This item is the archived peer-reviewed author-version of:

In vivo anterior scleral morphometry, axial length and myopia

Reference:

Consejo Alejandra, Rozema Jos.- In vivo anterior scleral morphometry, axial length and myopia
Contact lens & anterior eye / British Contact Lens Association [London] - ISSN 1367-0484 - (2018), p. 1-5
Full text (Publisher's DOI): <https://doi.org/10.1016/J.CLAE.2018.10.021>
To cite this reference: <https://hdl.handle.net/10067/1564640151162165141>

In vivo anterior scleral morphometry, axial length and myopia

Alejandra Consejo, MSc PhD,^{1,2} and Jos J. Rozema, MSc PhD^{1,2}

¹ Department of Ophthalmology, Antwerp University Hospital, Edegem, Belgium

² Department of Medicine and Health Sciences, University of Antwerp, Antwerp, Belgium

ABSTRACT

Purpose: To in-vivo quantify differences in anterior scleral shape between myopes and emmetropes and relate them with axial length and refractive power.

Methods: Forty-two participants (84 eyes) were included in this study. Twenty-five participants were categorised as emmetropes and seventeen participants were categorised as myopes. The refractive state was measured monocularly using a closed window autorefractometer. Axial length was acquired using an optical biometer and topographical data was obtained using a non-contact corneo-scleral topographer. Anterior scleral asymmetry was calculated from 3-dimensional data using a custom-made algorithm and further correlated to axial length and refractive power. Right and left eyes were analysed independently.

Results: The anterior scleral shape was highly correlated with axial length (OS and OD: $R = 0.76$, $p < 0.001$) and moderately correlated with refractive power (OS: $R = 0.48$, OD: $R = 0.53$, both $p < 0.01$). The more myopic the eye, the less asymmetric the anterior sclera.

Conclusions: Both axial length and refractive power are highly correlated with the anterior scleral shape. The refractive state of each patient should therefore be taken into consideration when analysing scleral shape when planning certain treatments or surgeries and when fitting scleral contact lenses.

KEYWORDS

Sclera; Anterior scleral shape; Axial length; Myopia; Myopia progression; Scleral lenses

INTRODUCTION

Myopia is an ocular condition that leads to blurry vision of distant objects. The disease affects almost two billion people worldwide, and this number is expected to increase to around 50% of worldwide population by 2050.^{1,2} Several approaches to myopia control offer hope to significantly reduce the number of people progressing to high myopia to slow down this trend. Some of these methods focus on the sclera, a tissue that expands excessively during myopia progression.^{3,4}

The sclera is a tough, fibrous, viscoelastic tissue whose biomechanical characteristics help determine the ocular size and the shape. Consequently, it plays a major role in determining the refractive state of the eye.⁵ Its anterior surface is rotationally asymmetric,⁶⁻⁸ helps protect the inner structures and provides an attachment for the extraocular muscle insertions. The sclera is a dynamic tissue that undergoes constant remodelling throughout life^{5,9} and its biomechanical properties alter

in response to the visual environment, resulting in ocular size and refractive state changes.⁵ Moreover, it is known that the visco-elastic properties of the sclera are noticeably less rigid in myopic eyes compared to healthy eyes.¹⁰⁻¹² Recently, differences between the scleral responses of myopes and emmetropes during accommodation were found.¹³ This agrees with previous animal-based research that suggested that myopic scleras are more malleable than emmetropic scleras.^{5,14}

This work hypothesizes that the anterior scleral morphometry might be related to the axial length, and consequently to the refractive state of the eye. Furthermore, this research aims to non-invasively quantify the in-vivo differences in anterior scleral shape between myopes and emmetropes.

METHODS

Participants

Forty-two participants (84 eyes) were included in this study. They were adult participants (30 females, 12 males) aged between 19 and 45 years (mean $\pm$ SD age: 26.7 ± 6.3 years). Twenty-five participants were categorised as emmetropes (refractive error between -0.50 D and $+0.75$ D) and seventeen participants were categorised as myopes (refractive error < -0.75 D). The study was approved by the Antwerp University Hospital Research Ethics Committee and adhered to the tenets of the Declaration of Helsinki. All participants gave written informed consent to participate after the nature and possible consequences of the study were explained. All participants were free of ocular disease, had less than 1.00 D of astigmatism in both eyes and current use of topical ocular medications was specified by the participants as part of a background questionnaire. Exclusion criteria included the presence of any corneal, conjunctival or scleral pathology, any history of ocular surgery, as well as contact lens wear.

