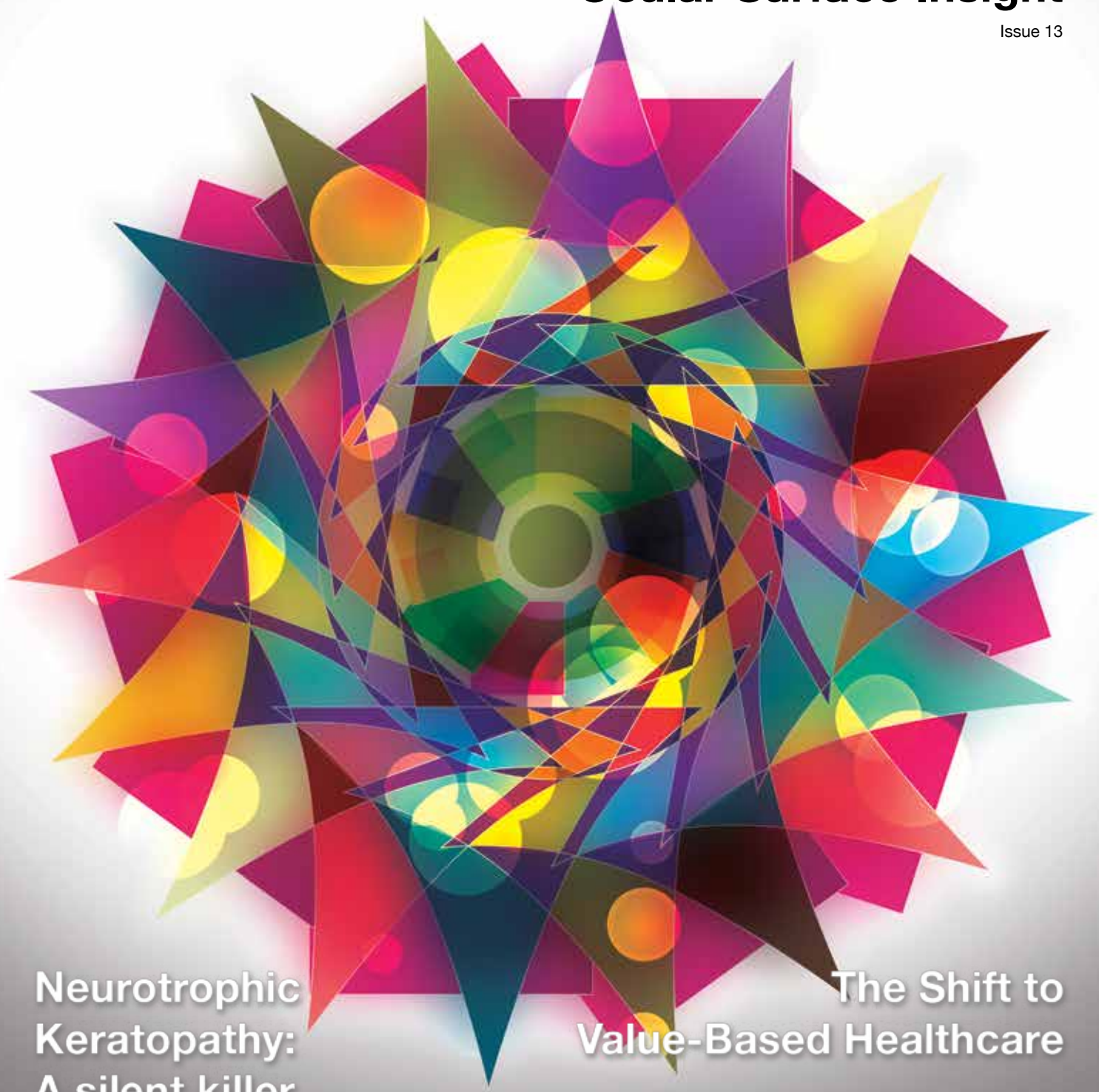
OSI

Ocular Surface Insight

Issue 13



Neurotrophic Keratopathy: A silent killer

The Shift to Value-Based Healthcare

Artificial Intelligence Grading and Telemedicine in Practice

Build, Manage and Grow Your Myopia & Dry Eye Practice.

Introducing the new

MYAH

Did you know that 50% of the world's population[1] may be myopic by 2050? European regions are not an exception.

MYAH offers all the technologies required to support myopia management: optical biometry, corneal topography and pupillometry — it is a one-time investment. In addition, MYAH is an all-in-one device that offers an evolving platform which provides the tools to add or grow Dry Eye Management.

Overview of MYAH

- **Corneal Topography including keratoconus screening and pupillometry**
- **Axial Length measurement by Optical Low Coherence Interferometry**
- **Progression reports for analyzing treatment efficacy**
- **Comprehensive suite of Dry Eye assessment tools**
- **Patient-friendly with rapid capture**
- **Compact, space-saving, easy to operate**

It has never been a better time to join the battle against the global myopia epidemic and to learn how to integrate myopia and dry eye management into your workflow.

LEARN MORE at **topconmyah.com**

TOPCON (GREAT BRITAIN) MEDICAL LIMITED
01635 551120 | medical@topcon.co.uk | www.topcon-medical.co.uk
TOPCON IRELAND
+353 1 223 3280 | medical.ie@topcon.com | www.topcon-medical.ie

TOPCON Healthcare
SEEING EYE HEALTH DIFFERENTLY

1. Holden, BA, Fricke, TR, Wilson, DA et al. Global prevalence of myopia and high myopia and temporal trends from 2000 through 2050. Ophthalmology. 2016; 123:1036–42. Available from: doi: DOI: 10.1016/j.ophtha.2016.01.006

Ocular Surface Insight

"If the doors of perception were cleansed, everything would appear to man as it is - infinite."

William Blake

Welcome to the Autumn 2021 issue of OSI.

Welcome to the OSI Magazine!

We are really excited about our upcoming **Joint Virtual Symposium with MCLOSA on the 26th of November.** We have a fantastic programme with so many inspirational speakers: Arthur Cummings, David Lockington, Gok Ratnarajan, Raman Malhotra, Colin Williams, Andrena McElvanney, Brian Tompkins, Amy Gallant-Sullivan, Sabrina Shah-Desai, Fiona Carley, Parwez Hossein, Sophie Jones. Our special guest and international speaker Prof. Rohit Shetty and finally this year's **MCLOSA Kersley Medal Lecturer** will be Prof. Francisco Figuereido. The full programme is available inside the magazine.

In this issue of the magazine, we have a diverse mix of articles. We have a very interesting piece from my former colleague Vivian Ho and her new team of colleagues at United Christian Hospital in Hong Kong about the potential dangers with Neurotrophic Keratopathy.

We have a fascinating read of a recent study in Tokyo on the effects of low strength Atropine instillation and Brian Tompkins is back with his final instalment "Top Tools I cannot live without when diagnosing Ocular Surface Disease" focussing on Telemedicine in Practice

We also have a very honest patient story about his long struggle with dry eye disease from childhood into adulthood. I personally find these patient perspective stories very important to keep raising the awareness of this disease.

Samer Hamada

Samer Hamada,
MD, MSc, DO (hons), FRCSEd, FRCOphth

About us

Ocular Surface Insight

Editor in Chief
Samer Hamada

Published by
VisionDuo Ltd.

Sales & Advertising
Denise Castell
denise@visionduo.com

Business Development & Marketing
Åsa Baudin
asa@visionduo.com

Conference & Educational Events
events@visionduo.com

Accounts
accounts@visionduo.com

Media No. 0001

Published November 2021

If you wish to receive your own future copies of OSI magazine, please email: subscriptions@visionduo.com.

Scan to go to the OSI website:

osimag.co.uk

Contributors

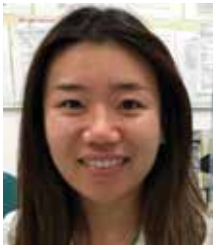
Mr Samer Hamada
Consultant Lead
Queen Victoria Hospital East Grinstead
Director and Lead Consultant
Eye Clinic London

Mr Brian Tompkins
BSC(Hons) FCOptom, FBLCA
Director & Optometrist
TK & S Optometrists Ltd.

Mr. Nathan Little
Chief Strategy Officer
Sparca AOS

Ms Vivian Ho
Associate Consultant Ophthalmologist
United Christian Hospital Hong Kong

Dr. Kenneth Li
Chief of Service and Consultant Ophthalmologist.
United Christian Hospital and Tseung Kwan O Hospital, Hong Kong.



Jacqueline W. T. Chan
Bachelor of Medicine and Bachelor of Surgery, CUHK (MBChB)
United Christian Hospital Hong Kong

KYORIN UNIVERSITY

Tadahiro Mitsukawa, Yumi Suzuki, Yosuke Momota, Shun Suzuki and Masakazu Yamada
Kyorin University School of Medicine, Tokyo, Japan

Editorial Panel:

Contents

What's in the news?

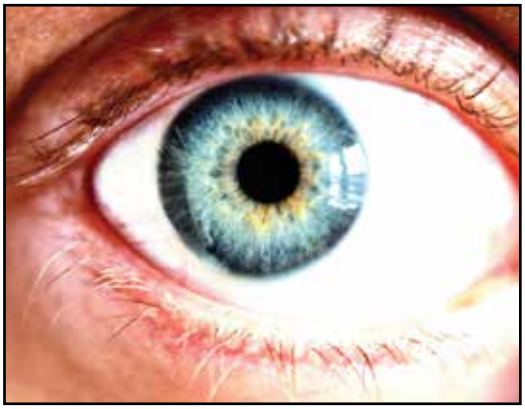
Clinical Outcomes and Patient Satisfaction After Corneal Neurotization

The aim of this study was to assess clinical outcomes of corneal neurotization (CN) and determine patient perception of postoperative results.

This was a retrospective study involving 29 eyes in 28 patients who underwent CN. Chart review data included demographic and clinical history; ophthalmic examination including visual acuity,

ocular surface quality, and corneal sensation; surgical technique; and postoperative course. Subjective self-reported patient outcomes of surgical success were also assessed. Only eyes with at least 6 months of follow-up were included in the statistical analysis.

A total of 24 eyes and 23 patients were included in statistical analyses. The median postoperative follow-up time was 12.2 months (interquartile range 10.9-18.5 mo). Twenty-three eyes (92%) achieved improvement in ocular surface quality. Eleven of 13 (85%) demonstrated healing of persistent epithelial defects at their last follow-up. Patients gained a median of 2.3 cm in Cochet-Bonnet esthesiometry measurements of sensation.



No significant difference was found between preoperative and postoperative visual acuity. All 17 patients who provided self-assessment of their surgical outcome indicated they would undergo CN again if given the choice. Most of the patients reported that the postoperative pain was tolerable, with a median pain score of 3.0 on a 10-point scale (interquartile range 0.0-4.0). Sixteen patients (94%) reported full or partial return of skin sensation along the donor nerve distribution.

Corneal Neurotization provides improvement in corneal health and sensibility, with high patient satisfaction and minimal postoperative pain and morbidity.

Authors: Leon Rafailov, Jane S Kim, Clayton Ellis Wisely, Edgar M Espana, Matias Soifer, Ilya M Leyngold
Publication: Cornea. 2021 Nov 1;40(11):1377-1386.doi: 10.1097/ICO.0000000000002759.

Should we care about the ocular surface in the anophthalmic patient?

The purpose of this study was to assess clinical and biomolecular changes of the conjunctival epithelium in anophthalmic patients wearing an ocular prosthesis.

Thirty-five unilateral anophthalmic patients were enrolled. Patients with blepharitis, lid abnormalities, and topical/systemic medication affecting the ocular surface were excluded. Symptom Assessment in Dry Eye (SANDE) questionnaire and tear function test (Schirmer Test Type I) were recorded. Conjunctival inflammation and meibomian gland dysfunction (MGD) were graded in the anophthalmic side and fellow eye. Impression cytology sampling of the upper, lower tarsal, and posterior/bulbar conjunctiva from the anophthalmic socket were collected and compared to healthy controls.

The result showed that the patients had significantly higher SANDE ($p < 0.001$), Schirmer I test ($p = 0.004$), conjunctival inflammation ($p < 0.001$), and MGD scores ($p < 0.001$) on the anophthalmic side compared to the fellow eye. Mucin 5AC, inflammatory markers (MMP-9, ICAM-1) expression ($p < 0.001$), and response to oxidative stress (NRF2-KEAP1 signaling pathway) ($p < 0.05$) were significantly upregulated in the posterior conjunctival surface in the anophthalmic socket.

Anophthalmic patients complained of more pronounced dry eye symptoms and presented more significant signs of inflammation and MGD on the anophthalmic side. The bulbar conjunctiva, behind the prosthesis, showed more significant hyperexpression of mucins, markers of inflammation, and increased response to oxidative stress compared to the tarsal conjunctiva. Patients wearing ocular prosthesis had signs of inflammation resembling dry eye disease.

Authors: Giulio Volpe, Maria De Piano, Giacomilde Mazzone, Alessandra Micera , Stefano Bonini, Alessandra Claudia Modugno
Publication: Eur J Ophthalmol. 2021 Oct 7;11206721211048803.doi:10.1177/11206721211048803.

BVI

All The Brands You Trust Now With a Single Vision

Beaver®
Knives and Blades

Visitec®
Cannulas

Malosa®
Single-Use Instruments

CustomEyes®
Custom Procedure Packs

PhysIOL
Premium IOLs

ARCAD
Surgical Fluids

Vitreo
Vitreoretinal Surgical Products

EndoOptiks®
Microendoscopy

Keeping Your Vision In Sight®

Since 1932, ophthalmic professionals have relied on us for dependable, high quality products. Now we've expanded our portfolio to support all aspects of ophthalmic surgery, from instruments and lenses to surgical equipment all with a single vision – yours.

