ORCA – Online Research @ Cardiff



This is an Open Access document downloaded from ORCA, Cardiff University's institutional repository:https://orca.cardiff.ac.uk/id/eprint/18123/

This is the author's version of a work that was submitted to / accepted for publication.

Citation for final published version:

Hayes, Sally , Khan, S., Boote, Craig , Kamma-Lorger, Christina S., Dooley, Erin Patricia, Lewis, J., Hawksworth, N., Sorensen, T., Daya, S. and Meek, Keith Michael Andrew 2012. Depth Profile Study of Abnormal Collagen Orientation in Keratoconus Corneas. Archives of Ophthalmology 130 (2) , pp. 251-252. 10.1001/archopthalmol.2011.1467

Publishers page: http://dx.doi.org/10.1001/archopthalmol.2011.1467

Please note:

Changes made as a result of publishing processes such as copy-editing, formatting and page numbers may not be reflected in this version. For the definitive version of this publication, please refer to the published source. You are advised to consult the publisher's version if you wish to cite this paper.

This version is being made available in accordance with publisher policies. See http://orca.cf.ac.uk/policies.html for usage policies. Copyright and moral rights for publications made available in ORCA are retained by the copyright holders.



Shimizu Foundation for Immunological Research Grant.

Online-Only Material: The eAppendix is available at http://www.archophthalmol.com.

Additional Contributions: Chikako Endo provided technical assistance.

- Yagi T, Sotozono C, Tanaka M, et al. Cytokine storm arising on the ocular surface in a patient with Stevens-Johnson syndrome. Br J Ophthalmol. 2011; 95(7):1030-1031.
- Ueta M, Sotozono C, Nakano M, et al. Association between prostaglandin E receptor 3 polymorphisms and Stevens-Johnson syndrome identified by means of a genome-wide association study. J Allergy Clin Immunol. 2010;126(6): 1218-1225, e10.
- Ueta M, Matsuoka T, Yokoi N, Kinoshita S. Prostaglandin E2 suppresses polyinosine-polycytidylic acid (polyI:C)-stimulated cytokine production via prostaglandin E2 receptor (EP) 2 and 3 in human conjunctival epithelial cells. Br J Ophthalmol. 2011;95(6):859-863.
- Ueta M, Matsuoka T, Yokoi N, Kinoshita S. Prostaglandin E receptor subtype EP3 downregulates TSLP expression in human conjunctival epithelium. Br J Ophthalmol. 2011;95(5):742-743.
- Ueta M, Kinoshita S. Innate immunity of the ocular surface. Brain Res Bull. 2010;81(2-3):219-228.
- Takayama K, García-Cardena G, Sukhova GK, Comander J, Gimbrone MA Jr, Libby P. Prostaglandin E2 suppresses chemokine production in human macrophages through the EP4 receptor. J Biol Chem. 2002;277(46):44147-44154.

Depth Profile Study of Abnormal Collagen Orientation in Keratoconus Corneas

n a previous study,¹ we used femtosecond laser technology to cut ex vivo human corneas into anterior, mid, and posterior sections, after which x-ray scatter patterns were obtained at fine intervals over each specimen. Data analysis revealed the predominant orientation of collagen at each sampling site, which was assembled to show the variation in collagen orientation between central and peripheral regions of the cornea and as a function of tissue depth. We hypothesized that the predominantly orthogonal arrangement of collagen (directed toward opposing sets of rectus muscles) in the mid and posterior stroma may help to distribute strain in the cornea by allowing it to withstand the pull of the extraocular muscles. It was also suggested that the more isotropic arrangement in the anterior stroma may play a role in tissue biomechanics by resisting intraocular pressure while at the same time maintaining corneal curvature. This article, in conjunction with our findings of abnormal collagen orientation in full-thickness keratoconus corneas,2,3 received a great deal of interest from the scientific community and prompted the following question: how does collagen orientation change as a function of tissue depth when the anterior curvature of the cornea is abnormal, as in keratoconus? Herein, we report findings from our investigation aimed at answering this question.

Methods. The Baron chamber used in our previous study¹ was adapted to enable corneal buttons to be clamped in place and inflated (by pumping physiological saline into the posterior compartment) to restore their natural curvature. A button diameter of 8 mm or larger was deemed necessary to ensure tissue stability during this process.

The next step, obtaining fresh, full-thickness, keratoconus buttons of sufficient diameter, proved to be problematic owing to the increasing popularity of deep anterior lamellar keratoplasty. Recently, however, the opportunity arose to examine an 8-mm full-thickness (300-340 µm minus epithelium) keratoconus corneal button with some central scarring and a mean power greater than 51.8 diopters (Figure 1). The tissue was obtained in accordance with the tenets of the Declaration of Helsinki and with full informed consent from a 31-year-old patient at the time of penetrating keratoplasty. Using techniques detailed previously,¹ the corneal button was clamped in the chamber and inflated. The central 6.3-mm region of the button was then flattened by the applanation cone and a single cut was made at a depth of 150 µm from the surface using an IntraLase 60-kHz femtosecond laser (Abbott Medical Optics Inc),¹ thus splitting the cornea into anterior and posterior sections of roughly equal thickness. Wide-angle x-ray scattering patterns were collected at 0.25-mm intervals over each cor-



Figure 1. Corneal topography of the keratoconus cornea (recorded 12 years previously).³ The broken lines show the 6.3-mm region of the cornea cut with the femtosecond laser (circle) and the region of greatest corneal steepening depicted in Figure 2 (rectangle).



