

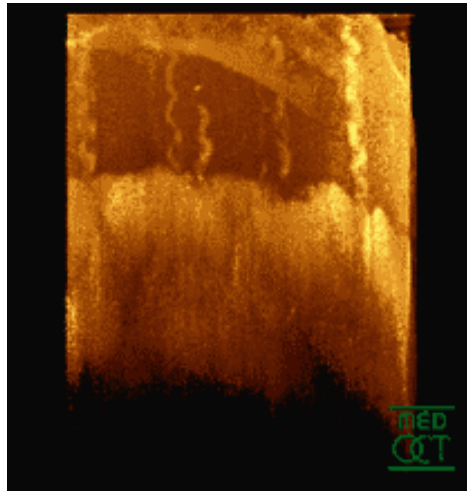
Optical Coherence Tomography (OCT) for the Neurologist

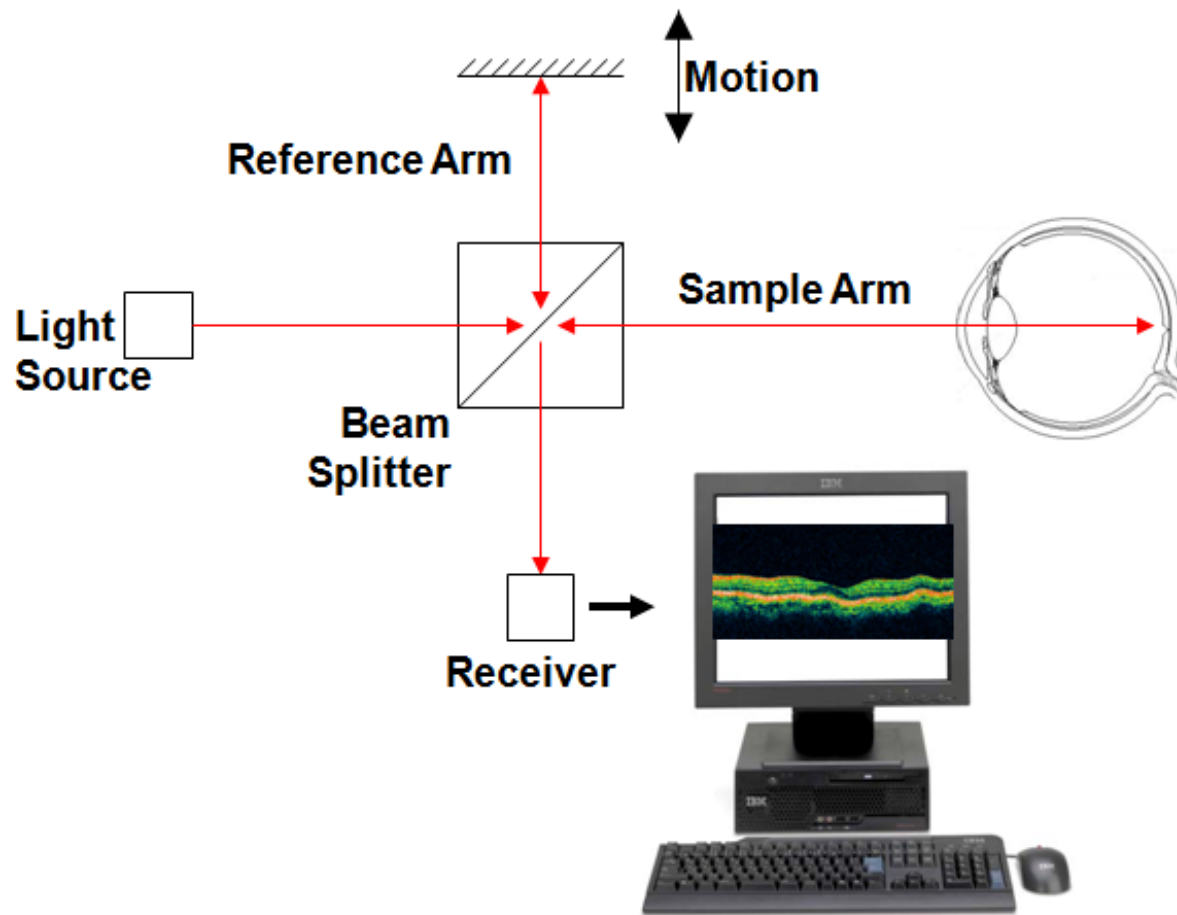
Alaa Bou Ghannam, MD
Neuroophthalmology Fellow

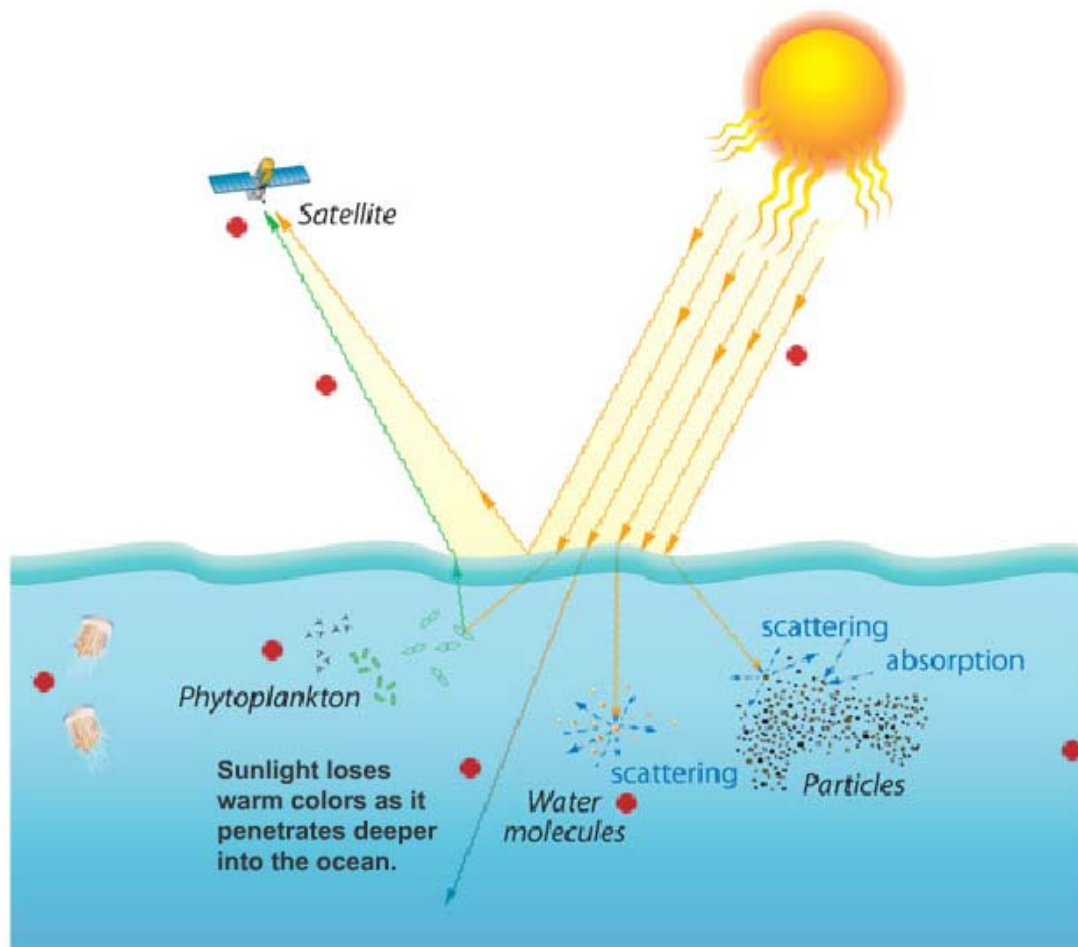
OCT

- Non-invasive diagnostic.
- Interferometry: cross-sectional map of the retina that is accurate to within at least 10-15 microns.
- Introduced in 1991

- Optical beam is directed at the tissue,
- most light is not reflected but, rather, scatters off at large angles
- a small portion of this light that reflects from sub-surface features is collected.
- Relatively long wavelength light → penetrate into the scattering medium