INT Tel: + 44 1865 601 256 Option 3
Email: ordersuk@bvimedical.com

bvimedical.com

1526680-04 IN

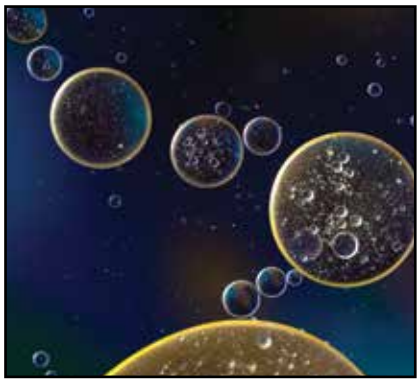
What's in the news?

An ion-paired moxifloxacin nanosuspension eye drop provides improved prevention and treatment of ocular infection

There are numerous barriers to achieving effective intraocular drug administration, including the mucus layer protecting the ocular surface. For this reason, antibiotic eye drops must be used multiple times per day to prevent and treat ocular infections.

Frequent eyedrop use is inconvenient for patients, and lack of adherence to prescribed dosing regimens limits treatment efficacy and contributes to antibiotic resistance. Here, we describe an ion-pairing approach used to create an insoluble moxifloxacin-pamoate (MOX-PAM) complex for formulation into mucus-penetrating nanosuspension eye drops (MOX-PAM NS). The MOX-PAM NS provided a significant increase in ocular drug absorption, as measured by the area under the curve in cornea tissue and aqueous humor, compared to Vigamox in healthy rats.

Prophylactic and treatment efficacy were evaluated in a rat model of ocular Staphylococcus aureus infection. A single drop of MOX-PAM NS was more effective than Vigamox, and completely prevented infection. Once a day dosing with MOX-PAM NS was similar, if not more effective, than three times a day dosing with Vigamox for treating S. aureus infection. The MOX-PAM NS provided increased intraocular antibiotic absorption and



improved prevention and treatment of ocular keratitis, and the formulation approach is highly translational and clinically relevant.

Authors: Aditya Josyula , Revaz Omiadze , Kunal Parikh , Pranjali Kanvinde, Matthew B Appell, Pratikkumar Patel, Hiwa Saeed , Yogesh Sutar, Nicole Anders, Ping He, Peter J McDonnell, Justin Hanes, Abhijit A Date, Laura M Ensign

Publication: Bioeng Transl Med. 2021 Jun 22;6(3):e10238.doi: 10.1002/btm2.10238

What's in the news?

Combination of 0.05% Azelastine and 0.1% Tacrolimus Eye Drops in Children With Vernal Keratoconjunctivitis: A Prospective Study

The aim in this prospective study was to compare the efficacy of the combination of 0. 05% azelastine and 0.1% tacrolimus eye drops with 0.1% tacrolimus monotherapy in paediatric patients with vernal keratoconjunctivitis (VKC).

Seventy-six patients with VKC were randomized 1:1 into monotherapy group with 0.1% tacrolimus or combination therapy group with 0.1% tacrolimus and 0.05% azelastine. The Ocular Surface Disease Index (OSDI) scores and the signs of conjunctival hyperemia, corneal involvement, and palpebral conjunctiva papillae were assessed at baseline and at 1, 2, and 6 weeks after treatment.

The two groups were comparable in age, sex, duration of VKC, OSDI, and clinical signs of VKC at baseline. Significant improvements in OSDI score and clinical signs were observed in both groups at all follow-up visits (all $p < 0.001$), compared with baseline. The combination therapy group showed a larger decrease in OSDI score from baseline (10.30 ± 0.9) compared with monotherapy group (7.30 ± 0.7, $p = 0.0085$) at 1 week.

Greater improvements in conjunctival hyperemia and conjunctival papillae were identified in the combination therapy group, compared with in the monotherapy group, at all follow-up visits (all $p < 0.05$). The corneal involvement scores in the combination group is significantly lower than the monotherapy group at 2 weeks after the treatment ($p = 0.0488$). No severe adverse effect was found in either group during the study.

The authors concluded that compared with a monotherapy of 0.1% tacrolimus, the combination of 0.05% azelastine and 0.1% tacrolimus eye drops lead to faster and greater improvements in clinical signs and symptoms of vernal keratoconjunctivitis in pediatric patients.

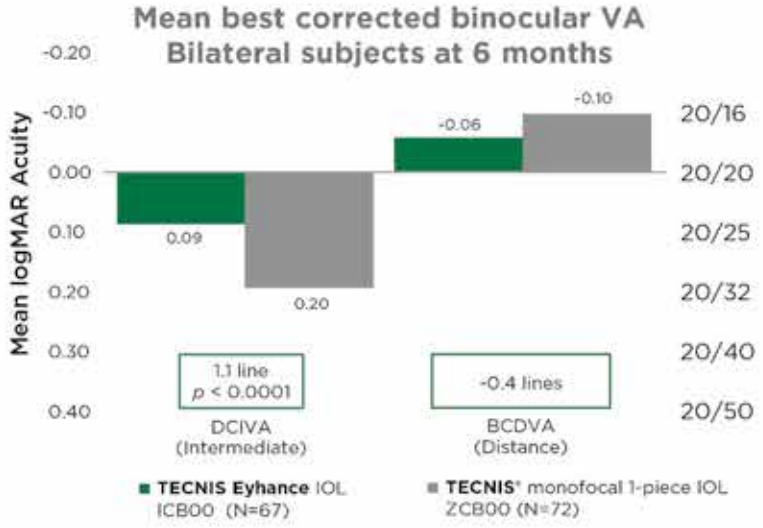
Authors: Minjie Chen, Anji Wei, Bilian Ke, Jun Zou, Lan Gong, Yan Wang, Chaoran Zhang, Jianjiang Xu, Jia Yin, Jiaxu Hong

Publication: Front Med (Lausanne). 2021 Sep 17;8:650083. doi: 10.3389/fmed.2021.650083. eCollection 2021.

TECNIS Eyhance IOL

A new generation of monofocal IOLs

Improved intermediate vision



TECNIS Eyhance IOLs (ICB00) offer a statistically significant improvement in monocular and binocular intermediate vision vs. **TECNIS®** monofocal 1-piece IOLs (ZCB00).[1]

- Improved intermediate vision[1]
- 20/20 distance vision[1*]

Give them more.

Enhance your patients' intermediate vision by using **TECNIS Eyhance** IOL.

Reference

1. Data on File, Johnson & Johnson Surgical Vision, Inc., Sep 2018. DOF2018CT4015.

*Based on a clinical study, N=134 achieved mean 20/20 monocular pooled distance BCDVA.

Enhanced vision within reach.

For healthcare professionals only.

Please read the Directions for Use for Important Safety Information and consult our specialists if you have any questions.

TECNIS Family of IOLs | LEADING INNOVATION | HIGH-QUALITY OUTCOMES | EXCEPTIONAL SATISFACTION |

Bring Vision to Life.

TECNIS
Eyhance IOL

See the Passion in Each Patient.

Johnson & Johnson VISION

CROSS OUT DRY EYE

ONE RANGE FOR ALL YOUR DRY EYE NEEDS

One Range | Simplicity | Widely recognised brand

- Preseruatiue FREE[1-3]
- Phosphate FREE[1-3]
- Contact Lens Friendly[1-3]
- Significant NHS Cost Sauings[4,5]

The NEW Xailin® eye health range. Preseruatiue & phosphate FREE formulation, contact lens friendly.[1-3]

1. Xailin® Tears Instructions for Use (IFU) 2. Xailin® Plus Instructions for Use (IFU) 3. Xailin® Intense Instructions for Use (IFU) 4. VISUfarma Data on File October 2021 5. www.ITIITIS.co.uk Last Accessed October 2021

VISUfarma
the eye health company

Please contact VISUfarma HQ for more information

+44 (0)113 4680661 | UKCustomerServices@VISUfarma.com

VISUfarma.com/UK

VFS3/UK/XL/0014 Date of Preparation: October 2021

Neurotrophic Keratopathy: A silent killer

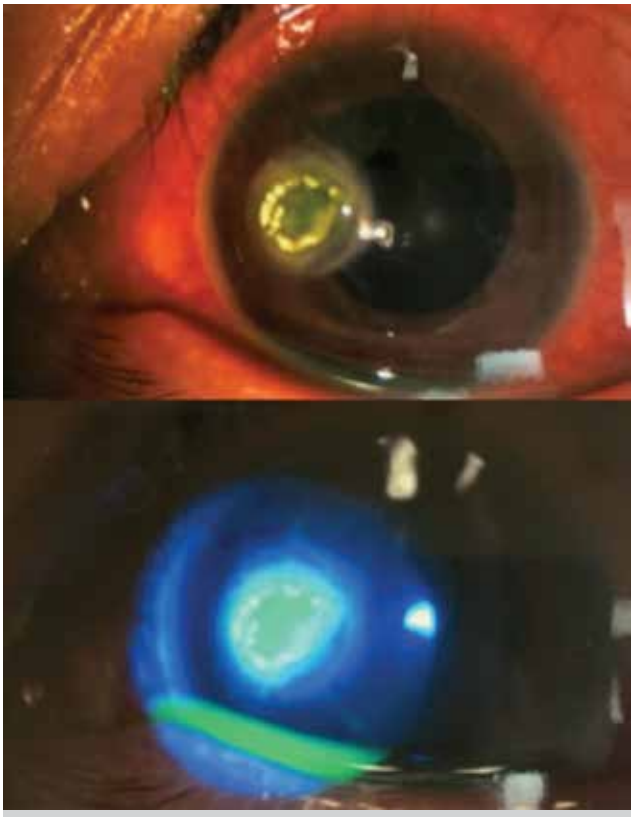
By **Jacqueline W. T. Chan[1,2], Vivian W. M. Ho[1,2], Kenneth K. W. Li[1,2]**

Background

Neurotrophic keratopathy (NK) is a rare, progressive, and degenerative corneal disease with a prevalence of 1.6 to 4.2 per 10,000 persons (Sacchetti 2014). It occurs when there is partial or complete loss of trigeminal innervation, resulting in reduced corneal sensation, impaired trophic supply; reduction of tear film production and alteration of corneal healing process. Without prompt medical or surgical treatment, this would quickly lead to spontaneous corneal epithelium breakdown, stromal thinning and even perforation, posing a serious threat to vision and negative impact of patients' quality of life.

Clinical cases

A 63-year-old Asian female presented to our Eye department with vesicular rash along the dermatome of ophthalmic branch of trigeminal nerve (V1) and redness over her left eye 3 weeks after her cataract surgery. Her past medical history included diabetes mellitus, hypertension, and metastatic carcinoma of lung with ongoing palliative chemotherapy. She had past ophthalmic history of right eye recurrent corneal erosion and left eye phacoemulsification with intraocular lens implantation performed in May 2021. At the time of presentation, patient was undergoing her 7the cycle of chemotherapy and was in an immunocompromised state with a low white cell and absolute neutrophil count. On examination, her presenting visual acuity (decimal) was 0.4 with a normal intraocular pressure. Her conjunctiva showed mild injection with mild anterior chamber activity.

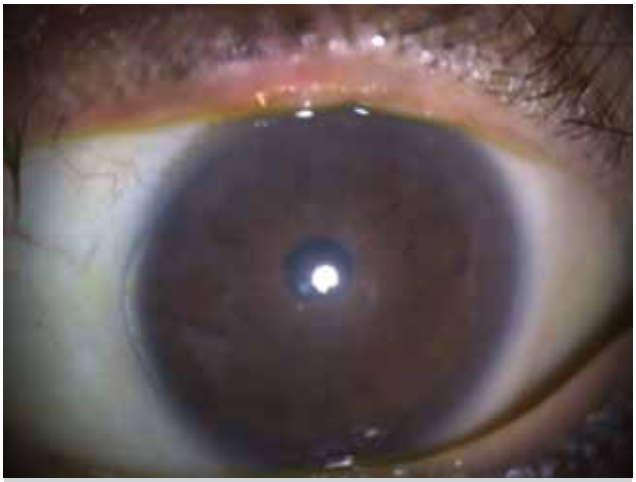


Persistent ED with BCL

Dendritic lesions was seen with corneal fluorescence stain. Otherwise, posterior segment examination was unremarkable. Hutchison sign was negative and extraocular movements were full. She was managed as Herpetic Zoster Keratouveitis and was started on topical acyclovir ointment, lubricants, and oral acyclovir of 800mg 5 times per day.

One week later, her visual acuity reduced from decimal 0.4 to 0.05. There was a large central epithelial defect of 8x 4mm with reduced corneal sensation. Preservative free intensive lubricants with empirical topical antibiotics cover were used together with oral acyclovir in prophylactic dose (400mg BD per day). Unfortunately, her epithelial defect persisted in a rolled edges appearance with hypopyon and Descemet's membrane folds. We stepped up our management by increasing dosage of oral acyclovir to 800mg 5 fives per day, preservative free lubricants to hourly during daytime and a trial of bandage contact lens. Her hypopyon and Descemet's membrane folds both resolved but the epithelial defect persisted.

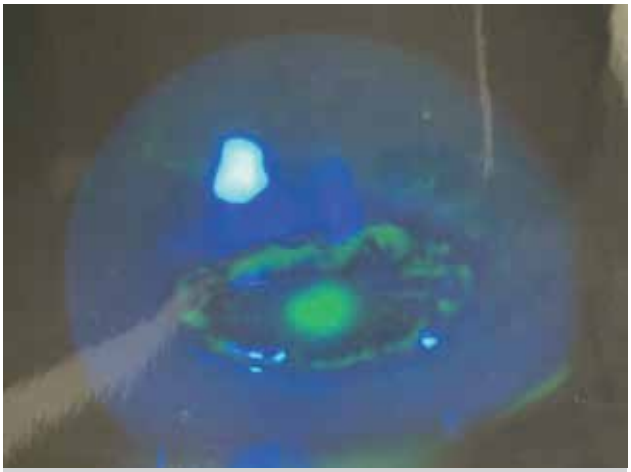
Eventually we performed a temporary tarsorrhaphy and the epithelial defect healed after 3 weeks, with her visual acuity returned to baseline.



ED healed with tarsorrhaphy

Our second case is a 96-year-old lady presented with left eye redness after accidentally injured by her own finger. Her past medical history included diabetes mellitus, hypertension, and myocardial infarction. She had past ophthalmic history of bilateral extracapsular cataract extraction with intraocular lens insertion performed more than 10 years ago.

