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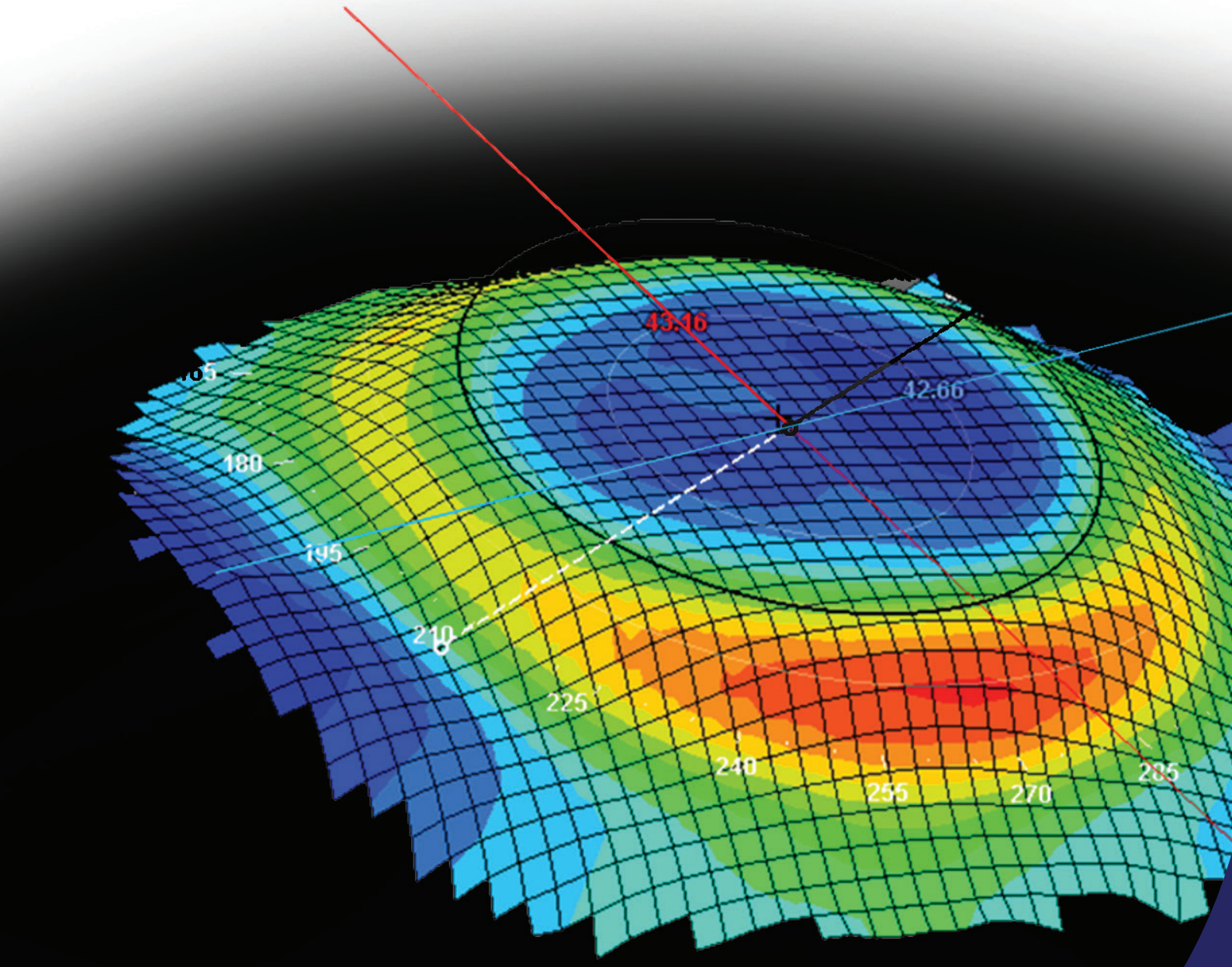
Optometry AUSTRALIA
ADVANCING OPTOMETRY



Corneal diseases

CFEH's Chairside reference

Contact lens trends

Efron, Morgan and Woods 18th annual survey results

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†meibomian gland dysfunction

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References: 1. Christensen M, Blackie CA, Korb DR, et al. An evaluation of the performance of a novel lubricant eye drop. Poster D692 presented at: The Association for Research in Vision and Ophthalmology Annual Meeting; May 2-6, 2010; Fort Lauderdale, FL. 2. Christensen, M, Martin, A, Meadows, D. An Evaluation of the Efficacy and Patient Acceptance of a New Lubricant Eye Gel. Presented at American Academy of Optometry 2011, Boston, MA. 3. Davitt WF, Bloomenstein M, Christensen M, et al. Efficacy in patients with dry eye after treatment with a new lubricant eye drop formulation. J Ocul Pharmacol Ther. 2010;26(4):347-353. 4. Aguilar A. Efficacy of a Novel Lubricant Eye Drops in Reducing Squamous Metaplasia in Dry Eye Subjects. Presented at the 29th Pan-American Congress of Ophthalmology in Buenos Aires, Argentina, July 7-9, 2011. 5. Geerling G, et al. The International Workshop on Meibomian Gland Dysfunction: Report of the Subcommittee on Management and Treatment of Meibomian Gland Dysfunction. IOVS. 2011;52(4):2050-2064. 6. Lemp MA et al. The definition and classification of dry eye disease: Report of the Definition and Classification Subcommittee of the International Dry Eye WorkShop (2007). Ocul Surf. 2007;5:75-92.

