Optic Disc Movement with Variations in Intraocular and Cerebrospinal Fluid Pressure

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PURPOSE. To determine the effect of intraocular pressure (IOP) and cerebrospinal fluid pressure (CSFP) on optic disc movement and lamina cribrosa displacement using confocal scanning laser tomography (CSLT).

METHODS. The anterior chamber and lateral ventricles were cannulated in mixed-breed dogs (n = 8) to allow modulation and control of IOP and CSFP, respectively. Optic disc topography was determined after baseline (set at IOP 15 mm Hg and CSFP of 0 mm Hg) and with each step-wise increase in IOP (steps of 3–5 mm Hg up to an average of 32 mm Hg) and with CSFP fixed at 0 mm Hg. After the pressure returned to baseline, images were obtained after each step-wise increase in CSFP (steps of 2 to 4 mm Hg up to an average of 12 mm Hg) with IOP fixed at 15 mm Hg. Data were analyzed by a new probabilistic method for CSLT and global parameters generated by the instrument software. The global parameter changes from baseline were analyzed as a function of the translaminar pressure difference (IOP minus CSFP).

RESULTS. Elevation in IOP resulted in significant posterior displacement of the disc surface, whereas elevation in CSFP resulted in significant anterior displacement. For a given degree of pressure change, an increase in CSFP resulted in larger changes than a corresponding increase in IOP. The deepest 5% of locations within the disc surface were displaced nonlinearly (with an inverse exponential function, r = 0.92) as a function of the difference in translaminar pressure. Most displacement occurred at low translaminar pressure differences, with little extra movement at differences higher than 15 mm Hg. The change in the volume subtended by the anterior lamina cribrosa showed a nonlinear relationship similar to the translaminar pressure difference (r = 0.98), with negligible volume change at high difference in pressures.

CONCLUSIONS. Most optic disc movement occurs with pressure changes in the low range of translaminar pressure differences. This is consistent with the mechanical properties of collagen. (Invest Ophthalmol Vis Sci. 2002;43:3236–3242)

The optic disc separates the eye from the optic nerve surrounded by subarachnoid space, forming a barrier between these two pressure compartments. The pressure in the eye is equivalent to intraocular pressure (IOP), whereas the subarachnoid space pressure is principally determined by intracranial cerebrospinal fluid pressure (CSFP). Pressure changes in either compartment alter the pressure distribution across the disc and hence the axial forces and transverse tension acting across optic disc tissue. The optic disc is the site of most visible damage in glaucoma, a disease associated strongly with elevated IOP, and therefore there is much interest in understanding the mechanical properties of the optic disc. Mechanical changes that occur in the connective tissue in glaucoma may affect the retinal ganglion cell axons and blood vessels.

Previous investigation of optic disc mechanics has examined the effect of IOP alone on axial displacement of the disc surface or lamina cribrosa. The neural tissue of the optic disc anterior to the lamina cribrosa is not subject to a pressure gradient, and its extravascular volume can therefore be assumed to remain constant during short-term IOP changes. Retinal arterial and venous diameters do not change significantly when IOP increases up to 40 mm Hg. It appears reasonable to assume that optic disc volume anterior to the lamina cribrosa remains constant with IOP changes below 40 mm Hg, and so the surface movement measured in these experiments most likely reflects underlying anterior lamina movement. A variety of techniques have been used for measuring the displacement of the whole or large parts of the disc with relatively large measurement error, constraining the experimental design to the use of large pressure steps. In vivo displacement measurements of the optic disc surface have been performed with optic disc imaging devices and histologic studies and by integrating the velocity of disc surface movement over time in response to changes in IOP. In vitro studies have also been performed, but they may have limitations due to postneculation changes in the optic disc tissue. They report maximum posterior disc surface displacement of 28 to 60 μm with IOP increases from 35 to 60 mm Hg. A systematic evaluation of the effect of CSFP on optic disc mechanics has not yet been reported.

Of greater interest than the optic disc tissue movement in response to a single large pressure change is its behavior across a range of pressure differences. The major structural component of the optic disc is collagen, which has highly nonlinear stress–strain properties with decreasing relative strain as stress increases. If similar properties have been used for measuring the displacement in lamina cribrosa collagen, then decreasing laminar displacement would be expected as IOP increases. The shape of the lamina cribrosa also influences its mechanical characteristics. Its approximation to a spherical surface and the use of Laplace’s tension relationship suggests the theoretical possibility that lamina displacement may increase with increasing IOP.