Her presenting visual acuity declined from baseline decimal 0.1 to finger-counting. On examination, there was a central corneal epithelial defect of 4x2mm with mild thinning and reduction in corneal sensation. There were no infiltrates or dendrites. We started her on topical empirical broad-spectrum antibiotics, preservatives-free lubricants, oral doxycycline and ascorbate acid to promote epithelium healing.



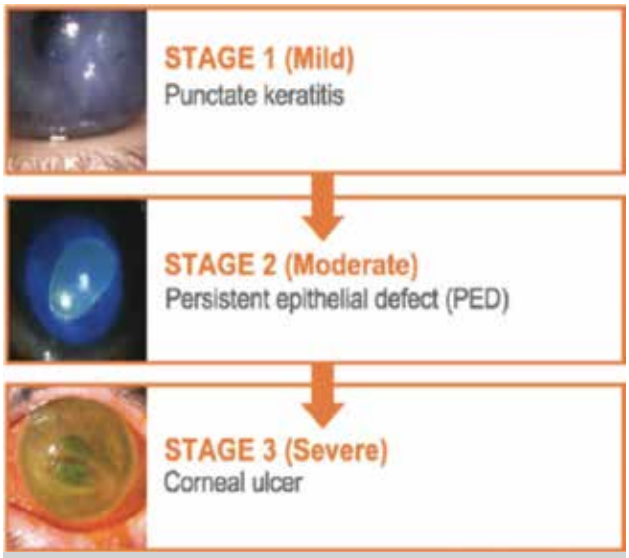
Persistent ED with BCL

On subsequent follow-up, her eye swab results showed no growth with negative autoantibodies blood test. After the epithelial defect failed to improve with maximal medical treatment and trial of bandage contact lens, she underwent temporary central tarsorrhaphy and epithelial defect resolved after 2 weeks.

Discussion

Causes of neurotrophic keratopathy can be classified into ocular, systemic, central and rarely congenital. The most common ocular causes include post-herpetic infection and after ocular surgeries, as demonstrated in our first case. Systemic cause includes diabetes mellitus and previous ocular surgeries which presented in both of our clinical cases. Other central causes include neurosurgical conditions, e.g., after acoustic neuroma removal.

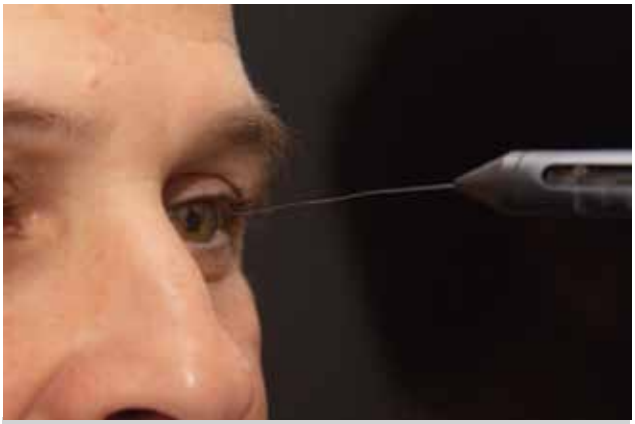
The pathophysiology of neurotrophic keratopathy begins with impairment of trigeminal nerve innervation to cornea. It diminishes corneal sensory innervation and trophic supply, which impairs trigeminal reflexes, tear film production and blink rate. All these factors results in corneal epithelial structural changes and impairment of corneal healing mechanism. This will eventually lead to spontaneous corneal epithelial breakdown, which starts the process of neurotrophic keratitis.



Mackie IA: Neuroparalytic keratitis; in Roy FH, Meyer SM, Fraunfelder F (eds): Current Ocular Therapy. Philadelphia, WB Saunders, 1995, pp 452-454.

Neurotrophic keratopathy can be graded into 3 stages using Mackie classification. Stage 1 refers to presence of punctate keratopathy, epithelial hyperplasia, stromal scarring, and corneal neovascularization. Stage 2 is the presence of persistent epithelial defect with smooth and rolled edges due to impaired healing. Descemet's folds, and stromal swelling may occur in this stage and may rarely progress to anterior chamber reactive inflammation with sterile hypopyon. Stage 3 is severe disease characterized by corneal stromal involvement, this may result in progressive corneal thinning and perforation.

To diagnose neurotrophic keratopathy, it is essential to take a detailed medical and drug history, especially any history of chemical injury, or chronic contact lens. Evaluation for systemic auto-immune disorders should also be considered in light of some of the other conditions associated with neurotrophic keratitis. On examination, we should look for any eyelid abnormalities e.g., lagophthalmos, entropion, ectropion and cicatricial scarring; check for corneal sensation and perform corneal staining to look for the presence of epithelial defect. For investigations, we can perform corneal scraping or swab to rule out co-existing bacterial, fungal, or viral infection as a potential cause for the defects. Other diagnosing method includes use of in-vivo confocal microscopy, which presence of plexus indicates good prognosis.



ED healed with tarsorrhaphy

Testing corneal sensitivity is a key step in diagnosing neurotrophic keratitis and differentiating it from other conditions that may present with epitheliopathy or decreased corneal sensation. Qualitatively, you may use a cotton swab, cotton wisp, non-waxed dental floss, or the tip of a tissue paper, which are readily available in an out-patient clinic setting. We should test the sensitivity of the normal eye first before the affected eye and perform the test before any anesthetic eyedrops instillation. Quantitatively, we can use Cochet-Bonnet aesthesiometer, which a nylon monofilament is touched to the corneal surface and perceived length of the filament is recorded as the corneal sensitivity.

The treatment of neurotrophic keratopathy involves both medical and surgical management. It is dependent on the stage of disease based on the Mackie classification. In stage 1, with presence of punctate keratitis, the goal at this stage is to improve the quality of the corneal epithelium, prevent epithelial breakdown and preserve corneal transparency. All offensive topical medications and systemic therapies such as neuroleptics, antipsychotics and antihistamines should be discontinued. The ocular surface

can be preserved using artificial tears without preservatives every 2-4 hourly and a lubricant ointment at bedtime.

In stage 2, our aim is to promote healing of epithelial defect and prevent progression of disease to corneal ulcer with stromal involvement. The presence of asymptomatic disease may enable rapid progression to corneal perforation. In these cases, on top of preservative-free lubricants, prophylactic topical antibiotics, oral doxycycline and ascorbate acid should be administered. Corneal or scleral contact lens can also be used to promote healing.

In stage 3, we should protect the ocular surface in preventing corneal thinning and perforation. In the event of large epithelial defects or corneal ulcers that do not respond to treatment with preservative free artificial tears or contact lens treatment, it is important to stop all treatment except artificial tears and prescribe antibiotic prophylaxis, as in previous stages. Autologous serum, cyclosporin, topical steroids and some new medications e.g., Cenegermin and Calcicol can be useful. Tarsorrhaphy has traditionally been considered the treatment of choice because it can be easily performed and is widely used. Alternatives to tarsorrhaphy include injection of botulinum toxin A to induce temporary ptosis of the upper eyelid or the use of an amniotic membrane transplant or conjunctival flap to cover the corneal surface, but this compromises aesthetics and visual function.

Cenegermin is a recombinant human nerve growth factor, which binds to lacrimal gland to affect tear secretion, stimulate innervation of corneal nerves, and growth of epithelium. Two independent, double-masked, multicentre, randomized controlled trials performed in both the US and EU (Pflugfelder et al, Bonini S et al).. Study participants were adults with stage 2 or 3 neurotrophic keratitis and non-responsive to existing treatments. More than 50% of patients in EU and US trial showed complete healing by week 4 of Cenegermin. In the European trial, 80% of patients who achieved complete corneal healing after just 8-week Cenegermin treatment cycle, remained healed after 1 year.

ReGeneraTing agent e.g., Cacicol composes of polysaccharides to mimic natural heparan sulfates which are component of the corneal extracellular matrix.
It promotes healing and maintain homeostasis of cornea's microenvironment. A case series (Review by Di Zazzo et al. 2019) shows Cacicol can aid complete corneal healing in 69% of eyes with a 4% recurrence. Some RCT results are pending for this medication.

Corneal neurotization is a rapidly evolving surgical procedure that involves the transfer of healthy donor sensory nerve axons to the denervated cornea in order to re-establish innervation (Malhotra et al 2018). It has shown success in restoring corneal sensation and trophic function by reinnervating the stromal and sub-basal layers of the cornea (Elalfy et al. 2021). However, it is a costly procedure and requires a multidisciplinary surgical approach with the involvement of multiple surgeons.

In summary, neurotrophic keratopathy is a progressive, degenerative corneal disease, with reduced corneal sensation. We should always look out for neurotrophic keratitis whenever there are patients presented with a painless corneal ulcer. Checking patient's corneal sensation is a key step in diagnosis. Without prompt management, it can lead to rapid progression and result in corneal perforation. A stepwise approach for treating neurotrophic keratopathy is therefore advised to prevent visual loss.

References:

Sacchetti M and Lambiase A (2014) Diagnosis and management of neurotrophic keratitis. Clinical Ophthalmology 8:571–9.

Mackie IA: Neuroparalytic keratitis; in Roy FH, Meyer SM, Fraunfelder F (eds): Current Ocular Therapy. Philadelphia, WB Saunders, 1995, pp 452-454.

Tiffany L M Yeung, Vivian Ho, Brian C Y Li & Kenneth K W Li (2021) Re: Ocular injuries resulting from commercial cosmetic procedures, Clinical and Experimental. Optometry, 104:5, 658-658,

Pflugfelder et al. Topical Recombinant Human Nerve Growth Factor (Cenegermin) for Neurotrophic Keratopathy: A Multicenter Randomized Vehicle-Controlled Pivotal Trial. Ophthalmology. 2020 Jan;127(1):14-26. Bonini S et al. REPARO Study Group. Phase II Randomized, Double-Masked, Vehicle-Controlled Trial of Recombinant Human Nerve Growth Factor for Neurotrophic Keratitis. Ophthalmology. 2018 Sep;125(9):1332-1343.

Antonio Di Zazzo et al. Neurotrophic keratopathy: Pros and cons of current treatments. The Ocular Surface, Volume 17, Issue 4, 2019, Pages 619-623

Malhotra R, Elalfy MS, Ruben K, et al. Update in corneal neurotisation. Br J Ophthalmol. 2018:1–10.

Elalfy M, Maqsood S, Hau S, Kannan RY, Nduka C, Hamada S, Malhotra R. Functional and Structural Changes Following Corneal Neurotisation in the Management of Neurotrophic Keratopathy: UK Single Centre Series. Clin Ophthalmol. 2021 May 24;15:2149-2160.

The Shift to **Value-Based Healthcare**

We are all aware of the growing need for more efficient and cost-effective healthcare systems and the global Covid pandemic has only exacerbated the need. A growing trend medical services delivery is value-based healthcare (VBC). VBC is described as a healthcare system where provider reimbursements are based on patient health results.[1]
The NEJM Catalyst group define it as "Value-based healthcare is a healthcare delivery model in which providers, including hospitals and physicians, are paid based on patient health outcomes. Under value-based care agreements, providers are rewarded for helping patients improve their health, reduce the effects and incidence of chronic disease, and live healthier lives in an evidence-based way."[1]
This new model of healthcare delivery is distinctly different from the fee-for-service model we are all too familiar with and the VBC model hopes to delivery that "value" by continually monitoring outcomes to cost of delivery, not just the cost of services provided. The theory is this will drive down costs in the system by removing unneeded services that do not demonstrate to improve patient outcomes.

Benefits of a VBC model touch every stakeholder in the healthcare delivery system, most notably providing decreased costs, increased efficiency, and better patient outcomes through more preventative healthcare.

While the benefits of a VBC model are clear there are significant hurdles to overcome for adoption, three of which are the shift in the payment structure and payment schemes for providers, the technology needed to delivery VBC, and patient ownership of care. Legacy healthcare systems are built from the ground up to provide services and care based on the fee-for-service model, including but not limited to the test ordering system, EMRs and financial systems. Converting these IT systems to accommodate and then support a VBC model will be time consuming and costly, with healthcare administrators left to balance the cost versus reward of the shift. In addition to legacy systems, new IT infrastructures will be needed to provision new care delivery technology such as telehealth services and at home testing. These will include not only new software systems for connecting providers and patients but also innovative remote test monitoring.

Value-Based Health Care Benefits

NEJM Catalyst (catalyst.nejm.org) © Massachusetts Medical Society

There are many tailwinds driving the shift to VBC, most recently Covid-19, however it would be shortsighted not to consider and properly weigh other factors that existed prior to the world as we know it today. Growing healthcare costs have been chronic problem for healthcare systems for some time, driven by the increase in aging population, chronic disease, and the current self-protective medicine approach. A 2013 article that studied physician data found "Physicians Foundation examined data on the leading key components and found that chronic disease conditions, life style – including obesity and addictions, administrative expenses, hospitals, pharmaceuticals, mandated insurance benefits, aging, end-of-life care, defensive medicine and health disparities have all had anywhere from a moderate to significant impact on rising overall health care costs"[2]
Given the driving factors it is clear a new healthcare model is needed and VBC seems to be the most viable.
There are several pilots in place in Europe at public and private healthcare systems to drive a shift towards VBC. One such example cited in the Phillips healthcare study is a Dutch network of 7 hospitals (Santeon) which instituted VBC and achieved reductions of nearly 30% in unnecessary inpatient stays and up to 74% in reoperation rates due to complications in breast cancer patients.[3]

The capturing of this new type of healthcare data will be critical to ensuring improved patient outcomes and the measuring the efficiency of the VBC model. Lastly, there is the end point of the care, the patient. The transition to VBC will require increased patient awareness about the need and necessity for preventative care, chronic condition management and a shift to better lifestyle choices. The empowering of the VBC model depends on the healthcare data which drives and informs providers and patients. The Phillips future index states the largest obstacles to digital health adoption are difficulties with data management, lack of interoperability between systems and lack of training on how to be utilize digital health technology.[3]

As those of us connected to the healthcare systems consider better ways to deliver or care responsibilities to patients VBC may be a system worth considering. There is an ever-growing need to drive down healthcare costs, increase efficiency and drive better patient outcomes, Value-Based Care may be the answer moving forward.