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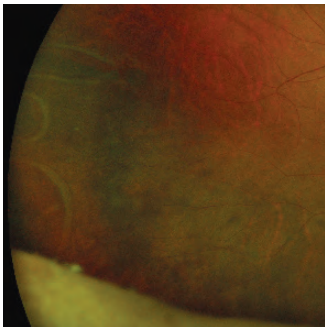
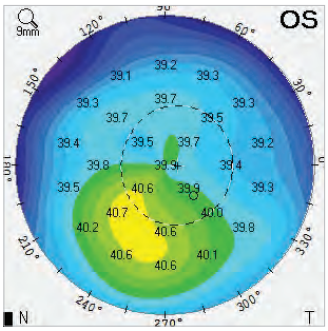
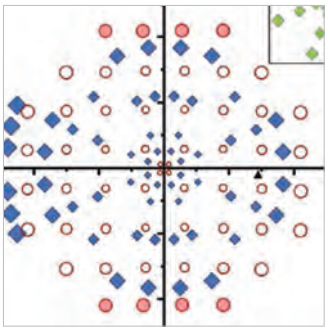
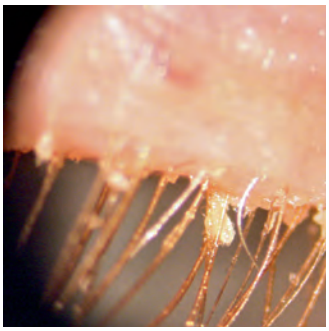
December 2017









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Cover
Corneal topography map. Image courtesy of Medmont

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Contact lens prescribing trends 2017

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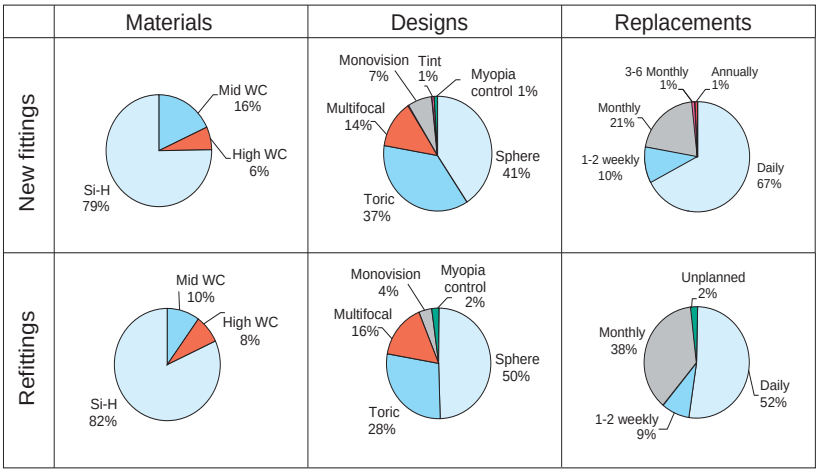


▲ Figure 1. Detailed results for soft contact lens prescribing, in the 2017 Australian survey (Si-H: silicone hydrogel; WC: water content)

THE 18TH ANNUAL survey of Australian contact lens prescribing was conducted between January and April 2017. The same format as in previous years was employed. An e-mail was sent to all members of Optometry Australia with a link to a questionnaire, and a request that this be downloaded, printed and completed to provide details of the first 10 patients fitted with contact lenses after receipt of the questionnaire. The survey was specifically designed to be straightforward to complete while capturing key information about their patients.

Practitioners were asked general questions about themselves. For each contact lens fitting, they were requested to complete the following details: date of fitting, new fitting or refitting, age and sex of patient, lens material, lens design, frequency of replacement, times per week of wear, modality (daily or extended wear) and care system. Practitioners were asked to return the questionnaire by e-mail, fax or post.

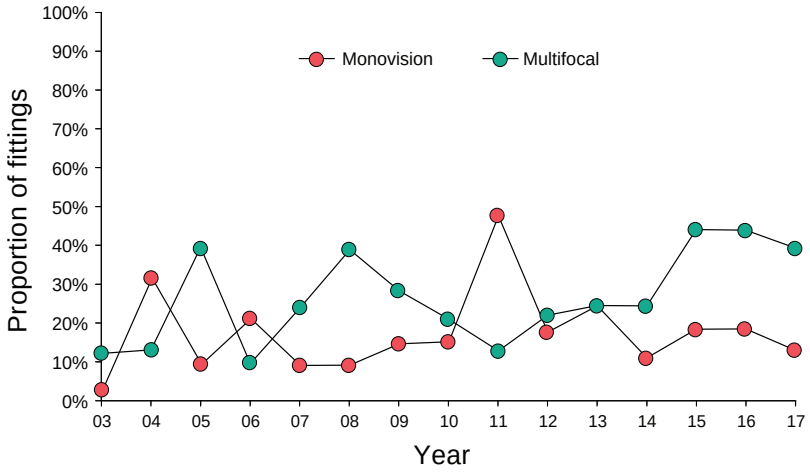
Completed questionnaires relating to 362 contact lens fittings were returned, providing a sound basis for a meaningful analysis. Each fitting was given an annualised weighting based on the number of lenses fitted during the survey period and the time taken to complete the fittings. This means that data generated by practitioners with a higher frequency of fitting contact lenses were afforded a higher weighting than those with a lower frequency of fittings.

The discussion below concentrates primarily on data relating to new lens fittings, as opposed to refittings. We believe that new fittings are a more sensitive barometer of current patterns and future trends, whereas refittings are more indicative of previous fitting behaviours.

In keeping with other markets around the world,[1] a majority of lenses (68 per cent) were fitted to females. The average age of contact lens wearers at the time of fitting was 37.3 ± 16.6 years. The age at fitting ranged from seven to 82 years.

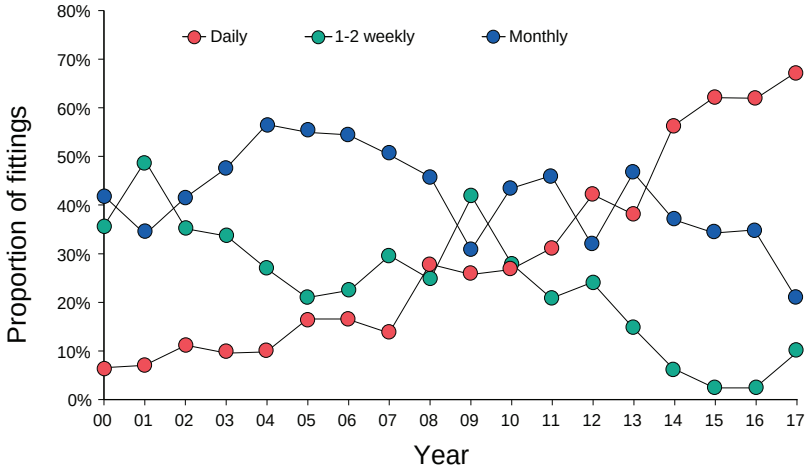
Soft lens materials and designs

Soft lenses are still the main type of contact lens fitted, accounting for 88 per cent of new fittings, representing a slight decrease from the past few years.[2]



▲ Figure 2. Percentage of all soft lenses prescribed for the correction of presbyopia to those over 45 years of age, in Australia between 2003 and 2017

