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The effect of intraocular pressure on chick eye geometry and its application to myopia

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Myopia is characterized by an increase in axial length of the eye, but the reasons for the axial elongation are still unknown. Higher intraocular pressure (IOP) has been associated with myopia and could be involved in eye enlargement. The purpose of this study was to investigate the effect of intraocular pressure on the geometry of the chick eye and to investigate whether an increase in IOP could cause the elongation of the eye. The IOP of ten 7-day old chick eyes was raised by injecting fluid into the eyes and the resulting deformation of the eyes was measured using digital cameras. In-vitro pressure–volume curves were obtained. The axial and equatorial strains (deformation normalized to the original dimension) were calculated. Our results showed that IOP increased exponentially with increasing injected volume. About 25 D myopia could be induced by the axial elongation created with an increase in IOP by 100 mmHg. As pressure increased from 0 to 140 mmHg, the chick eye elongated in the axial direction and initially contracted in the equatorial direction. The natural tendency of chick eyes is to elongate as IOP increases and this suggests that from a mechanical perspective IOP could play a role in myopia onset and progression. The results also suggest that oblate eyes might have higher risk of developing myopia.

Key words: *myopia, ocular biomechanics, intraocular pressure*

1. Introduction

Myopia is a refractive error of the eye affecting many people worldwide [1]–[3]. When myopia is defined as a mean spherical equivalent of –0.5 D (dioptres) or more, the prevalence of myopia in 1999–2004 in the United States reaches 50.1% [4]. The prevalence of myopia has increased significantly over the past decades in the United States [1] and in different parts of Asia [5] suggesting that environmental factors might have a significant impact in addition to heredity [6].

In most cases of human myopia (>95%), the refractive error is axial [7]. The traditional model of myopia stipulates that the anterior portion of the eye (the cornea, anterior chamber, and the lens) is normal, but the vitreous chamber is elongated and the posterior sclera is thinned [8]. More recently, ATCHISON et al. [9] found that myopic eyes are elongated more in the axial than in the vertical or horizontal dimension.

In part because of the association of myopia with glaucoma [10], the role of intraocular pressure (IOP) in myopia has been studied. Some authors reported higher IOP in children [11]–[13] and adults [14]–[16] with myopia suggesting that IOP causes ocular expansion and myopia while others did not find any association between IOP and myopia in children [17] and university students [18]. It is not clear from the literature whether the increase in IOP is a cause or an effect of myopia [19], [20]. Different studies investigated the effect of IOP on axial eye length [21], [22], but the effect of IOP on equatorial diameter seems to be absent in the literature.

Chicks are frequently used to study the development of myopia [21]. Chicks grow fast and develop myopia in a short time. It is not clear why chicks de-

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velop myopia in such a short time (3–4 days). Could a slight increase in IOP result in rapid change in chick eye geometry? What is the natural tendency of the chick eye to deform under the influence of increasing IOP? Does it expand equally in all directions? Is there a preferred deformation mode? Such information would be important to create and validate the computational models of eyes to study the development of myopia due to increased IOP resulting in tissue creep. The purpose of this study was to determine the change in geometry of the fresh chick eye with increasing IOP and to investigate whether the deformed geometry results in axial elongation, similar to the deformity in a myopic eye.

2. Methods

The chicks used in this study were Ross 308 obtained from a local poultry plant (Maple Leaf Poultry, New Hamburg, Ontario, Canada) on the day of hatching. The birds were kept in stainless steel brooders for seven days and were sacrificed by decapitation. The eyes were extracted, the extraocular muscles and fat were removed, and the eyes were stored in PBS at 4 °C for no more than 48 hours before the start of the experiment. Ethics approval for research with animals was granted by the Office of Research Ethics at the University of Waterloo.

Ten chick eyes from 6 birds were obtained and mounted on a custom built apparatus designed to inject a precise amount of fluid inside the chick eye (figure 1). The apparatus is composed of a computer-controlled syringe pump (NE-500, New Era Pump Systems Inc., Wantagh, USA), a 3 ml syringe, and a 26G × 1/2″ hypodermic needle connected in series using a 1/8″ diameter medical tubing. This arrangement can dispense fluid (water) to the chick eye attached to the end of the needle. A digital pressure gauge (DPG1000B-30G, Omega, Stamford, USA) is also connected using a T-connector so that the pressure inside the apparatus is measured. Two digital cameras (PowerShot A2000 IS, Canon, Tokyo, Japan) having a resolution of 3648 × 2736 pixels are mounted perpendicular to each other so that both the axial and equatorial deformation of the eye can be photographed.

