**Title: OCTA - A Novel imaging technique for Glaucoma**

Ms. Soundarya P 1. Prof. Tamilchudar R 2

1. Assistant professor, Department of Optometry, School of Allied health sciences, VMRF (DU) Salem
2. Professor, Department of Optometry, School of Allied Health Sciences, VMRD (DU) Salem

**Introduction**

Glaucoma is a group of ocular disorders characterized by progressive degeneration of retinal ganglion cells (RGC) and changes in neuroretinal rim tissue in the optic nerve head (ONH) accompanied by visual field constriction, which is the leading cause of irreversible blindness worldwide (1,2, 3). Approximately 11.2 million people aged > 40 years live with glaucoma in India (4). Of these, 3 million people are blind due to glaucoma, expected to double to 6 million by 2050 (5). Glaucoma goes undiagnosed in between 50% and 90% of cases in both developed and developing countries. Glaucomatous damage is preventable but irreversible, so early detection and improved glaucoma diagnosis are primordial (5).

**Pathogenesis of Glaucoma**

The pathophysiology of glaucoma is considered to be multifactorial. According to various theories, high intraocular pressure and vascular dysregulation are effective threat factors for glaucoma. It stresses within and across the laminar region with subsequent damage to a bundle of RGC axons and disruption of axonal transport, modified microcirculation of the optic nerve at the level of the lamina, and changes in the laminar glial and connective tissue. Multiple stresses such as RGC axon, endothelial cells, and astrocytes are likely to contribute to glaucoma, indeed though the factors contributing to its progression have not been completely understood (9) these degenerations of the nerves and cell bodies result in visual field loss, and also cause deformation and remodeling of the optic disc (10).

Two major theories have been proposed the mechanical theory and the vascular theory. Increased intraocular pressure (IOP) is a vital modifiable risk factor for the pathogenesis and development of glaucoma. Second, vascular factors also play pathogenic roles in glaucoma. Decreased ocular perfusion leads to tissue hypoxia, causing accumulation of reactive oxygen species and leading to damage to the optic nerve head (7, 8). Diagnosis is frequently delayed because it may be asymptomatic until late stages. So early detection and timely treatment are crucial in preventing vision loss in glaucoma patients.

**Optical Coherence Tomography Angiography**

Optical Coherence Tomography Angiography (OCTA) is an advanced imaging technique that has shown promising applications in the field of glaucoma diagnosis and management. OCTA is a new non-invasive imaging technique based on low-coherence interferometry performed to visualize the retinal and choroidal vasculature without the need for intravenous dye injection.

**Principle**

OCTA compares sequential OCT b – scans acquired at the same location to detect motion changes and construct a blood flow map. OCTA identifies blood vessels by detecting the erythrocyte movement in the OCT reflectance signal. This allows for the visualization and quantification of blood flow in the retina and optic nerve head, which is essential for understanding the vascular changes associated with glaucoma. The commercially available OCTA devices use different types of algorithms – SSADS (Spilt spectrum amplitude decorrelation angiography), OMAG -C (OCT Microangiography complex), and OCTARA (OCTA ratio analysis).

OCTA can evaluate the blood flow using various vascular parameters to investigate the glaucoma suspects, including vascular density and perfusion density in the optic nerve head, selected layers of the peripapillary retina, macula, and the optic disc flow index (9). Selective Capillary perfusion is measured which gives important information in the glaucomatous process. The commonly used parameters are vessel density which represents the percentage of the area by red blood cell movement

**Utilization of OCTA in Glaucoma**

1. **Assessment of Optic Nerve Head Perfusion:** OCTA can assess the blood flow in the optic nerve head, which is the region where the optic nerve exits the eye. Reduced blood flow in this area has been associated with glaucoma progression.
2. **Peripapillary Vessel Density Measurement:** OCTA can quantify the density of blood vessels around the optic nerve head, providing valuable information about the health of the retinal vasculature. Lower vessel density has been linked to glaucoma and can serve as an indicator of disease severity.
3. **Macular Vascular Changes:** OCTA can visualize the macular region, which is crucial for central vision. Changes in the macular vasculature have been observed in glaucoma patients and can offer insights into disease progression.
4. **Detecting Microvascular Abnormalities:** In glaucoma, microvascular abnormalities may not be evident with traditional imaging techniques. OCTA's high resolution enables the detection of these subtle changes, helping clinicians identify early signs of glaucoma.
5. **Monitoring Disease Progression:** Regular OCTA imaging can aid in monitoring the progression of glaucoma over time. Comparing sequential scans allows clinicians to identify changes in vascular patterns and assess treatment efficacy.
6. **Differentiating Glaucoma from Other Optic Neuropathies:** OCTA may help distinguish glaucoma from other conditions that affect the optic nerve and cause similar visual field defects.

