Appendix: The Theoretical Relationship Between E:Z Ratio and Anterior Chamber Depth Based on a Schematic Eye

Background

When an eye is viewed from the temporal side, perpendicular to the visual axis, a light ray emanating from the pupil is refracted by the cornea. The observer sees a virtual image which is anterior to the actual anatomical pupillary plane.

To find the relationship between E:Z ratio (limbus to image of mid pupil: limbus to cornea) and anterior chamber depth (ACD) we will first establish a theoretical expression for the forward displacement of the virtual image as a function of the actual anatomical pupil plane. Using this expression, the theoretical relationship between E:Z ratio and AC depth can be calculated (See hypothesis 1 in main manuscript).

In the following calculations we will assume a spherical corneal surface.

1. Virtual image height of the mid pupil point

A light ray emanating from the mid-pupil point on the actual anatomical pupil plane will be refracted by the cornea. The height of the virtual mid pupil, h, as viewed by an observer perpendicular to the visual axis can be determined by extending the ray coming from mid pupil point and refracting to produce a ray parallel to x-axis (Figure 1).
To find the virtual mid pupil image plane (which is the y value of the refraction point) for a given true pupil plane height (d), the aim is to solve the following expression:

\[ \sin \alpha = 1.37 \sin \beta \]
which is based on Snell’s law, assuming a combined corneal : aqueous refractive index of 1.37, where \( \beta \) is the incident angle and \( \alpha \) is the refracted angle from the normal at the refraction point.

We chose the mid pupil point, as this landmark is relatively easy to find on perpendicular photography and was used to define \( E \) for the measurement of \( E:Z \) ratio. We are however aware of the fact that the centre of the oval image of the pupil is only an approximation of the real pupillary centre image, given the refractive forward displacement increases as a function of distance from the viewer (See figure 6 in the main text).

2. Deriving a mathematical equation for sin \( \alpha \)

By assuming a perfectly spherical cornea

\[
y^2 + x^2 = R^2
\]

\[
y = \sqrt{R^2 - x^2}
\]

Therefore, and because the normal line at all points on the circle will extend from the origin AND angles made by a straight line across two parallel lines will be equal (Figure 2):

\[
\therefore \quad \sin \alpha = \frac{\text{opposite}}{\text{hypotenuse}} = \frac{y}{R} = \frac{\sqrt{R^2 - x^2}}{R}
\]
3. Deriving a mathematical equation for sin β

Angle β is formed between the normal line and a line connecting the central pupil point and the refraction point. To find angle β, we will use a standard equation for finding the angle between two straight lines

\[ \tan(\text{angle between two lines}) = \frac{m_1 - m_2}{1 + m_1 m_2} \]

where m1 is the gradient for line 1 and m2 is the gradient for line 2.

In our case,

\[ m_1 = \text{gradient of normal line} = \frac{y}{x} = \frac{\sqrt{R^2 - x^2}}{x} \]

\[ m_2 = \frac{y - d}{x} = \frac{\sqrt{R^2 - x^2} - d}{x} \]

\[ \therefore \tan \beta = \frac{\sqrt{R^2 - x^2} - \sqrt{R^2 - x^2 - d}}{1 + \frac{\sqrt{R^2 - x^2} - \sqrt{R^2 - x^2 - d}}{x}} = \frac{\sqrt{R^2 - x^2} - \sqrt{R^2 - x^2 + d}}{x^2 + \frac{R^2 - x^2 - d}{x} \sqrt{R^2 - x^2}} \]

To find $\sin \beta$ given $\tan \beta$,

\[
\sin \beta = \frac{x \cdot d}{H}
\]

\[
H^2 = d^2 x^2 + \left( R^2 - d \sqrt{R^2 - x^2} \right)^2
\]

\[
= d^2 x^2 + \left( R^4 - 2 d R^2 \sqrt{R^2 - x^2} + d^2 R^2 - d^2 x^2 \right)
\]

\[
= R^4 - 2 d R^2 \sqrt{R^2 - x^2} + d^2 R^2
\]

\[
= R^2 \left( R^2 - 2 d \sqrt{R^2 - x^2} + d^2 \right)
\]

\[
H = R \sqrt{R^2 - 2 d \sqrt{R^2 - x^2} + d^2}
\]

\[ \therefore \sin \beta = \frac{x \cdot d}{R \sqrt{R^2 - 2d \sqrt{R^2 - x^2} + d^2}} \]

Therefore, to solve for \( \sin \alpha = 1.37 \sin \beta \), one would solve for

\[
\frac{\sqrt{R^2 - x^2}}{R} = 1.37 \times \frac{x \cdot d}{R \sqrt{R^2 - 2d \sqrt{R^2 - x^2} + d^2}}
\]

4. **The relationship between the true pupil plane height (d) and the virtual pupil plane height (h) at the mid-pupil point for a given R.**

Due to the complexities of the algebraic calculations involved, Microsoft Excel SOLVER module was instead used to solve the x value that will produce the least difference between \( \sin \alpha \) and \( \sin \beta \) for a range of values of d in 0.25 mm intervals. The range of d in the table was chosen to generate an anatomically relevant AC depth range for the human eye.

For the calculations, R was assumed to be equal to the average biometrically measured corneal curvature of 7.8 mm obtained from Group A of our clinical study.

For each x coordinate x1, a vertical coordinate y1, which is the height of the virtual pupil plane (h), was calculated from the circle equation \( y = \sqrt{R^2 - x^2} \).
The value of y1 is the height of the virtual pupil plane (h) as shown in table 1.