Experimental measurements of optic disc and laminar displacement have been inconsistent to date. Disc surface displacement per unit change in IOP was found to either remain constant or increase with increasing IOP, whereas other evidence suggested that disc displacement decreased with increasing IOP. Recently, however, measurements with new
imaging techniques suggest that disc displacement remains constant with increasing IOP.\textsuperscript{14} If disc displacement increases with increasing IOP, then more laminar movement and greater laminar distortion would be expected at high IOP. This would be consistent with Maumenee’s hypothesis that glaucoma is in part caused by laminar movement that kinks retinal ganglion cell axons.\textsuperscript{15} In addition, laminar movement may be important in determining the diameter and flow resistance of the central retinal vein, because the central retinal vein wall collagen merges with that of the lamina cribrosa\textsuperscript{16} transferring laminar tension to the vein wall.

We used confocal scanning laser tomography (CSLT), a technique that allows quantitative measurements of optic disc topography, to perform in vivo experiments to measure disc displacement and volume changes. Of critical importance in measuring laminar movement is the ability to control and monitor CSFP, which has been shown to determine retrolaminar tissue pressure.\textsuperscript{1} This, combined with IOP, determines the pressure difference that acts across the optic disc and lamina cribrosa. IOP changes from 10 to 32 mm Hg have been shown to cause no significant change in choroidal volume or blood flow,\textsuperscript{17,18} and therefore we planned our protocol to vary IOP within this range. The possibility that optic disc tissue may become compressed under raised IOP prompted us to measure volume change when the IOP-CSFP difference was kept constant, while IOP was varied.

**METHODS**

**Animal Preparation**

Eight mixed-breed dogs were used under the guidance and approval of the University of Western Australia animal ethics committee and in accordance with the ARVO Statement for the Use of Animals in Ophthalmic and Vision Research. They were anesthetized with halothane inhalation for induction, followed by a continuous intravenous infusion of a 50:50 mixture of pentobarbitone and thiopentone, with ventilation providing with 80% nitrogen and 20% oxygen. Each animal was positioned prone with two cannulae in the left anterior chamber and lateral ventricles that allowed IOP and CSFP, respectively, to be monitored and altered. Systemic blood pressure was monitored through a femoral artery cannula, and arterial blood gases were measured periodically. The details of the animal setup are described elsewhere.\textsuperscript{3} A plano contact lens was applied to the cornea with methylcellulose to prevent corneal drying and minimize any induced astigmatism caused by the anterior chamber cannulae.

**Confocal Scanning Laser Tomography**

CSLT was performed (Heidelberg Retina Tomograph; Heidelberg Engineering GmbH, Dossenheim, Germany) to measure relative height or depth of the optic disc surface. The instrument and its operation have been described elsewhere.\textsuperscript{19} Briefly however, the device measures the topographic height at 65,536 (256 × 256) discreet points on the imaged area by image processing of 52 confocal optical sections through the optic nerve and retina in a 10° × 10°, 15° × 15°, or 20° × 20° area. In each animal, the same scan angle was used for all conditions.

**Experimental Protocol**

Two measurement protocols were used: varying IOP at fixed CSFP and varying CSFP with fixed IOP. After each pressure adjustment, we waited 15 minutes before acquiring any images. With each protocol, a set of six baseline images were taken with the tomograph. Six images were also taken at each step after the 15-minute wait. For the analysis, three best-quality images were taken from the images obtained at each pressure setting. The criteria used for selecting these images were (1) satisfactory grade in the built-in image quality-control analysis; (2) SD, after alignment, of less than 10 µm; and (3) manual inspection of aligned images.

1. At baseline, IOP was set at 15 mm Hg and CSFP to 0 mm Hg. After acquisition of the baseline image set, IOP was elevated in steps of between 5 and 5 mm Hg to an average of 32 mm Hg. In two experiments, IOP was reduced to 10 mm Hg first, then elevated in steps. IOP was then reduced to 15 mm Hg.
2. A second set of baseline images were taken at an IOP of 15 mm Hg and CSFP of 0 mm Hg. CSFP was then elevated in steps of between 2 and 4 mm Hg to an average of 12 mm Hg. In two experiments, the CSFP was reduced to ~2 mm Hg and ~4 mm Hg.
3. A third set of baseline images were taken with a baseline IOP of 14 mm Hg and CSFP of 0 mm Hg. CSFP and IOP were both elevated in equal 3-mm Hg steps.

**Data Analysis**

We analyzed the change in optic disc topography by a method described recently.\textsuperscript{20} Essentially, the 256 × 256-pixel image matrix was divided into an array of 64 × 64 superpixels, so that each superpixel contained 16 (4 × 4) pixels.\textsuperscript{21} An analysis of variance technique to analyze the topographic difference between the two sets of three images under two conditions (e.g., baseline and follow-up) was used. The analyses provide a topographic difference map and the likelihood of these localized changes being within the normal corresponding test-retest variability limits that are derived. The topography difference map is displayed as a pseudocolor image, with green representing anterior displacement and red representing posterior displacement. The corresponding probability values of these displacements are displayed on a gray-scale map.