The 18th annual survey by Efron, Morgan and Woods



▲ Figure 3. Percentage of all soft lenses prescribed for daily, 1-2 weekly and monthly disposal, in Australia between 2000 and 2017

Figure 1 is a composite of pie charts detailing the key findings of the 2017 survey in relation to soft lenses. Silicone hydrogels are still the dominant material, representing 79 and 82 per cent of materials prescribed as new fittings and refittings, respectively. The balance is a mixture of mid-water and high-water content hydrogel materials. No low-water content hydrogel lenses were recorded as being fitted in 2017. This represents a remarkable change in the market from 1977, at which time 87 per cent of lenses fitted were made from a low-water content material (38 per cent water content hydroxyethyl methacrylate, known as HEMA).[3]

The key categories of lens designs are spherical, toric, multifocal, monovision, coloured (tinted) and myopia control, with spherical and toric designs representing 78 per cent of new fittings. About one quarter of soft lenses prescribed are in toric form (37 per cent of new fittings and 28 per cent of refittings).

Figure 2 shows trends in the level of prescribing of contact lenses for presbyopia between 2003 and 2017. It can be seen that apart from one 'reversal' in 2011, multifocal lenses have been prescribed to a greater extent than monovision correction since 2007. This preference for multifocal lenses appears to have increased and consolidated over the past four years, perhaps reflecting significant advances in multifocal lens design and increasing availability in preferred materials and frequency of lens replacement. Coloured (tinted) lenses represented only one per cent of new fittings this year.

Myopia control lenses incorporate special designs for arresting the rate of progression of myopia.[4] These lenses represented one per cent of new fittings and two per cent of refittings in 2017 (compared to no fittings being recorded previously),[2] perhaps indicating that practitioners are now willing to try this new approach, after much discussion on practitioner forums and at clinical meetings over the past few years.

Soft lens replacement and wearing modality

Trends in the three key lens replacement modalities (daily, two-weekly and monthly) prescribed between 2000 and 2017 are illustrated in Figure 3. The relentless increase in the popularity of daily disposable lenses is clear; more than two-thirds of the new soft lens fittings this year were daily disposable lenses. If this rate of prescribing daily disposable lenses continues at the same rate as has been apparent over the past 17 years, virtually all soft lenses prescribed in Australia may be this lens type by the end of this decade.

Multipurpose solutions remain the lens care option of choice for those wearing reusable lenses, representing 95 per cent of prescribed care regimens. The

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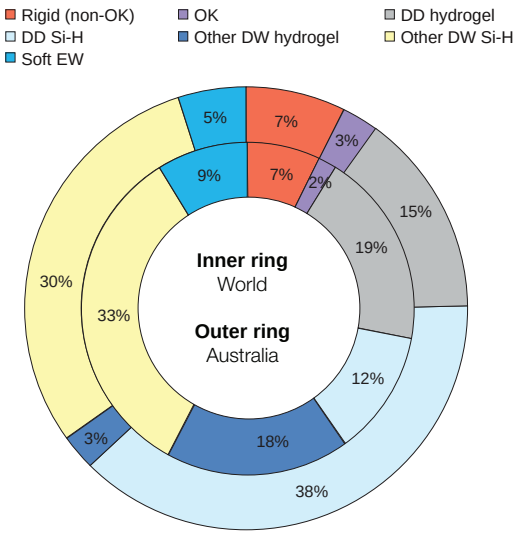

▲ Figure 4. Percentage of all contact lenses prescribed in Australia (outer ring) compared with the world average (inner ring). DD: daily disposable, DW: daily wear, EW: extended wear, OK: orthokeratology, Si-H: silicone hydrogel

Trends 2017

From page 3

balance comprises almost exclusively peroxide systems.

Rigid lenses

Conventional and orthokeratology rigid contact lenses represented 7.3 per cent and 2.7 per cent of all contact lens fittings, respectively. This increase in rigid lens prescribing compared with recent years[2] perhaps reflects a renewed interest in large diameter rigid lenses, and orthokeratology for temporary myopia relief and/or myopia control.

Australia versus the World

We have conducted annual contact lens fitting surveys in about 40 countries over the past few years.[1] This provides an opportunity to benchmark against international colleagues, and this year we compare contact lens prescribing in Australian against world trends (Figure 4). Seven key categories of lens type are represented. The outer and inner rings display the Australian and world-wide fitting data,[1] respectively.

The most striking difference in contact lens prescribing between Australia and the rest of the world is the extent of fitting silicone hydrogel daily disposable lenses, which represent 38 and 12 per cent of all lenses fitted, respectively. Also, the use in Australia of 'other' daily wear hydrogel lenses, that is, excluding daily disposable lenses, is far less than the world average. There is also less prescribing of extended wear lenses in Australia compared with the rest of the world. Differences between Australia and the world average in respect of fitting other lens types are small.

Conclusions

The results of our 2017 survey yet again confirm the high rate of prescribing daily disposable lenses in Australia. Silicone hydrogels are very firmly entrenched as the material of choice, representing about 80 per cent of all soft lens fittings. As was the case last year, we note continuing strong use of multifocals compared with monovision, and toric contact lens fitting continues at high levels. ▲

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When dry eye heralds a greater threat

Vision and life-threatening complications of Sjögren's syndrome

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BVisSci MOptom

Dr Adrian Bruce

BSc(Optom) PhD PGCertOcTher

Australian College of Optometry

Study draws attention to the ocular and systemic disorders associated with SS.

AKPEK et al[1] published in the journal of the *American Academy of Ophthalmology* a study that highlighted the frequency of vision-threatening ocular manifestations as well as concomitant, potentially sinister systemic disorders associated with Sjögren's syndrome (SS). The study's main conclusions encourage clinicians to more carefully scrutinise dry eyes.

In the study, new and returning patients were investigated within a four-and-a-half year period at the Johns Hopkins Medical institutions in Baltimore, Maryland. All patients were co-assessed by a rheumatologist and ophthalmologist, and underwent extensive systemic and ocular examinations in order to reach a diagnosis of SS.

Systemic examinations included serologic testing, minor salivary gland biopsy, salivary gland scintigraphy, parotid gland ultrasonography, and magnetic resonance imaging or computed tomography scanning of the major salivary glands. Ocular investigations were performed and included a symptoms questionnaire (Ocular Surface Disease Index), full ophthalmic evaluations (visual acuities, slitlamp and dilated fundus examinations) as well as systematic dry eye testing.

