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Case Report Open Access

# Effect of Ocular Biomechanics on Intraocular Pressure Measurement in Mucopolysaccharidosis I-S (Scheie's Syndrome)

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## Abstract

**Purpose:** To study the effect of biomechanical properties of the cornea on the intraocular pressure in eyes affected with Mucopolysaccharidosis type I-S (Scheie's syndrome).

**Methods:** Four eyes of two patients in their mid-fifties diagnosed with Scheie's syndrome were investigated for corneal biomechanical properties. The corneal biomechanical profile was assessed by the use of Ocular response analyzer (ORA, Reichert Inc., of Buffalo, NY). Intraocular pressures were also checked using various tonometry devices to check for variability in the readings due to the corneal changes.

**Results:** The intraocular pressure (IOP) measurements were noted to be high in both the patients at their initial presentation. Both the patients were put on topical anti glaucoma treatment and one underwent glaucoma filteration surgery as well for IOP control. Both the patients underwent successful bilateral deep anterior lamellar keratoplasty (DALK) procedures. The post procedure IOP measurement had a dramatic improvement in both the patients. Corneal biomechanical profile was noted to be high pre DALK and reduced significantly after the lamellar surgery. The intraocular pressure readings were also measured using different tonometry devices and were noted to be lower after graft surgeries.

**Conclusion:** Corneal rigidity and hysteresis is high in patients with MPS type I-S. This is reflected in the raised intraocular pressures checked by use of applanation or indentation tonometry. Use of the ocular response analyzer has helped study the biomechanical properties of such corneas and helped in assessment of true values of intraocular pressures thus preventing inappropriate intervention options especially surgical options.

**Keywords:** Ocular rigidity; MPS; Hysteresis; Scheie syndrome; Mucopolysaccharidosis; Ocular response analyser

## Introduction

Lysosomal storage disorders are a group of more than 50 inheritable disorders [1,2]. They are individually very rare, but collectively have an incidence of one in 5000 live births. Scheie's syndrome [Mucopolysaccharidosis type I-S (MPS Type I-S)] is one of the disorders falling in this group. It is an autosomal recessive disorder of mucopolysaccharide metabolism [3]. The deficiency lies in the α-L-iduronidase enzyme resulting in systemic deposition of dermatan and heparin sulphate, which form important components of extracellular matrix surrounding the keratocytes and integral parts of cell membranes [4]. The ocular features include corneal clouding [5] and stromal oedema, increased scleral thickness [6], chronic disc swelling or atrophy [5,7] and retinal pigmentary degeneration [5].

Previous studies have also reported raised intraocular pressure (IOP) and open angle glaucoma in patients with MPS [8,9]. Quigley et al. [10] observed acute glaucoma in two patients with systemic MPS type I-S. Rummelt et al. [11] described a patient with Scheie's syndrome where they noted raised IOPs before penetrating keratoplasty, which returned to normal levels after transplantation. The plausible explanation was put down to an increase in the corneal rigidity.

## Cases Review

We present here the management dilemmas for two female siblings, aged 52 years and 56 years respectively, suffering with Scheie's syndrome and showing variable phenotypic features (systemic and ocular) of the disease with high intraocular pressures (IOPs) (Figures 1 and 4). The presenting pressures for sibling 1 were 30 mm Hg and 26 mm Hg and for sibling 2 the IOPs were 56 mm Hg and 54 mm Hg in right and left respectively. Due to high measured IOPs, the sibling 2 underwent bilateral sequential trabeculectomy procedure, which failed within a few months. They both subsequently underwent bilateral deep anterior lamellar keratoplasty (DALK) to reduce the corneal clouding (Figures 3 and 5). As hypothesized the raised IOPs resolved for sibling 1 (measuring 14 mm Hg on right and 16 mm Hg on the left respectively) but for sibling 2, the IOP reduction was only temporarily seen in the early post op period following which she had repeated high measurements in her right eye. Due to their variable phenotypic features and with persisting high IOPs in one of the 4 eyes we decided

to look at their corneal biomechanical profile. This was measured using the Ocular response analyzer (ORA; Reichert, Inc, of Buffalo, NY) and the new ultra high-speed non-contact tonometer Corvisc ST (Oculus, Wetzlar, Germany). We were able to get pre and post DALK readings for sibling 2 but only post op measurements for sibling 1 as she had undergone DALK prior to availability of both the machines (Figures 2 and 6).

