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***In vitro* biometry of a human spherophakia**

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Keywords

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Spherophakia is a congenital condition in which the crystalline lens exhibits a relatively more spherical shape than usual because of an increased axial thickness.^{1–5} It may present as an isolated entity, be a part of other disorders, such as Alport syndrome, homocystinuria, Klinefelter syndrome, Marfan syndrome, or Weill–Marchesani syndrome or in association with other conditions, such as familial buphthalmos or nanophthalmia.^{1,3,6–8} The estimated prevalence of megalocornea-spherophakia-secondary glaucoma syndrome is less than one in 1,000,000.⁹ Because of loose zonular attachments, accommodation is defective and dislocation or subluxation of the lens is common.^{8,10}

The ocular features usually associated with spherophakia are ectopia lentis, lenticular myopia and secondary glaucoma.¹ The myopia is primarily due to the spherophakic lens; however, increased axial length may also contribute.² The shallow anterior chamber and the forward movement of the lens are predisposing factors for an increase in intraocular pressure (IOP).^{10,11} Early diagnosis and management of pupillary block by peripheral laser iridotomy prevent the onset of angle-closure glaucoma.¹⁰ Chronic elevation in IOP may be due to unrelieved pupillary block and lensectomy may be required to control glaucoma.⁴ Past studies on spherophakia have found small lenses (microphakia or microspherophakia).^{7,11}

Here, we report detailed *in vitro* biometry of an isolated human spherophakic lens and draw comparisons with age-matched crystal-line lenses with no developmental abnormalities.

This study followed the tenets of the Declaration of Helsinki. Informed consent was obtained from the legal guardian of the study subject and the study protocol was approved by the Institutional Ethics Committee, L V Prasad Eye Institute, Hyderabad, India.

CASE HISTORY AND PROCEDURES

A 17-year-old female presented to the Ophthalmic Plastics Clinic, L V Prasad Eye Institute, Hyderabad, India, concerned about the appearance of her left eye. The patient had bilateral congenital glaucoma, which had been treated with trabeculotomy and trabeculectomy in both eyes. At presentation, there was no perception of light in the left eye and it was buphthalmic with a gross anterior staphyloma (Figure 1). Review of the patients medical records revealed a previous diagnosis of spherophakia by slitlamp biomicroscopic examination prior to left corneal opacification. There were no associated signs or symptoms suggestive of any systemic condition. The patient underwent left eye evisceration and implantation of a polymethylmethacrylate implant (No. 26 Conformer, Akriti Oculoplasty Logistics, Hyderabad, India).

During the evisceration procedure, the crystalline lens was carefully extracted. The zonules had already ruptured during the time of dissection. After around 20 hours of preservation in balanced salt solution (Alcon Laboratories Inc, Fort Worth, Texas, USA), *in vitro* biometry of the isolated lens was performed applying the principle of shadow photogrammetry.^{12,13} The coronal and sagittal profiles of the lens were illuminated by two light sources of the second generation mini-shadowgraph and were captured using a digital camera.¹⁴ The images were used to measure dimensions and curvatures of the isolated lens and image analysis was performed using a custom MATLAB (R2012b, MathWorks, Natick, Massachusetts, USA) based program. In a sagittal lens profile, the total axial thickness was divided into an anterior thickness and a posterior thickness by the lens equatorial diameter. Because of its fixed optical magnification and high resolution, the second generation digital mini-shadowgraph has a precision of $\pm$ six micrometres.¹⁴ The wet weight of the lens was then measured using an analytical balance (KERN ABS 120–4, Kern & Sohn GmbH, Balingen-Frommern, Germany). After one week of fixation in five millilitres of five per cent buffered formalin and two weeks of drying at 80 °C in a hot air oven (Sisco, Thane, India), the dry weight of the lens was measured.¹⁵ The data from the study lens were compared to those of nine control lenses approximately matched for age (15-year-old = 1; 16-year-old = 1; 17-year-old = 1; 18-year-old = 3; 19-year-old = 3).¹⁶

RESULTS

Macroscopically, the lens was clear and appeared to be devoid of any capsular damage. Figure 2A shows the coronal and sagittal profiles of the lens under study. Similar profiles for a control lens from a 17-year-old male donor are shown in Figure 2B for comparison. The nylon sutures that support the lenses in the tissue chamber of the apparatus were visible through the lenses in their coronal profiles, indicating that the lenses were transparent. As

seen in Figure 2A and B, the study lens was grossly spherophakic in comparison to the age-matched control lenses. Table 1 summarises the results of the lens biometry for the study lens and the control lenses. For thicknesses (total, anterior and posterior), cross-sectional area, volume and weights (wet and dry), the measurements of the study lens were outside the 95 per cent confidence intervals for the mean values of the control lenses.

Additional clinical information for the right eye was obtained from retrospective review of the patient's medical records. Examination under anaesthesia and B-scan ultrasonography showed evidence of bilateral optic disc cupping with cup-to-disc ratio of 0.9:1. An inferior arcuate scotoma was found during computerised visual field examination of the right eye. Open anterior chamber angles were noted during gonioscopic examination of the right eye, when IOP was controlled after combined trabeculotomy and trabeculectomy. Biometric measurements of the right eye showed an anterior chamber depth of 4.33 mm, axial length of 24.88 mm, central corneal thickness of 504 μm (Lenstar) and crystalline lens thickness of 4.61 mm (B-scan), with a refraction of $-4.25/-1.00 \times 180$. The spherophakia was found to be associated with congenital glaucoma, buphthalmos and myopia.