As a first step, the syringe, medical tubing, T-connector, and needle were connected together and filled with water by submersion. The remaining end of the T-connector was coupled to the digital pressure gauge (figure 1). A chick eye was cannulated at the intersection of the equator and the 90-degree meridian to ensure that the eye did not rotate on the needle during experimentation. Furthermore, the eye was cannulated with the optic nerve aligned with the needle so that each eye had the same orientation (figure 2). During the experiment, the eye was attached only to the needle with nothing else to hold it (figures 1 and 2).

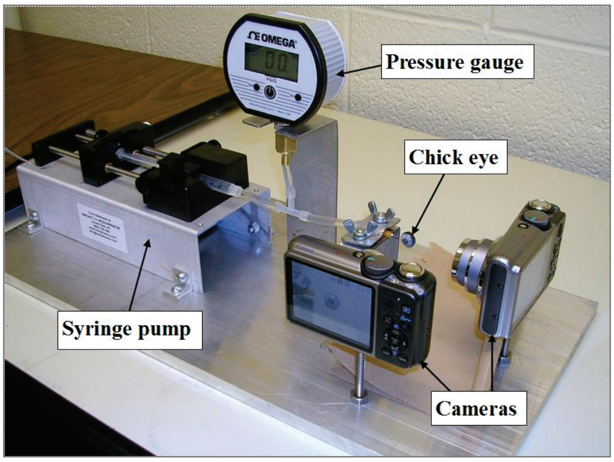


Fig. 1. Syringe pump apparatus used to vary the IOP in the chick eye and measure the deformations

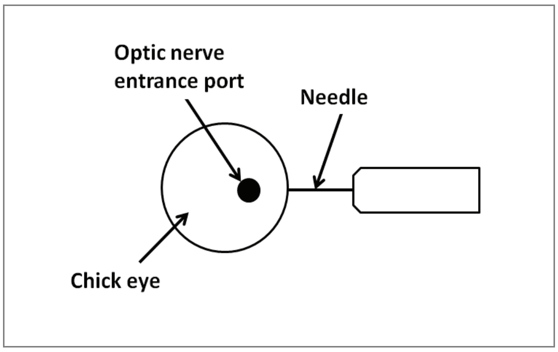


Fig. 2. Schematic of posterior view of the chick eye and the needle position relative to the optic nerve

A tiny amount of cyanoacrylate glue was applied to the puncture to seal it. The two cameras were mounted on their respective holders. Two pictures of the chick eye were taken at zero pressure, one showing the front and one showing the side of the eye. Twenty microliters of fluid was injected into the eye and the pressure was recorded. Two pictures of the chick eye were taken each time the pressure went up by a noticeable amount (~5 mmHg, 1 mmHg = 133.3 Pa). This procedure was repeated until 340 microliters of fluid were injected into the eye. At this point, the intraocular pressure was around 100 mmHg. Then, a single 60-microliter injection of fluid was administered followed by injections of 100 microliters until the eye ruptured. Rupture of the eye was determined when the intraocular pressure went back down to zero. In this experiment, intraocular pressure was raised beyond the physiological range and the eyes were tested to rupture to obtain the complete pressure–volume curve. The experiment was executed as fast as possible with just enough time between injections to record the pressure and take the pictures such that minimal creep could occur. The time elapsed between when the eye was taken out of the PBS solution and when it ruptured was no more than 30 minutes so that the eye did not dry out. On average, 50 photographs were taken for each eye, that is, 2 photographs (front and side views) per pressure value. The photographs were imported into the ImageJ software (U.S. National Institutes of Health, Bethesda, USA) to measure the axial length and the horizontal equatorial dimension (figure 3). The elongation of the eye in the axial and equatorial directions was measured from the photographs. The axial strain and the equatorial strains are defined as axial and equatorial elongations normalized to the respective dimensions of the undeformed eye. Accordingly, these strains were calculated by dividing the axial and equatorial elongations by the original axial and equatorial lengths of the eye respectively.