Table 1

<table>
<thead>
<tr>
<th>d</th>
<th>x1</th>
<th>sin α</th>
<th>1.37 x sin β</th>
<th>Absolute difference</th>
<th>y1 (h)</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.75</td>
<td>5.970252</td>
<td>0.643535</td>
<td>0.644248</td>
<td>0.0000714</td>
<td>5.019571</td>
</tr>
<tr>
<td>4</td>
<td>5.690364</td>
<td>0.683945</td>
<td>0.683999</td>
<td>5.4E-05</td>
<td>5.334769</td>
</tr>
<tr>
<td>4.25</td>
<td>5.391839</td>
<td>0.722605</td>
<td>0.72296</td>
<td>0.000355</td>
<td>5.636318</td>
</tr>
<tr>
<td>4.5</td>
<td>5.064155</td>
<td>0.760575</td>
<td>0.760543</td>
<td>3.14E-05</td>
<td>5.932481</td>
</tr>
<tr>
<td>4.75</td>
<td>4.710065</td>
<td>0.797095</td>
<td>0.796537</td>
<td>0.000558</td>
<td>6.217338</td>
</tr>
<tr>
<td>5</td>
<td>4.338222</td>
<td>0.83106</td>
<td>0.831035</td>
<td>2.53E-05</td>
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</tr>
<tr>
<td>5.25</td>
<td>3.938279</td>
<td>0.863173</td>
<td>0.862978</td>
<td>0.000196</td>
<td>6.732753</td>
</tr>
<tr>
<td>5.5</td>
<td>3.514832</td>
<td>0.892716</td>
<td>0.891835</td>
<td>0.000881</td>
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<tr>
<td>5.75</td>
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<td>0.918555</td>
<td>0.917922</td>
<td>0.000632</td>
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</tr>
<tr>
<td>6</td>
<td>2.647292</td>
<td>0.940643</td>
<td>0.94068</td>
<td>3.68E-05</td>
<td>7.337019</td>
</tr>
</tbody>
</table>

Plotting d against h shows the true pupil plane (d) forms a curvilinear relationship with the virtual mid-pupil height (h). This relationship can be approximated by the line $y = 1.0416 x + 1.2041$ (Figure 3).

The slope of this linear relationship is close to 1, therefore showing that the displacement (in mm) is fairly constant for an R value of 7.8 mm.

Figure 3: Plotting d against h shows the true pupil plane (d) forms a close to linear relationship with the virtual pupil plane (h) assuming R of 7.8 mm.

5. Establishing the image shift and the relationship between EZR and ACD

We will use the approximated expression shown above, \( y = 1.04d + 1.2 \).

The image shift forward is therefore \( y - d = 0.04d + 1.2 \).

\[
ACD = (vACD - CCT) + \text{image shift}
\]

\[
ACD = vACD - CCT + (0.04d + 1.2)
\]

Since \( d = R - ACD - CCT \), and assuming \( R=7.8 \text{ mm} \) and \( CCT= 0.55 \text{ mm} \):

\[
ACD = vACD - 0.55 + 0.04 (7.8 - ACD - 0.55) + 1.2
\]

\[
ACD = 0.96 \times vACD + 0.9
\]

by definition, \( vACD = Z - E \)

\[
ACD = 0.96 \times (Z - E) + 0.9
\]

We will express E as \( \frac{E}{Z} \times Z \) namely \( EZR \times Z \)

\[ ACD = 0.96 \times (Z - EZR \times Z) + 0.9 \]

Z depends on R and WTW with the equation \( Z = R - \sqrt{R^2 - \frac{WTW^2}{4}} \) (See figure 6 in the main manuscript), and using average R of 7.8mm and WTW of 12mm, this equation yields \( Z = 2.8 \text{ mm} \). For the distribution of this calculated Z value amongst all individual eyes in our series see figure 7 in the main manuscript.

Therefore, if using this average Z value:

\[ ACD = 0.96 \times (2.8 - 2.8 \times EZR) + 0.9 \]

\[ ACD = -2.688 \times EZR + 3.588 \]

This theoretically derived relationship between EZR and ACD shows a linear relationship of similar but not identical characteristics to our empirically derived relationship:

\[ ACD = -3.27 \times EZR + 4.18 \]

We hypothesise that this difference stems from approximations and assumptions of corneal sphericity we made in the theoretical calculation.

6. Measuring Z directly from calibrated photographs

An alternative way to study Z is to measure it directly, rather than calculate it theoretically. To achieve that we did calibrated photogrammetric analysis on a sample
of our patients. We took calibrated perpendicular lateral photographs of 24 patients (46 eyes). We used a tripod mounted Canon 450D with a set manual zoom (250 mm in a 55-250 mm lens) and a set focal length/object distance (107 cm, which is the minimal object distance for that zoom factor in the lens) and otherwise the same photography methodology described in the Methods section of the main manuscript. Using the same camera settings (zoom and focal length), a photo of a millimetric ruler was taken. All photographs were viewed with the same image viewer (IrfanView, www.irfanview.com) at the same zoom factor. The pixel:mm ratio was derived from the millimetric ruler photograph and found to be 82.89 pixels/mm. E and Z were determined in pixels as described in the Methods section of the main manuscript. The pixel value of E and Z in each of those photographs was then converted to millimeters by dividing it by 82.89 pixels/mm, in order to calculate the actual size of Z. The mean size of Z measured with this calibrated photogrammetric method was 3.0 mm, standard deviation=0.52 mm, range 1.77-4.1 mm.

If using this Z value of 3 mm in the above theoretical equation

\[ ACD = 0.96 \times ((Z - EZR \times Z) + 0.9) \]

The resulting relation is

\[ ACD = -2.88 \times EZR + 3.78 \]

which is closer to our empirically derived correlation than when using the theoretical, calculated value of Z=2.8mm.