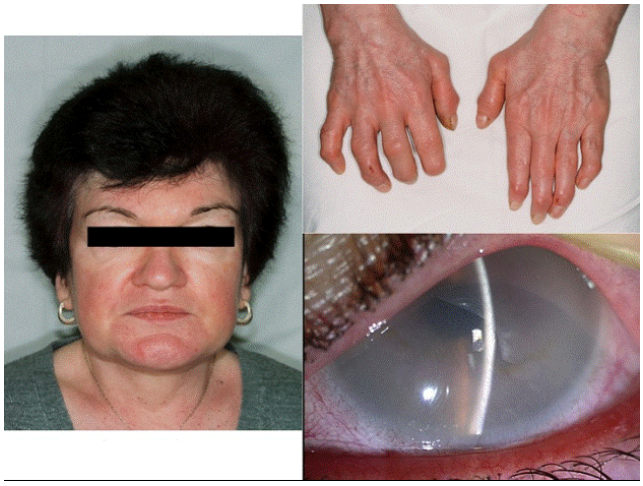

**Figure 1:** [Sibling 1] (Left) – Coarse facies; (Top Right)- hand abnormalities; (Bottom right)-corneal oedema with stromal haze prior to graft surgery.

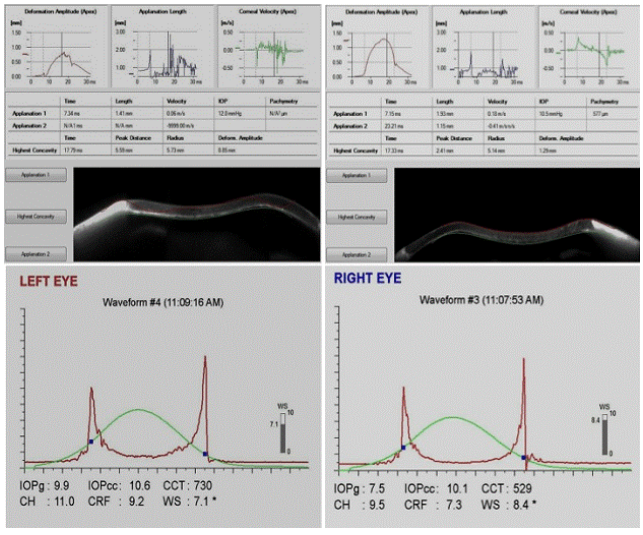


**Figure 2:** Images showing the corneal biomechanical profiles using the Corvisc ST (upper left (for left eye) and upper right (for right eye) respectively) and the waveforms picked up using the ORA (bottom left (for left eye) and bottom right (for right eye) respectively) for sibling 1.

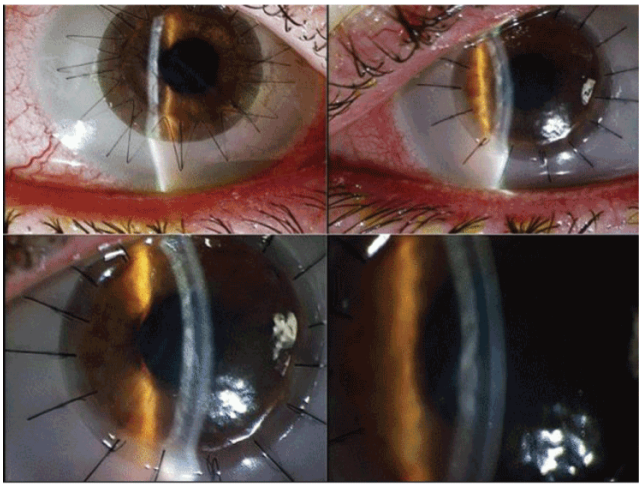

**Figure 3:** (Top right and left) – Post DALK images (Sibling 1) of right and left corneas with central clear donor button and surrounding recipient stromal haze; (Bottom left and right)- Magnified views of the left eye showing the clear donor button with some residual stromal haze in the post stroma of recipient cornea.