Dry eye was assessed in a sequential manner as follows:

1. Schirmer testing without topical anaesthesia
2. One drop of proparacaine with fluorescein into the lower conjunctival fornix
3. Assessment of tear film break-up time
4. Corneal staining scoring with the Oxford scoring system (scale of 0 to 5) after two minutes of instillation of fluorescein eye-drops
5. Conjunctival staining scoring with lissamine green and a single drop of preservative-free saline, also using the Oxford scoring system.

A diagnosis of SS was based on the American-European Consensus Group 2002 (Table 1). A minimum of four of six criteria or three of four objective criteria had to be met to make a conclusive diagnosis. These six criteria outlined subjective and objective ocular dryness, subjective and objective evidence of salivary gland involvement, presence of Sjögren-specific antibodies either A/Ro or B/La or both, and positive minor salivary gland biopsy.

Subjective: ocular dryness
Objective: ocular dryness
Subjective: evidence of salivary gland involvement
Objective: evidence of salivary gland involvement
Presence of Sjögren-specific antibiotics (A/Ro or B/La)
Positive minor salivary gland biopsy

▲ Table 1. Criteria for diagnosis of Sjögren's syndrome: based on American-European Consensus Group 2002

Only primary SS patients were included in the study, which meant that participants had to demonstrate a positive Sjögren-specific antibody A or B serologic result, or the presence of positive minor salivary gland biopsy. Secondary SS, which was defined as individuals who were diagnosed with another autoimmune connective tissue disease, for example, rheumatoid arthritis, systemic lupus erythematosus or scleroderma, were excluded.

At initial assessment	25%
Subsequently developed	10%
Nil	65%

▲ Table 2. Prevalence of ocular morbidity in Sjögren's syndrome

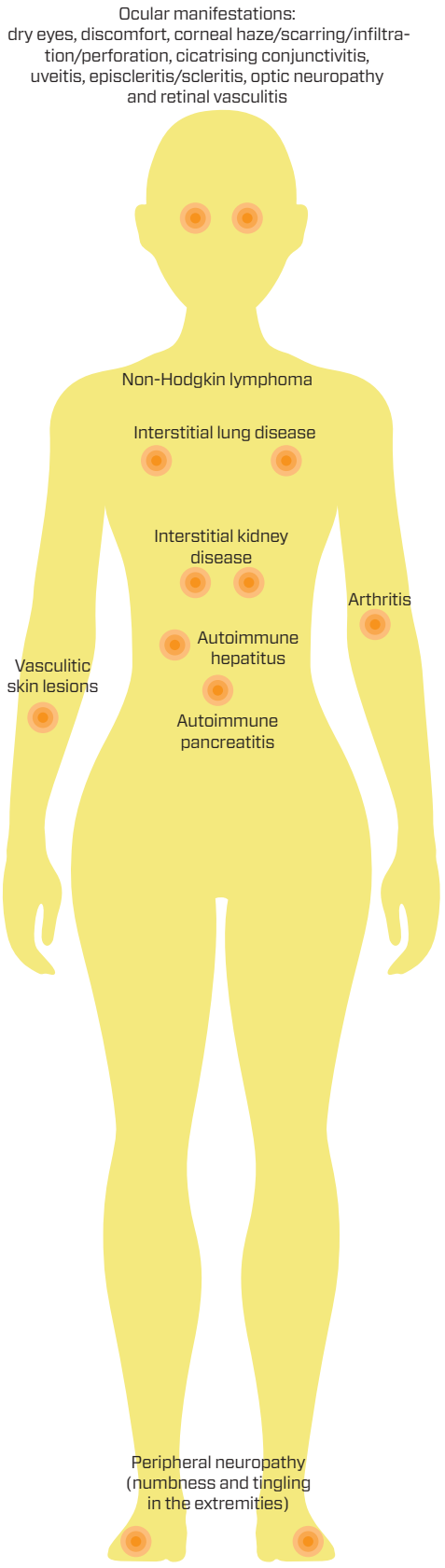
Of the primary SS cohort, a large majority (91 per cent) were women in their 50s (mean age = 51 ± 14 years) who experienced persistent dry eye symptoms spanning an average of 10.4 years. The study also found that extra-glandular ocular manifestations were present in 25 per cent of their patients (Table 2).

Among these, 13 per cent (22 patients) had vision-threatening complications including conditions such as corneal haze/scarring/infiltration/perforation, cicatrising conjunctivitis, uveitis, episcleritis/scleritis, optic neuropathy

Continued page 6

Sjögren's syndrome

From page 5



Concomitant systemic disorders associated with Sjögren's syndrome

and retinal vasculitis. The study reports close to half (55 per cent) of these individuals with more serious ocular manifestations did not have an established diagnosis of SS.

This study also investigated extra-glandular systemic manifestations of SS. Concomitant systemic involvement in those diagnosed with SS include: visceral (interstitial lung or kidney disease, autoimmune hepatitis, or pancreatitis) or non-visceral (vasculitic skin lesions, arthritis and peripheral neuropathies) diseases, with lymphoma being one of the more devastating complications.

Forty-two per cent (68 patients) of the patient cohort were classified as having an extra-glandular systemic manifestation of primary SS, five of whom had lymphoma (Table 3).

However, among the 22 patients who demonstrated vision-threatening manifestations of SS, 64 per cent (14 patients) reportedly had a concomitant extra-glandular systemic manifestation of SS ($p = 0.025$). This implied that the prevalence of SS-associated systemic manifestations, such as peripheral neuropathy, vasculitis and interstitial nephritis, were about four times higher in those diagnosed also with more serious ocular complications.

Perhaps more concerning is that the study highlights several other reports in agreement that SS is identified as an independent risk factor for non-Hodgkin's lymphoma. Primary SS is found to be the most strongly associated risk factor for malignancy in non-Hodgkin's lymphoma with a reported incidence rate of 18.8 per 100,000 patient-years.

Given these findings from this study, it may seem then that a delayed diagnosis of SS is unreasonable. At present, it is thought to be delayed by up to 10 years. However, SS is a challenging diagnosis that requires comprehensive and methodical objective and subjective assessments as well as multidisciplinary efforts between rheumatology and ophthalmology. In addition, this particular study cohort was derived from a large established tertiary care referral centre. When put into perspective, the numbers recorded in this study seem slightly exaggerated.