Data collection

The measurements were performed in a single visit. The refractive state was measured monocularly using a closed window autorefractometer. Axial length was acquired using an optical biometer (Lenstar 900, Haag-Streit, USA), which acquires and averages several measurements during each acquisition. Topographical data was obtained using a non-contact corneo-scleral topographer (Eye Surface Profiler (ESP), Eaglet Eye BV, Netherlands), a height profilometer that measures the corneo-scleral topography several millimetres beyond the limbus. The algorithms used in the ESP achieves similar levels of accuracy for corneal surface heights as Placido disk based videokeratoscopes.¹⁵ ESP measurements require the instillation of a fluorescein solution that is more viscous than saline. For this purpose BioGlo (HUB Pharmaceuticals) ophthalmic strips were impregnated with 1 mg of fluorescein sodium ophthalmic moistened with one drop of an eye lubricant (HYLO-Parin, 1mg/ml of sodium hyaluronate), and gently brought into contact with the upper temporal ocular surface. Four measurements were collected from each eye of each subject. Participants were instructed to open their eyes wide without using force during the ESP measurements to ensure maximal coverage of the corneo-scleral area. Measurements in which the corneo-scleral area was covered by eyelids were excluded. From the four measurements acquired per eye the one with the largest scleral area coverage was included for data analysis.

Analysis

After data acquisition the raw three-dimensional (3D) anterior eye height data (X , Y , and Z coordinates) were exported from the ESP for further analysis. The software incorporates an internal procedure to estimate the position of the corneal apex, as well as to ensure that the corneal data are not tilted or rotated (for details on the alignment procedure see¹³). This internal procedure also assures that all 3D maps are centred according to the same standard. Next, the sagittal height was calculated using custom-made software in all directions for the central cornea (0 – 4 mm), peripheral cornea (4 – 6 mm) and sclera (6 – 8 mm). Each of these annuli was divided in 10° sectors and the mean sagittal height in each sector was calculated.

In order to estimate the magnitude of anterior scleral asymmetry in each eye the sclera and the cornea were automatically separated at the level of the limbus, assuming a mean limbal diameter of 12 mm.¹⁶ The difference between 3D scleral topographies and a fixed reference surface was calculated and analysed by means of root mean squared error (RMSE).¹⁷ This low-variance, automatic method based on 3D topography grades scleral asymmetry in μm . A low value indicates a fairly regular anterior sclera, while a high value corresponds with an irregular anterior sclera. The scleral asymmetry calculated using this method correlates with refractive power and axial length in each individual participant.

The statistical analysis was performed using SPSS (v24.0; SPSS Inc., Chicago, Illinois, United States). The Shapiro-Wilk test was used to test the distribution type (Gaussian or non-Gaussian) of all continuous variables. Wilcoxon sign-rank test was performed to assess differences in scleral shape between emmetropes and myopes. To assess whether scleral asymmetry is correlated with axial length, refractive power and age the coefficient of correlation (R) was calculated. Fisher test was applied to determine the best possible fit to the relationship between scleral asymmetry and axial length. Goodness of fit was calculated by the coefficient of determination (R^2). Finally, the correlation between right and left eye was assessed using the Spearman correlation coefficient (ρ). The level of significance was set to 0.05 and a Bonferroni correction was applied to address the problem of multiple comparisons.

RESULTS

Anterior scleral asymmetry was found to be significantly different between myopes and emmetropes (Wilcoxon rank sum test, $p < 0.05/N$ (Bonferroni)). In emmetropes the anterior scleral shape was more irregular than in myopes. The RMSE difference in sagittal height between groups increases with the radial distance from corneal apex (Figure 1, Table 1).

Average and range values of scleral asymmetry, axial length and refractive power for both eyes of the group of myopes and the group of emmetropes are shown in Table 2.

Figure 1. Mean sagittal height 360 degrees around considering a central corneal annulus of 4 mm from the corneal apex, a peripheral corneal annulus of 4-6 mm radius and a scleral annulus of 6-8 mm radius, for the left eye of 17 myopic participants and 25 emmetropic participants. Error bars represent one standard deviation from the mean.

Table 1. Mean sagittal height (SH) in the three annuli under analysis (central cornea, peripheral cornea and sclera) for left (OS) and right (OD) eye of 25 emmetropes and 17 myopes. Root mean squared error (RMSE) calculated as the difference between the average of each group (myopes vs emmetropes) was also considered. Values in bold denote statistical significant difference.