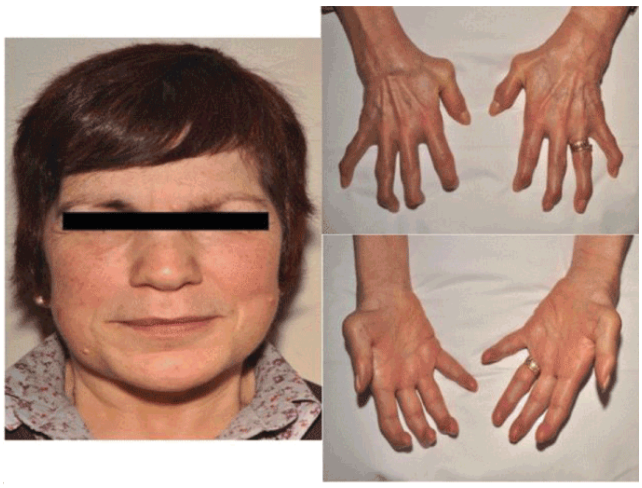

**Figure 4:** Case 2: (Left) – Coarse facies; (Top and Bottom Right)- hand abnormalities.

The biomechanical profiles (Tables 1 and 2) clearly show the reduction of the corneal hysteresis, and corneal resistance factors post DALK. The IOP measurements using various tonometry devices also showed false high readings prior to having undergone lamellar surgeries (Tables 1 and 2).

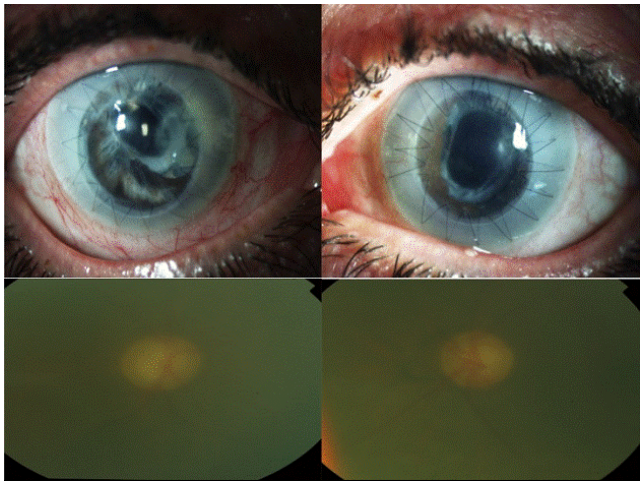

**Figure 5:** (Top left and right): Post DALK images and Disc appearance for Sibling 2. There was excessive PAS in the right eye (top left) with corectopia and inflammation post op. (bottom left and right): fundus images of optic discs showing advanced glaucomatous changes in the right eye (bottom left) due to secondary uncontrolled glaucoma.

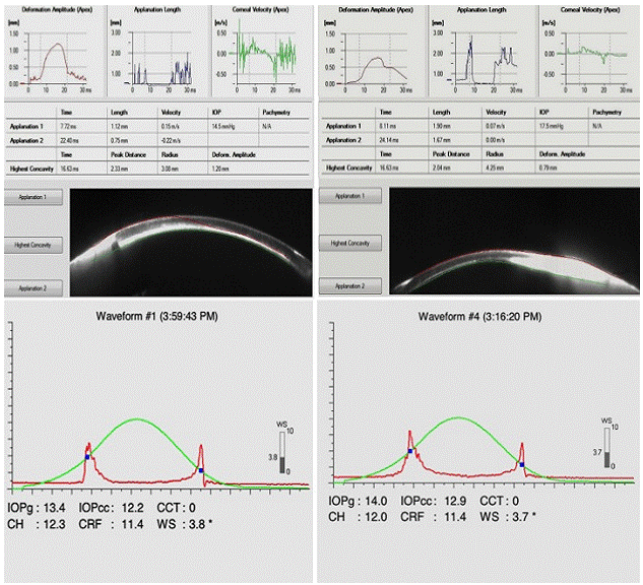


**Figure 6:** Images showing the corneal biomechanical profiles using the Corvisc ST (upper left (for left eye) and upper right (for right eye) respectively) and the waveforms picked up using the ORA (bottom left (for left eye) and bottom right (for right eye) respectively) for sibling 2.

