Glaucomatous optic neuropathy is believed to start in the optic nerve head, the lamina cribrosa in particular, hence there is critical need for approach to imaging this region of the eye in-vivo.

Understanding the complex interplay of intraocular pressure changes and lamina cribrosa is vital to our understanding of the disease progression.

With newer imaging techniques, namely enhanced depth spectral domain ocular coherence tomography, it is now possible to image the anterior lamina and thus study its characteristics with respect to glaucomatous changes.

There is a growing need for in vivo longitudinal studies that address the intraocular pressure-induced changes in the optic nerve head, in management of glaucoma.

Imaging of the deep optic nerve and laminar surface may provide new endpoints to predict the development and progression of glaucoma.

GON is characterized by optic nerve head cupping and visual field defects that could be detected with long-term rigorous monitoring of patients. There is not yet a good screening test for the disease, hence emphasis should be on prevention of progression of the disease by risk reduction. Currently, the only proven method to prevent the progression glaucomatous disease is lowering the intraocular pressure (IOP). The precise mechanism by which IOP contributes to the development and progression of glaucoma is not completely understood [1,2]. This is, in part, due to the variability in individual susceptibility to IOP [3]. To better understand this individual susceptibility, it is essential to understand this relationship between IOP and glaucomatous optic neuropathy (GON) for effective management of the disease.

Clinically, the recognition of glaucomatous optic nerve damage is by the deepening and enlargement of the optic cup and thinning of the neuro-retinal rim [4]. The sclera is the main load-bearing tissue of the eye and deformations of the sclera due to the IOP changes are transmitted to the optic nerve head (ONH), the most susceptible part of the corneo-scleral shell. The cupping of the ONH in glaucoma, in most cases, is due to a combination of the two components – prelaminar part and laminar cupping [5-8]. Prelaminar cupping of the ONH is characterized by progressive loss of the prelaminar tissues leading to increase in the depth and width of the optic cup (cup/disc ratio changes). Laminar cupping is a progressive posterior movement of the lamina cribrosa (LC) due to connective tissue remodeling that leads to progressive loss of the retinal ganglion cell (RGC) axons. The lamina is composed of a network of beams of connective tissue fibers that provide structural and functional support to the RGC axons as they pass through it into the optic nerve.

GON is believed to begin within the LC, changes include thinning, deformation, and compression of the connective tissue fibers and enlargement of pores [9,10]. Recent studies suggest that the trans-lamina cribrosa pressure difference (IOP vs. retrolaminar cerebrospinal fluid pressure around the optic nerve) is of importance in the pathophysiology of GON [10,11]. The altered biomechanical environment within the ONH and the LC may contribute to the disruption of the RGC axons and the subsequent loss of vision in GON. It is conventional belief that as IOP increases, the LC deforms posteriorly. Burgoyne et al. [12] developed ocular biomechanical models that show that as IOP changes, the LC and peripapillary sclera changes are much more complex and do not necessarily result in linear LC changes. Hence, there is a need for search for an association between changes in IOP and LC deformations [13].

The mainstay of clinical assessment of GON is by evaluation of the ONH by stereoscopic ophthalmoscopy. Newer imaging techniques have gained importance in recent years especially those with the ability to detect a longitudinal change in the optic disk. These include confocal scanning laser tomography, time domain optical coherence tomography, spectral domain ocular coherence tomography (SD-OCT) and scanning laser polarimetry. Post mortem studies in experimental glaucoma models of monkey eyes suggest that the earliest structural changes in ONH include a displacement of the LC, widening of scleral canal opening, and thickening of prelaminar tissue [5,6,13,15]. In vivo imaging of the ONH using high resolution imaging like the SD-OCT is thus essential to detect such early changes in these structures for better management of the disease.

OCT as a Measure of ONH changes

Optical Coherence Tomography (OCT) is a high-resolution, non-invasive imaging modality, first described by Huang et al [16], that generates an optical three dimensional section representative of the subsurface of the tissue being imaged, with a resolution approaching 10um in the axial plane with the initial time-domain units [17]. Newer technological improvements include SD-OCT, where the reflected signal from tissues is captured by a spectrometer, thus eliminating the need for a moving reference mirror in the z-axis, greatly improving the resolution and imaging speed. In commercially available SD-OCT (Heidelberg engineering, Germany), the eye is illuminated with light from a broadband source. The scattered light from the tissue is combined with that from the reference arm to generate the interference signal. The anterior surface of the LC is well visualized on the SD-OCT, hence essential to detect such early changes in these structures for better management of the disease.
However, imaging of much deeper tissues with this technique is often limited due to the interference from more anterior tissues. Spaide et al [18], recently described an enhanced depth imaging (EDI) technique that improved the penetrated penetration and axial resolution in choroid imaging. This EDI involved positioning of the SD-OCT device close enough to the eye to get an inverted image of the fundus, thus getting a better image of the deeper structures (Figure 2). Using this EDI SD-OCT, Lee et al. [19], visualized the LC with higher reflectivity and better contrast from the surrounding tissues, compared to that taken with conventional SD-OCT. Thus, in vivo imaging with EDI SD-OCT is currently the best commercially available technique available to image deeper ONH structures like the LC.

**LCD changes to IOP alterations detected by SD-OCT**

Agoumi et al. [1] utilized SD-OCT to determine the effect of transient elevation of IOP on laminar position. The authors transiently increased IOP in normal and glaucoma patients with an ophthalmodynamometer (Inami, Tokyo, Japan) and obtained SD-OCT images of the eye. They observed that there was no change in LC position for this transient raise of IOP but rather a compression of prelaminar tissues alone. This was in contrast to a displacement and/or change in thickness of LC, and expansion of the scleral canal observed in monkey and enucleated human eye models [10,14,20,21]. An advantage for the Agoumi et al study model was the ability to monitor real-time LC changes with changes in IOP, in vivo. However, one of the limitations to this study was the inability to measure the entire laminar surface, due in part to shadowing from blood vessels.

Also, even with EDI imaging, it is still difficult to visualize the full thickness of the LC, due to signal attenuation in the deep optic nerve surface, due in part to shadowing from blood vessels.

Further studies are indicated to understand the complex interactions between IOP and ONH in the pathophysiology of GON. Understanding these interplays are essential for detection of the earliest clinically discernable ONH changes. This will likely provide new imaging targets to predict the development and progression of glaucoma.

**References**


