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Corneal Biomechanical Response Alteration After Scleral Buckling Surgery for Rhegmatogenous Retinal Detachment

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Credit author statement

Leonardo Taroni: Conceptualization, Methodology, Writing - Original Draft, Validation. **Federico Bernabei**: Data curation, Methodology, Investigation, Writing - Original Draft. **Marco Pellegrini**: Data curation, Formal analysis. **Matilde Roda**: Data curation, Investigation. **Pier Giorgio Toschi**: Investigation. **Ashraf M Mahmoud**: Software. **Costantino Schiavi**: Supervision, Project administration. **Giuseppe Giannaccare**: Writing - Review & Editing, Supervision. **Cynthia J Roberts**: Writing - Review & Editing, Validation, Supervision.

ABSTRACT
Purpose: To compare corneal biomechanics of eyes that underwent scleral buckle (SB) for rhegmatogenous retinal detachment (RRD) with fellow eyes (FEs) and to further investigate its effect on intraocular pressure (IOP) values.
Design: Retrospective, fellow-eye matched cohort study.
Methods: Eighteen (11 males and 7 females) consecutive patients treated with SB for RRD in one eye were enrolled. Goldmann applanation tonometry (GAT) was used to measure IOP. Biomechanical properties of the cornea were investigated by means of Ocular Response Analyzer (ORA, Reichert Instruments, Depew, New York, USA) for the calculation of the following values: corneal resistant factor (CRF), corneal hysteresis (CH), Goldmann-correlated IOP (IOPg) and corneal-compensated IOP (IOPcc). Custom software was used for analysis of the ORA infrared and pressure signals, and significance threshold was set to p=0.05.
Results: Operated eyes (OEs) showed significantly lower values of CH and CRF compared to FEs (respectively 9.0±1.8 vs 10.1±1.8 mmHg, $P<0.001$; 10.0±2.2 vs 10.9±2.2 mmHg, $P<0.001$). GAT was significantly lower compared to IOPcc in OEs (18.1±4.9 vs 19.8±4.8 mmHg, $P=0.022$) but not in FEs. The second applanation event (A2) was earlier in time, and the cornea was moving faster during A2 in the OEs than in the FEs.
Conclusions: SB for the treatment of RRD affects corneal biomechanical response, likely due to a less compliant sclera that limits corneal motion and reduces energy dissipation, reflected in a lower CH. This has potentially meaningful clinical implications as the accuracy of the measurement of IOP values may be affected in these eyes.

Corneal Biomechanical Response Alteration After Scleral Buckling Surgery for Rhegmatogenous Retinal Detachment

Full-Length Article

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Short title: Corneal Biomechanics After Scleral Buckling Surgery

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INTRODUCTION

Rhegmatogenous retinal detachment (RRD) is a sight threatening disease characterized by the separation of the inner neurosensory retina from the outer retinal pigment epithelium, secondary to one or more retinal breaks.[1] Although there is an increasingly widespread use of pars plana vitrectomy, scleral buckling (SB) still represents an effective procedure for the treatment of RRD, particularly in young phakic patients.[2] SB is an episcleral procedure that consists of the placement of an encircling element around the circumference of the eye, in order to cause the reduction of transvitreal traction and the closure of the retinal break(s), thus allowing retinal re-attachment.[3] The mechanical force exerted by the scleral buckle causes well know alterations of several ocular parameters such as an increased axial length (AL), a decreased anterior chamber depth (ACD) and induced corneal astigmatism. All these changes typically result in post-operative refractive shift.[4–11] It is reasonable to hypothesize that SB could impact not only geometric adaptation but also biomechanical response of the cornea and globe. Currently, corneal biomechanics can be assessed using either Ocular Response Analyzer (ORA) or CorVis ST. The former is a non-contact tonometer that provides the measure of two parameters of corneal biomechanics: corneal resistant factor (CRF) that reflects the maximum correlation with central corneal thickness, and corneal hysteresis (CH) that measures the viscoelastic response of the cornea.[12] CorVis ST is a device that employs an ultrahigh speed Scheimpflug camera to record dynamic deformation of the cornea providing response indices.