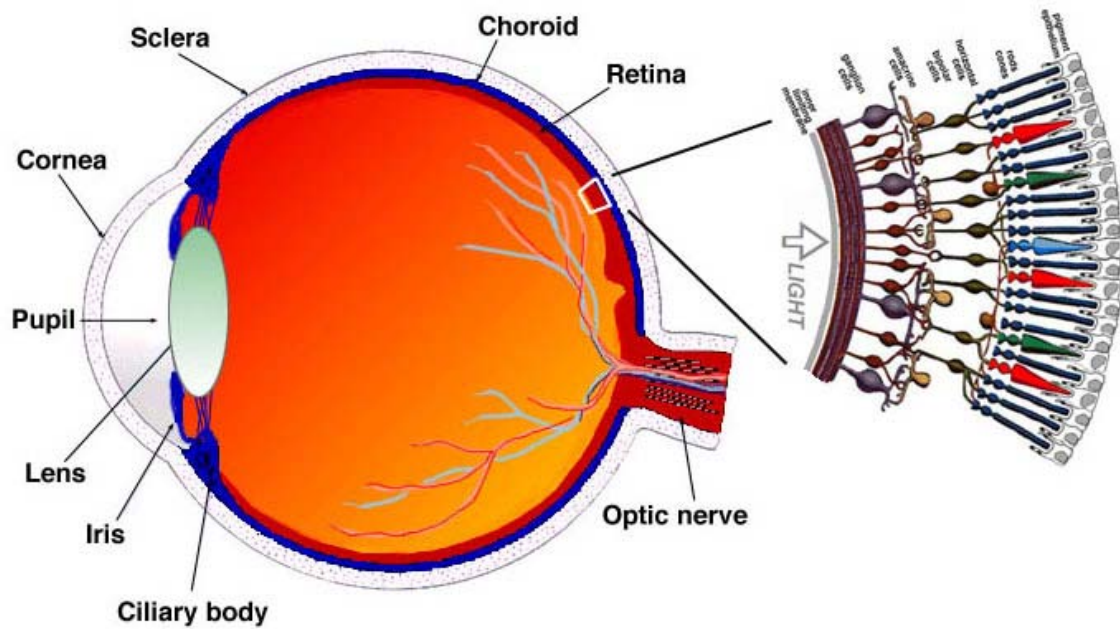
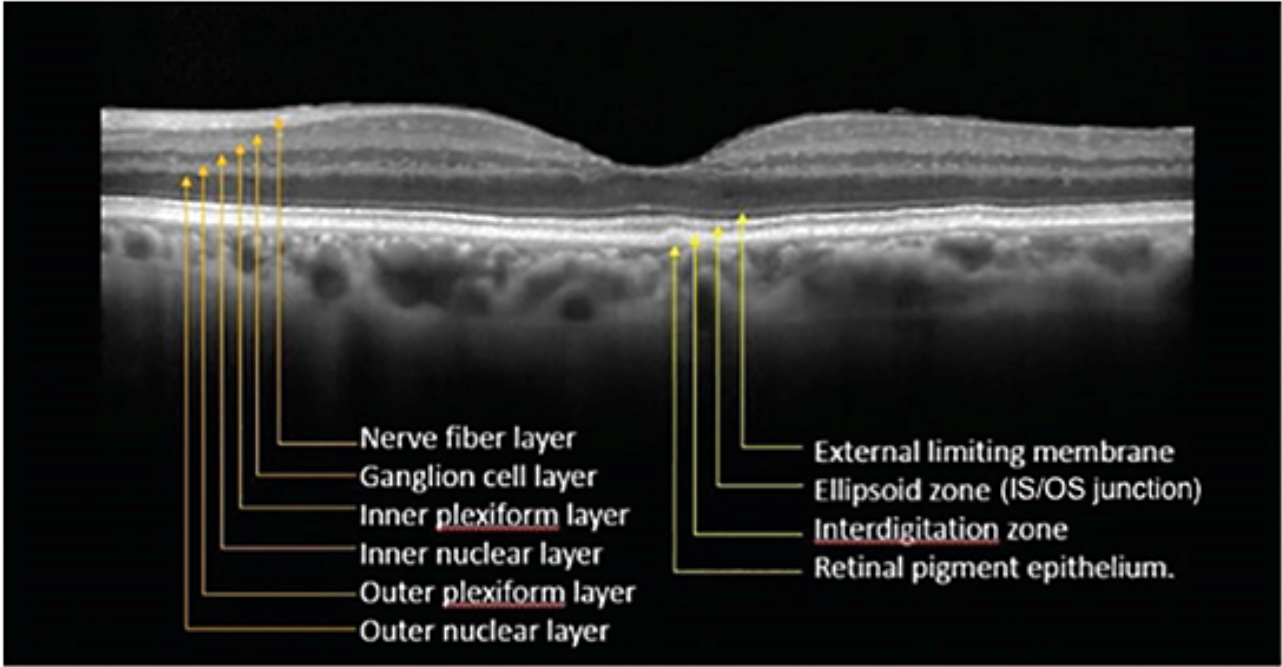
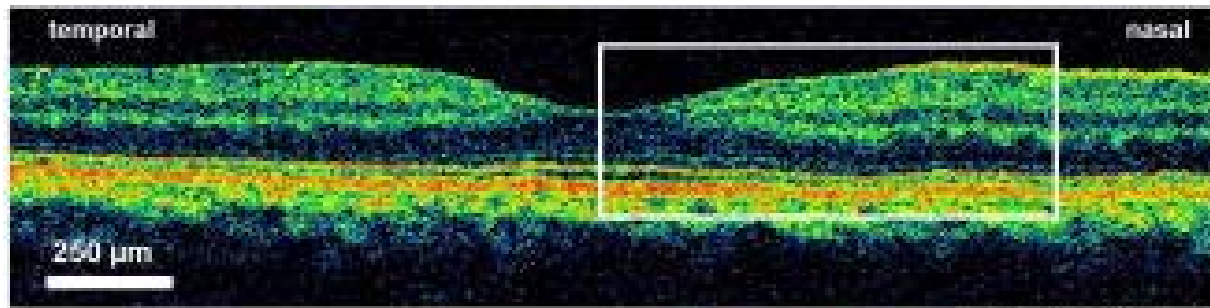
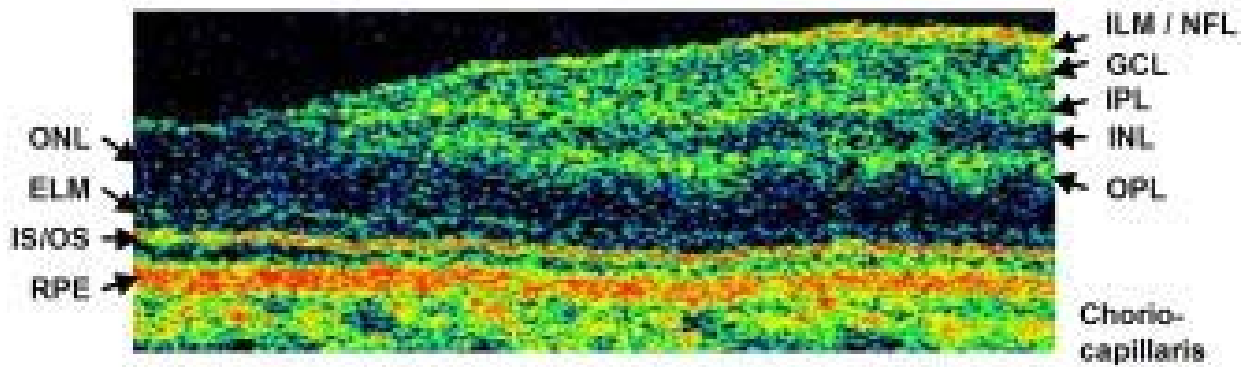


Fig. 1.1. A drawing of a section through the human eye with a schematic enlargement of the retina.





log reflection



1 **Key parameters**, compared to normative data, are displayed in table format.

2 **Nerve Fiber Layer (RNFL) thickness map** is a topographical display of RNFL. An hourglass shape of yellow and red colors is typical of normal eyes.

3 **The RNFL Deviation Map** shows deviation from normal. OCT *en face* fundus image shows boundaries of the cup and disc and the RNFL calculation circle.

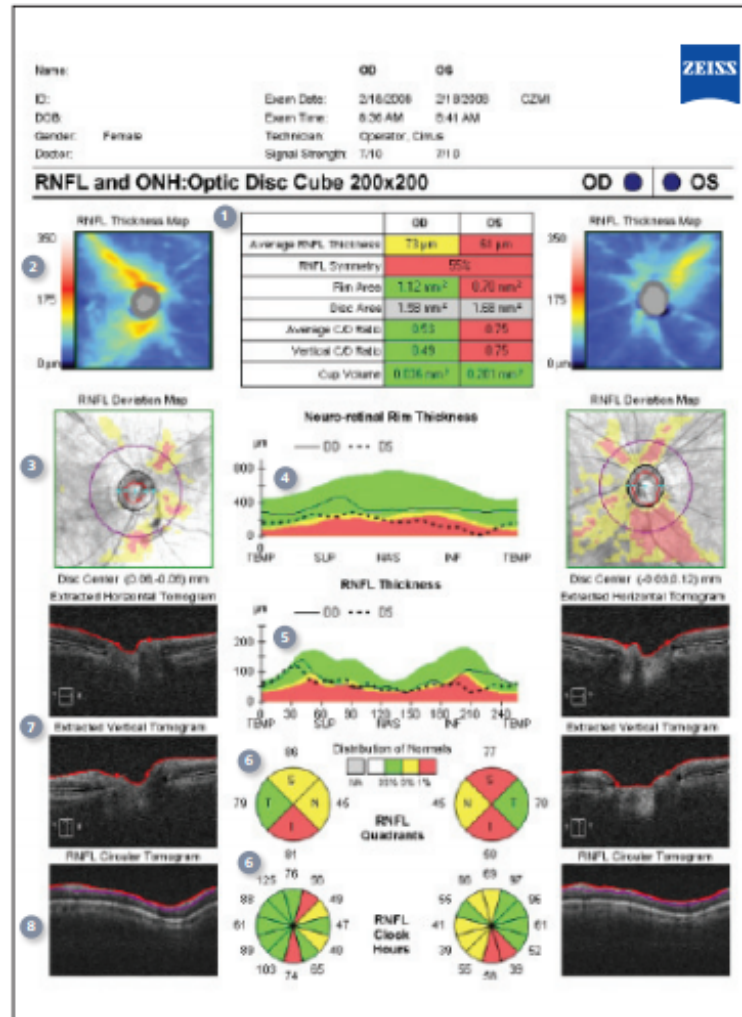
4 **Neuro-retinal Rim Thickness profile** is matched to normative data.

5 **RNFL TSNIT graph** displays patient's RNFL measurement along the calculation circle, compared to normative data.

6 **RNFL Quadrant and Clock Hour** average thickness is matched to normative data.

7 **Horizontal and vertical B-scans** are extracted from the data cube through the center of the disc. RPE layer and disc boundaries are shown in black. ILM and cup boundaries are shown in red.

8 **RNFL calculation circle** is automatically centered on the optic disc and extracted from the data cube. Boundaries of the RNFL layer segmentation is illustrated.