References:

1. https://catalyst.nejm.org/doi/full/10.1056/CAT.17.0558
2. Norbeck TB. Drivers of health care costs. A Physicians Foundation white paper - second of a three-part series. Mo Med. 2013;110(2):113–118. [PMC free article] [PubMed] [Google Scholar]
3. https://www.philips.com/c-dam/corporate/newscenter/global/future-health-index/report-pages/experience-transformation/2021/philips-future-health-index-2021-report-healthcare-leaders-look-beyond-the-crisis-global.pdf

What's in the news?

Olive Pomace Phenolic Compounds Stability and Safety Evaluation: From Raw Material to Future Ophthalmic Applications

Nowadays, increasing interest in olive pomace (OP) valorization aims to improve olive's industry sustainability. Interestingly, several studies propose a high-value application for OP extracts containing its main phenolic compounds, hydroxytyrosol and oleuropein, as therapy for ocular surface diseases. In this work, the stability and accessibility of OP total phenolic and flavonoid content, main representative compounds, and antioxidant activity were assessed under different pre-treatment conditions.

Among them, lyophilization and supercritical CO2 extraction were found to increase significantly most responses measured in the produced extracts.

Two selected extracts (CONV and OPT3) were obtained by different techniques (conventional and pressurized liquid extraction); Their aqueous solutions were characterized by HPLC-DAD-MS/MS. Additionally, their safety and stability were evaluated according to EMA requirements towards their approval as ophthalmic products: their genotoxic effect on ocular surface cells and their 6-months storage stability at 4 different temperature/moisture conditions (CPMP/ICH/2736/99), together with pure hydroxytyrosol and oleuropein solutions.

The concentration of hydroxytyrosol and oleuropein in pure or extract solutions was tracked, and possible degradation

products were putatively identified by HPLC-DAD-MS/MS. Hydroxytyrosol and oleuropein had different stability as standard or extract solutions, with oleuropein also showing different degradation profile. All compounds/extracts were safe for ophthalmic use at the concentrations tested.

Authors: Nikolaos Katsinas, Amalia Enríquez-de-Salamanca, Andreia Bento da Silva, Maria Rosário Bronze, Soraya Rodríguez-Rojo
Publication: Molecules. 2021 Oct 2;26(19):6002.doi: 10.3390/molecules26196002.

There's a Better Way.

When make-do methods aren't as effective, switch to one that is.

The TearLab® Osmolarity System is:

- **Established.** Trusted in over 20 Million eyes to date.
- **Empowering.** Accurate and objective dry eye disease diagnosis.
- **Essential.** Recognized by major societies in eye care.

To learn more, contact Louise Donohue on ldonohue@tearlab.com

TearLab®
OSMOLARITY SYSTEM

Empower your dry eye decisions with tear osmolarity

TearLab OSMOLARITY SYSTEM

www.tearlab.com

New algorithm (ASCRS) establish the essential nature of point-of-care testing for ocular surface disease diagnosis and treatment

Regardless of visual goals, be it comfortable contact lens wear, successful refractive surgery or premium cataract surgery, achieving optimal outcomes requires a healthy, optimised ocular surface.

The tear film is the first refractive surface of the eye - 70% of the total refractive power occurs at the tear film[1]. As such, ocular surface health is crucial for obtaining reliable refractive measurements. The accuracy of these measurements supports the success of surgical outcomes, and ultimately patients' satisfaction with their vision[2].

The American Society of Cataract and Refractive Surgeons (ASCRS) now recommends a specific ocular surface disease (OSD) algorithm to evaluate the ocular surface prior to surgery[1].

The new algorithm considers osmolarity and MMP-9 essential tests for the identification of Visually Significant Ocular Surface Disease (VS-OSD). VS-OSD adversely impacts surgical outcomes and should be addressed prior to surgery.

A Structured Approach

The ASCRS recommends that symptoms are captured through a validated questionnaire. Eye care providers can capture subjective information about patients' ocular surface discomfort, visual symptoms, and the overall impact of these conditions on day-to-day activities.

However, not all patients with VS-OSD present with symptoms, and additional testing should also be performed to avoid mis-or under-diagnosis. Therefore, the ASCRS regards osmolarity and MMP-9 tests as essential, particularly in evaluation of asymptomatic patients.

Objective data drives decision making

Performing objective tear testing has multiple benefits. Tests can be performed before the patients sees the clinician, thereby reducing chair time. Osmolarity provides value to rule-in AND to rule-out OSD. In addition, osmolarity helps direct an appropriate treatment plan, expands patient education and improves therapy compliance.

Conclusion

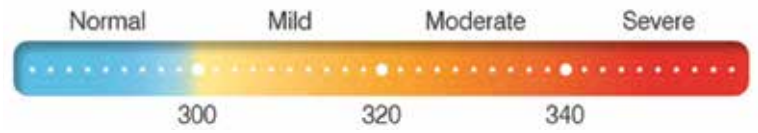
Use the ASCRS OSD algorithm to:

- incorporate a structure to identify VS-OSD
- improve diagnosis with essential point of care tests
- track therapy in weeks vs. months

... and thereby optimise surgical outcomes.

Osmolarity testing

Tear hyperosmolarity triggers a cascade of dry eye events that damage surface epithelial cells.[2] The TearLab Osmolarity System measures the osmolarity of tears with easy-to-interpret data, making the results informative whether normal or abnormal. An inter-eye difference of >8 mOsm/L or an elevated reading >300 mOsm/L is considered abnormal. Studies show that the toxicity of an abnormal tear osmolarity initiates cellular damage at levels >308 mOsm/L.[3] The TearLab Osmolarity Test provides a quick and simple method for



determining tear osmolarity using nanolitre volumes of tear fluid collected directly from the eyelid margin. This feature allows for tear collection in even the driest patients.

Benefits of Osmolarity testing

- ✓ Early, accurate DED detection
- ✓ Immediate, objective insight into ocular surface health
- ✓ Sets the stage for additional dry eye services
- ✓ Save chair time
- ✓ Efficient tracking of therapeutic response
- ✓ Enables you to have data-driven scientific conversations with your patients about their dry eye condition

Corneal Innervation in Health and Disease

By **Mr. Samer Hamada**

The cornea is the most richly innervated surface in the body making it 400 times more sensitive than the skin. It is densely supplied by unmyelinated sensory nerves (derived from the ophthalmic branch of the trigeminal nerve) and to a lesser extent by autonomic nerve fibres (arise from the superior cervical ganglion). Our knowledge about the complete corneal nerves architecture and functions remains very limited despite extensive laboratory investigations and research in the field. The interest in corneal nerves has accelerated in the recent years largely due to concerns about loss or disorganisation of corneal nerves after cornea laser vision correction. More recently, the role of corneal nerves dysfunction in the pathophysiology of dry eye disease is becoming widely discussed.

The use of in vivo confocal microscopy examination (IVCM) is revolutionary; however, it only allows a detailed examination of a small central area of the cornea, not of the entire cornea. Nerves were found to enter the corneal limbus from all quadrants in equal distribution moving towards the central cornea. They travel anteriorly and pass-through Bowman's membrane forming terminal bulbs from which the sub-basal nerves originate, which in turn innervates the corneal epithelium. There is no preferential concentration of nerve bundles in the 3 and 9 o'clock meridians. In clinical practice moving the LASIK flap hing should therefore, opposite to what is believed, make no difference to the degree to corneal nerve damage or speed of nerve recovery.

The corneal nerves have sensory and reflex functions, but also have important trophic effects on the cornea and play a significant role in the maintenance of a healthy ocular surface through the stimulation of corneal wound healing after corneal injuries. Damage or dysfunction of the corneal sensory innervation produces a degenerative condition known as neurotrophic keratitis characterised by decreased epithelial thickness, varying degrees of epithelial degradation, decreased epithelial cell mitosis, and impaired wound healing after corneal injuries. Several experimental and clinical studies have shown that there is a bidirectional control of corneal epithelium proliferation: sensory neurotransmitters enhance epithelial cell mitosis, while sympathetic mediators, epinephrine and norepinephrine, decrease epithelial cell mitosis. Corneal pain sensation can be triggered by mechanical, thermal, or chemical stimulation.

Neurotrophic keratopathy is caused by damage to corneal nerves. The damage could be central, peripheral or both as in some congenital or systemic diseases.

Table 1: Causes of corneal denervation

Genetic	Central nervous system	Systemic	Ocular
Riley–Day syndrome (familial dysautonomia)	Neoplasm	Diabetes	Post-herpes infections (herpes simplex & herpes zoster)
Goldenhar–Gorlin syndrome	Aneurysms	Leprosy	Chemical and physical burns
Mobius syndrome	Stroke	Vitamin A deficiency	Abuse of topical anaesthetics
Familial corneal hypoestesia	Postneurosurgical procedures		Drug toxicity (timolol, betaxolol, Trifluridine, Sulfacetamide, Diclofenac sodium, Oleoresin capsicum pepper spray, Hydrogen sulfide)
Familial trigeminal anesthesia	Acoustic neuroma		Postsurgical or laser treatment (trauma of ciliary nerves)
Congenital insensitivity to pain with anhidrosis	Trigeminal neuralgia		Corneal incisions
	Other surgical injury to the trigeminal nerve		Chronic ocular surface injury or inflammation
			Contact lens wear
			Orbital neoplasia
			Corneal dystrophies (lattice, granular)

Corneal Innervation after surgical interventions:

Corneal nerves are routinely damaged following modern refractive surgery. It has been reported that procedures like radial keratotomy, photorefractive keratectomy, and Laser In situ Keratomileusis (LASIK) produce localised injury of thick stromal nerves and the sub-basal plexus resulting in transient mild to severe epithelial changes with neurotrophic and/or dry eye features. Damaged corneal nerves may never restore its anatomical architecture or physiological functions. In one long term follow-up study, there has been incomplete regeneration of the sub-basal nerves for up to 5 years following LASIK. Furthermore, there is a significant reduction in the sub-basal nerve diameter and density following LASEK and these do not recover to pre-operative states even 6 months after surgery.

Total scissoring of corneal nerves such as after penetrating keratoplasty could lead to absence of sub-basal nerves for at least 12 months after the surgery and could take 2 years before it becomes detectable. However, stromal nerves in the central cornea could be observed as 7 months postoperatively. The indication for keratoplasty could affect the recovery of corneal nerves. For example, in keratoconus patients, the recovery of stromal corneal nerves is much faster than other indications. It has been proved that central corneal innervation is mainly affected in keratoconus, while the peripheral nerves remain intact. As a result, the regeneration of nerves after corneal transplantation will be faster in keratoconus cases.

There is no direct association between the sub-basal nerve regeneration and central corneal sensitivity, and this might be due to the inability of the current confocal microscopes to detect tiny regenerating nerves that are responsible for restoration of the corneal sensitivity after surgery or that there is substantial redundancy in corneal innervation and the density of nerves required for normal sensitivity is much less that what the cornea is endowed with. It could also mean that the present techniques to measure corneal sensitivity (Cochet Bonnett) are crude and are unable to pick up subtle loss of sensations.

Corneal Innervation in common eye diseases:

One of the most common causes of neurotrophic keratopathy is acute and chronic herpes simplex virus keratitis (HSVK). A profound reduction in the sub-basal nerve plexus is found and strongly correlate with loss of corneal sensation in those cases. Unexpectedly, the contralateral, clinically unaffected eye might also show a diminishment of sub-basal nerve plexus, suggesting bilateral nerve alteration in a clinically unilateral disease.

It is well known that Sjogren's syndrome is associated with increased prevalence of peripheral and cranial neuropathy. In addition, a relation has been suggested between corneal innervation and aqueous tear production. The results were inconsistent about the effect of dry eye on sub-basal nerve density. While some studies reported a significantly reduced sub- basal nerve density in both Sjogren's and non-Sjogren's syndrome dry eyes disease compared to normal, others observed no significant differences in the density. One of the interesting findings on confocal microscopy (IVCM) was sub-basal nerve tortuosity in Sjogren`s syndrome which was believed to be secondary to the release of nerve growth factors in response to the inflammatory process.

Although associated with reduced corneal sensation, long term contact lens wear does not appear to affect the morphology, distribution, or number of corneal nerves. Non-structural functional nerve changes have been attributed to the decreased corneal sensitivity in these subjects.

Mapping of the sub-basal nerve plexus in keratoconus has revealed abnormal architecture with a tortuous network of nerve fibre bundles at the apex of the cone; many of these bundles formed closed loops. At the topographic base of the cone, nerve fibre bundles appeared to follow the contour of the base, with many of the bundles running concentrically in this region.

OptiLight

A Bright Solution for Dry Eyes

The First and Only IPL FDA Approved for Dry Eye Management

OptiLight by Lumenis, offers you a new way to address dry eye disease with an effective and safe in-office treatment. OptiLight uses our patented Optimal Pulse Technology (OPT™) and OPT™ hand-piece for targeted, precise, controlled, light-based dry eye therapy.

Elevate your practice and patient care with OptiLight!

Lumenis®
Energy to Healthcare

www.lumenis.com/OptiLight

A patient's perspective – Dry Eyes Forever

By **Andrew Northover**

I've always had dry eye for as long as I can remember

I've always had dry eye for as long as I can remember. Even as a child. Of course, back then I just had "sensitive eyes" which would go red and itchy at the slightest change in environment. Dry dusty weather, windy weather, and I particularly remember after swimming when it was just the chlorine which was to blame.

As a teenager and in my twenties, I struggled with my "sensitive eyes" by trying to manage my environment as I had worked out myself when I would get problems. Smokey environments for example such as in pubs or nightclubs (yes back in the day people smoked inside!)

I was finally diagnosed with Dry Eye in my thirties almost by accident.

I was diagnosed with Rheumatoid Arthritis (RA) by the NHS after many years playing sports and putting the aches and pains down to wear and tear. During a consultation with my rheumatologist, I happened to mention my sensitive and sore eyes. I explained that is just how they have always been, and I just got on with life. The rheumatologist wasn't so dismissive of my long-term eye problem. He made a couple of phone calls and sent me straight down to the ophthalmology department.