		OS			OD		
		Mean SH $\pm$ SD (μ m)	RMSE (μ m)	p-value*	Mean SH $\pm$ SD (μ m)	RMSE (μ m)	p-value*
Central cornea (0 – 4 mm)	Emmetropes	530 $\pm$ 9	7	p = 0.13	534 $\pm$ 12	7	p = 0.11
	Myopes	528 $\pm$ 8			529 $\pm$ 10		
Peripheral cornea (4 – 6 mm)	Emmetropes	1790 $\pm$ 20	30	p = 0.034	1793 $\pm$ 42	25	p = 0.029
	Myopes	1770 $\pm$ 15			1778 $\pm$ 30		
Sclera (6 – 8 mm)	Emmetropes	3153 $\pm$ 256	140	p = 0.0010	3204 $\pm$ 214	100	p = 0.0011
	Myopes	3102 $\pm$ 145			3164 $\pm$ 188		

*Level of significance set to $p < 0.0014 = 0.05/N$ ($N=36$; Bonferroni correction)

The anterior scleral asymmetry decreases with increasing axial length (Figure 2). Scleral asymmetry and axial length were strongly correlated (OS: $R = 0.76$, $p < 0.001$; OD: $R = 0.76$, $p < 0.001$). However, the goodness of the fit improves when considering a second order rather than a first order polynomial equation (Fisher test, $p = 0.002$; Figure 2), in this case the coefficient of determination amounts to OS: $R^2 = 0.76$, $p < 0.01$; OD: $R^2 = 0.76$, $p < 0.01$ (or equivalently, OS: $R = 0.87$, $p < 0.01$; OD: $R = 0.87$, $p < 0.01$). According to the performed Fisher test, increasing from

second to third order does not lead to statistically significant results in the goodness of the fit. This result suggests that for axial lengths beyond approximately 24.5 mm the anterior sclera is fairly smooth, independently of the axial length itself.

Similarly, the scleral asymmetry decreases with increasing refractive power (OS: $R = 0.48$, $p < 0.01$; OD: $R = 0.53$, $p < 0.01$; Figure 3).

Table 2. Average and range values of scleral asymmetry (μm), axial length (mm) and refractive power (D) for the left (OS) and right (OD) eye of 25 emmetropes and 17 myopes.

	OS					
	Scleral asymmetry (μm)		Axial length (mm)		Refractive error (D)	
	Mean $\pm$ SD	Range	Mean $\pm$ SD	Range	Mean $\pm$ SD	Range
Emmetropes	41.4 $\pm$ 13.4	(21.0, 70.0)	23.5 $\pm$ 0.7	(21.6, 24.9)	0.43 $\pm$ 0.5	(-0.50, 0.75)
Myopes	26.3 $\pm$ 5.7	(17.0, 37.0)	25.1 $\pm$ 0.7	(23.4, 26.5)	-3.6 $\pm$ 2.3	(-8.25, -0.75)
	OD					
	Scleral asymmetry (μm)		Axial length (mm)		Refractive error (D)	
	Mean $\pm$ SD	Range	Mean $\pm$ SD	Range	Mean $\pm$ SD	Range
Emmetropes	42.1 $\pm$ 13.3	(22.4, 70.3)	23.5 $\pm$ 0.6	(21.6, 24.5)	0.40 $\pm$ 0.5	(-0.50, 0.75)
Myopes	28.5 $\pm$ 7.2	(17.6, 43.7)	25.1 $\pm$ 0.8	(23.6, 26.5)	-3.5 $\pm$ 2.1	(-8.25, -0.75)

Figure 2. Relationship between scleral asymmetry and axial length, for left (OS) and right (OD) eye of 42 participants. Data was fit to a second order polynomial equation.

Figure 3. Correlation between scleral asymmetry and refractive power, for left (OS) and right (OD) eye of 42 participants.

In addition, scleral asymmetry was not found to be correlated with age (OS: $R = 0.16$, $p = 0.16$; OD: $R = 0.17$, $p = 0.13$).

The scleral sagittal height was very strongly correlated between right and left eye (Spearman, $\rho = 0.89$; $p < 0.001$), as were the scleral asymmetry (Spearman, $\rho = 0.88$; $p < 0.001$), axial length (Spearman, $\rho = 0.95$; $p < 0.001$) and refractive power (Spearman, $\rho = 0.93$; $p < 0.001$).

DISCUSSION

To the best of the authors' knowledge, this is the first work that investigated in vivo anterior scleral morphometry and axial length. In the 84 ocular topographic maps and biometry of 42 participants the anterior scleral shape was highly correlated with axial length (OS and OD: $R = 0.76$, $p < 0.001$) and moderately correlated with refractive power (OS: $R = 0.48$, OD: $R = 0.53$, both $p < 0.01$). Therefore, the more myopic the eye, the less asymmetric the anterior sclera.

