INTRODUCTION

Glaucoma is a global burden. This disease causes irreversible blindness, and at the onset the person affected by glaucoma will experience tunnel vision. In the United States alone, there are 2.1 million blind people. Glaucoma is responsible for 1 in 15 of the blind people. Additionally, 1 in 45 visually impaired people have become visually impaired due to glaucoma. It is the second highest cause of blindness, behind cataracts.

Glaucoma is known to initiate in the lamina cribrosa, a porous, connective tissue in back of the eye. The lamina consists of beams, the connective tissue, and pores, the spaces between the beams through which nerve fibers pass on their way from the retina to the brain. Additionally, the lamina is surrounded by the sclera, the white part of eye. During elevated intraocular pressure, the nerve fibers suffer stretch and compression, which triggers events that eventually leads to their death and the loss of vision.

In the Laboratory of Ocular Biomechanics, many avenues are being explored to determine the cause of glaucoma. However, still more research is necessary to understand how the structure of the lamina cribrosa contributes to the mechanical and biological response to elevated intraocular pressure. Identifying a relationship between the location and shape of a pore and the strain it undergoes under elevated pressure will help predict understand glaucoma and predict patient susceptibility better.

OBJECTIVE

The purpose of this study was to determine if the location of a pore in the lamina cribrosa with respect to the sclera or the shape of the pore have an identifiable relationship with the strain in that pore. The aim is to determine what causes the onset of glaucoma by determining if the various shapes of pores cause the fibers to die. Additionally, knowing the shape patterns could help identify patients who are at risk of glaucoma. Patterns in patients’ eyes could be identified using ocular coherence tomography.

HYPOTHESIS/SUCCESS CRITERIA

The main success criteria for this study was determining if there is an association between pore strain and pore shape and location. The analysis will be conducted in Matlab and R programs, therefore, another success criteria is codes that run properly.

METHOD

The first step in determining the statistical significance of the shape on the strain of the pore was to identify the lamina cribrosa pores in histology images. This step was conducted in Matlab using binary images of the pores. Once the pore was identified, a code was written to quantify the shape based on several different parameters, including area, perimeter, convexity, aspect ratio, and eccentricity. As can be seen in Figure 1, lamina cribrosa pores can have very different sizes and shapes.

Figure 1. Binary image of lamina cribrosa pores to illustrate the differences in shape and size. Note the large differences between the two highlighted pores.

The next step was to determine the strain in the pores. The predicted strain was determined using finite element analysis. Data processing methods were utilized to assign the stretch percentage to each pore, as shown in Figure 2.

Figure 2. Data processing to determine the strain in individual lamina cribrosa pores.

The final step was to identify a relationship between strain and shape of the pores using a statistical software package, R. A linear mixed effects model was originally used, but was not suitable for the sample size. Instead, a fixed effects model was used. Models using different combinations of shape parameters
and data transformations were tested and the best fit model was selected using the Akaike Information Criterion (AIC).

RESULTS
The best fit model according to the AIC value for the max stretch of the pores, which is the 1st principal strain, was the log of max stretch with convexity being the only statistically significant shape parameter. The best fit model for the max compression of the pores, or the 2nd principal strain, was the linear relationship between max compression and the three parameters, convexity, area, and aspect ratio. While both relationships are important, only the relationship of max stretch with pore convexity will be further discussed in this abstract.

The shape parameter convexity refers to shapes that are more convex or less convex (concave). A convex shape is rounded outward, similar to a circle, whereas a concave shape is rounded inward. Figure 3 shows a convex pore and a more concave pore from the binary image.

Figure 3. Concave and convex lamina cribrosa pores from binary histology image

Figure 4 displays seven graphs that represent the seven different models that came from the data. The different models were due to the data coming from two different sheep, two different eyes from one of the sheep, and different sections from histology images. The peripheral regions are models that had sclera in the histology image, and the central regions had no sclera.

Figure 4. The max stretch of lamina cribrosa pores: modeling seven different models for pores in peripheral and central regions of the lamina cribrosa with log(max stretch) versus the convexity of the pores

All models indicate that as convexity of the pore increases, the percent stretch of the pore decreases. The pore shown in the top left of Figure 4 is one of the least concave in the model, and the pore has very high stretch. Additionally, the pore shown in the bottom right is the most convex pore in the model, and it reports a very low stretch.

DISCUSSION
There is an identifiable relationship between strain in lamina cribrosa pores and shape parameters. Additionally, all models report statistical significance, and there is no one model for all parameters. The objective and success criteria of the study were met.

Some limitations to the study include that the data was collected from sheep. While sheep eyes are around the same size as human eyes and they have lamina, the lamina has a slightly different structure, where the pores tend to be narrower and there is more collagen in human eyes. There are several reasons as to why the lab uses sheep eyes rather than human eyes; including, sheep eyes can be much less expensive to obtain than human eyes, and when eyes are collected from sheep, it is known that the eyes came from sheep that lived together in the same conditions. Processing and harvesting of tissue can be done in a consistent manner, so more statistical significance can be drawn from the eyes. However, it is difficult to draw conclusions to the human population because humans do not live the same way as sheep do.

An additional limitation to the study is there was no precise measure of distance from the sclera. The sclera factor was binary, taken into the models only as an image with sclera or an image without sclera. A shape parameter describing a pore’s distance from the sclera could improve the results.

The next step for the study is to determine the shape parameter for the distance of a pore from the sclera. Also, the same analysis will be completed for the connective tissue in the lamina cribrosa. Identifying risks factors for glaucoma could allow treatment to start earlier. The end goal would be to determine the causes of glaucoma in order to one day stop this disease.

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REFERENCES