Dry Eye diagnosis but no treatment

I went off the ophthalmology department thinking that it was a waste of time as my vision had always been perfect. I assumed ophthalmologists just checked your eyesight and gave you glasses to wear if you couldn't read one of those charts with letters on that you always remember seeing from childhood. (Snellen Chart).

He consultant ophthalmologist sat me down at one of his machines to take a look at my eyes. He then asked me a few questions about my eye problem. I described how they are often sore and itchy and that they were sensitive to changes in the environment.

The ophthalmologist declared, after asking me a few further questions, that I probably suffer from Dry Eye. Yes, I though to myself, I know that I've had it for over 20 years, but I call it "sensitive eyes". The ophthalmologist sent me back to rheumatology with a leaflet entitled "NHS Self-Care For Dry Eyes" which focussed on "good eyelid hygiene and avoidance of environmental factors".

I was disappointed as I had learnt nothing other that my "sensitive eyes" was actually a well known but poorly understood condition referred to by experts as "Dry Eye".

Eye drops, lots of eye drops

It wasn't until ten years after this diagnosis of Dry Eye that I tried my first eye drops. I had up until that point been wetting my eyes with fresh water as I found out that helped a lot. A friend just happened to mention to me that there were eye drops you could buy that would do the same thing. The eye drops were of course much more convenient than finding the nearest sink and splashing my face. That's when my eye drop journey started.

Eye Drops, the good the bad and the ugly

There are eye drops with all kinds of ingredients in them. They all claim to be good for your eyes and the next best thing for Dry Eye care. There are drops with Hyaluronate, drops with Hypromellose, drops with Glycerine amongst other ingredients. They all do the same thing and that is to wet the surface of the eye. There are so many drops it's quite a task to find one which is right for you.

Then there are the bad drops. The ones which contain preservatives and the ones claiming they have no preservatives but when you read the ingredients preservatives are still present. The real bad drops contain things like Benzalkonium Chloride, the worst preservative currently in use in dry eye products. These preservatives are damaging

to the eye surface especially if you use them daily all the time.

Then there are the just plain ugly drops which contain vasoconstrictors and must be avoided when trying to treat your dry eye problem. The "work" to remove the redness from your eyes by constricting the blood vessels. So, your eyes may look whiter but will feel a good deal worse.

Increasing awareness of the Dry Eye condition

After many years of trying different drops, I became aware of the increasing attention given to the problem of dry eye. This awareness increased especially during the recent lockdowns when many more people were working from home and staring at their computer screens all day long. This screen fatigue, as it is referred to, can make dry eye problems much worse. It was then that I began to notice the new and novel methods of treating dry eye.

Intense Pulse Light (IPL) treatment for dry eye

Some of these new treatments involve things like blocking the tear ducts to cause your tears to stay on the eye surface longer, or treatments to unblock the oil glands which send lubricating oils to the eye surface. I decided I needed to try something new as whilst the dry eye drops were giving me a certain amount of relief, I really needed to try another solution to see if I could get better results.

My options on the NHS were quite limited and I had been reading up about special light treatments for dry eye and this wasn't available on the NHS. These treatments are called Intense Pulsed Light treatments or IPL for short. So, I decided I would go private and find an ophthalmologist who offered this type of treatment.

The treatments I have been given so far are completely painless and take only about 5 mins per eye. I have had 3 treatments so far spaced 2 weeks apart. I can say for certain that I have already a much-reduced dry eye condition. My ophthalmologist says after the 4th treatment I may only need to be treated once per year.

Conclusion

Well, I suppose there is no conclusion as my dry journey continues but I can say that awareness of the condition has greatly increased. It is also evident that the problem of dry eye is much more prevalent today than it was when I first began to notice my symptoms. This is in part due to our "modern" way of living with air-conditioned homes or offices and staring at screens all day long. On the plus side though is that ophthalmologists seem to be taking the dry eye condition much more seriously these days and are making progress with treatments and services.

MCLOSA & OSI

The Medical Contact lens & Ocular Surface Association

Joint **Virtual** Symposium 26th November 2021

Join Medical Contact Lens & Ocular Surface Association (MCLOSA) and Ocular Surface Insight (OSI) for their first joint symposium.

This exciting virtual event will be moderated by OSI Editor-in-Chief Mr Samer Hamada.

Panel Session 1 – Ocular surface protection! - A superhero's approach	
09:00-09:15	Samer Hamada *Early detection of ocular surface failure*
09:15-09.30	David Lockington *Corneal melt*
09:30-09:45	Gok Ratnarajan *As seen by a glaucoma surgeon*
09:45-10:00	Raman Malhotra *As seen by an oculoplastic surgeon*
10:00-10:05	Discussion
10:05-10:15	Commercial Q & A
10:15-10:30	Colin Williams *Chronic Disease- the psychological effects.* *Hands-on advice on first line practical tips how to calm anxious patients.*
10:30-11:00	Andrena McElvanney *Therapeutic contact lenses – what is new?*
11:00-11:30	Prof Francisco Figueiredo *MCLOSA Kersley lecture*
Panel Session 2 - Environmental factors effect on the ocular surface	
11:30-11:45	Arthur Cummings *Work, hobbies and habits*
11:45-12:00	Rohit Shetty *Hormones, immune system and nerves*
12:00-12:15	Brian Tompkins *Contact lenses - Latest evidence*
12:15-12:30	Amy Gallant-Sullivan
12:30-12:45	Sabrina Shah-Desai *Cosmetics and Cosmetic Surgery (Beauty and the Beast)*
12:45-13:00	Discussion
13:00-13:40	Lunch – Commercial Presentation
13:40-14:10	Fiona Carley *Contact lens induced limbal stem cell deficiency*
Panel Session 3 - Sjogren's disease: How they see it?	
14:10-14:40	Rohit Shetty *An Ophthalmologist view*
14:40-14:55	Alaa Aldaadaa *An Oral Surgeons view*
14:55-15:05	Discussion
15:05-15:15	Commercial Q & A
15:15-15:45	Parwez Hossein *Contact lens related Microbial keratitis*
15:45-16:15	Sophie Jones *Management of refractive surprise*
16:15-16:20	Samer Hamada *Dry eye master class - why and who it is for?*
16.20-16.50	MCLOSA AGM

Santen *A Clear Vision For Life™*

DRY EYE FRUSTRATION?

NOW THERE IS A NEW SOLUTION FOR HOLDING ON TO HYDRATION

Acts like real tears on all 3 layers[1,2]

Cationorm®

POSITIVE ATTRACTION

PRESERVATIVE FREE

References: 1. Robert P et al. Eur J Ophthalmol 2016;26(6):546–55. 2. Lallemand F et al. J Drug Deliv 2012:604204.

All medical device adverse incidents (whether safety or quality related) should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store. Adverse incidents should also be reported to Santen UK Limited (Email: medinfo@santen.co.uk or telephone: 0345 075 4863).

PP-CATION-UK-0026; Date of Preparation: June 2020

Artificial Intelligence Grading and Telemedicine in Practice

By **Brian Tompkins**

High-quality examination techniques and the best possible prescribing are obviously key components to any eye care professional's long-term success but the importance of good communication to patients should never be underestimated.

How can we expect any patient to be invested in their eye health if they don't fully understand their condition, how to best manage it and the implications of what may happen if they let things slip?

Talking regularly to patients is essential and the way we talk to them makes a big difference. Clear and concise language, outlining their eye health in a way they understand, is so important and it's something we take particular pride in as a practice.

But it's not just about language. It's also about the method of communication.

Face-to-face conversations are ideal, you can gauge a patient's reaction and understanding from their body language and reinforce any points you feel may not have sunk in straight away.

Telephone calls are useful for any follow-ups while emails and text messages can serve a purpose for written details and 'bulletin-style' messages or reminders.

For several years now we have used a combination of all the above to ensure our patient communications are delivered in the right way, at the right time.

As with pretty much everything in life, the pandemic changed things. Our tried and trusted methods were thrown into the air, with face-to-face appointments cancelled and our preferred method of talking to our patients disappeared overnight.

Thankfully, modern technology afforded us a viable alternative and allowed us to enhance our day-to-day practices while engaging patients in ways we'd never been able to before.

AOS is an anterior imaging software platform that helps eye care professionals deliver better patient experiences both in and out of practice.

In practice, it has a suite of image enhancing and grading tools that can be used with or without a slit lamp. Out of practice, the AOS Vision mobile app allow patients to safely and quickly capture and transfer images and video of their eyes and the tele-optometry function makes video calls between us and our patients quick, easy and secure.

We use it to triage new patients, particularly those with complex issues, prior to their appointment. It gives us an idea of what we can expect to find and puts us one step ahead.

The imaging tools enable accurate and objective bulbar and lid redness grading and also give you an exact punctuate count on fluorescein images. You can also annotate images and use the ruler for accurate measurements.

A video component and new toric lens marker tool have recently been added that we are looking forward to using as part of our contact lens management programme.

We use it primarily for management of our contact lens and dry eye patients.

Capturing base line images when a new fit is conducted is vital and if you are able to add objective, accurate grading and generate a GDPR-compliant patient report to this then patient compliance is taken to the next level.

The grading we do also plays an important part in determining how suitable the patient is for lens wear – if they have issues due to bulbar or lid redness for example, they have a better understanding of their position if they can see images of their own eyes and we have attributed a 'score' to their pathology.

This uniform, independent grading gives consistent across multiple practitioners and can determine if patients require pre-CL fitting management, or assess the extent of their dryness, irritation or allergy to increase the rate of successful fits.

We use the AOS video call function to assist with the first application and removal of new fits and conduct remote video calls with existing wearers to check in with them and ensure they are still comfortable in their lenses. Our dropout rates are minimal because of the protocol we follow.

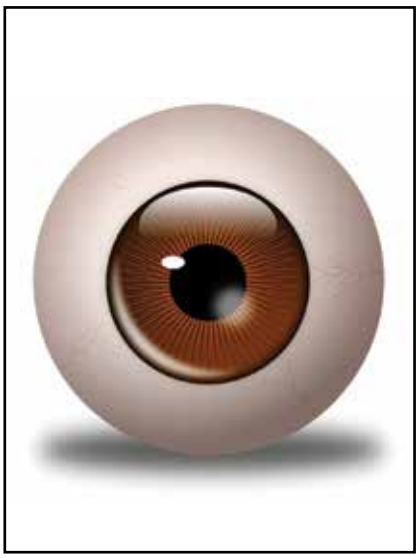
Care plans are a core part of our business model and being able to offer patients access to an app where they can take a picture or video and send it through to us whenever they have a problem has been great – it's another reason for them to sign up to a monthly subscription with us for all their eye care needs.

Patients love being able to see images of their eyes and we have seen the benefits of giving them a grade or 'score' they can work towards improving, while also generating reports for third party referrals. They have also responded really well to the remote video calls and are hugely appreciative of the time we are saving them.

It's all part of the patient theatre we aim to create and gives them something to tell their friends and family about. These changes were already in the pipeline but COVID-19 has fast-tracked them into everyday practice. What was possibly five years away is here now, and we are fully embracing it. It's here, and it's here to stay.

What's in the news?

Optimizing the ocular surface prior to cataract surgery



Ocular surface disease can significantly impact the outcomes of cataract surgery. Recent studies have examined the efficacy of several new dry eye disease (DED) therapies, the extent to which epithelial debridement affects keratometric measurements in epithelial basement membrane dystrophy (EBMD) and Salzmann nodular degeneration (SND), and the predictability of refractive error following combined pterygium and cataract removal.

This review aims to incorporate these newer studies in updating and further emphasizing the need for careful management and optimization of common ocular surface conditions prior to cataract surgery.

Common ocular surface conditions such as DED, EBMD, SND, and pterygium can cause significant irregular astigmatism and higher-order aberrations. Their resolution can substantially alter biometry measurements in preparation for cataract surgery, affecting the final visual outcome. Newer therapies for DED, such as topical lifitegrast and thermal pulsation treatment, can aid in this optimization process. If superficial keratectomy or excisions of lesions on the ocular surface are performed, sufficient healing time is needed to allow the ocular surface to reach stability prior to biometry measurements.

Authors: Xu He, Andy S Huang, Bennie H Jeng
Publication: Publication: Curr Opin Ophthalmol. 2021 Oct 25.doi: 10.1097/ICU.0000000000000814.

eyezin® XL
Sodium hyaluronate

THE DRY, THE ITCHY AND THE IRRITATED

THERE'S A NEW SHERIFF IN TOWN, READY TO FIGHT DRY EYES DAY AND NIGHT.

★★★★★ "Brilliant" Anne Bell

★★★★★ "Worked wonders" MJ Engle

★★★★★ "The best" Cp Chester

★★★★★ "Wow! Happy eyes" Aurelia

PRESERVATIVE FREE MULTIDOSE GEL DROPS DESIGNED TO PROTECT, HYDRATE AND RESTORE.

BRINGING LAW AND ORDER TO DRY EYES.

Intensive relief that lasts from sunrise to sunset.

Eyezin XL (Sodium Hyaluronate) Product Information

Presentation: 10ml bottle. **Main Ingredients:** Sodium hyaluronate, L-carnitine, Zinc chloride, Sodium Phosphate dibasic, Sodium phosphate monobasic, Sodium chloride, Virgin castor oil, Tween 80, Water. **Indications:** For the relief of medium to severe dry eye and to provide protection against the external environment. Also suitable for use overnight. **Dosage and method of use:** Instill 1 or 2 drops in the affected eye as required. **Warnings:** This product is not normally intended for continuous use for more than 30 days; if the symptoms persist consult your doctor. After administration, in rare cases, a slight temporary blurring of vision may occur due to the viscosity of the solution. If you wear soft contact lenses, remove them before applying product and do not replace the lenses for at least 15 minutes. After opening, use within 8 weeks. Consult doctor or pharmacist before using if pregnant or breast-feeding. **Contraindications:** Known hypersensitivity to ingredients. This product contains phosphates. It is not recommended for use in patients with significant damage to their corneal surface (such as pronounced erosion or corneal ulcer) as rare cases of calcification of the cornea during use of phosphate-containing eye drops have been reported in such patients. **Legal Category:** Class IIa Medical Device. **Cost:** £6.99 **Legal Manufacturer:** NTC S.r.l. Via Luigi Razza, 3-20124-Milan, Italy. **Distributer:** Aspire Pharma Ltd, Unit 4, Rotherbrook Court, Bedford Road, Petersfield, Hampshire, GU32 3QG, UK. **Date last reviewed:** September 2020. **Version number:** 1010448671 v 3.0

Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard. Adverse events should also be reported to Aspire Pharma Ltd on 01730 231148.

