve fiber layer (RNFL) thickness

- evaluate (average, inferior, and superior) RNFL thickness
  - particularly valuable in early to moderate glaucoma
  - less helpful with anomalous ONHs or advanced disease

Be suspicious of:

- an average RNFL thickness of ≤75μm
- an inter-eye asymmetry of 6 to 9μm

OCT: **green is not always good**

Retinal nerve fiber layer (RNFL) thickness

![RNFL thickness map](image)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>OD</th>
<th>OS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average RNFL Thickness</td>
<td>91 μm</td>
<td>87 μm</td>
</tr>
<tr>
<td>RNFL Symmetry</td>
<td>83%</td>
<td></td>
</tr>
<tr>
<td>Rim Area</td>
<td>1.12 mm²</td>
<td>0.99 mm²</td>
</tr>
<tr>
<td>Disc Area</td>
<td>1.36 mm²</td>
<td>1.46 mm²</td>
</tr>
<tr>
<td>Average C/D Ratio</td>
<td>0.41</td>
<td>0.56</td>
</tr>
<tr>
<td>Vertical C/D Ratio</td>
<td>0.38</td>
<td>0.58</td>
</tr>
<tr>
<td>Cup Volume</td>
<td>0.055 mm³</td>
<td>0.125 mm³</td>
</tr>
</tbody>
</table>

Don’t rely solely on global summary parameters: qualitatively assess the scan for accuracy or artifacts, and scrutinize the deviation and thickness maps for focal defects

OCT: glaucoma diagnosis

Macular (ganglion cell/inner plexiform layer: GCIPL) thickness

- evaluate minimum and inferior-temporal GCIPL thickness\(^1\)
- particularly valuable with anomalous ONHs, high myopia, and advanced disease\(^2,3\)
- less helpful in the presence of concurrent macular disease (including AMD, DME, ERM, and VMT)\(^4\)

Be suspicious of:

- an inter-eye asymmetry of ≥5μm
- asymmetry across the temporal raphe: quantitative (≥9μm) and qualitative\(^5,6\)

Why is macular involvement important?

Despite representing only 2% of the total retinal surface, the macula contains over 30% of the RGCs in the human retina, and is mapped to an area occupying 60% of the visual cortex.\textsuperscript{1-3}
Why is macular involvement important?

Visual field loss within 10° of fixation:
• is part of the definition of advanced (severe) glaucoma\(^1\)
• can have a significant impact on activities of daily living\(^2\)
• necessitates aggressive intervention to minimize progression

Glaucomatous damage of the macula is common in early disease, but can easily go undetected by “conventional” analyses\(^3\)

---

Macular damage is common

"More than 50% of the eyes with predominantly mild to moderate glaucomatous field loss showed defective locations in the ... superior paracentral region within an eccentricity of 3°.”¹

"Macular damage, as seen on 10-2 VF's, appears to occur almost as frequently as peripheral defects in patients with ... early glaucoma.”²

"Given the prevalence of early macular damage, patients should not be screened with only the 24-2 VF.”³

"... in addition to the disc cube scan, macula scans should be incorporated into clinical protocols for detecting glaucomatous damage ...”

The macular vulnerability zone

Most axons from the inferior-temporal macula project to the **macular vulnerability zone**, while those from the superior macula project to the less vulnerable temporal quadrant\(^1,2\)

---

The MVZ explains patterns of macular damage

The region within the **red borders** of the 10-2 grid corresponds to the **macular vulnerability zone**, while the region within the **blue oval** corresponds to the **section of the inferior macula projecting to the less vulnerable temporal quadrant**

Structure/function correlation
Macular structure/function correlation
Inferior macular damage

RGC damage in the inferior macula can be extreme and central, leading to superior VF loss that is deep and threatens fixation\textsuperscript{1}.

RNFL analysis (as an NSTIN curve, putting the macula centrally) shows extreme local thinning at the border of the temporal and inferior quadrants: the macular vulnerability zone.

\textsuperscript{1} Hood DC, et al. Early glaucoma involves both deep local, and shallow widespread, retinal nerve fiber damage of the macular region. *Invest Ophthalmol Vis Sci* 2014;55:632-49.
Seeing macular involvement: **TSNIT** versus **NSTIN**
RGC damage in the superior macula tends to be more subtle, leading to shallower inferior VF loss further from fixation\(^1\).

As a result, RNFL analysis can appear nearly normal, showing a relatively shallow depression at the border of the temporal and superior quadrants ...

... but look at the obvious macular RGC asymmetry

---

Diffuse macular damage

Macular damage can also be diffuse, with relatively widespread loss of macular RGC and RNFL and shallow VF depression.  

Be vigilant: diffuse damage is common, and easily overlooked

Even with diffuse damage, the inferior macula is more involved: note the deeper superior VF defect and more significant RNFL thinning in the macular vulnerability zone.

OCT: glaucoma diagnosis

**Suspicious RNFL assessment:**
- an average RNFLT of ≤75µm
- an inter-eye asymmetry of 6 to 9µm

**Suspicious GCIPL assessment:**
- asymmetry between eyes
- asymmetry above and below the horizontal raphe

**Suspicious ONH assessment:**
- NRR area <1mm
- statistically abnormal vertical C/D ratio

---

Which is better, one (OCT) or two (AVF)?