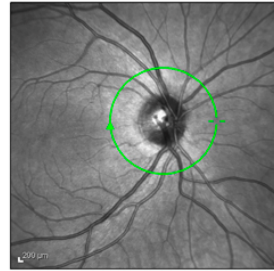


Patient: 000000 000000
 Patient ID: 000000
 Diagnosis: ---

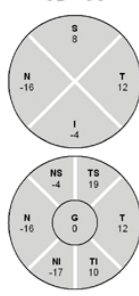
DOB: Oct/10/1980
 Exam.: Jun/25/2009
 Comment: ---

Gender: F

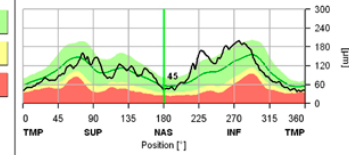
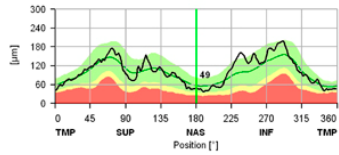
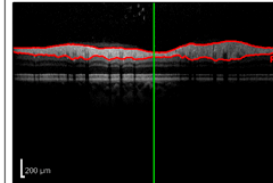
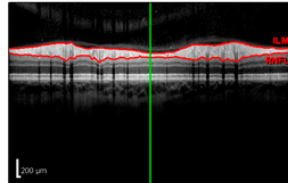
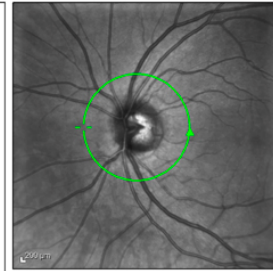
OD



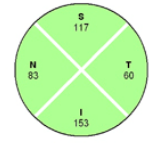
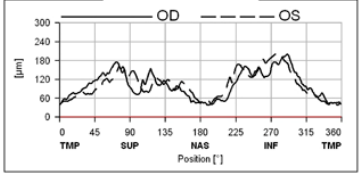
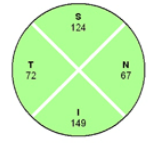
**Symmetry
 OD - OS**



OS



Within normal limits (p>0.05)
 Borderline (p<0.05)
 Outside normal limits (p<0.01)



Classification OD
 Within normal limits

Classification OS
 Within normal limits

Notes:
 Date: 6/25/2009 Signature: _____

516 Delaware Street SE
 Minneapolis, MN 55455
 Phone: 612.625.4400

FAQs

Does the Test Need Any Preparation?

No. Most patients older than 3 to 5 years of age should be able to have the test performed in a seated position with chin and head positioned in a manner similar to a slit lamp.

FAQs

Does the Procedure Need Any Dilation / Eye Drops?

Dilation or eye drops are not usually needed.

Infrequently, dilating drops may be needed, particularly in patients with cataracts or other media opacities, very small pupils (2 mm or less), or poor vision interfering with fixation.

FAQs

What Is the Duration of the Test?

Test duration depends on the OCT imaging protocol and device used. The most common optic nerve head/peripapillary and macular OCT studies can be completed in less than 10 minutes.

FAQs

What Is Being Measured?

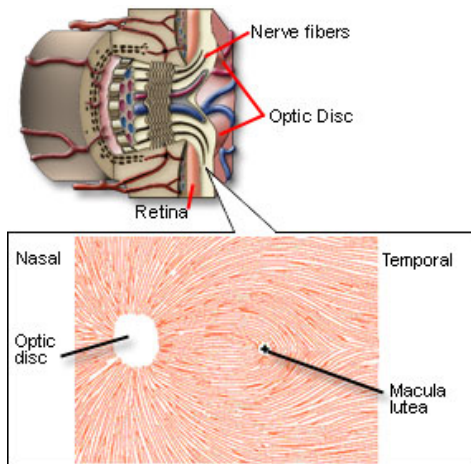
- retinal nerve fiber layer (RNFL) thickness around the optic nerve (peripapillary RNFL thickness)
- Central retina and macula.
- From a neurologic point of view, both types of imaging are important both to document the extent of optic neuropathy (RNFL thinning) and to exclude macular pathology as a cause for visual loss (macular imaging)

Time Domain vs. Spectral Domain

- Time domain: acquire 400 A-scans per second using 6 radial slices oriented 30 degrees apart.
 - Accurate 10-15 microns
- Spectral domain: scans approximately 20,000-40,000 scans per second.
 - diminishes the likelihood of motion artifact,
 - enhances the resolution
 - approach 3 micron resolution

Artifacts

- Signal Strength
 - High myopia
 - Corneal scars
 - Cataract
 - Vitreous opacity
- Movement artifacts



- Temporal RNFL axons have a specific arrangement in the retina, with a clear horizontal demarcation between the superior and inferior arcuate bundles.
- Fibers from the macula form the papillomacular bundle.
- Nasal fibers converge radially

Optic Neuritis and OCT



Physiologic values

- RNFL loss with age
 - 0.017% / year (~10-20 μm loss over 60 years).
- peripapillary RNFL thickness
 - 92.9 μm as measured by Cirrus SD-OCT
 - 100.6 μm as measured by Spectralis SD-OCT.
- Macular volume
 - 10.1 mm^3 on Cirrus SD-OCT
 - 8.75 mm^3 on Spectralis SD-OCT

Optic Neuritis

- As a sporadic event or in the context of multiple sclerosis (MS).
- 1 in 5 MS patients → first clinical manifestation of their disease.
- The Optic Neuritis Treatment Trial
 - Young (mean age: 32 years), white (85%), and women (77%)
 - Pain at the time of symptom onset (92 %)
 - Vision loss tends to progress over hours to days
 - May range from mild (Snellen visual acuity equivalent of 20/20) to severe (no light perception) initially

Optic Neuritis

- Visual recovery after optic neuritis
 - within weeks,
 - more than 90% of patients achieving a visual acuity of 20/40 after 1 year
- But
 - heat-induced vision loss (Uhthoff phenomenon),
 - altered motion perception
 - decreased spatial vision at low-contrast levels

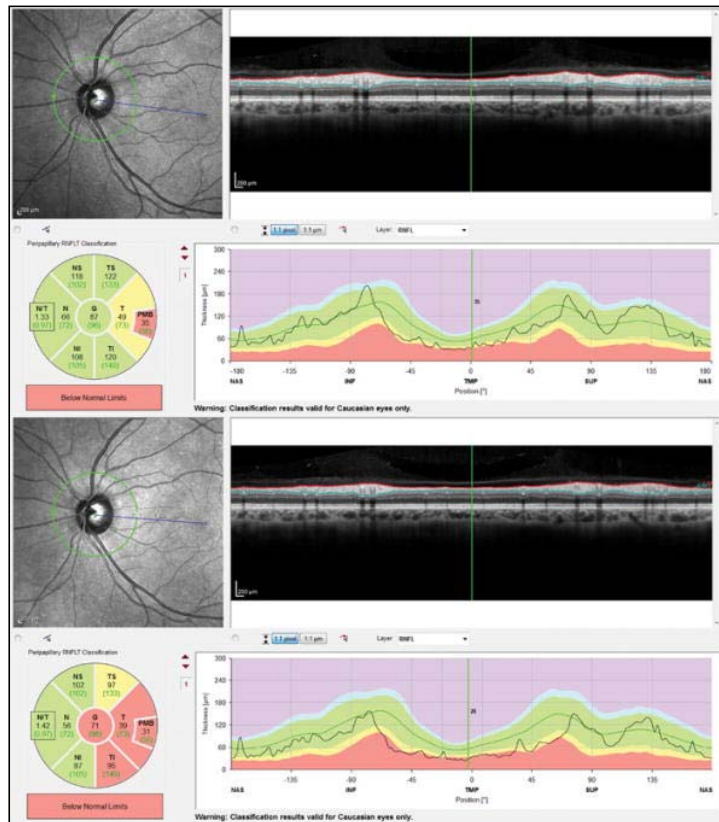
Acute ON and OCT

- Peripapillary RNFL measurements
 - Often elevated in the optic neuritis eye, presumably due to axoplasmic flow stasis.
 - OCT-measured macular volume and ganglion layer measures are generally comparable between affected and unaffected eyes of patients at the time of symptom onset.

- Costello et al, 2006
 - 20 to 40 μm thinning of the peripapillary RNFL within 3 to 6 months following acute ON.
 - “window of opportunity” for potential intervention with therapies that could protect and repair the CNS.
- More recent
 - retinal cell ganglion loss occurs within weeks of acute ON, pushing the time window to intervene much earlier.

- mean time to 90% RNFL loss: 2.38 months;
- 99% RNFL loss: 4.75 months
- Kupersmith et al
 - ganglion cell layer thinning develops rapidly within the first month in ON before any observable RNFL loss

Fig. 3



Optical Coherence Tomography for the Neurologist.
 Nolan, Rachel; Narayana, Kannan; Galetta, Steven; MD 1, 2; Balcer, Laura; MD, MSCE; 1, 2
 Seminars in Neurology. 35(5):564-577, October 2015.
 DOI: 10.1055/s-0035-1563579

Fig. 3 Optic neuritis. (Top) Baseline peripapillary optical coherence tomography (OCT) imaging in a patient 2 months after acute optic neuritis. Visual acuities were 20/20+ OD and 20/20-1 OS in both eyes at distance. Visual fields were intact to confrontation. With a red target, she reported red desaturation in the upper temporal quadrant of her left eye. She perceived 10/10 Ishihara color plates correctly with the right eye, and only 4/10 in the left. She had a left relative afferent pupillary defect (RAPD). On funduscopy, optic discs appeared normal without swelling or pallor, in the right; the left optic disc was pale, particularly in the temporal sector. Magnetic resonance imaging showed prominent enhancement of the left optic nerve and questionable mild enhancement of the right optic nerve. (Bottom) Six months after the initial optic neuritis attack. Peripapillary retinal nerve fiber layer measurement in the affected eye decreased by 16 [µm] since baseline OCT.