ASPIRE PHARMA

aspirepharma.co.uk

1010448123-4 v 1.0 June 2021

Effects of 0.01% Atropine Instillation Assessed Using Swept-Source Anterior Segment Optical Coherence Tomography

By **Tadahiro Mitsukawa, Yumi Suzuki * , Yosuke Momota, Shun Suzuki and Masakazu Yamada**

Department of Ophthalmology, Kyorin University School of Medicine, 6-20-2 Shinkawa, Mitaka, Tokyo 181-8611, Japan; mitsukawa@ks.kyorin-u.ac.jp (T.M.); momota@ks.kyorin-u.ac.jp (Y.M.); suzuki-s@ks.kyorin-u.ac.jp (S.S.); yamadamasakazu@ks.kyorin-u.ac.jp (M.Y.)
* Correspondence: yumis@ks.kyorin-u.ac.jp

1. Introduction

Myopia is the leading cause of preventable visual impairment in childhood and adolescence [1,2]. An increasing prevalence of myopia has been reported in East and Southeast Asia, including China, Korea, and Japan [1–6]. In addition, the number of patients with myopia has increased in the United States and Europe, mainly among school-aged children and young adults [2,7,8]. As a result, the global prevalence of myopia, including pathologic myopia, is increasing, and has gained prominent attention as a social health problem. Complications resulting from myopia can incur large social and economic costs [9]. Therefore, the prevention of myopia progression has become increasingly important.

Myopia is generally present at the school-going age in patients. However, with the use of appropriate treatment modalities targeting children with myopia, it is possible to reduce the lifetime risk of retinal complications by reducing the severity of final myopia [10]. Several methods for the prevention of myopia progression have been reported to date, and they are broadly classified into nonpharmacological and pharmacological treatments. The former includes optical approaches such as the use of special spectacles, contact lenses, and orthokeratology [11–15]. The latter relies on the use of atropine eye drops, which are an established pharmacotherapy for the prevention of myopia progression [16–18].

Owing to its antimuscarinic action, atropine has long been used in ophthalmology in the form of 1% atropine eye drops for accommodation paralysis, and as an anti- inflammatory agent for conditions such as keratitis and iritis [19]. A study in 2006, Atropine for the Treatment of Myopia (ATOM-1), reported that the use of 1% atropine was effective in halting the progression of myopia [16]. However, over a 2 year period, the researchers observed photophobia resulting from dilated pupils and impaired near vision due to accommodation paralysis in eyes treated with 1% atropine. These side effects greatly interfered with the daily lives of patients. In addition to the rapid progression of myopia after discontinuation of the eye drops, a 1% concentration was considered inappropriate for myopia control [20]. As a result of this, that same research group subsequently conducted a study using various low-concentration atropine treatments. In 2012, they reported the results of a clinical study that assessed the inhibitory effect of atropine on myopia progression (ATOM-2), using 0.5%, 0.1%, and 0.01% atropine eye drops [17]. In their survey of the prevention of 2 year myopia progression, the researchers found that the group that received the lowest concentration of atropine (0.01%) achieved approximately half the inhibitory effect of the placebo group (–0.49 diopters (D) compared with –1.20 D). Furthermore, the instillation of 0.01% atropine resulted in minimal adverse reactions when compared with the instillation of 0.1% and 0.5% atropine [17]. Consequently, the use of low-concentration atropine to reduce myopia progression has garnered attention because of its limited effect on visual function. However, in the ATOM-2 study, Chia et al. [17] reported that a small proportion (6%) of the patients required combined photochromatic progressive glasses because they developed impaired near vision and photophobia. In a study of the use of low-concentration atropine for preventing myopia progression, Yam et al. [18] assessed patients using a visual function questionnaire and found that atropine instillation had no effect on general vision, near vision activities, social functioning, or color vision. Although the instillation of 0.01% atropine eye drops only has a subtle effect on the pupil diameter and accommodative amplitude, concerns remain regarding the undesirable effects of atropine on patients' daily life [17].

Nonetheless, there are limited data regarding the short-term effects of low-concentration atropine instillation on pupil diameter and accommodative function in young adult sub- jects [21]. In our previous study, we successfully analyzed ocular biometric components (OBCs), including changes in the crystalline lens during accommodation, and the effects of cycloplegics, using a commercially available anterior segment optical coherence tomography (AS-OCT) system [22]. In recent years, AS-OCT has been used for in vivo studies of ocular lens behaviour during accommodation. A newly developed swept-source AS-OCT system (CASIA 2, Tomey Corp., Nagoya, Japan) has enabled detailed biometry measurements to be obtained from the corneal surface to the posterior surface of the lens by elongating the range of the imaging depth and increasing the sensitivity [23,24]. In the present study, we used the AS-OCT system to quantitatively evaluate the effects of 0.01% atropine eye drops on OBCs in the anterior segment of the eye.

The current study aims to determine how the instillation of 0.01% atropine produces morphological changes in the eye by assessing ocular biometric components (OBCs) before and after instillation, using anterior-segment optical coherence tomography.

2. Subjects and Methods

2.1. Participants

This study followed the guidelines outlined in the Declaration of Helsinki from the World Medical Association. All participants received a full explanation of the procedures and they provided written informed consent before they agreed to participate in the study. The study protocol was approved by the Institutional Review Board of Kyorin University School of Medicine (Project H30-099).

In this study, we examined young adults rather than children, as low-concentration atropine eyedrops for myopia have not been approved for children in Japan.

The study participants included 17 healthy volunteers (10 men and 7 women) aged 24–35 years (mean ± standard deviation: 28.9 ± 3.6 years). None of the participants had a history of eye disease, except for refractive errors, and all had a best-corrected visual acuity of 20/20 or better. The exclusion criteria were a history of any ocular disease, ophthalmic surgery, or laser treatment. We also excluded participants who were taking systemic medications that could affect accommodation.

We examined each participant's noncycloplegic refraction using an ARK-1 autore- fractor (NIDEK Co. Ltd., Gamagori, Japan). We considered the effect that the degree of refractive error would give to accommodation factors, as 17 participants had refractive errors from approximately -11 D to 0 D [25]. However, in this study, to ensure partici- pants' ability to accommodate 5 D or greater, we also examined the accommodation of the participants using the ARK-1 autorefractor.

2.2. Procedures and Assessments

We examined both eyes of all participants using the CASIA 2 swept-source AS-OCT system. The AS-OCT device has a swept-source laser that operates at a central wavelength of 1310 nm and a scan rate of 50,000 A-scans per second. The maximum imaging area is 16.0 mm × 16.0 mm, and the maximum imaging depth is 11.0 mm. This device enables simultaneous biometry measurements to be obtained for all anterior segment structures, including the cornea, anterior chamber, and crystalline lens.

All OCT images were obtained in a dimly lit examination room. During the mea- surements, the participants were instructed to fixate on the coaxial accommodative target image present in the OCT device. The negative or positive lens was set to compensate for the participant's spherical ametropia for near-equivalent spherical refractive correction. Next, we added a −5.0 D lens to stimulate physiological accommodation using an optical system in the OCT system. The active eye tracker of the OCT system was centered on the participant's eye. Two experienced operators (M.Y. and S.S.) collected all images.

Measurements were performed with and without a single instillation of 0.01% atropine eye drops. To prepare the 0.01% atropine eye drops, commercial 1% atropine sulfate hydrate (Nitten ATROPINE Ophthalmic Solution 1%; Nitten Pharmaceutical Co. Ltd., Nagoya, Japan) was diluted with saline. OCT images of the eye were obtained before instillation, and at 1, 24, and 48 h after instillation. The OBCs measured using AS-OCT included pupil diameter, anterior chamber depth (ACD), lens thickness (LT), and the horizontal radii of the lens' anterior curvature (LAC) and lens' posterior surface curvature (LPC). The boundaries of both the cornea and lens were outlined for anterior segment biometry. The positioning of the anterior and posterior surfaces of the lens on the horizontal meridian was traced, and the radius of the crystalline lens was determined using measurements that permitted circular fitting to the anterior and posterior lens surfaces.

The participants' accommodative amplitude was measured using the ARK-1 autore- fractor before instillation, and at 1, 24, and 48 h after instillation of the 0.01% atropine eye drops. Objective measurement of accommodation was performed with the participant focus- ing on a target that moved to a near point from a distance. Additionally, we conducted the measurement of participants' axial length using an optical axial length measuring device (OPTICAL BIOMETER OA-2000, Tomey Corp., Nagoya, Japan).

The participants were also instructed to answer questionnaires 1, 24, and 48 h after atropine administration about the difficulties they experienced with near vision and photo- phobia, separately, in which they rated their symptoms on a scale ranging from 0 (none) to 10 (inability to perform daily tasks).

2.3. Statistical Analysis

The Statistical Package for the Social Sciences version 27.0 for Windows (IBM Armonk, NY, USA) was used for all statistical analyses. The Mann–Whitney U test and Wilcoxon signed-rank test were used to perform comparisons. p-Values < 0.05 were considered to indicate statistical significance.

3. Results

3.1. Baseline Characteristics of the Participants

Table 1 presents the baseline biometric parameters of both eyes before the instillation of 0.01% atropine eye drops. The noncycloplegic refraction of the right eye ranged from −0.38 to −10.88 D, and that of the left eye ranged from +0.38 to −11.25 D; there was no significant difference in refraction between the right and left eyes ($p = 0.691$, Mann–Whitney U test). There was also no significant difference in accommodation between the right and left eyes, and both eyes were able to accommodate more than 5 D. We did not find any significant differences in any baseline biometric parameters between the right and left eyes before the instillation of 0.01% atropine eye drops (Mann–Whitney U test). Therefore, we present the findings of only the right eyes.

Table 1. Baseline biometric parameters of both eyes before instillation of 0.01% atropine eye drops.

	Right Eye		Left Eye		*p*-Value *
	Median	IQR	Median	IQR	
Baseline biometric parameter					
Spherical equivalent (D)	−5.88	6.50	−5.37	6.94	0.69
Axial length (mm)	25.39	2.37	25.45	2.52	0.95
Accommodation amplitude (D)	6.48	1.49	6.53	1.07	0.95
Central corneal thickness (μm)	537	42	527	42	0.97
Anterior chamber depth (mm)	3.28	0.35	3.33	0.31	0.62
Pupil diameter (mm)	4.38	1.26	4.59	0.79	0.55
Lens thickness (mm)	3.61	0.25	3.61	0.27	0.96
Radius of the lens' anterior surface curvature (mm)	11.65	1.97	12.04	3.39	0.57
Radius of the lens' posterior surface curvature (mm)	5.73	0.60	5.81	0.67	0.86

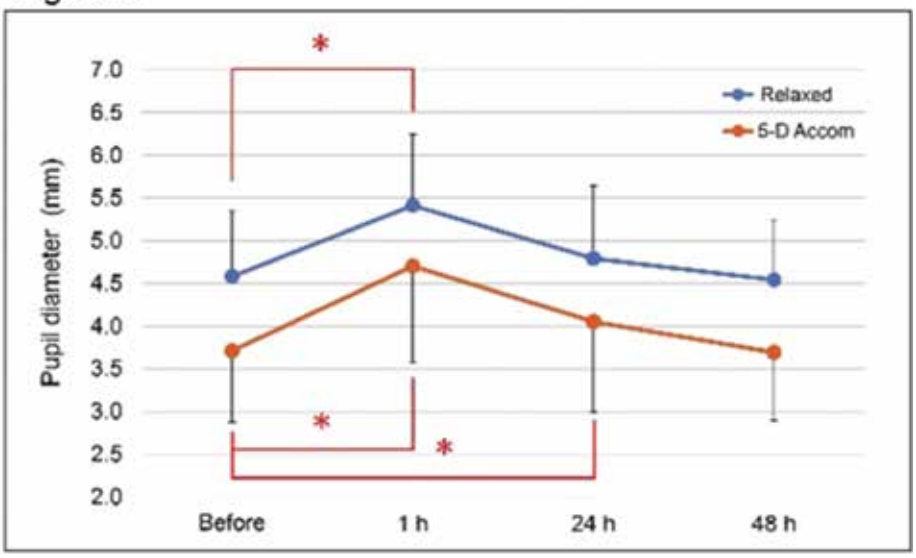
IQR, interquartile range; D, diopters; * Mann–Whitney U test.

3.2. Effects of 0.01% Atropine on Pupil Diameter

Figure 1a presents a comparison of pupil diameters in the relaxed state, and those with the 5 D accommodative stimulus, before and 1, 24, and 48 h after instillation of 0.01% atropine eye drops. The pupil diameter was significantly larger 1 h after atropine instillation than before the atropine instillation (from 4.58 ± 0.77 to 5.41 ± 0.83 mm) in the relaxed state ($p < 0.05$, Wilcoxon signed-rank test). With the 5 D accommodative stimulus, the pupil diameter at 1 and 24 h was significantly larger than that before atropine instillation (from 3.71 ± 0.84 mm to 4.70 ± 1.13 and 4.05 ± 1.06 mm, respectively, $p < 0.05$, Wilcoxon signed-rank test). In contrast, there was no significant difference in the pupil diameter 24 and 48 h after atropine instillation compared with that before atropine instillation in the relaxed state, or in the pupil diameter 48 h after atropine instillation compared to before atropine instillation with the 5 D accommodative stimulus.

However, with the 5 D accommodative stimulus, ACD at 1 h was significantly larger than that before the instillation (from 3.08 ± 0.16 mm to 3.10 ± 0.18 mm, $p < 0.05$). LPC at 1 and 24 h was significantly larger than that before the instillation (from 5.21 ± 0.43 mm to 5.36 ± 0.35 and 5.50 ± 0.50 mm, respectively, $p < 0.05$).