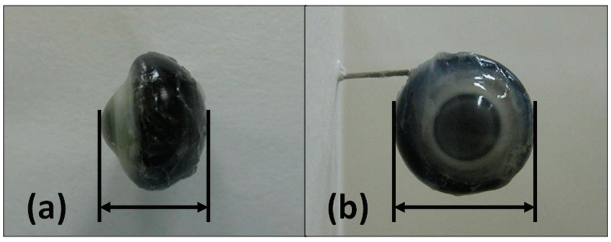
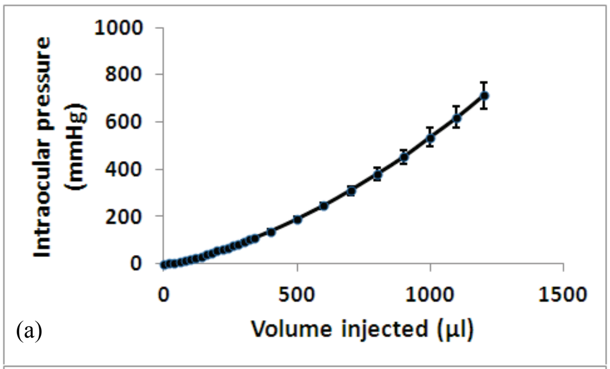


Fig. 3. Photographs of a chick eye showing
(a) the axial length and (b) the horizontal equatorial dimension

3. Results

3.1. Pressure–volume relationship

The experimental pressure–volume relationships are shown in figures 4a and 4b. On average, the chick eyes ruptured when the IOP reached 869 mmHg. Most eyes ruptured at the back of the eye near the optic nerve entrance port, a few ruptured at the limbus, and none ruptured at the needle insertion point. This makes sense because there is a stress concentration near the optic nerve entrance port [8]. When examining the pressure–volume curve of individual eyes, the eyes from the same bird had similar pressure–volume curves as expected.



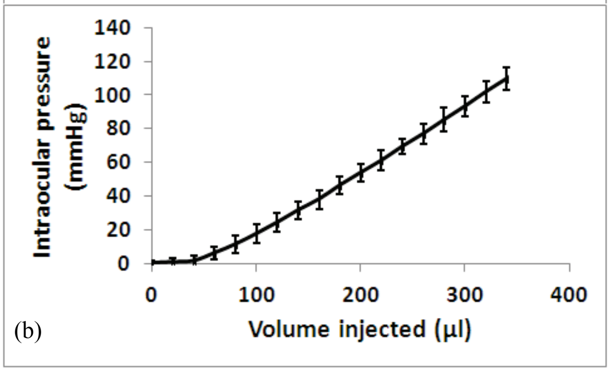


Fig. 4. Average pressure–volume curve of 7-day old chick eyes (n = 10, ±*SD*). (a) At full range of IOP until the rupture. (b) At lower IOP representing the physiological range of IOP. The curves are not linear; as the volume increases, the eye gets stiffer

3.2. Strain–pressure relationship

The way chick eyes deform as pressure increases is somewhat counterintuitive though makes sense from mechanical perspective. As expected, the axial length increases when pressure increases, but not at a constant rate. This is depicted by the positive and non-linear axial strain curve (figure 5). As seen in figure 6, the average elongation when the intraocular pressure is equal to 100 mmHg (which is physiologically possible) was about 1 mm. This axial elongation of 1 mm is equivalent to ≈25 dioptres of myopia for 7-day old chick eyes as per the conversion given by IRVING et al. [23]. Also, the average axial elongation at rupture was 1.70 mm which represents 44 dioptres of transient myopia. Interestingly, almost 60% of the total axial deformation occurs by the time intraocular pressure reaches 100 mmHg. This shows how a relatively small increase in the IOP could cause a substantial change in the axial length of the eye causing myopia.

Interestingly, the horizontal equatorial dimension contracts as pressure increases from 0 to 140 mmHg (figure 5). After that point, the horizontal equatorial strain starts to increase to become positive at a pressure of 540 mmHg. At any given point, the axial strain is at least 10 times greater than the horizontal equatorial strain.

