OCT Angiography: A promising tool in Glaucoma

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Abstract
Optical Coherence Tomography Angiography, a non-invasive imaging modality detects blood flow through the motion contrast generated by erythrocytes (RBC). It provides a quantitative assessment of microcirculation of the retina and choroid in various layers.

Keywords: OCTA, Glaucoma, SSADA, Vessel density, Flow index, Microvascular dropouts, Radial peripapillary slab, Choroidal slab

Introduction
Optical Coherence Tomography Angiography, a non-invasive imaging modality detects blood flow through the motion contrast generated by erythrocytes (RBC). It provides a quantitative assessment of microcirculation of the retina and choroid in various layers.

Principle
OCTA uses laser light reflectance of surface of moving red blood cells to accurately depict vessels through different segmented areas of the eye. The scan consists of multiple individual A-scans, compiled into a B-scan to produce cross-sectional structural information. Same tissue area is imaged multiple times, and differences are analyzed between scans (over time), thus permitting detection of zones containing high flow rates (with marked changes between scans) and zones with slower/ no flow (similar among scans).

OCTA Algorithms
Various commercially available OCTA devices incorporate several algorithms to interpret variances in OCT signal.

- Split spectrum amplitude decorrelation angiography (SSADA) in Angiovue, RTVue-XR SD-OCT, Optovue Inc, Fremont, CA, uses variation in intensity of OCT signal to identify blood vessels.
- Full spectrum amplitude decorrelation angiography (FS-ADA) in Spectralis OCT2 Module, Heidelberg Engineering, Heidelberg, Germany, uses variation in entire intensity spectrum of OCT signal to identify blood vessels.
- OCT Ratio analysis (OCTARA) in DRI OCT Triton, Topcon, Japan) uses full spectrum of OCT signal for blood vessel delineation, thereby preserving axial resolution.
- Optical microangiography OCTA algorithm (OMAG) in Angioplex, Cirrus HD-OCT, Carl Zeiss Meditec Inc., Dublin, CA, uses variation in intensity as well as phase difference of OCT signals for vessel delineation.

OCTA Scans and Parameters
Quantification is done using various parameters

- Vessel density: Ratio of area occupied by vessels divided by total measured area.
- Flow index: Average decorrelation value in SSADA algorithm.
- Parapapillary deep-layer microvascular dropout (MvD): Complete loss of chorio-capillaries in localized regions of parapapillary atrophy.

Figure 1: OCTA images. a) Radial peripapillary capillary (RPC) network. b) Superficial Radial vascular network in the macular region (Source: Akman A et al. Optical coherence tomography in glaucoma: A practical guide. Springer, 2018: p.351)
Deeper slab: Extends from 15 µm below inner plexiform layer to 30 µm below retinal pigment epithelium reference line in RTVue –XR SD OCT or from IPL to RPE in Cirrus HDOCT.9,11

Relevance of OCTA in Glaucoma
Functional damage in glaucoma is assessed by visual field testing and structural damage by thinning of retinal ganglion cell layer and retinal nerve fiber layer by optical coherence tomography. Ocular coherence tomography provides objective information on retinal layers’ thickness, with a high repeatability and reproducibility and has been in use both for pre-perimetric disease and diagnose progression in advanced glaucoma.13,14,19

The limitations in OCT in advanced glaucoma come from the floor effect where OCT parameters reach a base, beyond which little change is visible with increasing severity of glaucoma.14 This effect is delayed for OCTA where vessel density eventually reaches the floor, for very advanced disease. Thus, OCTA detects changes in advanced glaucoma which are invisible to OCT.