We also used the global indices provided by the tomograph. A circular contour line was placed 500 µm from the disc margin. This contour line was not used to define the optic disc margin, as in conventional clinical use. The reference height was always set at 300 µm below the average height of the reference ring, which is automatically placed in the periphery of the image (in the flat peripapillary retina) and used to align serial topography images. The absolute mean axial depth of the reference ring was noted for each image and pressure condition in the experimental protocol to determine whether there was a shift in the position of the peripapillary retina (due to axial movement of the retinal surface or choroidal compression with the IOP or CSFP modulation). All subsequent depth measurements including the reference height were made relative to the normalized reference ring depth after image alignment.

Maximum cup depth (MaxD) was defined as the mean depth of the deepest 5% of pixels within the circular contour line, representing the average depth of the deepest portion of the cup. These could be seen on the surface maps and were in the center of each optic disc. In this region, there is a minimum of tissue between the lamina cribrosa and the disc surface; therefore, movement of this region may be most representative of movement of the central lamina cribrosa. No laminar pores or other potentially confusing anatomic anomalies were seen in any of our animals.

Regarding volume measurements, the curved surface was used as the reference surface. The geometric center of the circular contour line was used as the curved surface center with surface lines radiating out to the contour line. The curved surface has an appearance similar to that of a circus tent roof. Volume below the curved surface (Fig. 1; VolC) was that bounded by the curved surface and the disc surface below the curved surface. Volume above the curved surface (Fig. 1; VolAC) is that bounded by the curved surface and the neural tissue surface above the curved surface.

We assume that optic disc neural volume anterior to the lamina cribrosa (VolN) will remain constant in the face of changing IOP or...
The change in the volume subtended by the anterior lamina cribrosa, \(\Delta VolS\), is determined by movement of the anterior lamina. Hence, \(VolC\) minus \(VolAC\) at two conditions would be equivalent to \(\Delta VolS\).

Curve fitting was performed on computer (SigmaPlot; SPSS Science, Chicago, IL).

RESULTS

Stability of Reference Ring

The average shift in the absolute reference ring position for any pressure condition relative to baseline across all animals was \(-2.20 \mu\text{m}\). In individual animals, the average shift ranged from \(-35.67\) to \(24.78 \mu\text{m}\). The average maximum and minimum shifts were 14.72 and \(-42.33 \mu\text{m}\), respectively. These data suggest that the peripapillary retina (and therefore the reference height) did not shift meaningfully after modulation of either IOP or CSFP. It should be noted that during image alignment, these changes are accounted for to measure changes from baseline accurately.

Probability Map Analysis

An example of the probability map analysis is shown in Figure 2. When IOP was increased incrementally from 20 to 33 mm Hg at constant CSFP (0 mm Hg), the central disc surface moved posteriorly by up to 64 \(\mu\text{m}\) (Fig. 2B). The corresponding probability map confirmed that most of the movement occurred in the central disc region. When CSFP was increased incrementally from 0 to 10 mm Hg at constant IOP (17 mm Hg), large anterior movement occurred across the whole optic disc surface (Fig. 2D). Even a small increase in CSFP caused large and significant anterior disc displacement.

Global Indices

The difference was calculated between each global index measured and the index taken at IOP of 15 mm Hg and CSFP of 0 mm Hg in each animal. Hence, the change in the global indices describing the deepest portion of the cup and the volume subtended by the anterior lamina, \(\Delta MaxD\) and \(\Delta VolS\), respectively (Fig. 1), were calculated at each pressure setting and in each animal. For the results when the IOP-CSFP difference was constant, \(\Delta VolS\) was normalized to that at IOP of 24 mm Hg and CSFP of 10 mm Hg. For grouped analysis, \(\Delta MaxD\) and \(\Delta VolS\) were binned at pressure intervals of 3 to 5 mm Hg.

As the translaminar pressure increased, \(\Delta MaxD\) increased nonlinearly and then reached an asymptote (Fig. 3). The maximum depth increased by 80 \(\mu\text{m}\) as the pressure difference increased from 3 to 20 mm Hg. The relationship is described by the following function with \(r = 0.92\)

\[
\Delta MaxD = -0.15 e^{-0.24(IOP-CSFP)}
\]

As the translaminar pressure increased, \(\Delta VolS\) increased nonlinearly (Fig. 4A). The relationship was described by the following function with \(r = 0.98\)

\[
\Delta VolS = 0.18 \ln \left( \frac{IOP-CSFP-1.45}{13.53} \right)
\]

No significant change in \(\Delta VolS\) was found when IOP was elevated from 14 to 32 mm Hg, maintaining the IOP-CSFP difference at 14 mm Hg (Fig. 4B).