In clinical practice, corneal biomechanical modifications could alter routine intraocular pressure (IOP) measurements, affecting glaucoma and ocular hypertension (OHT) diagnosis and management.[13] The purpose of the present study was to compare corneal biomechanical response of eyes which had undergone SB for RRD with fellow eyes (FEs) and to further investigate its effect on the accuracy of IOP measurements.

METHODS

Study Design and Patients

This study included patients treated for RRD at a single tertiary-referral center (S.Orsola-Malpighi University Hospital, Bologna, Italy) between January 2016 and May 2019. The study was performed in accordance with the principles of the Declaration of Helsinki and was approved by the local Institutional Review Board. Written informed consent was obtained from all subjects included in the study. Consecutive patients older than 50 years treated with SB for RRD in one eye were screened for enrollment. SB was performed by the same surgeon (P.G.T.) in phakic patients with RRD due to single retinal break or small confluent multiple breaks without significant lens opacification. Eyes with SB were included as the study eye and the FEs served as control. Exclusion criteria were: any previous ocular surgery in both eyes, keratoconus, corneal dystrophy, diabetes, contact lens wearing, tear film instability, use of glaucoma medications, keratometry < 40 diopters (D) and > 46 D, spherical equivalent ≥ 7 D, anisometropia ≥ 1.5 D and any ocular infection within 3 months prior to enrollment.

Biometric and keratometric data were measured using Lenstar (Lenstar, Haag-Streit, Köniz, Switzerland) that is an OLCR (optical low-coherence reflectometry) biometer that employs dual zone keratometry with 32 marker points to provide measurement of the astigmatism and axis, equivalent to the "Gold Standard" manual keratometry. White-to-white (WTW), lens thickness (LT), AL and ACD were analyzed in all eyes. Goldmann applanation tonometry (GAT) was used to measure IOP.

Episcleral Surgery Technique

A 360-degree limbal conjunctival peritomy incision was made and traction sutures were placed beneath the insertions of the exposed rectus muscles to facilitate positioning the globe. A 2.5 mm wide silicone band was passed around the circumference of the globe and beneath the rectus muscles at a distance of 14 mm from the limbus. The band was anchored with single interrupted suture with bites parallel to the limbus placed in the center of each quadrant, the ends of the band were then joined in the opposite quadrant of the retinal break(s) with a silicone sleeve. In all cases, drainage procedure was performed by a sclerotomy just below the retinal break(s) then sutured by a single scleral stitch. Ab externo cryotherapy was done in the retinal break(s) location. In order to increase the buckling effect an adjunctive biconvex silicone 9 mm wide element was placed beneath the band above the retinal break(s). The ends of the encircling silicone band were then pulled until the desired buckle effect was reached. A paracentesis was done and SF6 injection was performed 4 mm posterior to the limbus.

Ocular Response Analyzer Measurements

The Ocular Response Analyzer (ORA, Reichert Instruments, Depew, New York, USA) measures two applanation pressure points during a dynamic bi-directional applanation process generated by a precisely metered air pulse. The first applanation pressure event (A1) occurs as the air puff pushes the cornea inward, through applanation, to a concave shape during the loading phase. The second applanation pressure event (A2) occurs as the cornea returns from the concave state during the unloading or recovery phase, through outward applanation, to its baseline convex state. The difference between these two applanation pressures (P1 and P2, respectively) is defined as the CH, while CRF is calculated as a linear function of the two values. The average of both pressures provides Goldmann-correlated IOP (IOPg), while the corneal-compensated IOP (IOPcc) is the empirically determined IOP value that compensates for corneal biomechanical effects.[12,14]
All the ORA examinations were performed at least 4 months after the surgery by two operators (M.R. & F.B.), both masked to the subject's characteristics. Before each examination, central corneal thickness (CCT) values obtained with an ultrasonic pachymeter (Dicon P55, Paradigm Medical Industries Inc., Salt Lake City, UT, USA) were inserted in the software. Because of the potential confounding effect of diurnal IOP variation, all measurements were obtained between 10 am and 12 pm. All included ORA measurements had a waveform score > 7.0.[15] The average values of 4 measurements with desirable curves were recorded for statistical analysis.
Custom software was used to extract parameters from both the infrared and air pressure signals exported by the ORA. P1 and P2 represent the first and second applanation pressures, respectively. Full-width-half max (fwhm1 and fwhm2, respectively) represents how long it takes the cornea to move through applanation in seconds. A smaller value means the cornea has a greater velocity. Time 1 and Time 2 represent the timing of A1 and A2. Pmax is the maximum magnitude of the air pressure pulse, and tPmax is the timing of this value. Note that the ORA produces an air puff magnitude that is a function of the timing of A1, such that an earlier A1 produces a lower Pmax. A subject with a lower IOP will thus receive a lower magnitude air puff. Peak 1 and Peak 2 represent the maximum values of the infrared signal during A1 and A2, and represent the stiffness of the corneal response, such that a high peak represents a stiffer cornea.[12]