Chronic Optic neuritis

- Earliest studies of ON in MS
 - peripapillary RNFL thickness was reduced by an average of 33 to 46% by time-domain OCT in eyes with an ON
 - Fellow eyes of patients with a history of ON had RNFL thickness reductions of 27to 28%.
 - Eyes with a history of ON also had macular volume reductions of 11%.

- Retinal segmentation techniques:
 - initial months % decrease in ganglion layer thickness correlates with increased outer nuclear layer and photoreceptor layer thicknesses,
 - outer layer measurements subsequently decline between months 4 and 12 postevent.

- Recurrent optic neuritis → worse OCT measures of neuroaxonal integrity
- Yeh and colleagues
 - 9-µm (9%) decrement in RNFL thickness for each additional episode of optic neuritis in a pediatric population
- OCT floor effect
 - mean RNFL values do not generally decrease 30 µm regardless of the extent of optic nerve injury

- Optical coherence tomography can be used to confirm an optic neuropathy based on the presence of peripapillary RNFL thinning
- Optic atrophy, and associated peripapillary RNFL thinning, may take weeks to develop.
- In acute ON, peripapillary RNFL thickening may actually be present even in cases where the clinical ophthalmoscopic examination does not reveal evidence of optic disc swelling (retrobulbar ON).



MS and OCT

MS and OCT

- One of the ongoing challenges in MS is to establish sensitive biomarkers of relapse-related and subclinical CNS injury that contribute to neurologic disability.

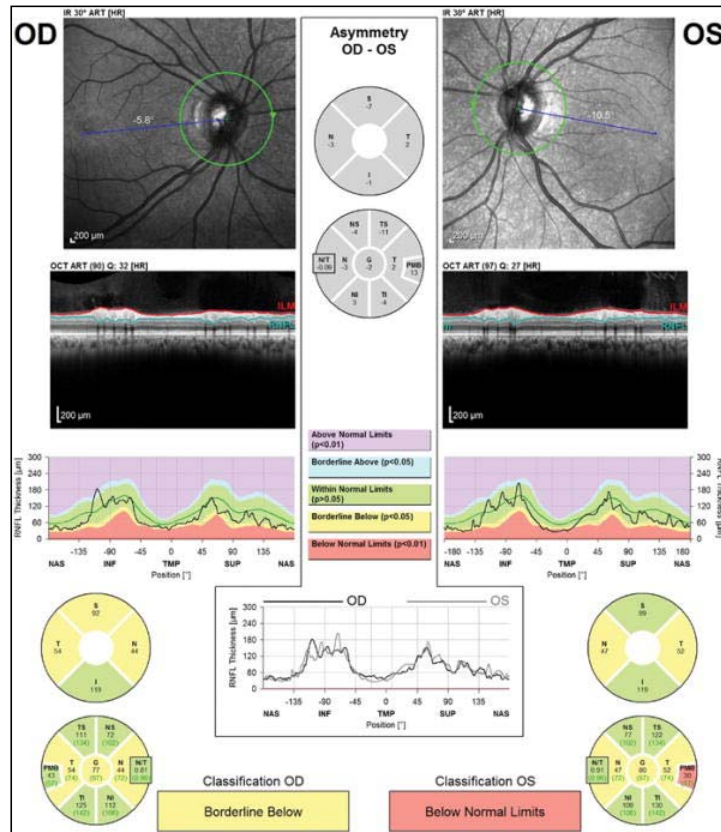
MS and OCT

- Petzold et al, 2010
 - peripapillary RNFL thinning by time- domain
 - 20.38 μm in MS eyes with a history of acute ON.
 - 7.08 μm in MS patients with no history of ON.

MS and OCT

- Thinning of the peripapillary RNFL has been observed in
 - Eyes with ON
 - asymptomatic fellow eyes of MS patients (thickness between 91.08 and 109.3 μm)
 - eyes of MS patients without a clinical history of acute ON

Fig. 4



Optical Coherence Tomography for the Neurologist.
 Nolan, Rachel; Narayana, Kannan; Galetta, Steven; MD 1, 2; Balcer, Laura; MD, MSCE; 1, 2
 Seminars in Neurology. 35(5):564-577, October 2015.
 DOI: 10.1055/s-0035-1563579

Fig. 4 Patient with multiple sclerosis (MS; with no history of optic neuritis). Peripapillary optical coherence tomography imaging in a 45-year-old African American woman diagnosed with MS 26 years prior to imaging date. She was on glatiramer acetate for 14 years and intravenous immunoglobulin for 9 years. At the time of imaging, patient's secondary progressive multiple sclerosis was fairly stable.

MS and OCT

- In MS patients with no history of acute ON
 - Average peripapillary RNFL thicknesses is reduced
 - Subclinical anterior visual pathway axonal loss in patients with MS, even in eyes without history of ON.
 - For every 1-line decrease in low-contrast letter acuity score, mean RNFL thickness values decreased by 4 μm
 - Potential role for OCT in trials that may examine neuroprotective and other disease-modifying therapies.

Subtypes of MSA

- CIS:
 - Even in CIS eyes without prior optic neuritis, the ganglion layer measures were reduced
- PPMS
 - Abnormal RNFL
 - does not manifest clinically overt optic neuritis with same propensity as patients who have experienced RRMS
- Secondary progressive MS
 - greatest degree of thinning (mean RNFL thickness = 70.8 μm)
- Macular thinning predominant (MTP)
 - Normal RNFL
 - Sparing of GCL
 - Proposed new MS phenotype

- RNFL thickness reflects the volumes of brain white and gray matter as well as the normalized volumes of whole brain and white matter.
- Retinal nerve fiber layer thickness also is reduced among patients with the greatest degrees of brain atrophy, reductions in brain parenchymal fraction and the highest volumes of T1 and T2 lesions.

- multicenter study
- 849 subjects
 - RNFL < 87 microns, 2x risk of EDSS –determined disability worsening up to 3 yrs
 - 4x the risk 3-5 years.
 - OCT may be used to track manifestations of neurodegeneration that lead to permanent neurologic disability in MS.

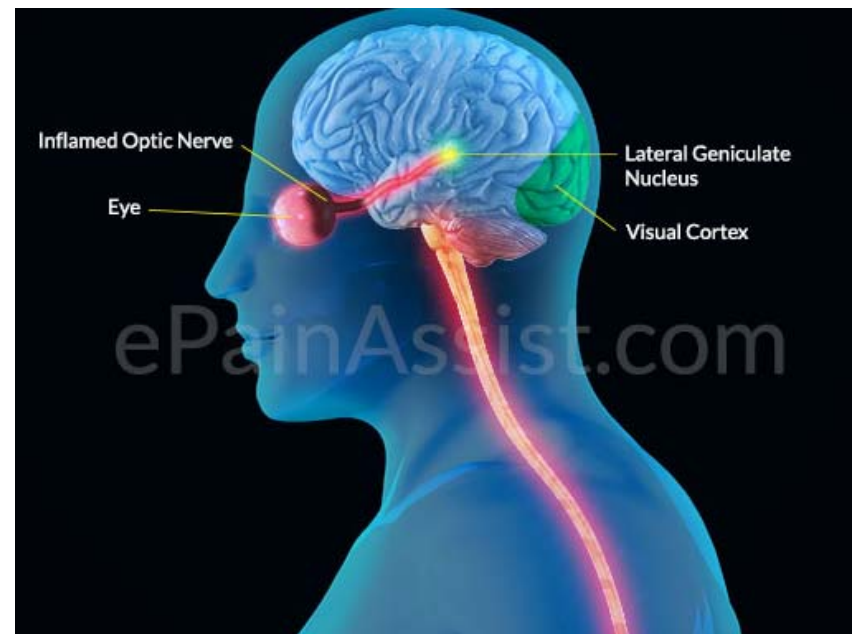
Fingolimod

- Fingolimod
 - macular edema in 0.3 to 1.2% of patients;
 - history of uveitis and other ocular pathology elevates this risk.
 - Macular edema resolves when fingolimod treatment is discontinued.
 - Happens in the first 3 months
 - Ophthalmologic evaluations, including OCT scans of the macula, are recommended before initiating treatment and follow-up at 3- to 4-month

Microcystic Inner Nuclear Layer Abnormalities

- Associated with reductions in vision.
- Microcystic inner nuclear layer abnormalities are not specific to MS with a history of ON

NMO and OCT



NMO

- Visual prognosis after an episode of ON may be worse
- Thinning: 50 -83 microns (vs. 20 microns in MS)
- Superior and inferior quadrants are more affected by RNFL (vs. temporal in MS)
- Unaffected eyes are comparable to controls
- Prominent microcystic macular edema may be seen with apparent thickening of the inner nuclear layer

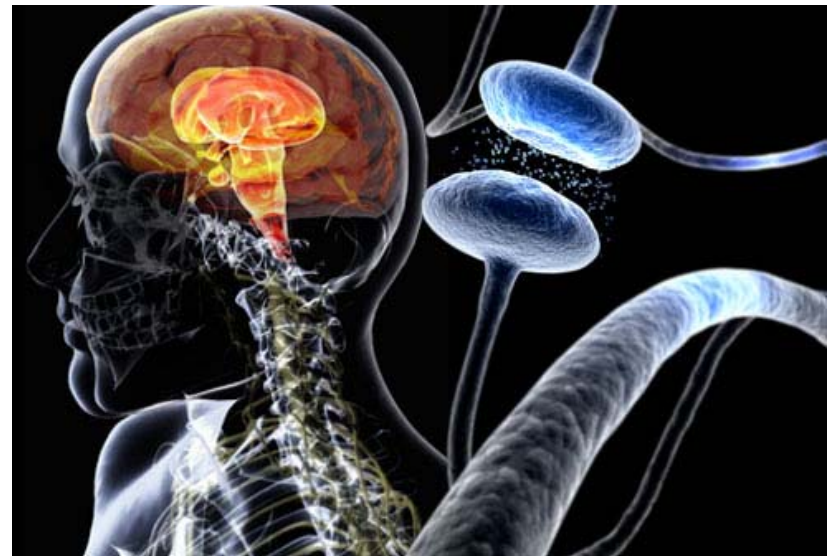
Alzheimer's and OCT



Alzheimer Disease

- In a recent meta-analysis
 - Significant reductions in peripapillary RNFL thickness
 - Choroid, macular, and ganglion cell layer thicknesses are also reduced
 - Detection of abnormal deposits in the retina using fundus autofluorescence is a potential use of OCT in mild cognitive impairment and AD.
 - Such findings could be incorporated in the future into screening and early diagnosis protocols, thus identifying patients who could most benefit from clinical trials or new therapies.