Figure-a



3.3. Effects of Atropine on Other Biometric Parameters Measured Using AS-OCT

Figure 1b–e shows a comparison of biometric parameters (ACD, LT, LAC, LPC) be- tween before and 1, 24, and 48 h after the instillation of 0.01% atropine eye drops in the relaxed state and with the 5 D accommodative stimulus. Other than pupil diameter, none of the biometric parameters showed changes in the relaxed state at any point in time when compared to before the instillation.

Figure-b

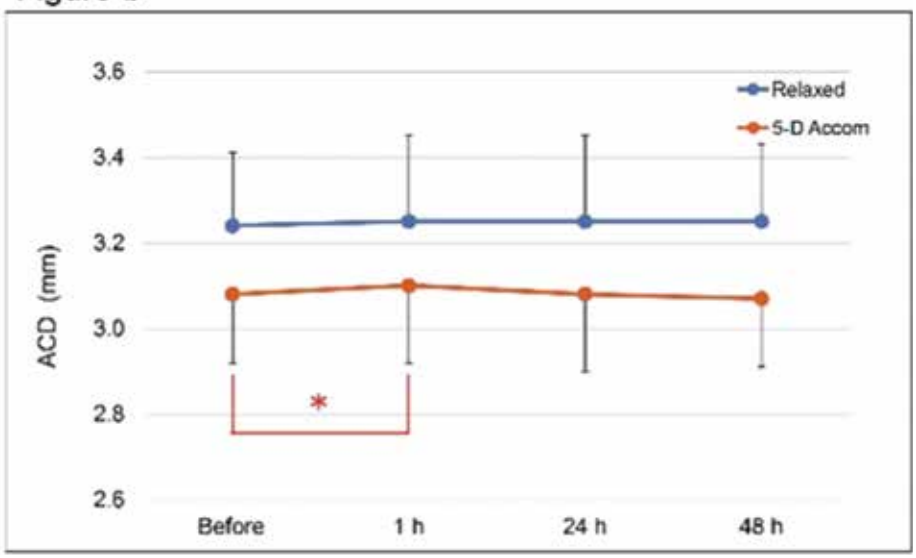


Figure-c

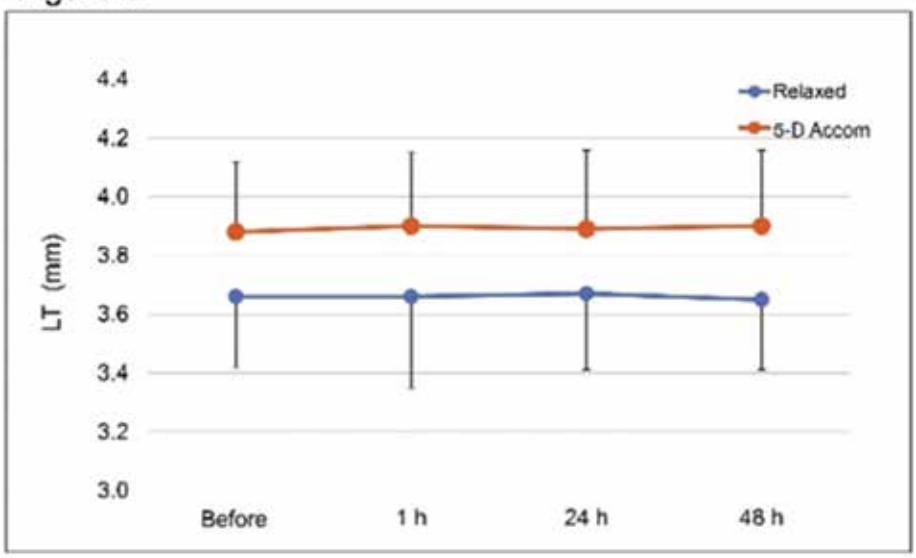


Figure-d

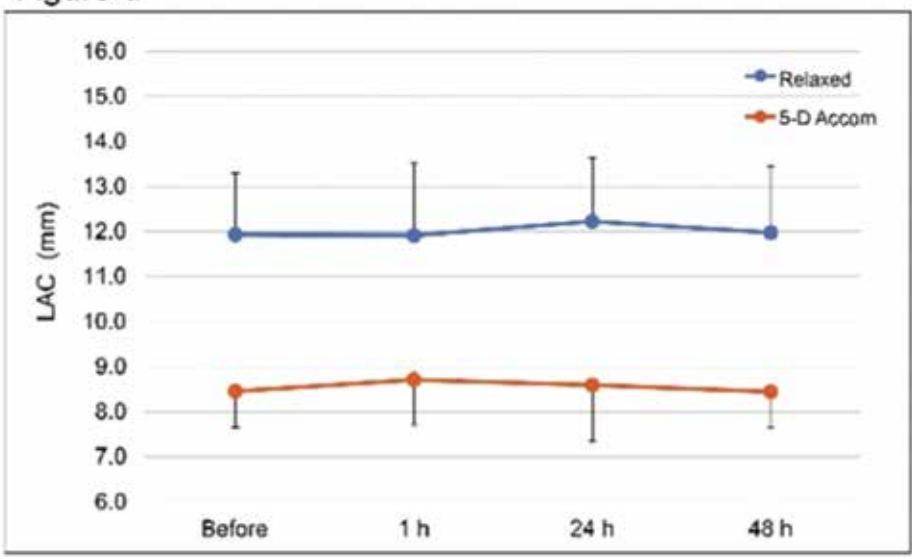
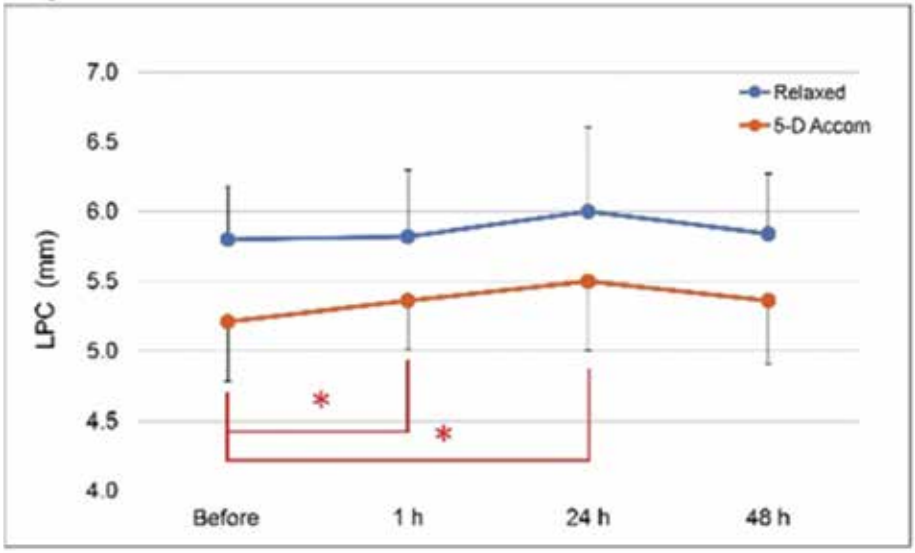


Figure-e



3.4. Effects of Atropine on Refraction, Accommodation Amplitude, and Subjective Symptoms

Table 2 shows the spherical equivalent 1, 24, and 48 h after the instillation of 0.01% atropine eye drops. There were no significant changes in the mean spherical equivalent from the values before the instillation ($p = 0.10$, $p = 0.86$, and $p = 0.55$, respectively).

Table 2 shows the accommodative amplitudes 1, 24, and 48 h after the instillation of 0.01% atropine eye drops. There were no significant changes in the mean accommodative amplitude at any point in time when compared with that before the instillation ($p = 0.76$, $p = 0.50$, and $p = 0.07$, respectively).

In terms of the two subjective symptoms, we found no serious adverse events re- lated to atropine. None of the participants reported photophobic sensation, although three participants reported mild difficulty with near vision (rated as 1/10 and 3/10 in one and two participants, respectively) 1 h after the atropine instillation.

Table 2. Change in refraction, accommodation amplitude, and subjective symptoms after the instillation of 0.01% atropine eye drops.

of the imaging depth and improving performance sensitivity [23,24]. Our prior study revealed an increase in LT and a decrease in ACD, LAC, and LPC with accommodation, which suggested that steepening and anterior movement of the lens during accommodation occurred. After the application of cycloplegics (cyclopentolate), there was a decrease in LT, which resulted in an equivalent increase in ACD [22]. Therefore, the CASIA 2 swept-source AS-OCT system could detect changes in OBCs during accommodation.

Accordingly, we used the same technique in this study to assess OBCs before and 1, 24, and 48 h after the instillation of 0.01% atropine. Although no participants reported photophobic sensations, 0.01% atropine had a minor effect on pupil diameter. While the pupil diameter increased significantly 1 h after instillation in a relaxed pupil state, it returned to the pre-instillation level at 24 h. The pupil diameters at 1 and 24 h were significantly larger with a 5 D accommodative stimulus, but they returned to the pre-instillation level at 48 h. Kaymak et al. [21] reported the short-term effects of 0.01% atropine instillation on pupil diameter and accommodation amplitude in 14 young adults. The reported pupil diameters before and 24 h after instillation were 3.3 ± 0.5 and 3.9 ± 0.8 mm, respectively, which indicated a significant increase ($p < 0.02$). Our study also confirmed that instillation of 0.01% atropine caused a slight and transient increase in pupil diameter.

Table 2. Change in refraction, accommodation amplitude, and subjective symptoms after the instillation of 0.01% atropine eye drops.

	Pre-Instillation		1 h after Ocular Instillation		24 h after Ocular Instillation		48 h after Ocular Instillation	
	Median	IQR	Median	IQR	Median	IQR	Median	IQR
Spherical equivalent (D)	−5.88	6.50	−6.25 (p, 0.10)	6.44	−6.13 (p, 0.86)	6.13	−6.13 (p, 0.55)	6.19
Accommodation amplitude (D)	6.48	1.49	6.49 (p, 0.76)	1.38	6.40 (p, 0.50)	1.09	6.59 (p, 0.07)	1.00
Subjective symptoms	0.00	0.00	0.00 (p, 0.11)	0.00	0.00	0.00	0.00	0.00

D, diopters; h, hour; p, p-value (Wilcoxon signed-rank test).

4. Discussion

Recent studies have shown that atropine effectively inhibits the progression of myopia and axial elongation [16–18,26,27]. Treatment guidelines for the inhibition of myopia progression, developed by Wu et al. [27], ranked low-concentration atropine eye drops as the key component to successful inhibition. The reported side effects of low-concentration atropine eye drops were limited to photophobia due to mydriasis and impaired near vision resulting from the impairment of accommodative amplitude [17,18,21]. Although these adverse events were rare and mild, objective measurements of changes in OBCs after 0.01% atropine instillation might be important. With this background in mind, we assessed the effects of low-concentration atropine eye drops on OBCs using AS-OCT. Our results revealed significant but subtle changes in OBCs.

In our previous study, we used a commercially available AS-OCT system (CASIA 2) to measure the OBCs, including lens parameters [22]. This system enables detailed biometric measurements to be obtained from the corneal surface to the posterior lens surface by increasing the range

In the relaxed state, none of the assessed OBCs (ACD, LT, LAC, and LPC), other than pupil diameter, showed significant changes at any of the assessed points in time compared to before the instillation. In contrast, with the 5 D accommodative stimulus, ACD 1 h and LPC 1 and 24 h after atropine instillation were significantly larger than those before the treatment ($p < 0.05$). However, there were no differences in either LT or LAC. Therefore, we confirmed that the cycloplegic effect following the instillation of 0.01% atropine eye drops was marginal. Our results suggest that measuring OBCs using the AS-OCT system is useful for detecting subtle changes that result from low-concentration atropine instillation. The AS-OCT results corresponded with the measurement of the accommodation amplitude. In our study, we found no decrease in the accommodation amplitude as a result of the instillation of 0.01% atropine. Only a few participants reported experiencing some difficulties with near vision 1 h after atropine instillation. Similarly, Kaymak et al. [21] reported no difference in the accommodation amplitude before and 24 h after 0.01% atropine instillation ($p = 0.06$).

Our study has some limitations. First, the participants were young adults rather than school-aged children, which could

have influenced the results. Low-concentration atropine instillation has been used to inhibit myopia progression in school- and preschool-aged children to address the trend of early-onset myopia and the increase in the number of preschool- and school-aged patients with myopia. In this respect, the ocular permeability of atropine and its pharmacokinetics might differ between children and adults. The accommodation amplitude also differs between school-aged children and young adults. Hence, as the participants were young adults aged 24-35 years, the results might not be directly applicable to school-aged children. Second, we observed only the short-term effects of a single instillation of 0.01% atropine. Our study showed that at a dose of 0.01% atropine, short-term effects included a slight increase in pupil diameter and minor accommodation paralysis. However, the long-term effects of low-concentration atropine instillation are not clear, and further studies are needed to clarify this issue. Third, similar to most other studies using AS-OCT, we were unable to analyze the entire lens shape through the pupil [28–33]. Because of the variability in the measurements and the asphericity of the lens, the curvature radius obtained by fitting the circular curve might not precisely express the shape of the lens. Finally, although the effect of atropine eye drops on vergence reactions should have been evaluated, we did not examine this in the present study.

In conclusion, we assessed the effects of 0.01% atropine eye drops by performing ocular biometry using the CASIA 2 AS-OCT system. Similar to the findings in previous reports, we did not observe significant photophobia or subjective difficulty in near vision. However, our measurements did suggest a change in the pupil diameter, ACD, and LPC, which are part of the assessed OBCs, which resulted from a subtle reduction in accommodation. In other words, morphologically, we were able to confirm an increase in the pupil diameter and a decrease in the accommodation response of OBCs with a 5 D accommodative stimulus following the instillation of 0.01% atropine. Moreover, we demonstrated that AS-OCT could evaluate subtle changes evoked by low concentration atropine administration.