In “early” (pre-perimetric) glaucoma, VF progression becomes **clinically detectable** at an average RNFL thickness of ~75μm\(^1,2\)

However, -3dB MD equates to a 50% loss of retinal ganglion cells\(^3\)
- the logarithmic scale of AVF analysis masks early loss\(^4\)

OCT is also less variable, facilitating earlier detection of change\(^5\)

---

Which is better, one (OCT) or two (AVF)?

In advanced glaucoma (MD ≥ -12dB), both RNFL and GCIPL reach a measurement floor at ~50μm (glial/vascular/non-RGC tissue)\(^1,2\)

![RNFL and GCIPL graphs]

VF loss remains detectable, albeit with significant variability\(^3\)

However, GCIPL tends to reach its floor later, and a larger area remains above the floor, allowing ongoing progression analysis\(^4\)

---

Which is better, one (OCT) or two (AVF)?

Early (including pre-perimetric) glaucoma:
- clinical exam and OCT (RNFL ≥ GCIPL > ONH)
- obtain baseline 24-2 and 10-2 for future reference

Moderate glaucoma:
- clinical exam and OCT (RNFL ≥ GCIPL > ONH)
- AVF (24-2, and 10-2 guided by GCIPL abnormalities)

Advanced glaucoma:
- 10-2 > 24-2 AVF (or 24-2 with stimulus size V)
- clinical exam and OCT (GCIPL > ONH ≥ RNFL)

**Utilize all the tools at your disposal:**
progression is detected by only one method >90% of the time\(^1,2\)

Leverage OCT in **early** disease and AVF in **advanced** disease\(^3\)

---

OCT: detecting progression

**Optical coherence tomography: Guided Progression Analysis**

Event-based analysis:
- highlights change from baseline in both RNFL and GCIPL thickness that exceeds normal variability
  - change on one occasion: **possible loss**
  - change on two or more successive occasions: **likely loss**

OCT: detecting progression

**Optical coherence tomography: Guided Progression Analysis**

Trend-based analysis:
• plots thickness over time to quantify rate of change in:
  • average, superior, and inferior RNFL thickness
  • average C/D ratio
  • average, superior, and inferior GCIPL thickness

Retinal nerve fiber layer (RNFL) thickness

- widening of an existing (inferior-temporal) RNFL defect
- repeatable inter-visit change in average RNFLT $\geq 5\mu m$
- a rate of average RNFL thinning $\geq 2$ to $3\mu m/year$

In suspects who go on to develop VF loss (manifest disease), the rate of RNFL loss is $\sim 2\mu m/year$, 4x the normal age-related loss

OCT: detecting progression

Retinal nerve fiber layer (RNFL) thickness

- widening of an existing (inferior-temporal) RNFL defect
- **repeatable** inter-visit change in average RNFLT ≥5μm
- a rate of average RNFL thinning ≥2 to 3μm/year

• smaller changes are more significant in advanced disease
• allow for age-related thickness loss of up to 0.5μm/year

OCT: detecting progression

RNFL loss may be clearer in *en face* images than thickness maps\(^1\)

- change in reflectivity may precede change of thickness\(^2\)

1. Hood DC, et al. Details of glaucomatous damage are better seen on OCT en face images than on OCT retinal nerve fiber layer thickness maps. *Invest Ophthalmol Vis Sci* 2015;56:6208-16.
OCT: detecting progression

Progressive RNFL loss: clinical exam and *en face* imaging
OCT: detecting progression

Macular (ganglion cell/inner plexiform layer: GCIPL) thickness
- widening of an existing (inferior-temporal) GCIPL defect
- repeatable inter-visit change in average GCIPLT ≥4μm
- a rate of average GCIPL thinning ≥1 to 1.5μm/year

The advantage of GCIPL in advanced glaucoma

# OCT: anterior segment in glaucoma

## Central corneal thickness

- optical and ultrasound CCT measurements may not be interchangeable (impact on risk calculation?)

## Angle assessment

- (static) OCT does not replace (dynamic) gonioscopy, but can provide ancillary quantitative and qualitative data

---

Putting it into practice

Macular and RNFL analyses are complementary, and GCIPL thinning can precede RNFL loss\textsuperscript{1,2}

\textbf{Obtain and critically analyze both RNFL and macular scans}

Current OCT segmentation algorithms aren’t foolproof:
- carefully inspect each scan to ensure quality/accuracy\textsuperscript{3}

Recognize the limitations of reference databases\textsuperscript{4}

Never rely solely on summary parameters: \textbf{qualitatively assess} and \textbf{look for focal change} in both RNFL and macular scans\textsuperscript{5}

\textbf{“Any result on SAP or SDOCT ... needs to be interpreted along with the total clinical picture ...”}\textsuperscript{6}

5. Hood DC, De Moraes CG. Four questions for every clinician diagnosing and monitoring glaucoma. \textit{J Glaucoma} 2018;27:657-64.
Are there any questions about my presentation?

Yes.

Did you brush your teeth too aggressively and accidentally stab yourself in the brain?

Can you be more specific?

Frontal lobes?