Statistical Analysis
The SPSS statistical software (SPSS Inc., Chicago, Illinois, USA) was used for data analysis, and SAS was used to analyze the parameters produced by the custom software. Values are expressed as mean ± standard deviation. Continuous variables between operated eyes (OEs) and FEs were compared using the Student's t-test. A *P* value < 0.05 was considered statistically significant.

RESULTS

Thirty patients treated with SB for RRD were initially identified. Of these, 12 patients did not satisfy the inclusion/exclusion criteria and were excluded from the final analysis. In particular, 2 presented high myopia, 8 had previous eye surgery, 1 used topical anti-glaucoma drugs and 1 was lost to follow up. Finally, 18 patients were enrolled in the study. Mean age was 61.6 ± 6.4 years; 11 patients (61.1% of the total) were males and 7 (39.9%) were females.
OEs were significantly longer than fellow eyes (25.79 ± 1.49 mm vs 25.31 ± 1.63; *P* = 0.004), while no significant differences were found for K1 and K2 values between the eyes (respectively, 42.3 ± 1.1 vs 42.5 ± 1.3 D, *P* = 0.072 and 43.2 ± 1.2 vs 43.4 ± 1.2, P = 0.072). In addition, CCT, GAT, ACD, LT and WTW did not significantly differ between eyes (respectively 551.1 ± 24.6 vs 518.3 ± 134.7 µm, *P* = 0.292; 18.1 ± 4.9 vs 17.9 ± 3.9 mmHg, *P* = 0.868; 3.09 ± 0.45 vs 3.15 ± 0.46 mm, *P* = 0.089; 4.23 ± 0.21 vs 4.19 ± 0.26 mm, *P* = 0.257; 12.38 ± 0.54 vs 12.44 ± 0.54 mm, *P* = 0.144).
Corneal biomechanics and signal analysis parameters in OEs and FEs are reported in Table 1. In all patients, the waveform score was ≥ 7, with a mean value of 8.3 ± 0.9 in OEs and 8.1 ± 0.8 in FEs (*P* = 0.461). OEs showed significantly lower values of CH (all *P* < 0.001), while IOPcc was significantly higher in OEs compared to FEs (Figure 1). In OEs, GAT was significantly lower than IOPcc (18.1 ± 4.9 vs 19.8 ± 4.8 mmHg, *P* = 0.022) (Figure 2). Conversely, in FEs no significant difference between GAT and IOPcc was found (17.9 ± 3.9 vs 18.4 ± 3.4 mmHg, *P* = 0.389).
Signal analysis showed significantly lower Time 2 (p=0.005) and fwhm 2 (p=0.021) in OE's compared to FE's. No other parameter was different between eyes.

DISCUSSION

It's well known that SB for RRD could modify different anatomical structures of the eye globe, thus affecting refractive status.[3] Consistent with a previous study, our results showed that encircling scleral buckle lead to an increased AL in the absence of significant induced astigmatism.[2] Moreover, ACD reduction and LT modifications could also occur after SB, contributing to the postoperative refractive change.[9,16–18] The presence of the encircling scleral buckle generates an annular tangential pressure that serves to stiffen the scleral response, thus limiting corneal deformation. The theory of a stiffened sclera limiting corneal deformation under an air puff has been demonstrated both theoretically and in human donor eyes.[19–21] Indeed, the ORA signal parameter analysis in the current study demonstrated that A2 is shifted to an earlier time point and the corneal is moving faster at A2 in the OEs, with smaller Time2 and fwhm2, respectively. Both these parameters occur in the unloading or recovery phase, likely the result of a less compliant sclera in the OEs. The lower CH means the eye is less able to dissipate energy with a less compliant sclera in the OEs. The lower CH means the eye is less able to dissipate energy with a less compliant sclera in the OEs. The type of scleral buckle (e.g. materials and shape) and the surgical technique are surgeon-related factors that may influence the whole biomechanical modification.[22]