As the measured post DALK readings taken from sibling 1 were similar to those of sibling 2, it was reasonable to assume that the hysteresis of the cornea had reduced and this reflected in the reduction of their IOPs. Unfortunately sibling 2 had worsening of the IOPs as she started showing signs of open angle glaucoma with trabecular meshwork blockage by the excessive deposition of GAGs [8,9]. Her IOPs started to increase and her optic discs started to show signs of optic disc neuropathy. She underwent electrodiagnostic investigations (EDTs), which showed severely reduced responses to flash- visual evoked response (flash-VER) and pattern-visual evoked responses (pattern-VER). This was consistent with optic disc atrophy, which is well known to occur in this disease [5,7]. On comparison with EDTs done 3 years ago the amplitude and latency values of pattern-VER were noted to have reduced and prolonged further respectively, which could point to further reduction in optic nerve fibres secondary to progressive glaucoma. Retinal nerve fiber layer scan (Spectralis Spectral Domain-Optical Coherence Tomography, Heidelberg Engineering, Heidelberg, Germany) of the optic discs were carried out which also showed gross reduction of neuronal fibers (Figure 7). She is therefore now under care of glaucoma team for further management options.

| Devices | Right Eye | Left Eye |
|---|---|---|
| Tonopen | 06 | 10 |
| GAT | 07 | 11 |
| **ORA** | | |
| IOPcc | 10.1 | 10.6 |
| IOPg | 7.5 | 9.9 |
| CH | 9.5 | 11 |
| CRF | 7.3 | 9.2 |

**Table 1:** Intraocular pressure measurements using different tonometry devices and ORA after bilateral DALK procedures for sibling 1 (pre-DALK measurements not available as ORA was not introduced in 2003).

| Devices | Right eye | | | Left eye | | |
|---|---|---|---|---|---|---|
| | Pre DALK | Post DALK | 12M Visit | Pre DALK | Post DALK | 12M Visit |
| **TONOPEN** | 21 | 14 | 32 | 23 | 12 | 18 |
| **GAT** | 26 | 15 | 36 | 27 | 14 | 19 |
| **ORA** | | | | | | |
| **IOPcc** | 16.3 | 09 | 28.4 | 19.3 | 10.7 | 15.8 |
| **IOPg** | 18.3 | 14.4 | 27.6 | 21.7 | 15.6 | 17.7 |
| **CH** | 19.2 | 10.9 | 8.5 | 16.8 | 10.8 | 12.3 |
| **CRF** | 19.2 | 8.8 | 14.5 | 18.5 | 10.5 | 12.7 |

**Table 2:** IOP measurements (in mm Hg) using various tonometry devices in case 2. Readings were taken both pre-DALK and immediate post DALK (within 1 month) and at the visit after 12 months post DALK.