**Parameters of OCTA (11)**

Many parameters are available in OCTA to differentiate the glaucomatous eye from the normal eye.

1. **Vessel Density (VD)**

It is also known as vessel area density or capillary density. It is represented as a ratio of the area of blood vessels in an image to the area of percentage which shows non-perfusion. This parameter can detect areas of ischemia and drop-out zones in both the retina and choroidal layers. The early changes of the disease occur at the capillary level so OCTA can be used as an early diagnostic tool.

1. **Blood Vessel Caliber (BVC)**

Vessel diameter, vessel width, or vessel diameter index are the other names of BVC. It measures vessel dilation or attenuation caused by different ocular pathologies. It is the ratio of vessel area to the length of the vessel.

1. **Blood Vessel Tortuosity (BVT)**

In normal vasculature and flow, blood vessels travel smoothly in the tissue to transport the blood efficiently. Due to ocular pathologies, blood vessels may not be smooth causing vessel tortuosity which causes abnormal blood transport. BVT measures the degree of vessel distortion in an area of the image.

1. **Vessel Perimeter Index (VPI)**

VPI measures the ratio between the overall contour length of blood vessel boundaries and the total blood vessel area in the segmented vessel map. It is a quantitative parameter that shows the ischemia and vessel dropout caused due to different ocular conditions.

1. **Foveal Avascular Zone (FAZ)**

The foveal avascular zone is a zone free of any vasculature in the fovea. The enlargement in the FAZ is a pathological sign and occurs due to different ocular conditions such as DR and vein occlusions. FAZ enlargement is caused by the dropout of parafoveal and perifoveal capillaries which can be captured by OCTA.

1. **Branchpoint Analysis (BPA)**

Bifurcation in vascular structure can be affected by decreased blood transport. BPA measures the angle and width features of the blood vessels. Vessel branching angles and child branching angles are measured to quantify the bifurcation in vascular structure. This parameter can be used to classify DR objectively.

1. **Flow analysis**

Flow analysis includes Flow Index (FI), adjusted FI, Flow Void (FV), vascular connectivity, and other parameters. These are developed to detect the changes in the blood flow. OCTA captures the decorrelation value of each pixel of the captured image. The average decorrelation value within a region of a particular area in the retina is known as Flow Index (FI).

**OCTA in Different types of glaucoma**

1. **Primary open-angle glaucoma (POAG)(12,13,14)**

The reduction of microvascular density within the Retinal Nerve Fibre Layer (RNFL) in the parapapillary retina in POAG eyes at the location of glaucomatous damage. In POAG patients, it is observed that there is localized attenuation of the microvascular network in the parapapillary retina. This represents the degeneration of capillaries that occurs along with the loss of RNFL. Circumpapillary VD (cpVD) losswas found to be the more valuable diagnostic criteria than macular VD (mVD) loss for POAG. mVD decrease was faster than GCC thinning associated with the severity of the disease. This parameter is useful for evaluating the progression.

1. **Primary Closed Angle Glaucoma (17)**

Vessel density in superotemporal RNFL thickness was significantly lower in PAC patients compared to healthy individuals.

1. **Normal-tension Glaucoma (15, 16)**

For NTG patients, different studies found mVD losscan be used as a diagnostic utility compared to cpVD loss.

Macular intercapillary area enlargement could be a potential biomarker for early NTG.

**Limitation of OCTA**

1. Projection artifacts and motion artifacts are common limitations of OCTA
2. Sometimes, the SSDA algorithm provides poor-quality images of the optic disc and macular regions
3. The scan time for OCTA varies from 3 to 6 seconds, which may induce a higher incidence of motion artifact. Patients with advanced glaucoma or dense cataracts may face difficulty in fixing, resulting in poor quality results.
4. OCTA does not account for vascular attenuation and dropout.