Parkinson's and OCT



Parkinson Disease

- Peripapillary RNFL thinning has been reported in several small case series
- Temporal quadrant has been most commonly identified as thin compared with controls.⁷
- Macular thinning and volume loss from the inner retina has also been reported

Papilledema and OCT

- When used in combination with other well-known clinical measures (vision, color vision, and visual fields), OCT can play a role in monitoring disease progression.
- It may prove to be a helpful quantification tool for monitoring patients with papilledema.
- For lower grades of papilledema, peripapillary RNFL thickness measurement is useful to quantify the severity of disc swelling.
- In moderate to severe papilledema, where the average RNFL thickness is often $> 200 \mu\text{m}$, software algorithms for calculating thickness may fail in over a third of the cases on time-domain OCT.



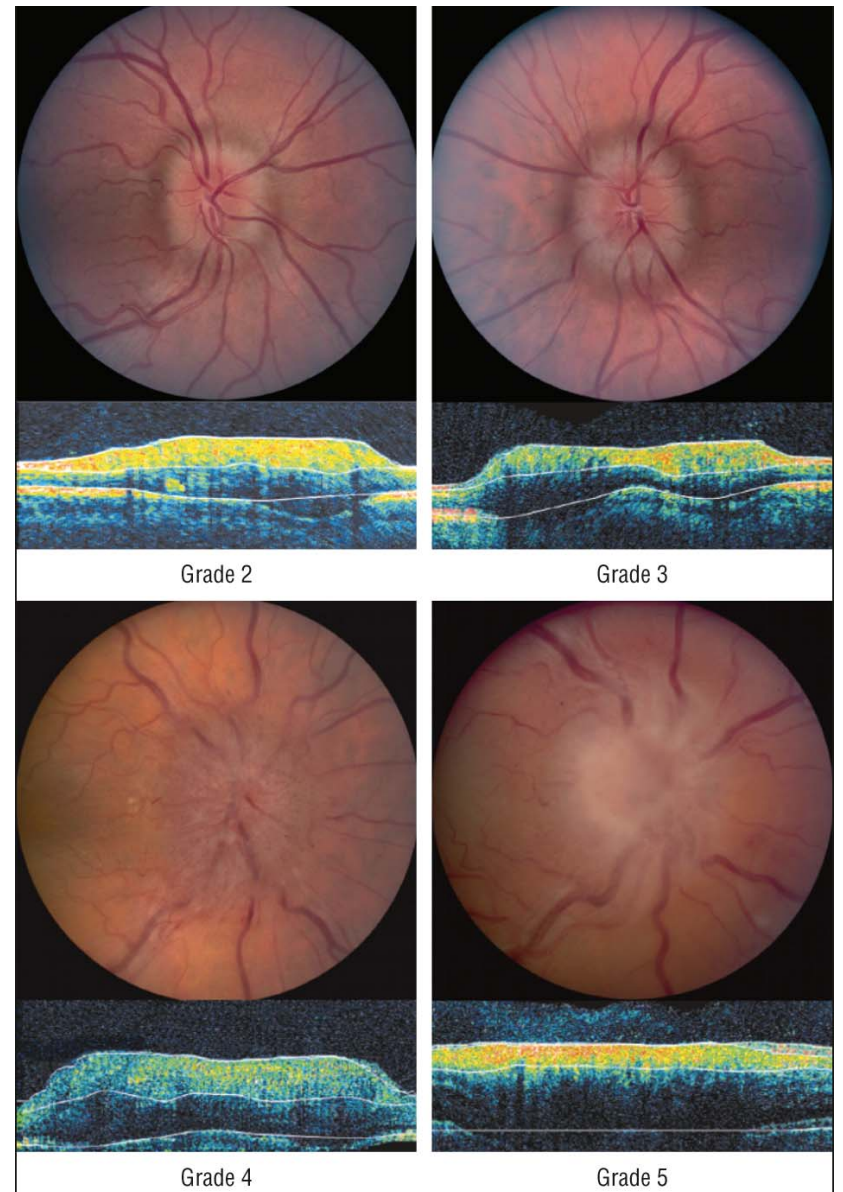
Papilledema

Pseudotumor cerebri

- Increased intracranial pressure of unknown cause,
- associated with papilledema.
- Swelling of the optic nerve head is believed to arise from compression of the retrolaminar optic nerve → obstructs axoplasmic flow

Papilledema

- Scott and colleagues



Papilledema

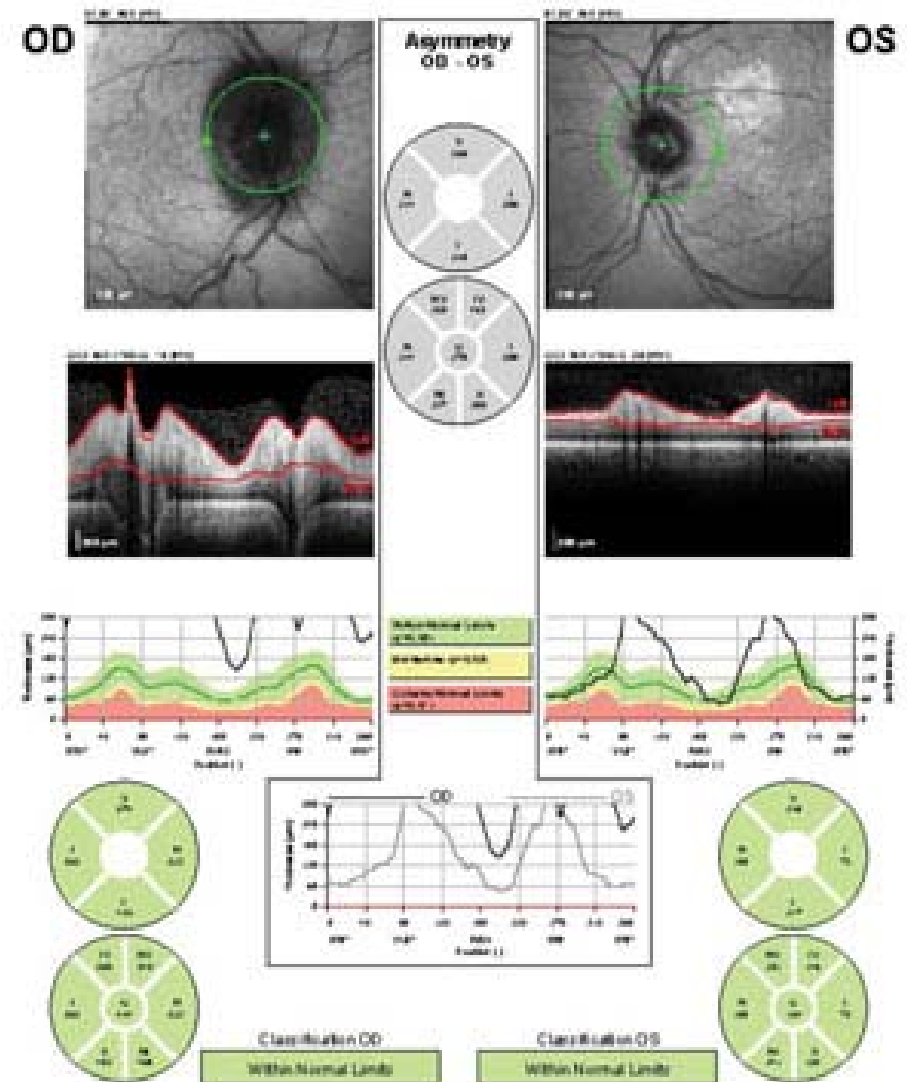
- Acutely
 - severe optic disc edema correlated with marked elevations in RNFL thickness and corresponding increases in macular volumes.
- With time and treatment
 - RNFL values diminish and optic disc edema abates.
- In chronic stages
 - RNFL values, macular volume and ganglion layer thickness decrease → optic atrophy

- IIHTT

- macular ganglion cell layer/inner plexiform layer thinning → visual acuity
- Increased peripapillary RNFL thickness → higher elevations in intracranial pressure (ICP) in newly diagnosed IIH patients.
- These findings make OCT a potentially valuable supplement to subjective assessment of papilledema in IIH.