Even though the underlying reasons for myopia development are not yet understood, it is well known that myopia develops primarily due to excessive axial growth. The presented results confirm that the sclera may indeed be of fundamental importance in myopia progression.³⁻⁵ This may be visualized by considering the emmetropic sclera as a half-inflated balloon. When not fully inflated certain shape irregularities may still be seen in the balloon surface. However, when the balloon is completely filled with air its surface will be entirely regular and the surface irregularities will disappear. This illustrates why the anterior sclera was more regular in long-eyed myopes than in shorter-eyed emmetropes (Figure 1). This connects with previous reports that the sclera remodels itself throughout life,^{5,9} the visco-elastic properties of the sclera are markedly different in myopic eyes,¹⁰ and the myopic scleras are more malleable and less rigid.^{12,14} Although these previous works were mostly based on cadaveric or animal eyes, recent work demonstrated that accommodation affects the scleral shape differently in myopes and emmetropes, supporting the higher malleability of the myopic sclera.¹³ The typical axial elongation and scleral thinning at the posterior pole seen in myopia^{18,19} may also be the result of scleral remodelling.²⁰ Similarly, a recent work on school-age children with progressive myopia reported biomechanical abnormalities of the corneo-scleral area.⁴ As the sclera affects the restraint or facilitation of eye growth, different myopia control strategies have been proposed based on strengthening the sclera, such as scleral reinforcement and collagen cross-linking.³ However, most current techniques for myopia control are highly invasive and show a variable outcome between patients.³ Gaining better knowledge on the anterior scleral shape in myopic eyes could therefore assist practitioners with planning the most adequate treatment for a given patient.

Besides its importance in myopia research, the anterior scleral shape is also gaining interest in the field of scleral lenses.^{6-8,22-25} These lenses rest entirely on the sclera, without touching the cornea, and have repeatedly proven to improve vision in case of severe refractive errors or refractive surgery related complications.²⁴ The reported findings highlight the importance of considering the refractive state of the cornea when fitting scleral lenses. Sclera and cornea are not independent from one another as corneal astigmatism is in a way correlated with scleral astigmatism in astigmatic eyes.^{7,26,27} The refractive state of each patient should therefore be taken into consideration when analysing scleral shape. It would be of interest to further investigate subjects with of corneal astigmatism greater of 2 D^{7,27} with different levels of myopia to assess the correlation of scleral asymmetry, axial length and astigmatism.

The non-invasive methodology to determine the scleral asymmetry is highly accurate as it is directly based on the 3-dimensional maps of the anterior sclera. The corneo-scleral topographer used provides an RMS error of $< 10 \mu\text{m}$ for the central 8 mm area of a calibrated artificial surface and $< 40 \mu\text{m}$ for an extended measurement area of 16 mm.¹⁵ In addition, in a static optimized position the repeatability of the instrument was reported to be very high (standard deviation of the RMS error $< 0.05 \mu\text{m}$).¹⁵ Similarly, a clinical study based on ESP reported very high intra subject repeatability.²⁸

This study has some limitations with regards to the coverage of the corneo-scleral area, however, which plays a key role in the measuring process and the accurate description of the scleral shape. Since the methodology is very robust in presence of missing values, eye lids are not expected to affect the measurements by much, apart from a reduced accuracy due to an incomplete scleral map. In such cases the analysis may be restricted to the still exposed nasal and temporal quadrants.

In conclusion, the presented results show that both axial length and refractive power are highly correlated with the anterior scleral shape. The anterior sclera is easily accessible to the clinician in-vivo and in a non-invasive manner. It would be of interest to investigate whether anterior scleral shape could be used as a predictor for myopia development, or whether anterior scleral symmetry is rather the inevitable consequence of myopia.