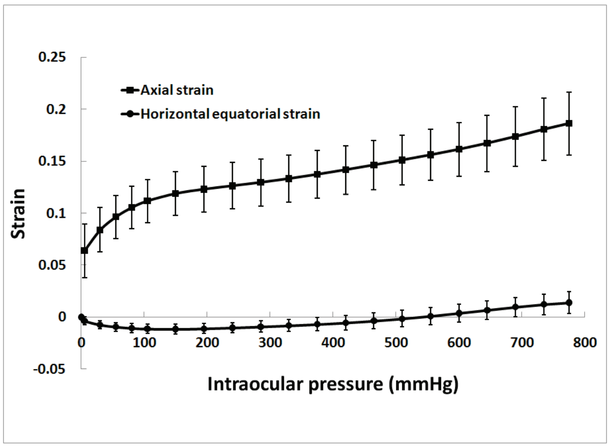


Fig. 5. Average strain–pressure curve of 7-day old chick eyes ($n = 9$, ±*SD*). The deformation is different in both axial and horizontal equatorial directions

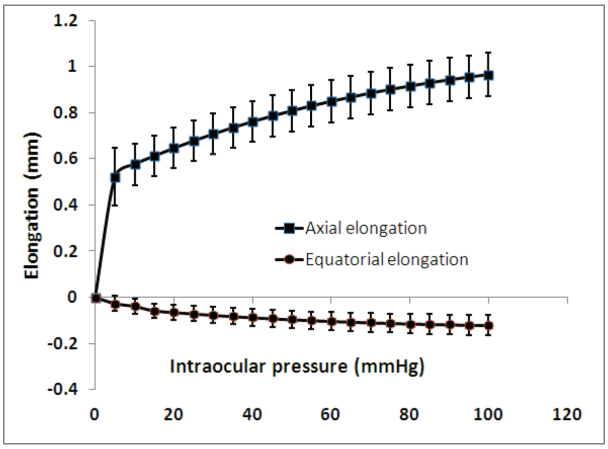


Fig. 6. Average elongation–pressure curve for chick eyes within physiologically possible range of pressure. Negative elongation in the equatorial direction represents contraction

4. Discussion

The deformation of chick eyes as intraocular pressure increases is accompanied by axial elongation which is in agreement with other studies in humans [22] and chicks [21]. The axial elongation would lead to transient axial myopia and permanent myopia if the eyes were stressed beyond their elastic limit [24]. The elastic limit of chick eyes was not determined in this study so it is not possible to tell at what pressure the chick eyes started to yield and become permanently myopic. Whether chick eyes would reach their yield point and become permanently myopic under an IOP of 100 mmHg is unknown but is possible due to creep in the sclera. In this study, we did not study the effects of creep. Higher strain could result due to tissue creep even at lower IOP. For instance, KU and GREENE [25] obtained significant amount of strain by subjecting rabbit eyes to IOP pulses of 150 mmHg over a period of 4 hours. The initial contraction of chick eyes in the horizontal equatorial direction is opposite to findings in humans [9], tree shrews [26], and chicks [23] where myopic eyes are found to be larger than normal eyes in the equatorial direction.

The fact that chick eyes deform more in the axial direction could be explained by the intrinsic material anisotropy and non-homogeneity of the chick eye. Different studies in humans [27], [28] and pigs [29] showed that the cornea is less stiff than the sclera which would cause the cornea to deform more than the sclera, contributing to axial deformation. In the present study, the deformation of the cornea itself was not measured, but it appeared to bulge outward as IOP increased. In addition, chicken eyes have a bony structure, the scleral ossicle, located near and posterior to the limbus [30] that could increase the rigidity of the eye in the equatorial direction.

However, increased rigidity in the equatorial direction would not explain why the chick eye initially shrinks in this direction. One explanation could be the oblate geometry of the chick eye (the average initial axial length was 9.12 mm and the average initial horizontal equatorial length was 12.62 mm). PHILLIPS and McBRIEN [26] constructed a basic finite element model of a tree shrew eye showing that oblate tree shrew eyes elongate in the axial direction but contracted in the equatorial direction. The same behaviour seems to be true in the case of chick eyes.