Author Contributions: Conceptualization, Y.S. and M.Y.; methodology, T.M., Y.S. and M.Y.; software, Y.M.; validation, Y.S. and M.Y.; formal analysis, Y.S.; investigation, S.S. and Y.M.; resources, M.Y.; data curation, Y.S.; writing—original draft preparation, Y.S.; writing—review and editing, T.M., Y.S. and M.Y.; visualization, T.M. and Y.S.; supervision, M.Y.; project administration, T.M., Y.S. and M.Y.; funding acquisition, M.Y. All authors have read and agreed to the published version of the manuscript.

Funding: This research was supported by a grant from the Ministry of Health, Labour and Welfare, Japan (Grant number 19FA1010).

Institutional Review Board Statement: This study followed the guidelines outlined by the Declaration of Helsinki of the World Medical Association. The study protocol was approved by the Institutional Review Board of Kyorin University School of Medicine (project H30-099).

Informed Consent Statement: All participants received a full explanation of the procedures and provided written informed consent before agreeing to participate in the study.
Data Availability Statement: All data relevant to this study were included in the article.

Conflicts of Interest: The authors declare no conflict of interest. The funders had no role in the design of the study; in the collection, analysis, or interpretation of data; in the writing of the manuscript; or in the decision to publish the results.

References:

1. Morgan, I.; Ohno Matsui, K.; Saw, S. Myopia. Lancet 2012, 379, 1739–1748. [CrossRef]
2. Holden, B.A.; 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. [CrossRef]
3. Jung, S.; Lee, J.; Kakizaki, H.; Jee, D. Prevalence of myopia and its association with body stature and educational level in 19-year-old male conscripts in seoul, south korea. Investig. Ophthalmol. Vis. Sci. 2012, 53, 5579–5583. [CrossRef] [PubMed]
4. Lee, Y.; Lo, C.; Sheu, S.; Lin, J. What factors are associated with myopia in young adults? A survey study in taiwan military conscripts. Investig. Ophthalmol. Vis. Sci. 2013, 54, 1026–1033. [CrossRef]
5. Sun, J.; Zhou, J.; Zhao, P.; Lian, J.; Zhu, H.; Zhou, Y.; Sun, Y.; Wang, Y.; Zhao, L.; Wei, Y.; et al. High prevalence of myopia and high myopia in 5060 chinese university students in shanghai. Investig. Ophthalmol. Vis. Sci. 2012, 53, 7504–7509. [CrossRef] [PubMed]
6. Wu, J.F.; Bi, H.S.; Wang, S.M.; Hu, Y.Y.; Wu, H.; Sun, W.; Lu, T.L.; Wang, X.R.; Jonas, J.B. Refractive error, visual acuity and causes of vision loss in children in shandong, china. the shandong children eye study. PLoS ONE 2013, 8, e82763. [CrossRef] [PubMed]
7. Vitale, S.; Sperduto, R.D.; Ferris, F.L. Increased prevalence of myopia in the united states between 1971–1972 and 1999–2004. Arch. Ophthalmol. 2009, 127, 1632–1639. [CrossRef] [PubMed]
8. Dayan, Y.B.; Levin, A.; Morad, Y.; Grotto, I.; Ben-David, R.; Goldberg, A.; Onn, E.; Avni, I.; Levi, Y.; Benyamini, O.G. The changing prevalence of myopia in young adults: A 13-year series of population-based prevalence surveys. Investig. Ophthalmol. Vis. Sci. 2005, 46, 2760–2765. [CrossRef] [PubMed]
9. Rudnicka, A.R.; Kapetanakis, V.V.; Wathern, A.K.; Logan, N.S.; Gilmartin, B.; Whincup, P.H.; Cook, D.G.; Owen, C.G. Global variations and time trends in the prevalence of childhood myopia, a systematic review and quantitative meta-analysis: Implications for aetiology and early prevention. Br. J. Ophthalmol. 2016, 100, 882–890. [CrossRef]
10. Dolgin, E. The myopia boom. Nature 2015, 519, 276–278. [CrossRef]
11. Gwiazda, J.; Hyman, L.; Hussein, M.; Everett, D.; Norton, T.T.; Kurtz, D.; Leske, M.C.; Manny, R.; Marsh-Tootle, W.; Scheiman, M.; et al. A randomized clinical trial of progressive addition lenses versus single vision lenses on the progression of myopia in children. Investig. Ophthalmol. Vis. Sci. 2003, 44, 1492–1500. [CrossRef]
12. Zhu, Q.; Liu, Y.; Tighe, S.; Zhu, Y.; Su, X.; Lu, F.; Hu, M. Retardation of myopia progression by multifocal soft contact lenses. Int. J. Med. Sci. 2019, 16, 198–202. [CrossRef]
13. Hiraoka, T.; Sekine, Y.; Okamoto, F.; Mihashi, T.; Oshika, T. Safety and efficacy following 10-years of overnight orthokeratology for myopia control. Ophthalmic Physiol. Opt. 2018, 38, 281–289. [CrossRef]
14. VanderVeen, D.K.; Kraker, R.T.; Pineles, S.L.; Hutchinson, A.K.; Wilson, L.B.; Galvin, J.A.; Lambert, S.R. Use of orthokeratology for the prevention of myopic progression in children: A report by the american academy of ophthalmology. Ophthalmology 2019, 126, 623–636. [CrossRef] [PubMed]
15. Prousali, E.; Haidich, A.B.; Fontalis, A.; Ziakas, N.; Brazitikos, P.; Mataftsi, A. Efficacy and safety of interventions to control myopia progression in children: An overview of systematic reviews and meta-analyses. BMC Ophthalmol. 2019, 19, 106. [CrossRef] [PubMed]
16. Chua, W.H.; Balakrishnan, V.; Chan, Y.H.; Tong, L.; Ling, Y.; Quah, B.L.; Tan, D. Atropine for the treatment of childhood myopia. Ophthalmology 2006, 113, 2285–2291. [CrossRef] [PubMed]
17. Chia, A.; Chua, W.H.; Cheung, Y.B.; Wong, W.L.; Lingham, A.; Fong, A.; Tan, D. Atropine for the treatment of childhood myopia: Safety and efficacy of 0.5%, 0.1%, and 0.01% doses (atropine for the treatment of myopia 2). Ophthalmology 2012, 119, 347–354. [CrossRef]

18. Yam, J.C.; Jiang, Y.; Tang, S.M.; Law, A.K.; Chan, J.J.; Wong, E.; Ko, S.T.; Young, A.L.; Tham, C.C.; Chen, L.J.; et al. Lowconcentration atropine for myopia progression (LAMP) study: A randomized, double-blinded, placebo-controlled trial of 0.05%, 0.025%, and 0.01% atropine eye drops in myopia control. Ophthalmology 2019, 126, 113–124. [CrossRef]
19. Mauger, T.F.; Craig, E.L.; Havener, W.H. Havener's Ocular Pharmacology, 6th ed.; Mosby-Year Book: St. Louis, MI, USA, 1994; pp. 140–146.
20. Tong, L.; Huang, X.L.; Koh, A.L.; Zhang, X.; Tan, D.T.; Chua, W.H. Atropine for the treatment of childhood myopia: Effect on myopia progression after cessation of atropine. Ophthalmology 2009, 116, 572–579. [CrossRef] [PubMed]
21. Kaymak, H.; Fricke, A.; Mauritz, Y.; Löwinger, A.; Klabe, K.; Breyer, D.; Lagenbucher, A.; Seitz, B.; Schaeffel, F. Short-term effects of low-concentration atropine eye drops on pupil size and accommodation in young adult subjects. Graefes Arch. Clin. Exp. Ophthalmol. 2018, 256, 2211–2217. [CrossRef]
22. Mitsukawa, T.; Suzuki, Y.; Momota, Y.; Suzuki, S.; Yamada, M. Anterior segment biometry during accommodation and effects of cycloplegics by swept-source optical coherence tomography. Clin. Ophthalmol. 2020, 14, 1237–1243. [CrossRef]
23. Shoji, T.; Kato, N.; Ishikawa, S.; Ibuki, H.; Yamada, N.; Kimura, I.; Shinoda, K. In vivo crystalline lens measurements with novel swept-source optical coherent tomography: An investigation on variability of measurement. BMJ Open Ophthalmol. 2017, 1, e000058. [CrossRef]
24. Shoji, T.; Kato, N.; Ishikawa, S.; Ibuki, H.; Yamada, N.; Kimura, I.; Shinoda, K. Association between axial length and in vivo human crystalline lens biometry during accommodation: A swept-source optical coherence tomography study. Jpn. J. Ophthalmol. 2020, 64, 93–101. [CrossRef]
25. Millodot, M. The effect of refractive error on the accommodative response gradient: A summary and update. Ophthalmic Physiol.Opt. 2015, 35, 607–612. [CrossRef]
26. Li, F.; Yam, J. Low-concentration atropine eye drops for myopia progression. Asia-Pac. J. Ophthalmol. (Phila) 2019, 8, 360–365. [CrossRef]
27. Wu, P.C.; Chuang, M.N.; Choi, J.; Chen, H.; Wu, G.; Ohno-Matsui, K.; Jonas, J.B.; Cheung, C.M.G. Update in myopia and treatment strategy of atropine use in myopia control. Eye 2019, 33, 3–13. [CrossRef] [PubMed]
28. Du, C.; Shen, M.; Li, M.; Zhu, D.; Wang, M.R.; Wang, J. Anterior segment biometry during accommodation imaged with ultralong scan depth optical coherence tomography. Ophthalmology 2012, 119, 2479–2485. [CrossRef] [PubMed]
29. Gambra, E.; Ortiz, S.; Perez-Merino, P.; Gora, M.; Wojtkowski, M.; Marcos, S. Static and dynamic crystalline lens accommodation evaluated using quantitative 3-D OCT. Biomed. Opt. Express 2013, 4, 1595–1609. [CrossRef] [PubMed]
30. Zhong, J.; Tao, A.; Xu, Z.; Jiang, H.; Shao, Y.; Zhang, H.; Liu, C.; Wang, J. Whole eye axial biometry during accommodation using ultra-long scan depth optical coherence tomography. Am. J. Ophthalmol. 2014, 157, 1064–1069. [CrossRef] [PubMed]
31. Sun, Y.; Fan, S.; Zheng, H.; Dai, C.; Ren, Q.; Zhou, C. Noninvasive imaging and measurement of accommodation using dual-channel SD-OCT. Curr. Eye Res. 2014, 39, 611–619. [CrossRef]
32. Zhang, J.; Ni, Y.; Li, P.; Sun, W.; Liu, M.; Guo, D.; Du, C. Anterior segment biometry with phenylephrine and tropicamide during accommodation imaged with ultralong scan depth optical coherence tomography. J. Ophthalmol. 2019, 2019, 6827215. [CrossRef] [PubMed]
33. Neri, A.; Ruggeri, M.; Protti, A.; Leaci, R.; Gandolfi, S.A.; Macaluso, C. Dynamic imaging of accommodation by swept-source anterior segment optical coherence tomography. J. Cataract. Refract. Surg. 2015, 41, 501–510. [CrossRef] [PubMed]

What's in the news?

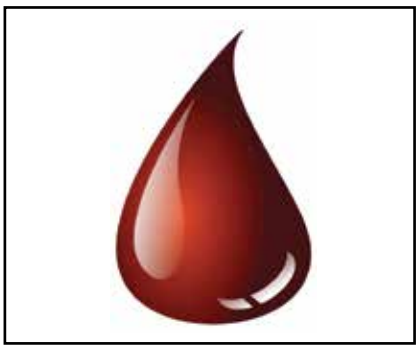
Patient-reported outcome measures for a large cohort of serum eye drops recipients in the UK

Serum eye drops (SED) are an important treatment for patients with chronic and severe ocular surface disease (OSD). Despite a long history of use, there is a paucity of information on patient-reported outcomes, particularly comparing autologous SED (Auto-SED) and allogeneic SED (Allo-SED). National Health Service Blood and Transplant is the national provider of SED service for patients in the UK.

The purpose was to evaluate and compare patient-reported outcome measures (PROMs) in patients receiving Auto-SED and Allo-SED for severe OSD.

PROMs were retrospectively collected from all new patients commencing treatment with Auto-SED and Allo-SED between January 2017 and September 2018, using the Ocular Surface Disease Index (OSDI) 12-item questionnaire. A linear mixed model was used to evaluate the change in OSDI scores between baseline and follow-up.

During the study period, 279 patients who received either Auto-SED (n = 71) or Allo-SED (n = 208) were included in the analysis. Baseline and follow-up OSDI scores were available for 161 of these (49 Auto-SED and 112 Allo-SED). There was a significant reduction in mean OSDI score for both Auto-SED (59.06-24.63, $p < 0.001$) and Allo-SED (64.21-34.37, $p < 0.001$). There was no significant difference between Auto-SED and Allo-SED patients in terms of the reduction in the OSDI score ($p = 0.27$).



The results showed that both Auto-SED and Allo-SED were associated with improvements in the quality of life of patients with chronic and severe OSD. Auto-SED and Allo-SED were equally effective in relieving the symptoms of OSD.

Authors: R J Lomas, A Chandrasekar, C Macdonald-Wallis, S Kaye , S Rauz , F C Figueiredo
Publication: Eye (Lond). 2021 Sep 16.doi: 10.1038/s41433-021-01560-8.

UKISCRS

United Kingdom & Ireland Society of Cataract & Refractive Surgeons

Irish
MEETING

Thursday 9th December 2021

The Conrad Hotel, Dublin

Visit **www.ukiscrs.org.uk** for all details

info@daybreakmedical.com
+44 (0) 208 894 6601

DAYBREAK MEDICAL

• ILLUMINATE •

Exciting New Diagnostic and Treatment Options for Dry Eye

Please see www.mydryeyedisease.com

DRY EYE TREATMENT

"

I have had excellent feedback from patients whom I have treated with the IPL LacryStim device. I highly recommend the Lacrystim for it's ease of use and excellent training and backup provided by the suppliers.

DR. PIETER GOUWS, UK

LACRYSTIM™

TREATMENT OF DRY EYE

We now also distribute all Ellex and Quantel Medical Ultrasound and Laser products

www.daybreakmedical.com