The anatomical composition of the cornea is responsible for its viscoelastic nature and thus for its biomechanical deformation response. Elastic materials deform instantly and reversibly under external stress and do not dissipate energy under mechanical stress; the deformation is proportional to the force applied and it is fully recovered upon unloading, following the same path as during the loading phase. On the other hand, losing energy through a loading cycle, viscous materials do not necessarily regain their original shape when the force is removed, and in viscoelastic materials, the unloading pathway is different than the loading pathway, demonstrating a lag in response. The difference in pathways is characterized by the corneal hysteresis, with P2 less than P1. However, biomechanical response of the cornea under an air puff load could be influenced from both alteration of its biological constituent elements (ectasia, dry eye), structural modification (refractive surgery, stiffness of the tissue),[23–25] or by a change in the compliance of the sclera, either stiffer or softer.[19–21]

Previous studies have identified CCT as being an independent risk factor for development and progression of glaucoma, underlining the existing relationship between IOP measurements and cornea.[26–29] It has also been suggested that corneal biomechanics has a greater impact on IOP estimation than CCT.[13,24] Moreover, IOP and corneal biomechanics have mutual influence as both the cornea and the sclera exhibit stiffer behavior as IOP increases.[23] In clinical practice, routine IOP measurement is still performed by mechanical methods, but most nomograms do not take into account corneal biomechanical modification.[13,30,31] In our study, GAT values were significantly lower compared to IOPcc values in OEs. It is known that IOPcc was empirically developed and has been shown to provide a more accurate estimation of IOP under conditions of a more compliant cornea, such as after refractive surgery.[32] However, it has not been evaluated under conditions of a less compliant cornea or sclera. The current study indicates that is likely that IOPcc is overestimating IOP under the condition of a less compliant sclera in OE's, which may limit corneal deformation. GAT has minimal corneal displacement, only to applanation. However, an air puff induces a concave state of the cornea, which would be more influenced by a less compliant sclera. Hence, IOP values measured with conventional tools may affect the proper diagnosis and follow-up of glaucoma/ocular hypertension in these eyes. Furthermore, on one hand it has been demonstrated that eyes affected by primary open angle glaucoma (POAG) are at higher risk to develop RRD. On the other hand, the incidence of POAG in eyes treated for a previous RRD is 4 to 12 times higher as compared with healthy eyes.[33,34] Therefore, given these epidemiological data, our results suggest that IOP must be carefully evaluated in this kind of patients, taking into account the iatrogenic changes affecting not only the cornea but also the sclera in its influence on the deformation response.

A recent study validated a new algorithm to overcome IOP measurement systematic error in patients with altered corneal biomechanics related to soft cornea with the Corvis ST.[35] However, it is not known how this algorithm will perform with an altered sclera. Therefore, it would be desirable to develop new tools able to adjust the IOP measurements in patients who also present a modified scleral response, including those who have undergone SB.

To the best of our knowledge, this is the first clinical study that showed the potential influence of scleral properties on IOP measurements. The retrospective nature represents the main limitation of this study because it hampered the evaluation of IOPcc and GAT before and after SB in order to detect their postoperative changes and their association with corneal biomechanics. Another limitation is the small sample size that didn't allow a stratification of patients according to anatomical and clinical characteristics (e.g. IOP and AL). However, since several factors could influence corneal biomechanical assessment, a

significant number of SB patients did not satisfy the study criteria and were excluded from the final analysis.[36,37]
Future prospective clinical studies are mandatory to elucidate corneal and scleral biomechanical modification and the clinical implications in RRD patients treated with SB.
In conclusion, based on our findings, SB for the treatment of RRD affects corneal biomechanical deformation response by limiting corneal motion and reducing dissipation of energy via a stiffer sclera. In these patients, conventional algorithm for glaucoma diagnosis and follow-up may not be appropriate. Future prospective clinical studies are mandatory to elucidate corneal and scleral biomechanical modification and the clinical implications in RRD patients treated with SB.