One systemic finding	39%
More than one finding	16%
No findings	45%

▲ Table 3. Prevalence of extraglandular systemic manifestations of primary Sjögren's syndrome.

This article helps to expand the primary care practitioner's knowledge of potentially ominous manifestations of Sjögren's syndrome and is meaningful enough to tingle one's sixth sense with the unusual dry eye patient. It serves as a good message to not carelessly dismiss the patient with persistent dry eye. ▲

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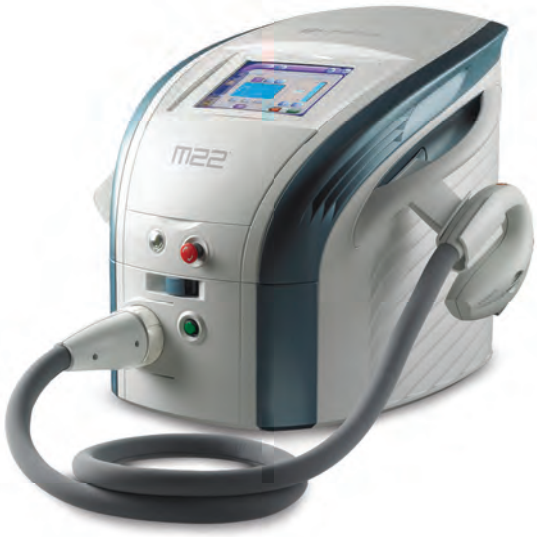

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Energy to Eye Care

Ultra-widefield imaging in clinical practice

Michael Wicks

BScOptom(Melb)

ADVANCES in technology are expanding opportunities in optometry for earlier detection and treatment of a multitude of sight- and life-threatening pathologies.

Standard examination procedures typically proceed from anterior to posterior segment, via slitlamp, tonometry, binocular indirect ophthalmoscopy (BIO), OCT and retinal camera. Considering that numerous studies show that pathologies are often initially evident in the periphery long before problems manifest in the central pole, a thorough examination of the retina is essential for a comprehensive examination.

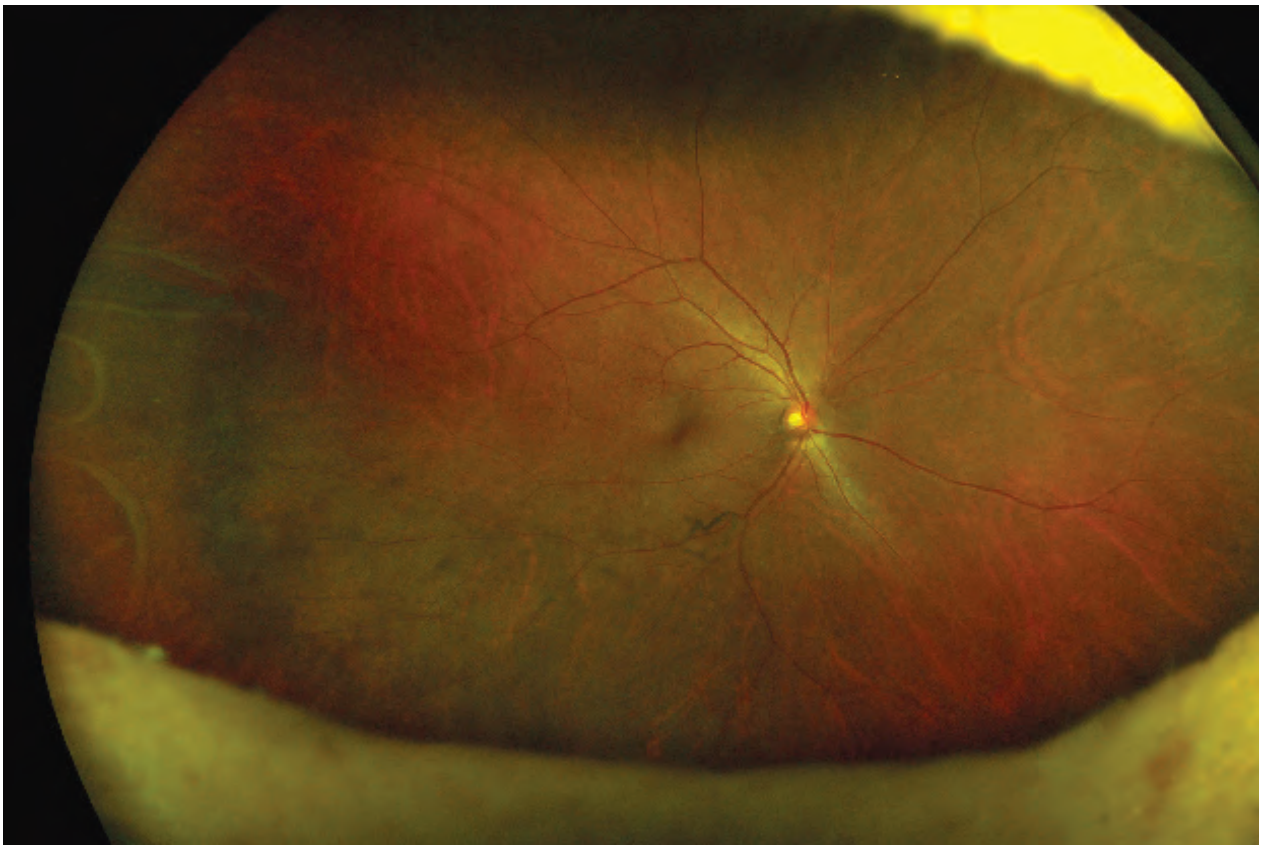
Following pretest and examination of the anterior chamber, standard BIO will often direct the rest of the examination, and when a fundus issue is detected, time-consuming stratagems are often necessary to obtain a better view and a retinal image for documentation.

The introduction of ultra-widefield (UWF) imaging into our practice has altered examination protocol, essentially reversing the order of how we utilise our technology and examine patients.

The Daytona Plus UWF allows a 200-degree, high definition, digital view of the retina in a single non-contact image in less than 0.4 seconds. This image is called optomap. Daytona Plus image modalities include a colour composite view, red channel (choroidal) view, green channel (sensory retina) view and autofluorescence. The evolution of optomap image resolution has improved to a degree that it is comparable to our retinal camera; however, our ability to access and assess 82 per cent of the retina via optomap has resulted in a notable increase in pathology discoveries.