DISCUSSION

This study reports the *in vitro* biometry of an isolated human spherophakic lens measured using the technique of shadow photogrammetry. To the best of our knowledge, there have been no detailed studies of *in vitro* dimensions of a spherophakic lens. The lens obtained in our study was transparent enough to make comparisons with the age-matched normal donor lenses.

Although the equatorial diameters are comparable, the total thickness of the study lens is 44 per cent greater than that of the control lenses. A similar result was obtained by Cabot and colleagues¹⁷ from lens thickness comparisons using extended-depth spectral-domain optical coherence tomography (OCT) in a 26-year-old woman with Weill–Marchesani-like syndrome and a control subject of the same age. Cabot and colleagues¹⁷ also reported that the equatorial diameters were 6.2 mm and 6.7 mm. McGavie⁷ reported an average equatorial diameter of 6.75 mm for eight lenses removed from patients with Weill–Marchesani syndrome with sagittal diameters (total thickness) 25 per cent greater than normal. The spherophakic lens diameters described in these two studies (6.2 to 6.75 mm) were very low compared to normal controls of the same age (8.0 to 9.0 mm). Fujiwara and colleagues¹¹ found a lens from a 20-year-old man with the same syndrome to have an equatorial diameter of 7.0 mm and a sagittal diameter greater than normal; however, it is not known how the measurements were obtained in the above studies. Interestingly, our study shows that, relative to controls, the anterior thickness of the study lens was 67 per cent greater, whereas the posterior thickness was 26 per cent greater. The cross-sectional area and volume, which are dependent on thickness are also higher for the study lens.

For the spherophakic lens, the anterior and posterior radii of curvature in the central 6.0 mm of the surfaces appear similar to those of the control lenses. This suggests that any increase in curvature observed in spherophakia occurs in the lens periphery, that is, outside the central 6.0 mm zone. A steep anterior lenticular curvature has been noted in OCT and

ultrasonic biomicroscopic studies of spherophakia.^{10,17–19} The small difference between the anterior and posterior curvature observed in our study may be a distinguishing feature of spherophakia. These changes in curvature present typically as lenticular myopia.

The study lens was heavier than the control lenses in wet and dry weights by 53 and 47 per cent, respectively. McGavie⁷ found the weight of the lenses to be 20 to 25 per cent less than normal. Since wet and dry weights are higher by the same proportion in spherophakia, the increase in size is due to growth and not water uptake.²⁰ Such a heavy lens is more prone to dislocation or subluxation, leading to ectopia lentis and/or pupillary block.¹⁹ Hence, it is not only the size but also the weight of the lens in spherophakia that may predispose the eye to secondary glaucoma.

The dry weight provides a reliable measure of protein content and is not affected by saline preservation. The high value of dry weight found in our study lens suggests an increase in protein content; however, the dry weight concentration (ratio of dry weight to wet weight) in the study lens (30 per cent) is similar to that of the control lenses (31 ± 1 per cent) suggesting that the compaction process responsible for the development of gradient refractive index in normal lenses may also be intact in spherophakia. The increase in protein, together with the increase in lens size, indicates that there has been a change in the regulation of lens growth or a mutation resulting in a larger asymptotic lens size.

In short, our study provides a new perspective on spherophakia from the results of *in vitro* biometry. Although the study was performed on only one 17-year-old lens, considering the rarity of the disease, our results give insights into the biometry of an unusually large and heavy spherical crystalline lens. The normal length of the equatorial diameter and increased wet weight (unlike the past studies) together with the hypothesised increase in protein content, suggest that the study lens may be a variant of spherophakia.

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Figure 1.
Clinical photograph of both the eyes showing a gross anterior staphyloma of the left eye

Figure 2.

A. Coronal (left) and sagittal (right) profiles of the lens under study imaged using a digital mini-shadowgraph. B. Similar profiles of a control lens (17-year-old male) for comparison. The lenses were supported by 10–0 nylon sutures (prominent in sagittal profiles) in the tissue chamber of the apparatus. The nylon sutures were also visible through the lenses in the coronal profiles, indicating that the lenses were transparent. Scale bars represent five millimetres.

Table 1.

Summary of the results of lens biometry for the study lens and the control lenses

Isolated lens biometry	Study lens	Control lenses: mean $\pm$ standard deviation (95 per cent confidence interval)
Equatorial diameter (mm)	8.57	8.61 $\pm$ 0.21 (8.45 to 8.77)
Total thickness (mm)	5.84	4.07 $\pm$ 0.24 (3.89 to 4.26)
Anterior thickness (mm)	2.88	1.72 $\pm$ 0.19 (1.57 to 1.87)
Posterior thickness (mm)	2.96	2.35 $\pm$ 0.19 (2.20 to 2.50)
Cross-sectional area (mm ²)	38.64	26.28 $\pm$ 1.51 (25.12 to 27.44)
Volume (mm ³)	217.64	147.32 $\pm$ 9.24 (140.22 to 154.42)
Anterior radius of curvature [†] (mm)	6.54	7.63 $\pm$ 1.43 (6.53 to 8.73)
Posterior radius of curvature [†] (mm)	-5.32	-4.99 $\pm$ 0.48 (-5.36 to -4.62)
Wet weight (mg)	245.60	160.87 $\pm$ 12.55 (151.22 to 170.52)
Dry weight (mg)	73.10	49.58 $\pm$ 5.23 (45.56 to 53.60)

[†] (central six millimetres conic)