Figure 2. Collagen orientation in the normal (A) and keratoconus (B) posterior stroma (central 6.3 mm). The highlighted regions of the posterior (C and D) and anterior (E and F) stroma are expanded. Large vector plots showing high collagen alignment are downsized (key).

ARCH OPHTHALMOL/VOL 130 (NO. 2), FEB 2012 WWW.ARCHOPHTHALMOL.COM 251

©2012 American Medical Association. All rights reserved.

neal section on station IO2 at the Diamond Light Source.² The data were analyzed¹ to form vector plots—the radial extent of which, in any direction, is proportional to the number of fibrils preferentially aligned in that direction. These were assembled, and the larger plots scaled down, to show the predominant orientation of collagen throughout each tissue section.

Results. Abnormalities in collagen organization were seen in both the anterior and posterior stroma of the keratoconus cornea (**Figure 2**), with the most drastic disruption occurring within the region of greatest corneal steepening (Figure 1). In the posterior stroma, the normal orthogonal predominant orientation of collagen was absent; in the anterior stroma, the usual isotropic arrangement of collagen was replaced with more highly aligned unidirectional collagen.

Comment. The results indicate that a gross rearrangement of lamellae had occurred in both the anterior and posterior regions of the keratoconus corneal stroma (Figure 2). These findings support our belief that the specific arrangement of stromal collagen plays a significant role in the maintenance of normal corneal curvature.

Sally Hayes, PhD Saj Khan, MD Craig Boote, PhD Christina S. Kamma-Lorger, PhD Erin Dooley, MSc Jennifer Lewis, PhD Nick Hawksworth, MD Thomas Sorensen, PhD Sheraz Daya, MD Keith M. Meek, DSc

Author Affiliations: Structural Biophysics Group, School of Optometry and Vision Sciences, Cardiff University, Cardiff (Drs Hayes, Boote, and Kamma-Lorger, Ms Dooley, and Prof Meek), and Department of Ophthalmology, Royal Glamorgan Hospital, Llantrisant (Dr Hawksworth), Wales; Centre for Sight, West Sussex (Drs Khan and Daya), and Diamond Light Source, Harwell Science and Innovation Campus, Oxfordshire (Dr Sorensen), England; and Department of Ophthalmology, Havener Eye Institute, Ohio State University, Columbus (Dr Lewis).

Correspondence: Prof Meek, School of Optometry and Vision Sciences, Cardiff University, Maindy Road, Cardiff CF24 4LU, Wales (meekkm@cf.ac.uk).

Financial Disclosure: None reported.

Funding/Support: This work was funded by grants G0600755 from the Medical Research Council and MX-2932 from the Science and Technology Facilities Council. Prof Meek is a Royal Society Wolfson Research Merit Award Holder.

Role of the Sponsors: The funding organizations had no involvement in the design and conduct of the study; collection, management, analysis, and interpretation of the data; or preparation, review, or approval of the manuscript.

Previous Presentation: This paper was presented at the Eurokeratoconus II meeting; September 23, 2011; Bordeaux, France.

Additional Contributions: Abbott Medical Optics allowed the loan and use of the IntraLase FS60 femtosecond laser. Dr Valerie Smith and the staff at the Bristol Eye Bank, Bristol, England, provided the normal cornea used in this study, and Mr Ashraf M. Mahmoud, Ohio State University, provided technical assistance.

- Abahussin M, Hayes S, Knox Cartwright NE, et al. 3D collagen orientation study of the human cornea using X-ray diffraction and femtosecond laser technology. *Invest Ophthalmol Vis Sci.* 2009;50(11):5159-5164.
- Hayes S, Boote C, Tuft SJ, Quantock AJ, Meek KM. A study of corneal thickness, shape and collagen organisation in keratoconus using videokeratography and X-ray scattering techniques. *Exp Eye Res.* 2007;84(3):423-434.
- Meek KM, Tuft SJ, Huang Y, et al. Changes in collagen orientation and distribution in keratoconus corneas. *Invest Ophthalmol Vis Sci.* 2005;46(6):1948-1956.

Dacryops of Krause Gland in the Inferior Fornix in a Child

D acryops of the accessory lacrimal glands are extremely rare, with only 4 previous cases reported to involve Krause glands in the last 60 years.^{1.4} Dacryops of Krause glands have not been reported in the inferior fornix. The cause is often unclear, although numerous causes of secondary dacryops are known.^{1.4}

Report of a Case. An otherwise healthy 2-year-old girl had a left lower eyelid mass, noted since age 2 months



Figure 1. Findings in a 2-year-old girl. A, Left lower eyelid swelling (asterisk). B, Computed tomographic scan shows the cystic nature of the lesion (C) extending inferiorly, with enophthalmos of the left globe (G).

ARCH OPHTHALMOL/VOL 130 (NO. 2), FEB 2012 252 WWW.ARCHOPHTHALMOL.COM