During the first two months with the Daytona Plus use we have discovered in asymptomatic patients numerous retinal tears, peripheral lattice degeneration and small holes in the far periphery that have self-sealed. Some of these were patients we had seen previously and when we compare the optomap images to previous retinal photos, these pathologies are not evident.

Over this short time, the conclusion that we may be missing emergent



▲ Figure 1. Optomap of right eye; even with blink disruption, the horseshoe tears on the periphery are clearly visible

A 200-degree view of the retina yields a striking image of otherwise undetectable pathology

pathology has influenced how we proceed with examinations. The optomap ease of use and rapid image acquisition have similarly contributed to this adaptation. The Daytona Plus allows us to quickly obtain expansive images in populations that are difficult to dilate, refuse dilation or present with multiple issues that complicate a prolonged, comprehensive examination.

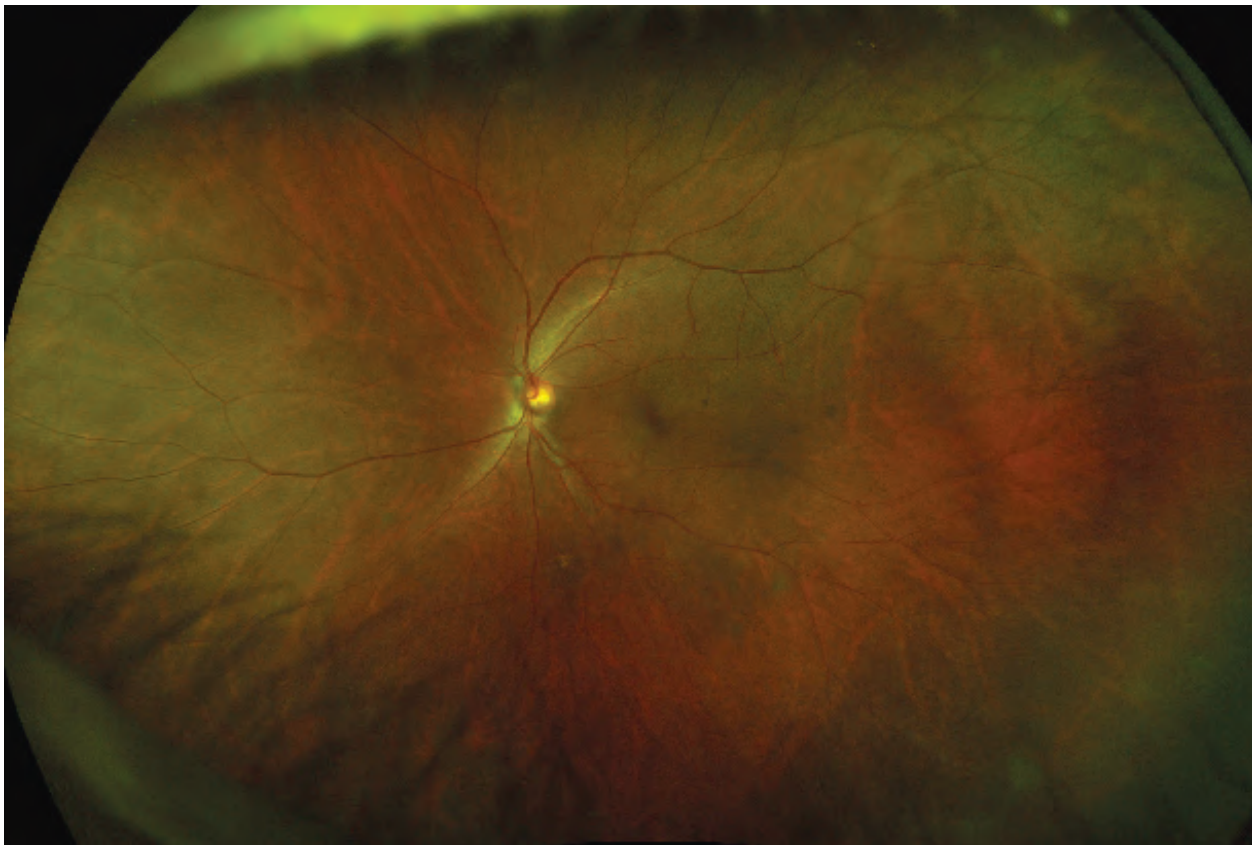
CASE REPORT

Que is a 64-year-old patient who presented six weeks ago with complaints of a shadow slightly obscuring his vision OD. He did not speak or understand English and was accompanied by his son who spoke only slightly more English, but attempted to translate directions.

Achieving desired results during his dilated retinal examination with BIO was difficult. When a direction was given, Que would retract from the light from the headset and look to his son for translation. This behaviour resulted in a protracted examination with insufficient information. I was able to clearly see a floater that did not have the appearance of retinal tissue. I also caught a glimpse of a possible issue superior temporal OD but I could not obtain a suitable view of the periphery. Although I did not anticipate any better result we brought him to the Daytona Plus for imaging.

However, the target in the device made little explanation necessary. I was able to quickly obtain a good 200-degree view of the retina of both eyes without trouble. On review of the images, three large horseshoe tears were clearly evident in the far periphery OD (Figure 1). Que was immediately referred to a retinal specialist and the tears were successfully sealed the following day.

Use of the Daytona Plus has resulted in greater efficiency that allows us to see more patients and ultimately translates into enhanced quality of care. Utilising the technology for screening accommodates a more comprehensive examination with an unparalleled scope for greater discovery and documentation. The optomap experience has been well received by patients and is less intrusive than other methods. The images provided by Daytona Plus have expedited and simplified the examination of my patients while providing powerful diagnostic and educational elements for our staff and patients. ▲



▲ Figure 2. Optomap of left eye

All lenses great and small

Damon J Ezekiel

BOptom FAAO FCLSA FSLS

Director, Ezekiel Eyes, WA

'Options' is the byword for fitting keratoconus patients

MY PHILOSOPHY for fitting keratoconus patients is to work through the options with them. The various options range from soft toric contact lenses, piggy-back soft lenses with corneal RGPs, and corneal RGPs, to gas permeable mini-scleral and gas permeable scleral contact lenses.

The range of options available depends on the severity of the patient's cone. Ultimately, this will determine the path that will give the patient the best visual acuity improvement.

CASE REPORT

PC, a 30-year-old patient, presented to my office concerned about his quality of life. He had been diagnosed with keratoconus when he was 22 years old and he admitted his vision had been poor for a few years before the diagnosis.