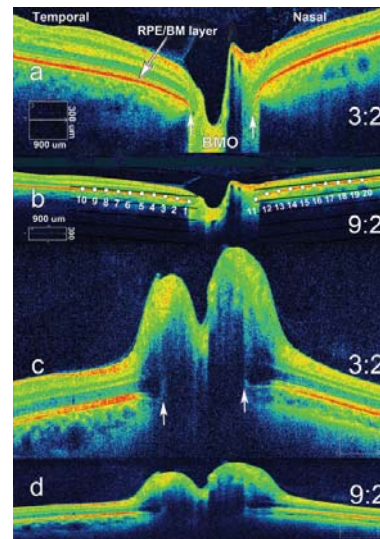
OCT and papilledema

- limited in the evaluation of more severe grades of papilledema



From: Effects of Lowering Cerebrospinal Fluid Pressure on the Shape of the Peripapillary Retina in Intracranial Hypertension

Invest. Ophthalmol. Vis. Sci.. 2014;55(12):8223-8231. doi:10.1167/iovs.14-15298



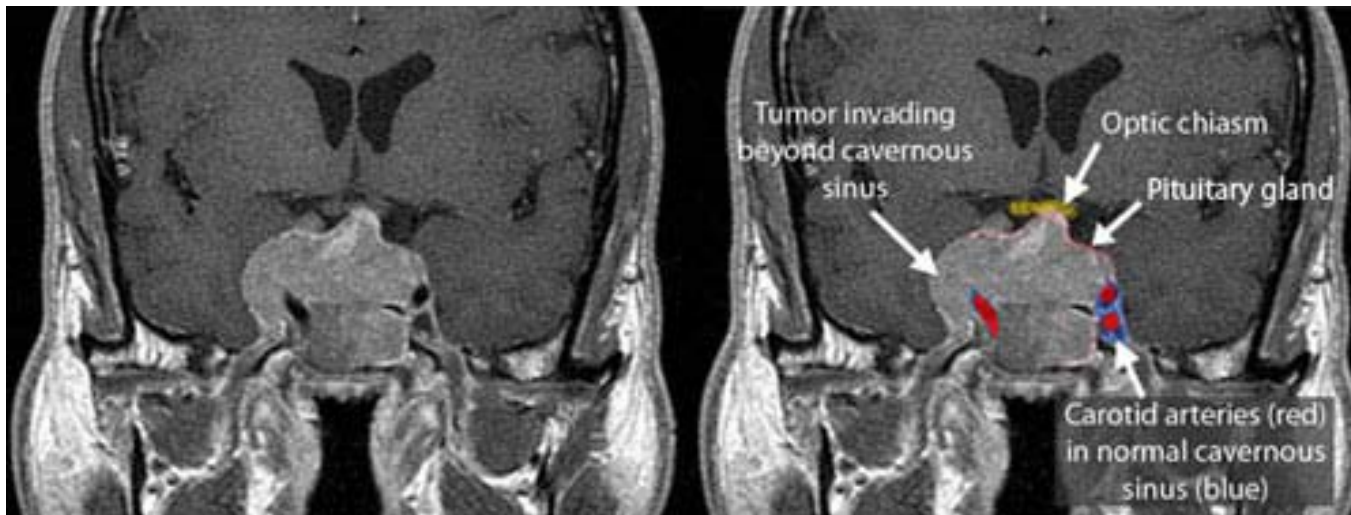
Spectral-domain OCT 9-mm axial raster images of a normal eye and the eye of a patient with papilledema, illustrating aspect ratio, semi-landmark placement, and shape of the ppRPE/BM layer. (a) Normal eye. Spectral-domain OCT raster scan using the standard jpg image (9-mm scan with aspect ratio of 3:2; 750 × 500 px). This image demonstrates the V-shape of the RPE/BM layer that slopes away from the vitreous, typically seen in normal subjects. (b) Normal eye. Corrected 9-mm image that eliminates vertical stretch with an aspect ratio of 9:2 (750 × 167 px). The numbered points demonstrate the placement of 10 equidistant semi-landmarks that define the shape of the RPE/BM layer (starting at the border of the BMO). The semi-landmarks span a distance of 2500 μm on each side of the BMO. (c) Papilledema. An example of a 9-mm raster image (3:2 aspect ratio; 750 × 500 px) demonstrating the inverted U-shape deformation, indenting the globe toward the vitreous. (d) Papilledema. Same as (c) after correcting the aspect ratio (9-mm scan, aspect ratio of 9:2, 750 × 167 px).

- After intracranial pressure lowering
 - Peripapillary retinal pigment epithelium–basement membrane layer changed to one that appeared more V-shaped
 - The magnitude of the change with respect to shape, mean RNFL thickness, and displacement of the peripapillary retinal pigment epithelium–basement membrane layer was greater in patients who underwent CSF shunting, relative to patients treated medically or with lumbar puncture.

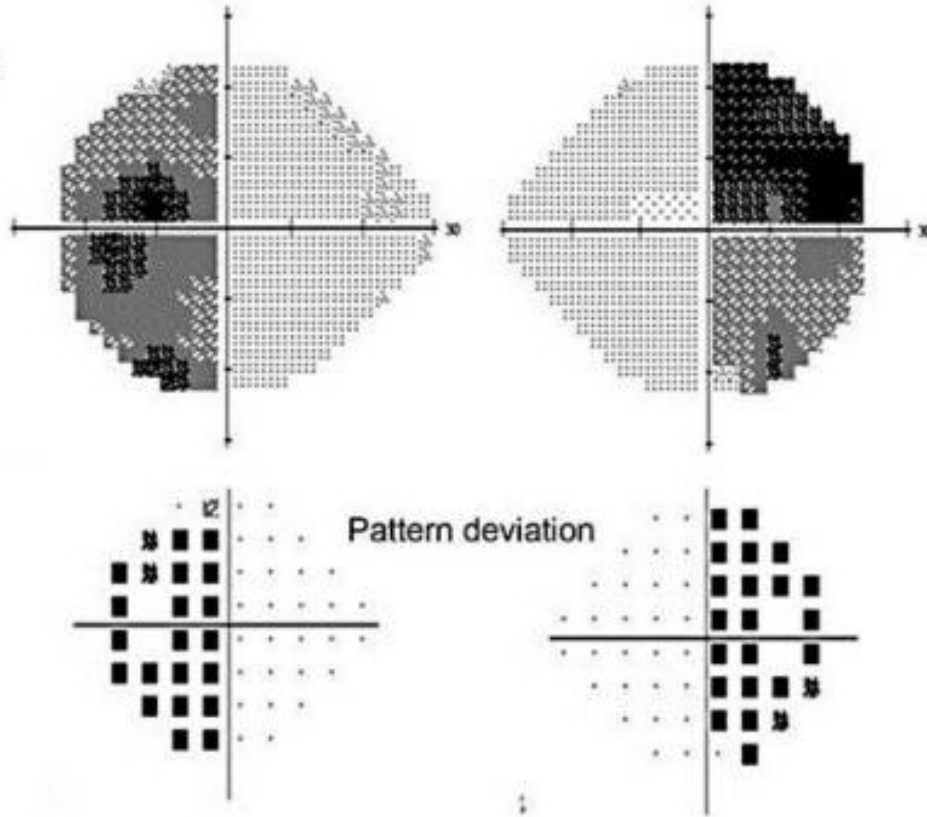
- Sibony and colleagues
 - 3 types of folds in IHH patients with papilledema
 - peripapillary wrinkles
 - retinal folds
 - choroidal folds.

Pituitary tumors and OCTA

- Lesions with suprasellar extension → vision loss due to mass effect on the ante

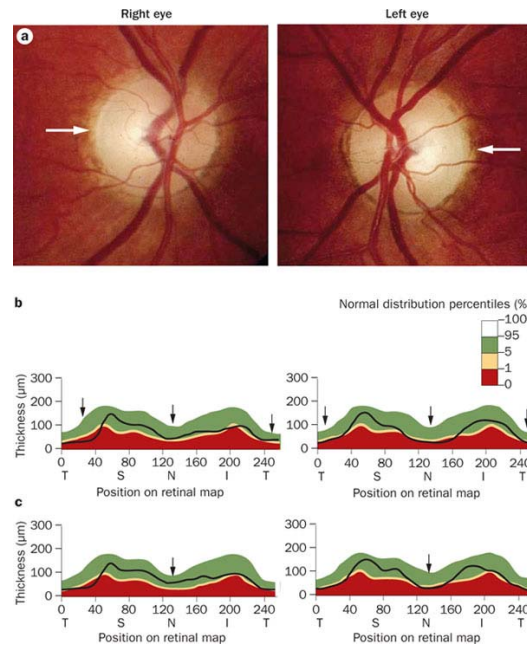


C



- Various factors that have been proposed to have an impact on postoperative visual outcomes in pituitary patients I
 - rate of tumor growth
 - severity of optic chiasm compression
 - tumor size
 - preoperative OCT optical measured RNFL thickness
 - duration of visual dysfunction visual pathway.