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CAPTIONS

FIGURE 1. Ocular Response Analyzer signals in a patient underwent scleral buckling surgery.

The operated eye (Part A) showed lower values of Corneal Hysteresis and Corneal Resistant Factor and higher value of Corneal-Compensated IOP, compared to the contralateral healthy eye (Part B).

FIGURE 2. Operated eyes IOP Measurements: Box-plot analysis.

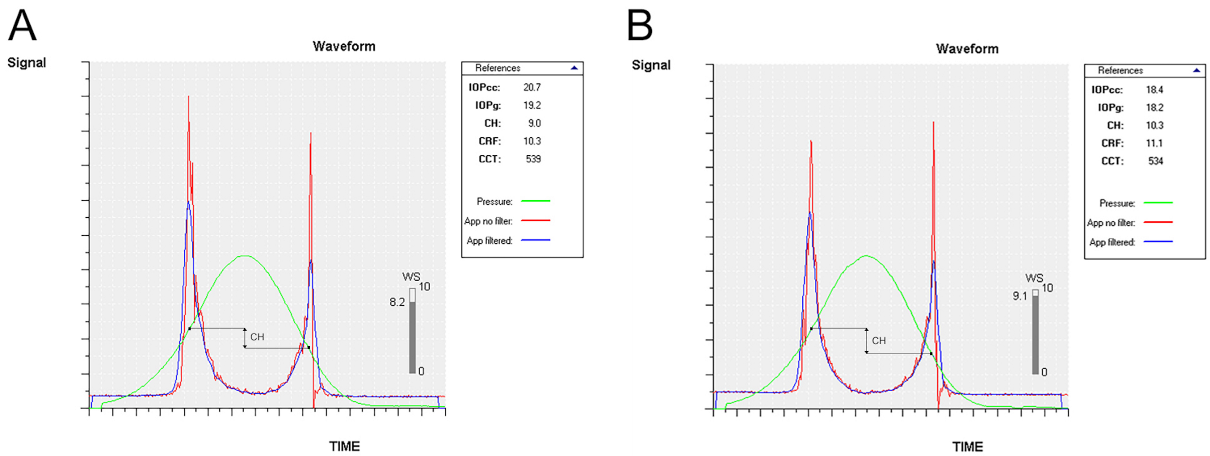
Box-plot analysis of Goldmann applanation tonometry (GAT) and corneal-compensated IOP (IOPcc) in eyes treated with scleral buckling for rhegmatogenous retinal detachment. Operated eyes showed significantly lower GAT values compared with IOPcc.

Table 1: Biomechanical and signal analysis parameters in eyes treated with SB for rhegmatogenous retinal detachment and fellow eyes.

Parameter	Operated eyes	Fellow eyes	*P* *
CH (mmHg)	9.0 ± 1.8	10.1 ± 1.8	**< 0.001**
CRF (mmHg)	10.0 ± 2.2	10.9 ± 2.2	**< 0.001**
IOPcc (mmHg)	19.8 ± 4.8	18.4 ± 3.4	**0.021**
P1 (mmHg)	242.9 ± 39.2	242.4 ± 30.8	0.910
P2 (mmHg)	171.8 ± 36.30	166.3 ± 26.4	0.185
fwhm1 (s)	12.8 ± 2.8	12.5 ± 3.7	0.815
fwhm2 (s)	7.7 ± 3.0	9.9 ± 3.2	**0.021**
Time 1 (s)	8.2 ± 0.6	8.2 ± 0.5	0.773
Time 2 (s)	18.7 ± 0.2	18.8 ± 0.2	**0.005**
Peak 1 (mmHg)	785.2 ± 151.1	823.0 ± 89.2	0.3
Peak 2 (mmHg)	655.6 ± 160.6	667.1 ± 146.8	0.795
Pmax (mmHg)	453.6 ± 50.6	457.3 ± 42.6	0.490
tPmax (s)	12.8 ± 0.5	12.8 ± 0.4	0.637

SB, scleral buckling; CH, corneal hysteresis; CRF, corneal resistance factor; IOPcc, corneal-compensated intraocular pressure; P, applanation pressures; fwhm, full-width-half max. Significant *P* values (< 0.05) are in bold.