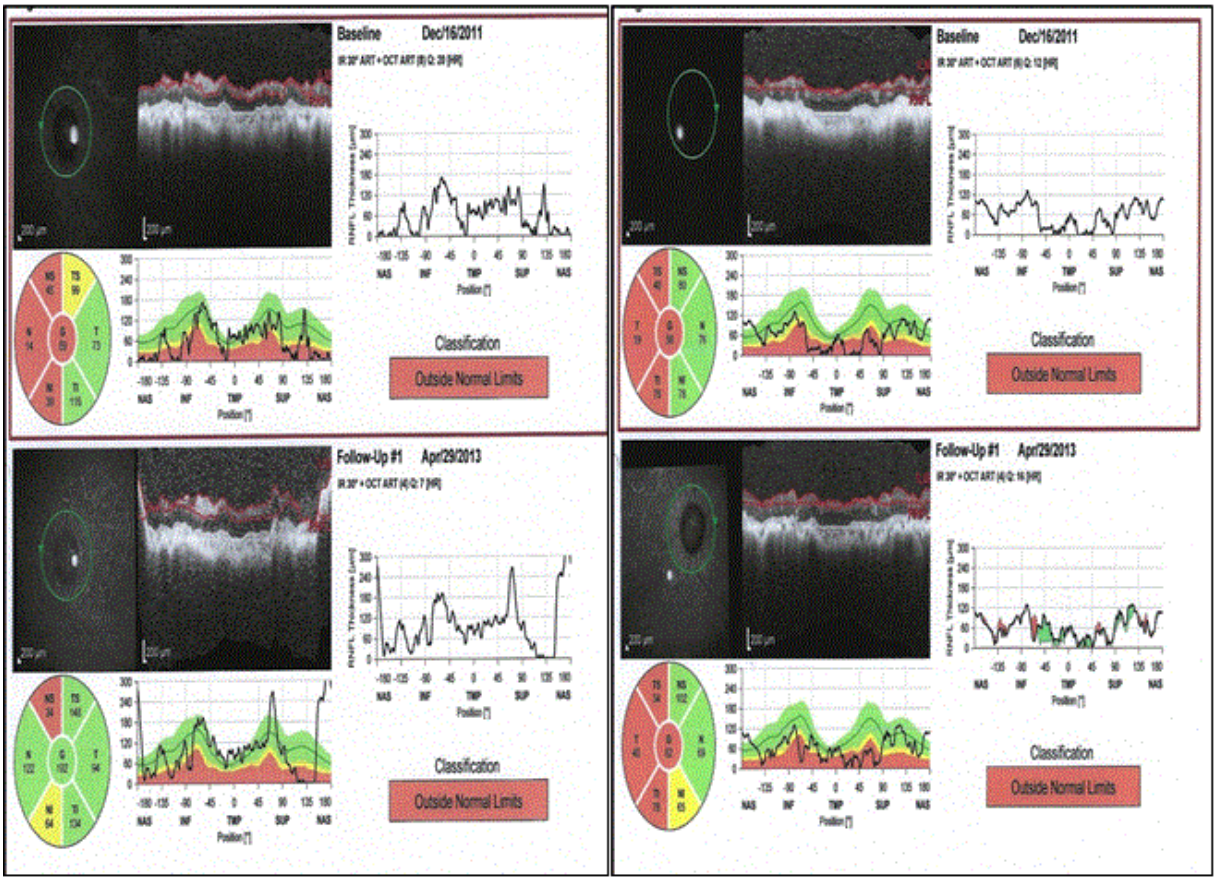


**Figure 7:** Retinal nerve fibre layer (RNFL) scans (left – left eye and right –right eye) done for sibling 2 using the spectral domain- optical coherence tomography. It shows thinning of RNFL secondary to glaucomatous optic neuropathy and optic atrophy.

## Discussion

The Scheie syndrome is a less aggressive form of the MPS Type I. The patients have less physical symptoms and survive well into the adulthood [5] as we see with our two siblings, who are now in their mid-fifties. The ocular features include cornea clouding, retinal pigmentary degeneration, glaucoma and optic nerve abnormalities [7]. Rummelt et al. [11] described the light and electron microscopy features of cornea in their patient with Scheie syndrome with deposition of glycosaminoglycans (GAGs) in the basal corneal epithelial cells and within the stroma leading to corneal clouding, stromal oedema and increased corneal rigidity. The ocular features were more focused on the cornea with variable affect to trabecular meshwork drainage and posterior segment involvement. The main reason of trabecular drainage block leading to rise in intraocular pressures was implied on accumulation of incompletely degraded GAGs in the trabecular meshwork leading to open angle glaucoma with progressive and permanent loss of vision and light hypersensitivity. There have been some reports of shallowing of anterior chamber and angle closure glaucoma in the intermediate spectrum disorder [9] but this was not the case for sibling 2 who had open angles highlighted on gonioscopy.

The physiological biomechanical properties of corneal tissue respond to stress as a viscoelastic material and for a given level of stress, the resultant corneal strain is time dependent. This viscoelastic response is seen as an immediate deformation followed by a rather slow deformation [12]. The immediate elastic response of the ocular tunics comes from the collagen fibres, and the steady state response reflects the properties of the corneal matrix [13]. This viscoelastic property can be measured as corneal hysteresis (CH), which is reflected as damping of the cornea. Various parameters, which affect the hysteresis, include corneal thickness and ocular rigidity [12]. According to Glass et al. [14] the main force that balances the pressure or the IOP is the resistance to stretching (Elasticity). This force takes the form of tension in the corneal collagen lamellar fibres. In their in-vitro model they described effect on hysteresis by varying the viscosity and elasticity separately. A further link between hysteresis and central corneal thickness was picked up by Shah et al. [15] and found a moderately positive correlation in normal eyes. There was also a comparison of the central corneal thickness and the corneal resistance factor (which reflects more of the elastic nature of cornea) and also found a positive correlation between the two variables. This was clearly noted in the difference in the hysteresis values of both the patients due to the variation in their corneal thickness [15,16].

Sun et al. [17] in their paper highlighted a very interesting finding that the increasing IOP beyond the normal range had an inverse effect on hysteresis (Figures 8 and 9). As the intraocular pressure increased the corneal hysteresis values showed negative trend and started to

decrease, which was further clarified upon by Shimmyo [18] in reply to Sun et al. [17], as the stretching or corneal fibres at higher pressures caused a shallow concavity beyond applanation giving a reduced difference in the two amplitudes, that made the hysteresis. This was also noted in sibling 2 who had lower values of hysteresis in range of 4-5 when IOP was measuring more than 40 mmHg.

