THE RELATIONSHIP BETWEEN CORNEAL BIOMECHANICS AND OPTIC NERVE HEAD BIOMECHANICS IN GLAUCOMA AND OCULAR HYPERTENSION

THESIS

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LIST OF ABBREVIATIONS

CCT	**:**	Central Corneal Thickness
CH	**:**	Corneal Hysteresis
CRF	**:**	Corneal Resistance Factor
CSLO	**:**	Confocal Scanning Laser Ophthalmoscope
DCT	**:**	Dynamic Contour Tonometry
GAT	**:**	Goldmann Applantion Tonometer
GPS	**:**	Glaucoma Probability Score
HRT	**:**	Heidelberg Retinal Tomograph
IOP	**:**	Intra Ocular Pressure
IOPcc	**:**	Corneal Compensated IOP
IOPg	**:**	Goldmann Correlated IOP
MRA	**:**	Moorfields Regression Analysis
OHTS	**:**	Ocular Hypertension Treatment Study
ONH	**:**	Optic Nerve Head
ORA	**:**	Ocular Response Analyzer
POAG	**:**	Primary Open Angle Glaucoma
RGC	**:**	Retinal Ganglion Cells

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INTRODUCTION

Increased intra ocular pressure (IOP) is the primary risk factor for the development of glaucomatous optic neuropathy. The optic nerve head is suggested to be the primary site of retinal ganglion cells axons atrophy. The mechanism of loss involves both mechanical and vascular effects. Substantial literature studied the changes that occur to the lamina cribrosa in response to elevation of the IOP in several models including monkey eyes (1, 2), human eyes (3) and computer modeling techniques (4-6).

Quigley studied lamina cribrosa in normal and glaucomatous eyes and correlated structural alterations to the lamina cribrosa with the clinical severity of the glaucoma (7). Levy and coworkers found that lamina cribrosa displaced minimally adjacent to the sclera and maximally at the centre concluding that lamina cribrosa displacement could cause shearing of the optic nerve head axons owing to differential displacement of the connective tissue (8, 9).

In vivo human eyes the lamina cribrosa compliance can be estimated using the confocal scanning laser ophthalmoscope (CSLO) by comparing the position of the

base of the cup relative to the retinal surface before and following IOP pressure changes (3,10-12).

Some studies have investigated corneal thickness as a contaminating factor in measuring IOP. Others have investigated central corneal thickness (CCT) as an independent indicator of glaucoma risk, concluding that a thin CCT is a risk factor for development and progression of POAG and this observation has been made in ocular hypertensive patients, glaucoma suspects, and glaucoma patients (13, 14). Although this risk can be explained by the effect of CCT on IOP measurement such that eyes with thin corneas present at later stages of disease progress, Lesk et al. have showed that patients with open angle glaucoma and ocular hypertension with thin corneas have a more mobile (compliant) lamina cribrosa (15).

If the relationship between corneal thickness and optic nerve head compliance is driven by the biomechanical properties of these two structures, then a better relationship would be found between a measure of the biomechanical properties of the cornea and optic nerve head compliance. It seems that future diagnostic procedures in glaucoma will be directed toward the measurement of anterior segment properties beyond simple geometric thickness.

Currently ocular response analyzer (ORA) has allowed a reproducible and repeatable method to measure the biomechanical properties of the cornea in vivo by measuring the corneal hysteresis (CH) (16, 17). Congdon and co-workers found that low CH was predictive of visual field progression in cohort of glaucoma patients indicating an independent association between CH and glaucoma damage (18).

While the relationship between glaucoma susceptibility and corneal biomechanical variables (beyond their effects on IOP measurement) is being vigorously studied, substantial efforts are also being directed at answering questions about how biomechanical factors in the posterior segment might be related to those in the anterior segment.

Wells et al. reported that in glaucoma patients CH was associated with increased deformation of the optic nerve head during transient elevation of the IOP (19).

In this study we examined patients with glaucoma and ocular hypertension to determine the presence or absence of a correlation between CH and optic nerve head topographical changes induced by chronic IOP reduction.

Such a relationship between biomechanical properties of the cornea and the lamina cribrosa would contribute to the growing body of evidence that ocular biomechanics influence the susceptibility of the optic nerve head to glaucomatous damage.

AIM OF THE WORK

The primary objective is to examine the relationship between corneal hysteresis and optic nerve head topographical changes induced by IOP reduction i.e. between the biomechanical properties of the cornea and the optic nerve head.

Primary Hypothesis: Eyes with more compliant corneas will have greater anterior displacement of the base of the cup and greater reductions in cup volume than those with less compliant corneas and the correlation will be stronger than that observed between optic nerve head (ONH) topographical change and central corneal thickness.

ANATOMY OF THE OPTIC NERVE HEAD

The optic nerve head (ONH), also known as the optic disc or papilla, forms the point of exit of the retinal ganglion cell (RGC) axons through the scleral canal. It is composed primarily of neural fibers (1.2-1.5 million retinal ganglion cell axons), glial cells, extracellular matrix supportive tissue and vascular elements (20-26). The ONH is delineated from the adjacent peripapillary tissue by a scleral rim of connective tissue, the border tissue of Elschnig (27). The diameter of the ONH and anterior portion of the optic nerve is approximately 1.5 mm (28).

The ONH may be divided into four anatomic regions, from front to back (29-33):

Surface nerve fiber layer: this region is continuous with the nerve fiber layer of the retina. It is composed of the non-myelinated axons of RGCs in transition from the superficial retina to the neuronal component of the optic nerve.

Prelaminar region: this is the region between the surface nerve fiber layer and the lamina cribrosa, at the

level of the choroid and outer retina. It consists of the nerve fibers arranged in bundles, surrounded by glial tissue septa and astrocytes.

Lamina cribrosa region: lies adjacent to the sclera, and provides the main support for the optic nerve as it exists the eye and penetrates the sclera coat.

Retrolaminar region: this region lies immediately posterior to the lamina cribrosa. It is marked by the beginning of axonal myelination and is surrounded by the leptomeninges of the central nervous system.

Differences among these four regions reflect the conditions to which the axons are exposed to as they pass through the ONH. These differences include axon myelination posterior to the lamina cribrosa, sources of blood supply, and the change in tissue pressure from intraocular pressure to that of the cerebrospinal fluid.

ANATOMY OF THE LAMINA CRIBROSA

The lamina cribrosa is a complex collagenous, relatively elastic structure that consists of a series of fenestrated sheets of connective tissue (approximately 10) and provides the main support for the axons of the optic nerve (20, 29,30). The sheets of the lamina cribrosa span the sclera opening at the back of the eye inserting into the outer half of the sclera. They are arranged in a series of parallel stacked plates.

Each of these sheets contains fenestration or pores that are vertically aligned to allow the passage of the neural elements of the optic nerve. Central pores allow transit of the central retinal artery and central retinal vein. In humans, the pores of the lamina cribrosa are histologically larger and fewer superiorly and inferiorly and the laminar sheets are thinner when compared to the nasal and temporal aspects of the optic nerve (34) (Figure 1). This correlates with the reported preferential loss of axons at the superior and inferior poles of the ONH in glaucomatous optic neuropathy. Enlargement of the laminar pores and alteration of the shape of the cup both peripherally and posteriorly are characteristic signs of glaucomatous optic