* Student's t-test


A
Waveform
Signal
References
IOPcc: 20.7
IOPg: 19.2
CH: 9.0
CRF: 10.3
CCT: 539
Pressure:
App no filter:
App filtered:
WS
10
8.2
0
CH
TIME
B
Waveform
Signal
References
IOPcc: 18.4
IOPg: 18.2
CH: 10.3
CRF: 11.1
CCT: 534
Pressure:
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App filtered:
WS
10
9.1
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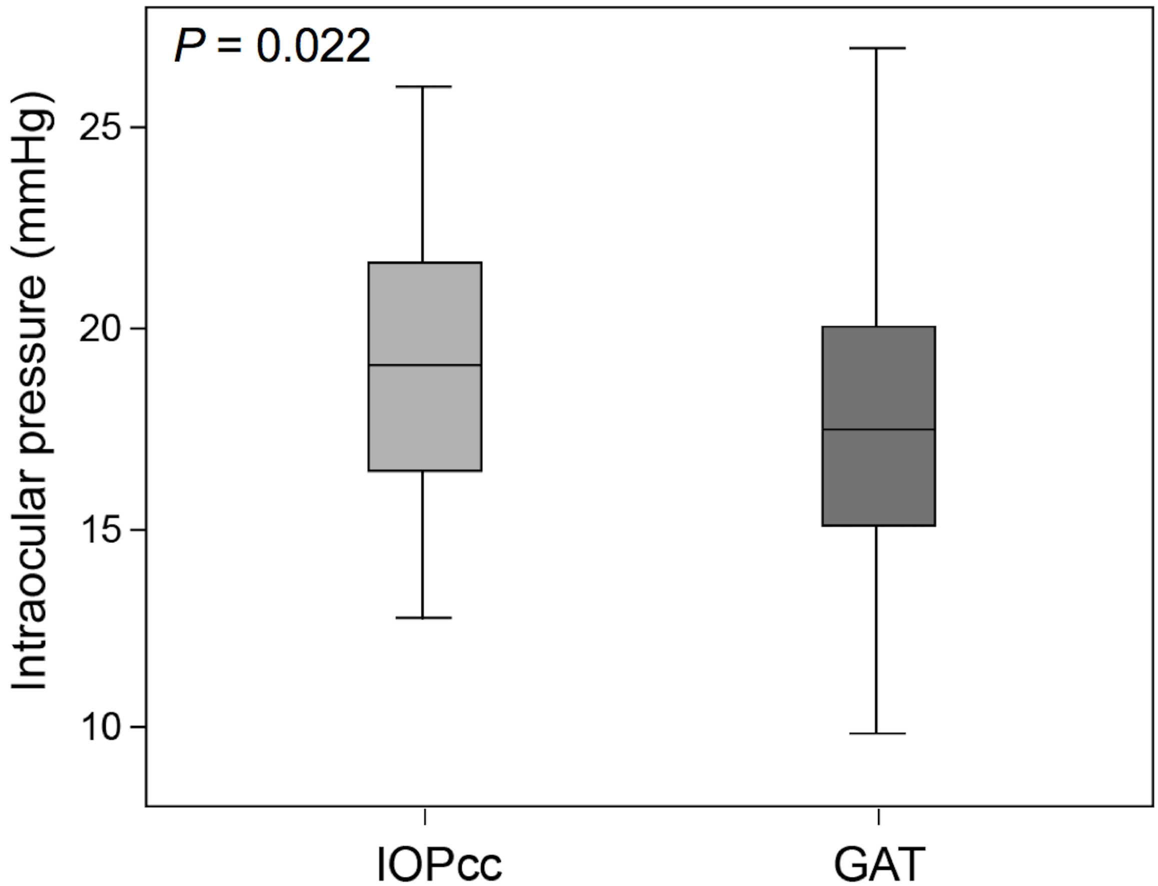
CH
TIME


P = 0.022
Intraocular pressure (mmHg)
25
20
15
10
IOPcc
GAT

Highlights

- Encircling scleral buckle induces scleral stiffness, limiting corneal deformation.
- Scleral buckling surgery affects corneal biomechanical response.
- A concave state of the cornea is more influenced by a less compliant sclera.
- Routine IOP measurement accuracy may be affected in operated eyes.