PC was only just managing with the spectacle prescription: R Plano/-5.25 x 45, VA 6/48; L -0.50/-1.75 x 100, VA 6/9.5. His Flat and Steep K readings were R 49.36/54.96 and L 46.40/48.47.

PC worried whether he would be able to continue to hold down a job and drive, which are aspects of life that most of us take for granted. He was at a crossroad in his life, as his lack of vision was becoming a liability for him as well as for other road users.

In discussions with PC, it emerged that he had tried only soft disposable toric contact lenses, which were not satisfactory due to very poor visual acuities and comfort. We decided to start with corneal gas permeable contact lenses.

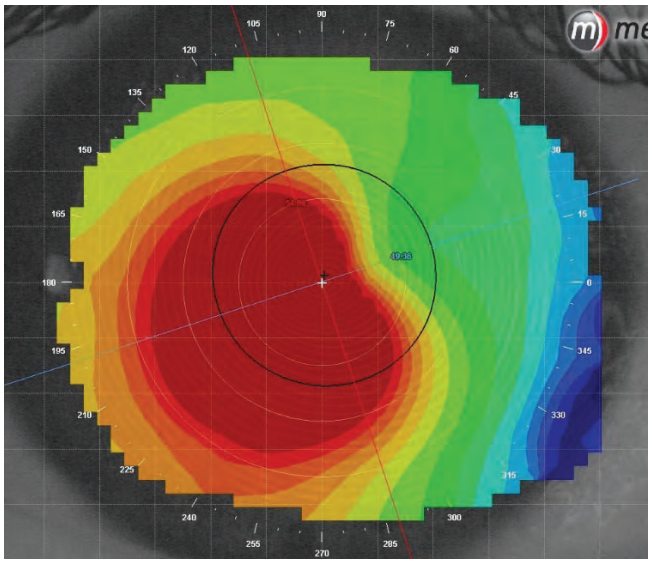
I trial-fitted PC with the Keracon lens in a 9.6 diameter. After a few trial fittings to establish a good three-point touch fit, PC's visual acuities improved to R 6/7.5- and L 6/6-.

At the first aftercare consultation review, PC was wearing the lenses full time with great vision and reasonable comfort. No contact lens adjustments were required; another review was scheduled for two weeks later.

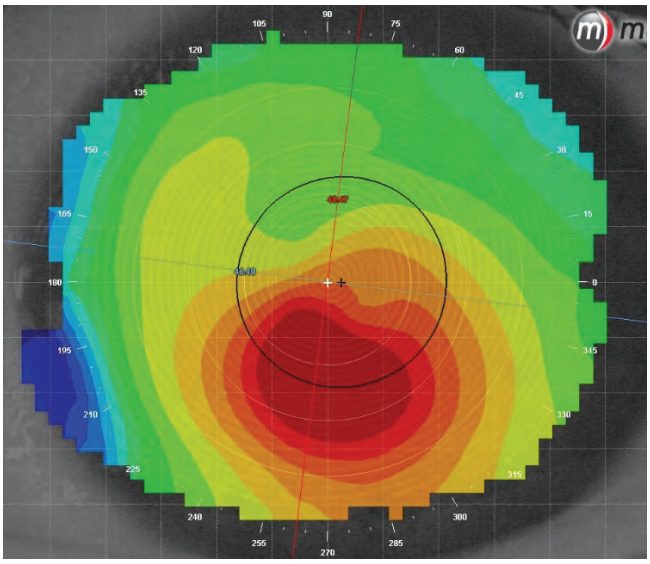
At the following aftercare consultation, PC informed me that he had been to his work site north of Perth and been surrounded by dust, heat and wind. His comfort was a real issue. The fit of the lens in my clean, cool consulting room was great and the vision was good.

The next option we discussed was to move PC into a gas permeable mini-scleral lens. He returned the following day with no lens wear and we undertook the trial fitting of the gas permeable SoClear mini-scleral lenses.

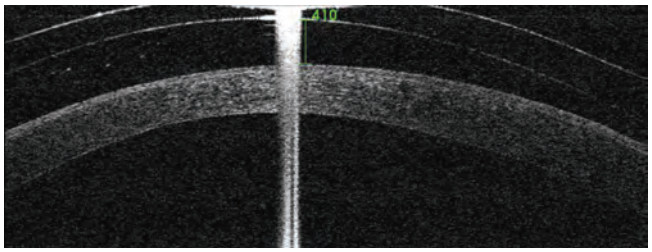
The gas permeable SoClear mini-scleral lens is made by Dakota Sciences in the USA, and Gelflex Laboratories is



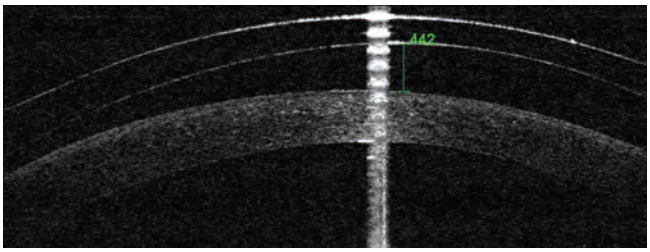
▲ Figure 1. Corneal topography map reveals the extent of PC's keratoconus, right eye



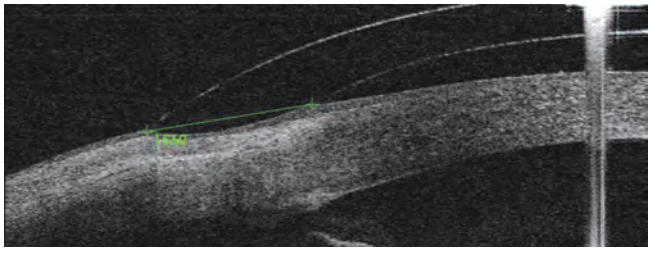
▲ Figure 2. Corneal topography map reveals the extent of PC's keratoconus, left eye



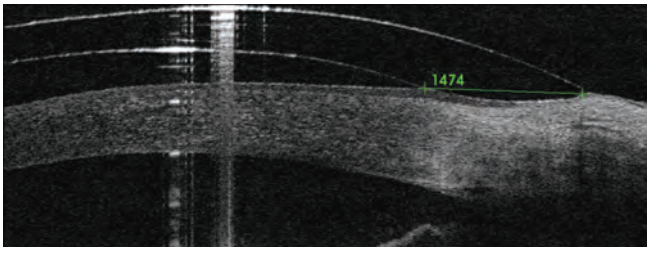
▲ Figure 3. Right eye central fit



▲ Figure 4. Left eye central fit



▲ Figure 5. Right eye landing zone



▲ Figure 6. Left eye landing zone

the agent for these lenses. It is a sealed design, nice and thin, made in the Boston XO2 material, and I find that it is a terrific lens for my patients.