**Conclusion**

We conclude that undiagnosed and untreated glaucoma can lead to visual impairment, visual field loss and also cause an economic burden to society. Early glaucoma detection remains a challenge in the community. A comprehensive assessment, including visual field testing, structural OCT, and clinical examination, is essential for the accurate diagnosis and management of glaucoma. However, OCTA vascular biomarkers with clinical structural measurements also aid in the early diagnosis of glaucoma. Recent literature shows that the utility and availability of OCTA among Indian eye care practitioners were less. So, the clinical significance of OCTA in India should evolve for early diagnosis of glaucoma.

**References:**

1. George, R., Ramesh, S. V., & Vijaya, L. (2010). Glaucoma in India: estimated burden of disease. *Journal of glaucoma*, *19*(6), 391-397
2. Shon, K., Wollstein, G., Schuman, J. S., & Sung, K. R. (2014). Prediction of glaucomatous visual field progression: pointwise analysis. *Current eye research*, *39*(7), 705-710.
3. Kanski, J. J., & Bowling, B. (2011). *Clinical ophthalmology: a systematic approach*. Elsevier Health Sciences.
4. Bojikian, K. D., Chen, P. P., & Wen, J. C. (2019). Optical coherence tomography angiography in glaucoma. *Current opinion in ophthalmology*, *30*(2), 110-116.
5. Saxena R, Singh D, Vashist P Glaucoma: An emerging peril Indian J Community Med 2013 38 135 7
6. Yanagi, M., Kawasaki, R., Wang, J. J., Wong, T. Y., Crowston, J., & Kiuchi, Y. (2011). Vascular risk factors in glaucoma: a review. *Clinical & experimental ophthalmology*, *39*(3), 252-258.
7. Ko ML, Peng PH, Ma MC, Ritch R, Chen CF. Dynamic changes in reactive oxygen species and antioxidant levels in retinas in experimental glaucoma. Free Radic Biol Med 2005; 39: 365–73.
8. Fard, M. A., & Ritch, R. (2020). Optical coherence tomography angiography in glaucoma. *Annals of Translational Medicine*, *8*(18).
9. Weinreb, R. N., Aung, T., & Medeiros, F. A. (2014). The pathophysiology and treatment of glaucoma: a review. *Jama*, *311*(18), 1901-1911.
10. Nickells, R. W., Howell, G. R., Soto, I., & John, S. W. (2012). Under pressure: cellular and molecular responses during glaucoma, a common neurodegeneration with axonopathy. *Annual review of neuroscience*, *35*, 153-179.
11. Yao, X., Alam, M. N., Le, D., & Toslak, D. (2020). Quantitative optical coherence tomography angiography: a review. *Experimental Biology and Medicine*, *245*(4), 301-312.
12. Yarmohammadi, A., Zangwill, L. M., Diniz-Filho, A., Suh, M. H., Manalastas, P. I., Fatehee, N., ... & Weinreb, R. N. (2016). Optical coherence tomography angiography vessel density in healthy, glaucoma suspect, and glaucoma eyes. *Investigative ophthalmology & visual science*, *57*(9), OCT451-OCT459.
13. Bojikian, K. D., Chen, P. P., & Wen, J. C. (2019). Optical coherence tomography angiography in glaucoma. *Current opinion in ophthalmology*, *30*(2), 110-116.
14. Lee, E. J., Lee, K. M., Lee, S. H., & Kim, T. W. (2016). OCT angiography of the peripapillary retina in primary open-angle glaucoma. *Investigative ophthalmology & visual science*, *57*(14), 6265-6270.
15. Lee, S. Y., Son, N. H., Bae, H. W., Seong, G. J., & Kim, C. Y. (2021). The role of pattern electroretinograms and optical coherence tomography angiography in the diagnosis of normal-tension glaucoma. Scientific reports, 11(1), 12257.
16. Chang, P. Y., Wang, J. Y., Wang, J. K., Yeh, S. C., & Chang, S. W. (2020). Asymmetry analysis of optical coherence tomography angiography macular perfusion density measurements in preperimetric and perimetric glaucoma. Scientific Reports, 10(1), 14781.
17. Rao, H. L., Pradhan, Z. S., Weinreb, R. N., Riyazuddin, M., Dasari, S., Venugopal, J. P., ... & Webers, C. A. (2017). Vessel density and structural measurements of optical coherence tomography in primary angle closure and primary angle closure glaucoma. *American journal of ophthalmology*, *177*, 106-115.