REFERENCES

1. Holden BA, Jong M, Davis S, Wilson D, Fricke T, Resnikoff S. Nearly 1 billion myopes at risk of myopia-related sight-threatening conditions by 2050—time to act now. *Clin Exp Optom* 2015;98:491-493.
2. Logan N, Guggenheim J, To C. Myopia: mechanisms, manifestations and management. *Ophthalmic Physiol Opt* 2018;38:207-209.
3. Backhouse S, Gentle A. Scleral remodelling in myopia and its manipulation: a review of recent advances in scleral strengthening and myopia control. *Annals of Eye Science* 2018;1:15
4. Iomdina E, Tarutta E, Markossian G, Aksenova J, Smirnova T, Bedretdinov A. Sclera as the target tissue in progressive myopia. *Pomeranian J Life Sci* 2015;2:146-152.
5. Rada JAS, Shelton S, Norton TT. The sclera and myopia. *Exp Eye Res* 2006;82:185-200.
6. Consejo A, Llorens-Quintana C, Bartuzel MM, Iskander DR, Rozema JJ. Rotation asymmetry of the human sclera. *Acta Ophthalmol* 2018 (in press, doi: 10.1111/aos.13901).
7. Ritzmann M, Caroline PJ, Börret R, Korszen E. An analysis of anterior scleral shape and its role in the design and fitting of scleral contact lenses. *Cont Lens Anterior Eye* 2018;41:205-213.
8. Bandlitz S, Bäumer J, Conrad U, Wolffsohn J. Scleral topography analysed by optical coherence tomography. *Cont Lens Anterior Eye* 2017;40:242-247.
9. Geraghty B, Jones SW, Rama P, Akhtar R, Elsheikh A. Age-related variations in the biomechanical properties of human sclera. *J Mech Behav Biomed Mater* 2012;16:181-191.
10. McBrien NA, Gentle A. Role of the sclera in the development and pathological complications of myopia. *Prog Retin Eye Res* 2003;22:307-338.
11. McBrien NA, Jobling AI, Gentle A. Biomechanics of the sclera in myopia: extracellular and cellular factors. *Optom Vis Sci* 2009;86:E23-30.
12. McMonnies CW. An examination of the relation between intraocular pressure, fundal stretching and myopic pathology. *Clin Exp Optom* 2016;99:113-119.
13. Consejo A, Radhakrishnan H, Iskander DR. Scleral changes with accommodation. *Ophthalmic Physiol Opt* 2017;37:263-274.
14. Levy AM, Fazio MA, Grytz R. Experimental myopia increases and scleral crosslinking using genipin inhibits cyclic softening in the tree shrew sclera. *Ophthalmic Physiol Opt* 2018;38:246-256.
15. Iskander DR, Wachel P, Simpson PN, Consejo A, Jesus DA. Principles of operation, accuracy and precision of an Eye Surface Profiler. *Ophthalmic Physiol Opt* 2016;36:266-278.

16. Consejo A, Llorens-Quintana C, Radhakrishnan H, Iskander DR. Mean shape of the human limbus. *J Cataract Refract Surg* 2017;43:667-672.
17. Consejo A, Behaegel J, Van Hoey M, Iskander DR, Rozema JJ. Scleral asymmetry as a potential predictor for scleral lens compression. *Ophthalmic Physiol Opt* 2018 (In press, doi: 10.1111/OPO.12587).
18. Mitchell P, Hourihan F, Sandbach J, Wang JJ. The relationship between glaucoma and myopia: the Blue Mountains Eye Study. *Ophthalmology* 1999;106:2010-2015.
19. Xu L, Wang Y, Wang S, Wang Y, Jonas JB. High myopia and glaucoma susceptibility: the Beijing Eye Study. *Ophthalmology* 2007;114:216-220.
20. Norman RE, Flanagan JG, Rausch SM, Sigal IA, Tertinegg I, Eilaghi A, et al. Dimensions of the human sclera: thickness measurement and regional changes with axial length. *Exp Eye Res* 2010;90:277-284.
21. Elsheikh A, Phillips JR. Is scleral cross-linking a feasible treatment for myopia control? *Ophthalmic Physiol Opt* 2013;33:385-389.
22. Consejo A, Behaegel J, Van Hoey M, Wolffsohn JS, Rozema JJ, Iskander DR. Anterior eye surface changes following miniscleral contact lens wear. *Cont Lens Anterior Eye* 2018 (In press, doi: 10.1016/j.clae.2018.06.005)
23. Vincent SJ. The rigid lens renaissance: A surge in sclerals. *Cont Lens Anterior Eye* 2018; 41:139-143
24. Schornack MM. Scleral lenses: a literature review. *Eye Contact Lens* 2015;41:3-11.
25. van der Worp E, Bornman D, Ferreira DL, Faria-Ribeiro M, Garcia-Porta N, González-Meijome JM. Modern scleral contact lenses: a review. *Cont Lens Anterior Eye* 2014;37:240-250.
26. Consejo A, Rozema JJ. Scleral Shape and Its Correlations With Corneal Astigmatism. *Cornea* 2018;37:1047-1052.
27. Macedo-de-Araújo RJ, Amorim-de-Sousa A, Queirós A, van der Worp E, González-Meijome JM. Relationship of placido corneal topography data with scleral lens fitting parameters. *Cont Lens Anterior Eye*. 2018 (In press, doi: 10.1016/j.clae.2018.07.005)
28. Consejo A, Bartuzel MM, Iskander DR. Corneo-scleral limbal changes following short-term soft contact lens wear. *Cont Lens Anterior Eye* 2017;40:293-300.