Early pre-perimetric disease also can be picked up earlier than structural OCT, with emphasis on early vascular changes.40,41

• Primary open angle glaucoma (POAG): Reduced flow index and vessel density within both Optic nerve head slab and in peripapillary region (RPC slab) have been demonstrated in eyes with POAG compared with normal. 3,15 Reduced vessel densities in superficial macular regions also have been reported with more pronounced decrease correlated with severity of disease.12,16 Choroidal slab documents deep-layer microvascular dropout in glaucomatous eyes.17,18

Vascular derangement by OCTA has been confirmed by reporting negative correlation of foveal avascular zone with inner retinal layer thickness and visual field indices.38

Normal tension glaucoma (NTG): OCTA parameters are lower with significant correlation with both OCT and visual field indices primarily with mean deviation.19,20 This finding however is not corroborated by other studies.20,21 The technology is being used to evaluate early macular circulation in open angle glaucoma, normal tension glaucoma and ocular hypertension (OHT). Impaired vasculature before significant disease has been demonstrated in both OAG and NTG with lower superficial vessel density than control normal.36 Vessel loss differences have been identified with lower deep vessel density in NTG group compared to controls and larger FAZ compared to OHT group.36

Primary angle closure glaucoma (PACG): OCTA measurements are reduced in PACG eyes especially after acute episode of angle closure.14,22,23 Mean vessel density has been found to be less in PACG eyes compared to severity matched POAG eyes.24 Inferior temporal peripapillary vessel density loss has been identified to be more in POAG eyes than PACG eyes despite similar vision and intraocular pressure.39 Angle closure eyes document more evenly distributed reduction of vessels.

• Pseudo-exfoliation glaucoma: Studies have reported greater reduction of vessel densities compared to POAG eyes of similar disease severity.25,26

• High Myopia: For glaucoma in high myopia visual field is often difficult to interpret. Shin JW et al proved OCTA to be better in linking these field parameters compared to OCT thickness. Microvasculature dropout in peripapillary choroid in high myopia eyes by OCTA aids in diagnosis, where segmentation errors make retinal nerve fiber layer thickness measures unreliable by conventional OCT.37

• Advanced glaucoma: Visual field indices show a higher concordance with OCTA than with OCT.39 This could be due to less pronounced floor effect seen in OCTA.31 Radial peripapillary capillary slab, has been found to be the better biomarker in advanced disease.32

Figure 2: Representative vascular, structural images of two eyes with mild-to-moderate and severe glaucomatous damage. a) Glaucomatous eye with mild neuroretinal rim loss, localized vascular drop-out of RPCs (yellow and green arrowheads), enlargement of foveal avascular zone FAZ and peripapillary retinal nerve fiber layer thinning. b) Glaucomatous eye with advanced cupping, widespread vascular drop-out of the RPC and macular region, irregular, enlarged FAZ and diffuse pRNFL loss (Source: Akman A et al. Optical coherence tomography in glaucoma: A practical guide. Springer, 2018: p.352)
• **Post trabeculectomy surgery:** Confirming the vascular theory, OCTA documented almost 60% improvement in peripapillary retinal microvascular post filtering surgery in POAG along with reduction in lamina cribrosa depth.\(^{27}\)

• **Anterior segment OCTA:** AS-OCTA images are found useful for objective assessment of conjunctival hyperemia and aid in understanding pathophysiology of post-trabecular aqueous humour outflow.\(^{28}\)

### Limitations

- **Motion artifacts:** OCTA detects RBC movements to generate contrast. Being extremely motion sensitive, the technology is prone to motion artifacts with movements like heartbeats, respirations, saccadic eye movements, blinking causing errors.\(^{33,34,14}\) Increasing scanning speed, decreasing image area and eye tracking technology are being used to reduce these.

- **Shadowing/ masking effect:** Signal attenuation may occur due to media opacities like cataract, hemorrhages, PVD, PED creating false negative OCTA flow pattern.

- **Projection artifacts:** It is caused by superficial vessel signal projecting onto deep retinal and choroidal circulation, affecting detection of microvascular dropouts (MvD).\(^{33,34,13}\) Newer generation OCTA like projection resolved OCTA reduce this.

### Conclusion

OCTA is a promising tool for diagnosing and monitoring glaucoma patients, especially in situations where OCT has limitations like advanced disease and myopia. The technology has corroborated vascular etiology of glaucoma and would be useful to identify effect of treatment on retinal blood flow parameters.

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