IOP in chicks has been measured previously and a range of values in normal eyes have been found. LAUBER et al. [31] report values between 7 & 17 mmHg. SCHMID et al. [32] report that the IOP changes with age and find an average IOP value of 18 mmHg for 7-day old birds. GLASSER et al. [33] report values of 9–34 mmHg. These values are for normal eyes and IOP's can raise to much higher values for eyes with light-induced avian glaucoma [31]. It can be seen from figure 5 that about 60% of the total deformation occur with raise in IOP of about 100 mmHg, which is physiologically possible. Myopia can be induced in chick eyes by having them view through defocusing lenses. If viewing through defocusing lenses were to raise the IOP, it seems that because of the oblate geometry of the chick eye, the increase in IOP could produce axial deformation in the eye causing myopia.

If the geometry of the eye influences its deformation, would experimental myopia be easier to produce in animals with oblate eyes? By defining the oblateness ratio as the equatorial diameter minus the axial length over the equatorial diameter, it is possible to compare the eye shape of different animals and the amount of myopia that can be achieved experimentally. For instance, IRVING et al. [23] produced a 9.70 D myopic shift in chick eyes (oblateness ratio of 0.277) by applying −10 D goggles for 7 days, while PHILLIPS and McBRIEN [26] obtained a 5.6 D myopic shift in tree shrew eyes (oblateness ratio of 0.143) using monocular deprivation of form vision for 5 days. Although the conditions of the two experiments are different, it seems to be easier to produce experimental myopia in the more oblate eye, which is the chick eye.

Assuming we could use the same reasoning in humans, would people with oblate eyes be more at risk for axial deformation and myopia? Are eyes before development of myopia oblate in shape? While it is a common knowledge that human eyes are spherical in shape, in a study of ocular shape, 71% of 77 hyperopic eyes were found to be oblate in shape [34]. However, there is no indication that hyperopic eyes progress more toward myopia than normal eyes. More research is needed to determine whether oblate eye geometry along with a decrease in scleral thickness is associated with axial elongation and myopic shift in humans.

The procedure used in this experiment is quite simple and care was taken to ensure the integrity of the measurements. Although the measurements were taken on post-mortem enucleated eyes, all measures were taken within 48 hours after death. A recent study showed that rabbit eyes can be stored for up to 72 hours in PBS at 4 °C without noticeable change in mechanical properties of the sclera [35]. Also, the eyes were cannulated at the intersection of the equator and the 90 degree meridian for maximum stability and to ensure that the eyes do not rotate on the needle. This is important to obtain accurate measurements of the eye from the digital photographs. It is possible that the cyanoacrylate glue used to seal the puncture stiffened the eye and influenced the data, but care was taken to ensure no excessive use. Also, a stiffer part of the eye would not explain the contraction in the equatorial direction. Therefore, it is unlikely the cyanoacrylate glue affected the conclusions of the study.

Refraction of an eye is a combination of many factors including eye length and optical properties such as corneal curvature and thus optical power. Corneal curvature will depend on the age and strain of the bird. For birds of a similar strain and age (7 days) to the ones used in the current experiment the corneal radius of curvature is approximately 3 mm [36]. This translates to a corneal power of 109 diopters and an overall power of the eye of 183 diopters. The corneal curvature in our experiments was not measured. The experiment was not setup to measure this from the outset. While such measurement could have provided interesting information about the relationship between corneal curvature and IOP, experimentally induced refractive errors have been shown by many authors including IRVING et al. [23] and SCHAEFFEL et al. [37] to be almost entirely the result of axial length changes. Therefore, it can be said that the experimental setup captures experimentally induced refractive errors in chick eyes.

In conclusion, intraocular pressure increments cause axial elongation and horizontal equatorial contraction followed by expansion in chick eyes. A small increase in IOP can cause substantial axial deformation of the eye. Chick eyes prefer to deform in the axial direction as opposed to the horizontal equatorial direction. The most plausible explanation for this deformation is the oblate geometry of chick eyes which tends to naturally become more spherical as IOP increases. The natural tendency of chick eyes is to elongate under increasing IOP and this suggests that IOP could play a role in myopia onset and progression. If change in IOP could cause myopia, the results also indicate that oblate eyes might have higher risk of developing myopia.

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