Figure 6 Optic nerve head photographs and OCT imaging from a patient with a compressive optic neuropathy due to a pituitary adenoma



O'Neill, E. C. *et al.* (2010) The optic nerve head in acquired optic neuropathies
Nat. Rev. Neurol. doi:10.1038/nrneurol.2010.5

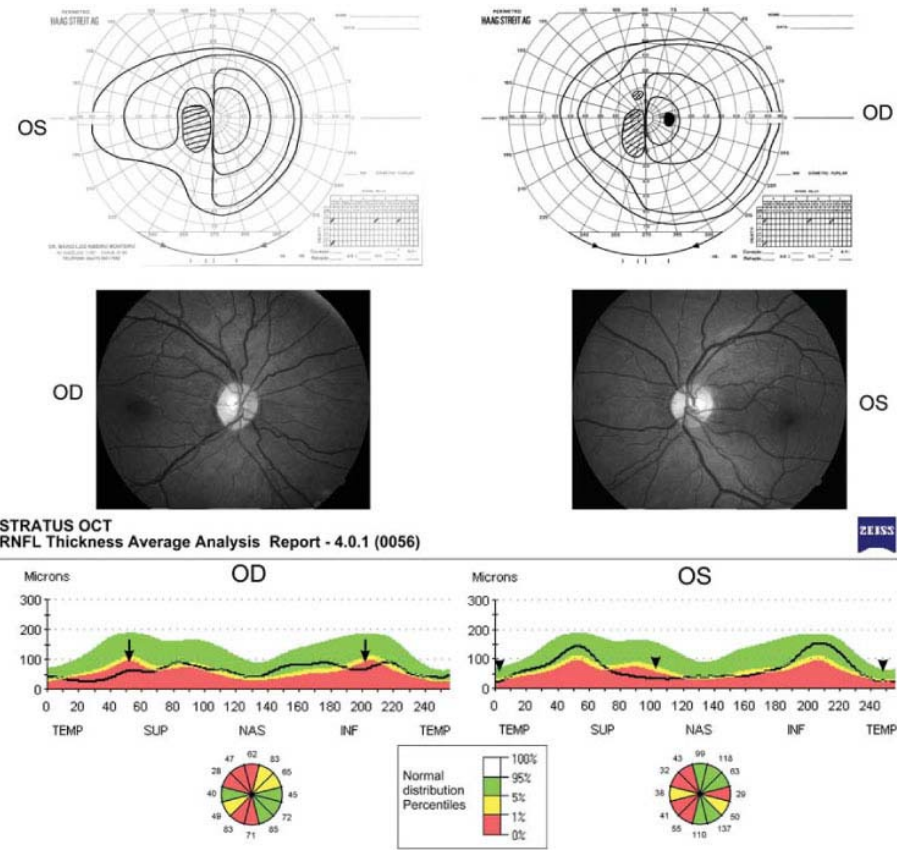
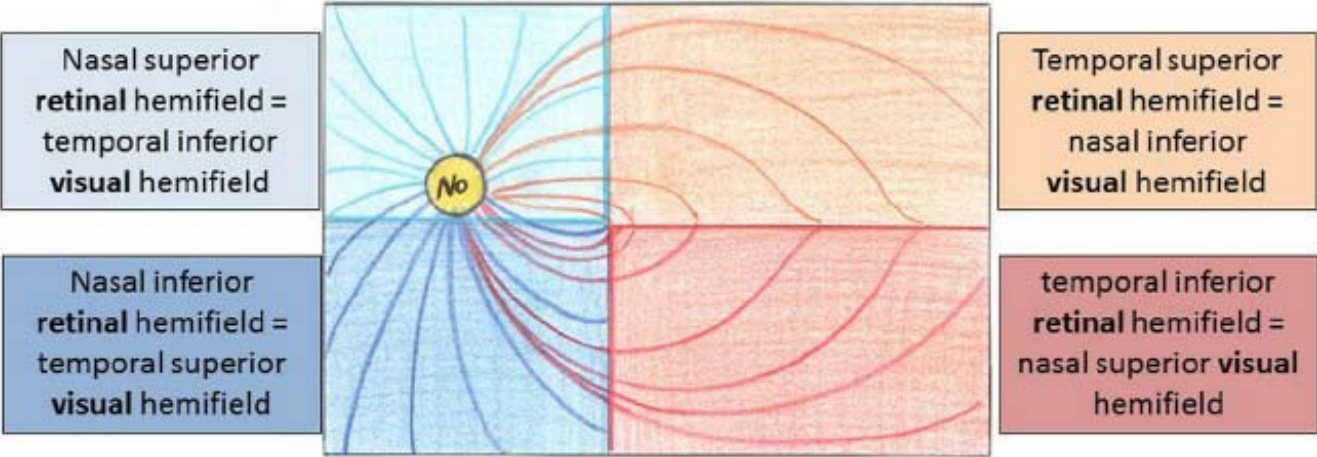
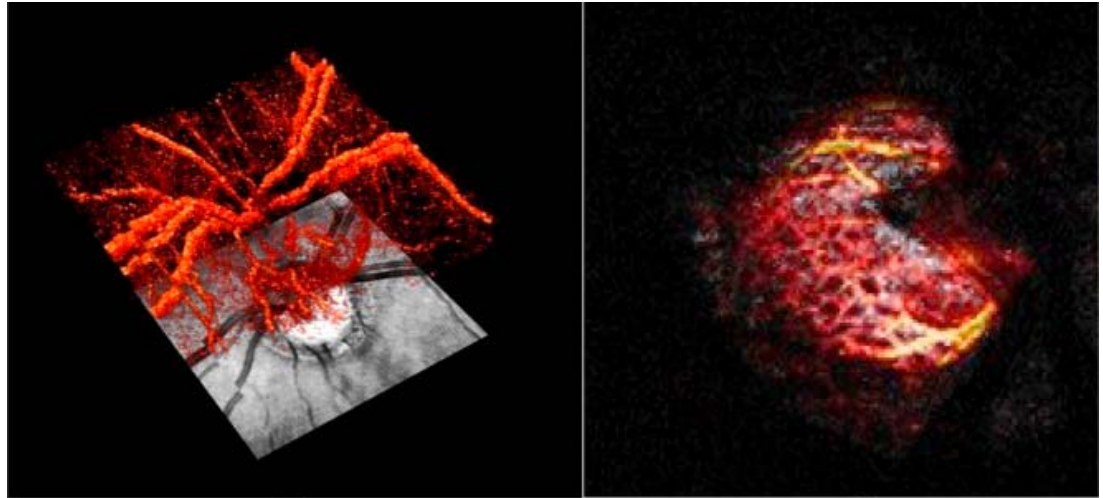


Figure 2: Case 2 - Goldmann visual fields showing incongruous left homonymous hemianopia. Middle, fundus photograph showing diffuse pallor in the right eye (OD) and band atrophy of the optic nerve in the left (OS). Below, Stratus - Optical coherence tomography showing retinal nerve fiber layer loss in the superior and inferior quadrant (arrows) in OD and in the temporal and nasal aspects of the optic nerve in OS (arrowheads)



- OCT can detect ganglion layer integrity that predate functional deficits in visual function

OCTA

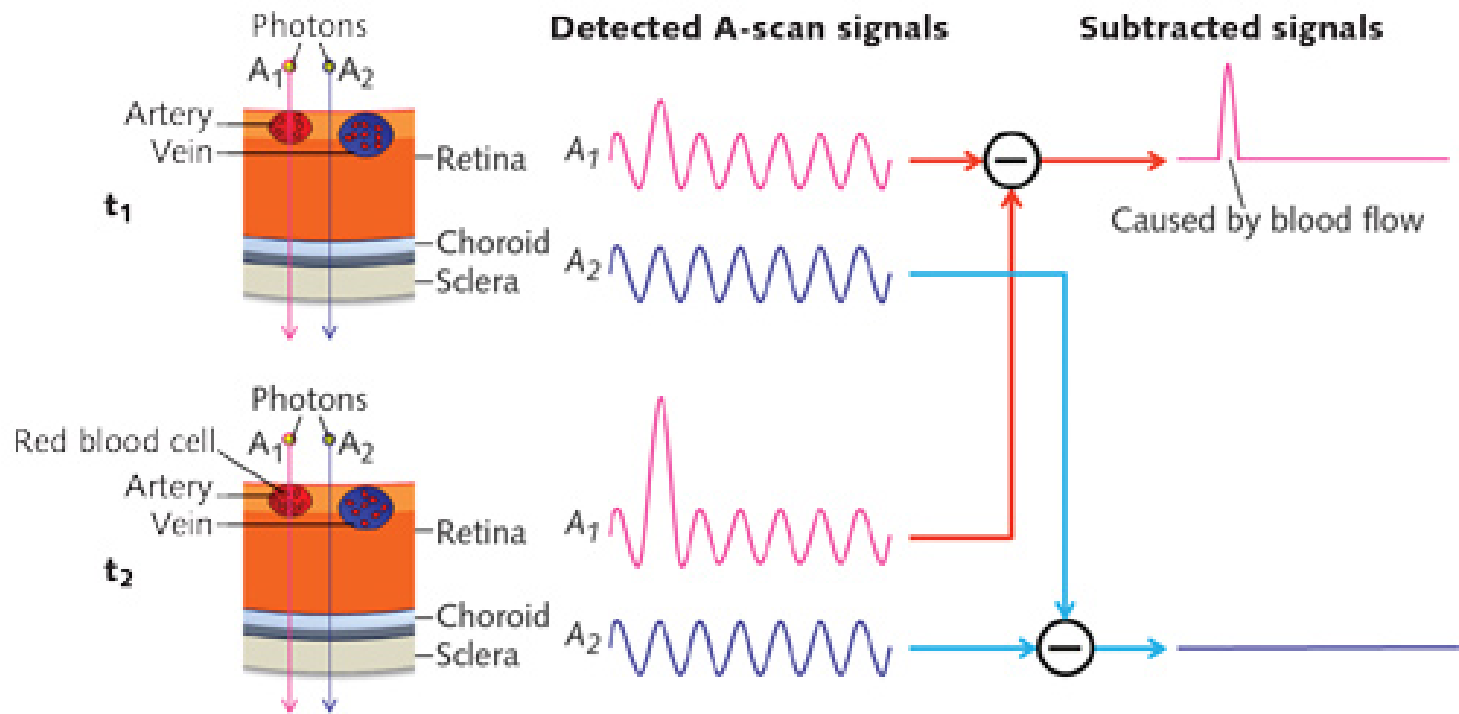


(a)

(b)