DISCUSSION

The results of this study help clarify the effects of acute changes in IOP and CSFP on optic disc position. A theoretical concern with these measurements was the effect of a change in IOP on the choroidal thickness and hence reference ring position, which was used to align serial images to determine topographic changes. The observation that there was no significant lamina volume change when IOP and CSFP increased equally (Fig. 4B) supports the assumption that there is no significant choroidal or disc tissue compression at these IOP ranges. Another explanation would be that the choroidal and optic disc tissue compress equally, which would not affect our conclusions regarding displacement of the lamina cribrosa.
Figure 2. Optic disc images obtained from one animal by CSLT during modulation of IOP (A, B) and CSFP (C, D). Baseline reflectivity (A, top left) and topography (A, bottom left) images before modulation of IOP. Baseline IOP and CSFP were 20 and 0 mm Hg, respectively. Difference map (A, top right) and probability map (A, bottom right) at baseline pressure conditions obtained between two sets of baseline images to illustrate background noise. Sequential elevation of IOP alone demonstrating progressive depression of disc surface in difference (B, top) and probability (B, bottom) maps. Baseline reflectivity (C, top left) and topography (C, bottom left) images before modulation of CSFP. Baseline IOP and CSFP were 17 and 0 mm Hg, respectively. Difference map (C, top right) and probability map (C, bottom right) at baseline pressure conditions obtained between two sets of baseline images to illustrate background noise. Sequential elevation of CSFP alone demonstrated progressive elevation of disc surface in difference (D, top) and probability (D, bottom) maps.
peripheral laminar displacement and not to a further increase in cup volume at high translaminar pressure differences is due to not asymptotic. These observations suggest that the increase in the maximum displacement of the cup, volume change was lowest at higher pressure differences, although, unlike changes in translaminar pressure differences of less than 15 mm Hg and mortality with attendant temperature changes may explain some of this difference. Small increases in CSFP had a much greater effect than equivalent increases in IOP, suggesting that greater movement occurred at lower translaminar pressure differences. This nonlinearity was suggested by the previous work of Levy, who noted that 53% of the movement occurred during the first 15-mm Hg IOP increase. We also found that $\Delta MaxD$ was nonlinearly related to the translaminar pressure difference (Fig. 3). The curve of best fit was a logarithmic increase to a maximum. This maximum displacement was stable at translaminar pressure differences greater than 15 mm Hg. This would suggest that at pressure differences of more than 15 mm Hg, almost no further posterior laminar movement occurred (Fig. 3). However, at pressure differences of less than 15 mm Hg, relatively large displacements occurred. Similarly, the $\Delta VolS$ with translaminar pressure difference was nonlinear (Fig. 4). $\Delta VolS$ was greatest at translaminar pressure differences of less than 15 mm Hg and lowest at higher pressure differences, although, unlike changes in the maximum displacement of the cup, volume change was not asymptotic. These observations suggest that the increase in cup volume at high translaminar pressure differences is due to peripheral laminar displacement and not to a further increase in cup depth at the most cupped locations. This nonlinearity is consistent with the known nonlinear stress–strain relation of collagen, whereby the change in strain decreases with increasing stress.

It is interesting to note that the in vitro compliance of the human eyeball is approximated by the following formula:

$$Vol = 20.2 \ln \left( \frac{IOP}{P_0} \right)$$

where $P_0$ is the initial IOP and $Vol$ is the change in volume. This is an exponential function similar to that best describing optic disc volume change found in the present study

$$\Delta VolS = 0.18 \ln \left( \frac{IOP - CSFP - 1.45}{13.53} \right)$$

Obviously, the increase in disc cup volume for a given change in pressure is much less than that of the whole eyeball. This is reflected in the differing exponential constants that are akin to the rigidity constants of tonography. There are two orders of magnitude difference between these exponential constants (0.18 and 20.2).

Currently, imaging techniques are used to measure changes in optic disc neural tissue, with increasing cup volumes usually being interpreted as due to the loss of axons, and worsening glaucoma. The results in this study raise the possibility that changes in IOP and CSFP between imaging sessions may induce changes in volume that are not related to the loss of neural tissue. Clinical studies with CSLT have shown changes in disc topography with pharmacologically and surgically induced changes in IOP. Another study has shown spontaneous variations in disc topography in patients with untreated idiopathic intracranial hypertension who have large variations in CSFP.

In summary, with a given change in either IOP or CSFP, there is relatively greater optic disc movement across lower

![Figure 3](https://iovs.arvojournals.org/pdfaccess.ashx?url=/data/journals/iovs/932900/)
translaminar pressure ranges than across higher ranges. This may have implications regarding the vulnerability of vital structures, such as ganglion cell axons and blood vessels in the optic disc.

References