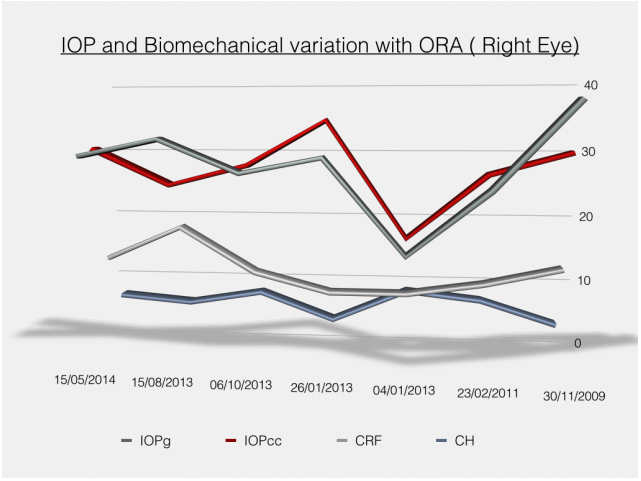


**Figure 8:** Scatter plot of IOP fluctuation in right eye of sibling 2 over a 5-year period causing fluctuation in the corneal biomechanics, which shows a strong correlation and supports viscoelastic nature of the cornea.

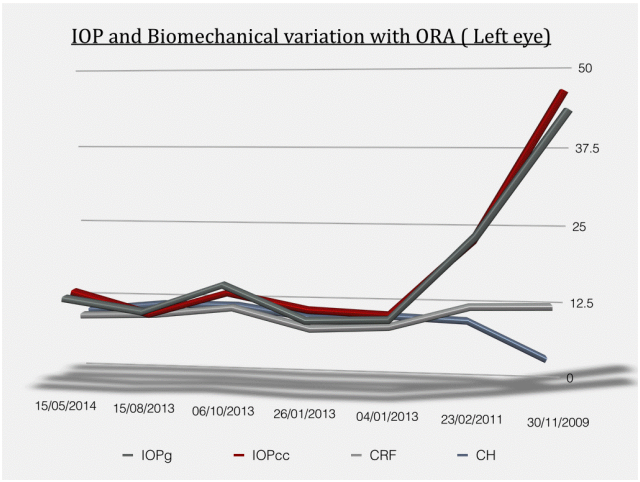


**Figure 9:** Scatter plot of IOP fluctuation in left eye of sibling 2 over a 5-year period causing fluctuation in the corneal biomechanics, which shows a strong correlation and supports viscoelastic nature of the cornea.

Another breakthrough in the measurement of corneal biomechanics and deformation happened by use of ultra-high speed Scheimpflug imaging technique to capture the corneal profile using the non-contact tonometer Corvisc ST (Oculus, Wetzlar, Germany) [19]. Hon et al. [20] in their recent paper presented the raw biomechanical data in their paper comparing the intra-examiner repeatability and the intersession reproducibility of the corneal deformation profile in healthy subjects. Although these values did not yet quantify corneal elastic modulus, their direct comparison to some readings taken in our 2 patients did show a slight decrease in the deformation amplitude. This may be due to presence of GAGs in the residual corneal layers adding to the rigidity of the cornea but needs further research to form a conclusion.

Thus in summary, the new Ocular response analyzer has helped us measure the biomechanical property of the cornea and highlighted that true IOP measurement which would be reflected wrongly if measured using the indentation and applanation tonometry devices like Goldmann applanation tonometry. Also with the new Corvisc ST we noted a reduction in the deformation amplitude in the eyes with increased central corneal thickness and also residual stromal disease concluding a reduced elastic modulus still present in the corneas. This may also highlight that the new Corvisc ST appears to have a good correlation with the ORA, which has been the only tool we have had till now to look at the biomechanical profile of the cornea. The changes in corneal hysteresis should be kept in mind by all ophthalmic professionals who either work at primary care level or in hospital-based care, when dealing with such individuals with metabolic storage diseases. As science and technology is advancing at phenomenal pace, this raises a question, whether such tonometry tools should be available at primary care level to give better information to patients and providing more accurate referral information.

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