OCTA

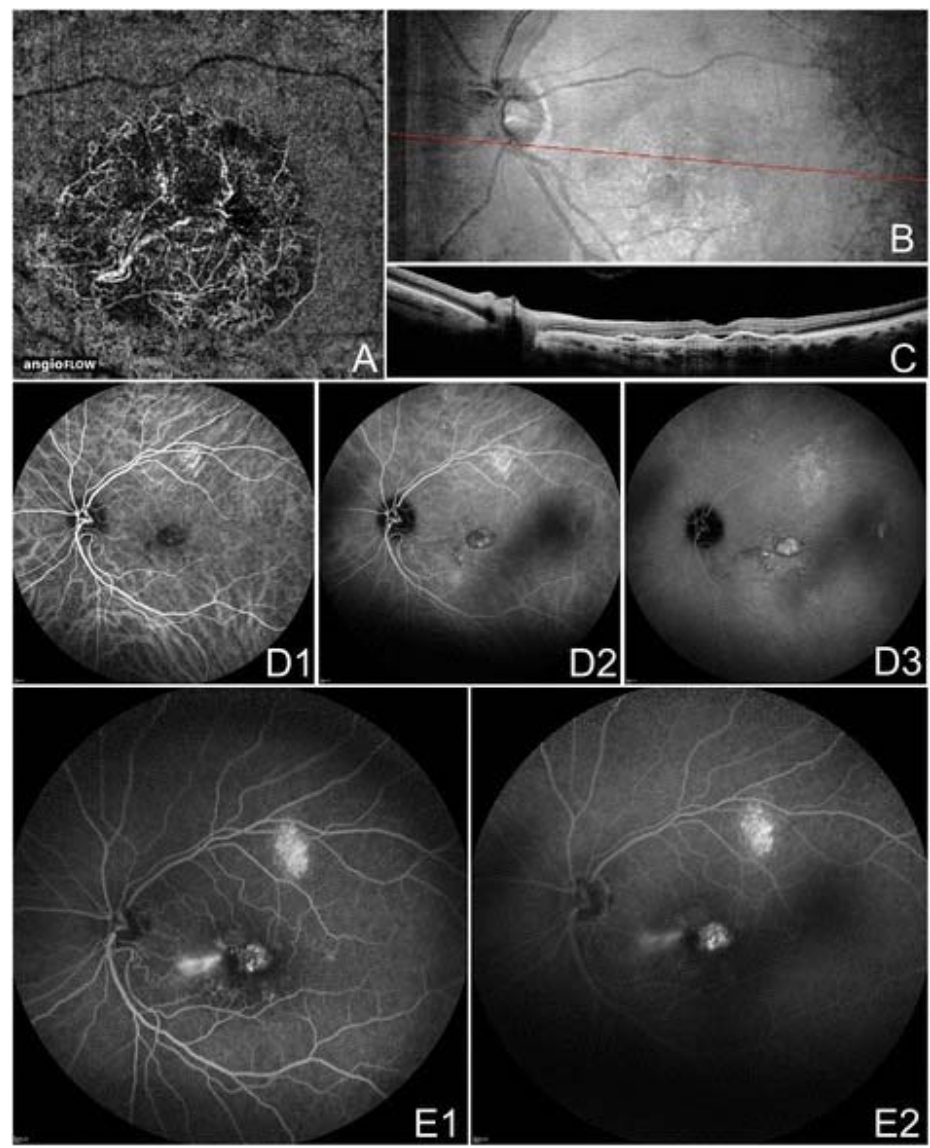
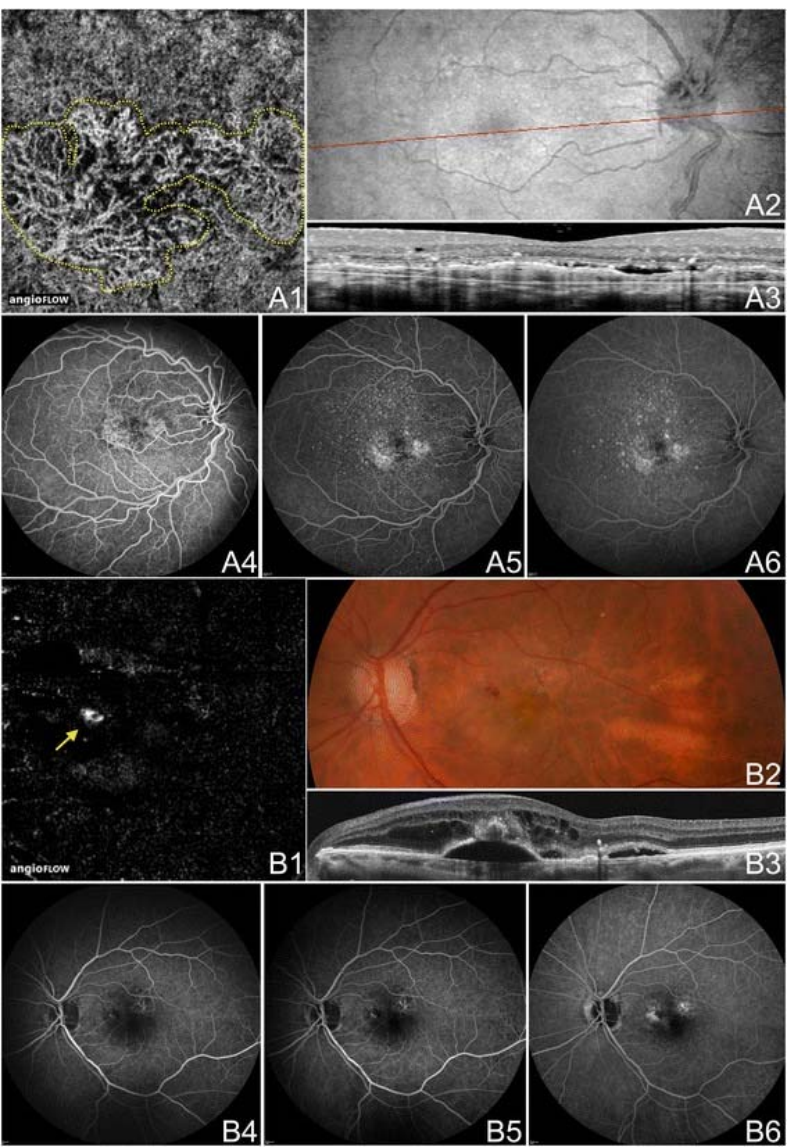
- Optical coherence tomography angiography (OCTA)
- Non-invasive imaging technique
- Available in 2014
- Employs motion contrast imaging to high-resolution volumetric blood flow information generating angiographic images in a matter of seconds.



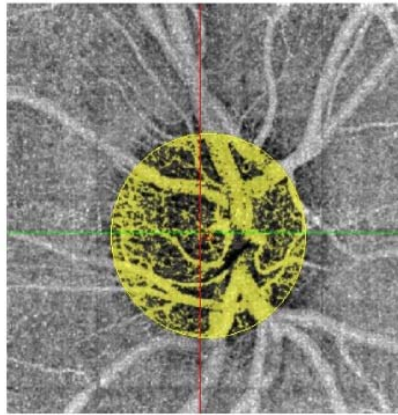
- Compares the decorrelation signal (differences in the backscattered OCT signal intensity or amplitude) between sequential OCT b-scans taken at precisely the same cross-section in order to construct a map of blood flow.
- Axial bulk motion from patient movement is eliminated so sites of motion between repeated OCT b-scans represent strictly erythrocyte movement in retinal blood vessels
- Requires higher imaging speeds than most currently available OCT systems

- OCTA

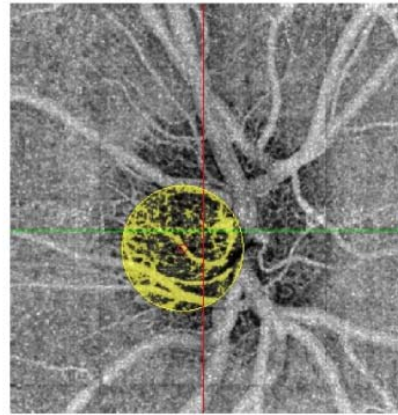
- non-invasive
- No Dye
- Each three-dimensional scan set takes approximately six seconds to obtain.
- The en-face images (OCT angiograms) can then be scrolled outward from the internal limiting membrane (ILM) to the choroid to visualize the individual vascular plexus and segment the inner retina, outer retina, choriocapillaris, or other area of interest.
- The en-face acquisition areas currently range from 2×2 mm to 12×12 mm
 - scan quality greatly decreased with a widened field of view since the same number of OCT b-scans is used for all scanning areas.
- The 12×12 mm : research
- The 3×3 mm OCT : higher resolution than the currently available FA/ICGA images



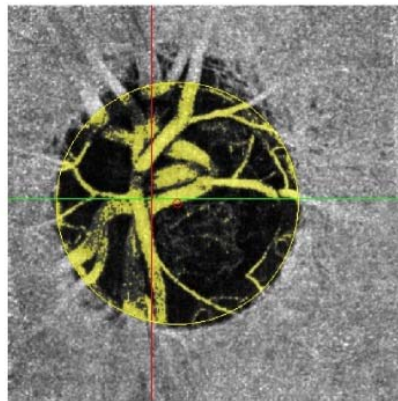
In glaucoma



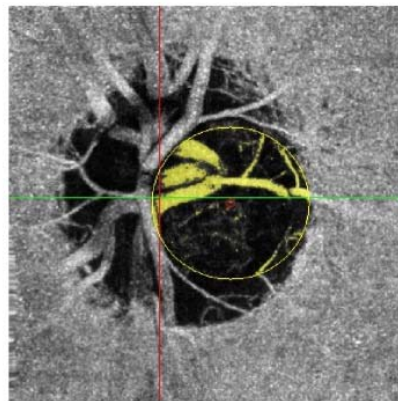
(a)



(b)



(c)



(d)

Future use

- Papilledema
- Optic neuropathies

Thank you