After a few trial lenses to establish the correct fitting, I decided on the following lens parameters: R 5.19/15.00/-19.50, L 5.27/15.00/-19.50.

Figures 3 and 4 show the central corneal tear layer at delivery of R 410 µm and L 442 µm. We aim for a central corneal tear layer of around 400 µm; with increased wearing time this central tear layer will drop to approximately 200 µm. A small central tear layer initially will become too tight as the lens drops onto the cornea. With increased wearing time, this will cause corneal staining. An excessively large corneal tear layer will cause dimple veiling and compromise the corneal health; vision will be poor as the lens will not drop back on the eye.

The landing zone of the SoClear lens is to fit the periphery of the lens on the sclera and clear the limbus. We measure this landing zone with our anterior OCT. A landing zone of approximately 1500 µm is great. If the landing zone is too small, the lens will become too tight and if the landing zone is too large, the bearing of the lens will encroach across the limbus and compromise the fit and lens comfort. In this case it was R 1560 µm and L 1474 µm as shown in Figures 5 and 6.

During PC's next aftercare consultation, he was achieving wearing his lenses with comfortable all day wear and achieving visual acuities of R 6/7.5 and L 6/6.

PC was very happy that his visual acuities and overall quality of life had greatly improved. He appreciated the effort of trying a modality of contact lenses and then moving on to the next level to enhance either the vision or the comfort. ▲

• Damon Ezekiel is the Practising Fellow of the Scleral Lens Education Society in Australia. In 2018, he will be the first Australian to become president of the International Society of Contact Lens Specialists.

Find something new with a change in view

Axial versus tangential maps

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OVER THE PAST 25 years, videokeratoscopy has transformed the measurement of corneal topography. One of the key advantages of being able to measure corneal topography is that it now allows us to detect keratoconus at an earlier stage.

Prior to the introduction of videokeratoscopy, it was probably thought that about 10 per cent of cases of keratoconus were unilateral. We now know that this is simply not correct. Subsequent evaluation of corneal topography shows us that nearly all of these 'unilateral' cases are bilateral with early but definite signs of keratoconus noted in the better eye. In fact, clinical experience tells us that true unilateral keratoconus is extremely rare and probably occurs in less than 0.5 per cent of cases of keratoconus.

Detecting early or sub-clinical keratoconus by assessment of corneal topography can still be challenging, especially when only very subtle corneal changes are noted. One way practitioners can improve their chances of diagnosing keratoconus is to use the 'tangential' (also known as 'instantaneous' or 'true') radius to measure the corneal shape.

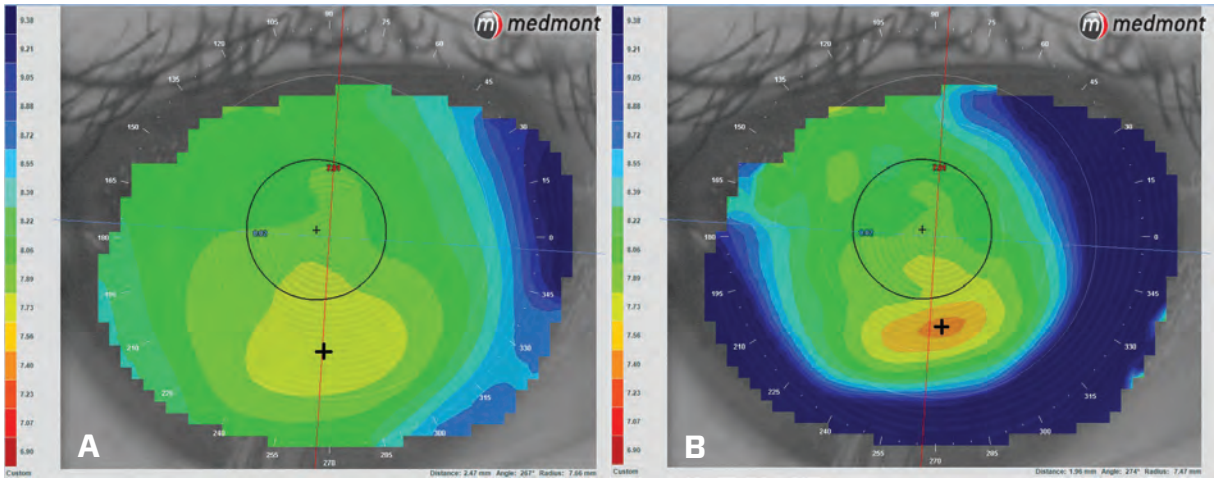
Two types of radii are used in videokeratoscopy: axial and tangential. The axial radius (also known as 'sagittal') is also the radius that is measured in keratometry. It is the distance from a point on the cornea to the optic axis of the videokeratoscope when it is aligned with the cornea. The axial radius tends to be the default setting for most clinicians when using videokeratoscopy.

The tangential radius is the other type of radius and it is independent of any axis; rather it is based on only the local curvature at each corneal point and therefore it is often referred to as the 'true' or 'instantaneous' radius).

With peripheral corneal flattening, the tangential radius will always be longer than the axial radius for each peripheral corneal point. Conversely, for peripheral corneal steepening the tangential radius will always be shorter (steeper) than the axial radius for each corneal location as you move away from the visual axis.

Local changes in corneal shape, such as those occurring in keratoconus, are seen most clearly when using tangential radius measurements. Figure 1A shows the axial map of a patient with very early 'sub-clinical' keratoconus in his right eye. Note that the patient has advanced keratoconus in his left eye. With this corneal map, it is not clearly evident that this eye has keratoconus. Figure 1B shows the tangential map of the same cornea. It can be seen from this corneal map that the patient definitely has keratoconus in this eye.

Note also that when comparing the two corneal maps, it can be observed that the tangential map reveals the corneal apex to be closer to the centre of the map and also shows the true central curvature, which is much greater (steeper) than that obtained with the axial map. ▲



▲ Figures 1A and 1B. Axial map (A) and tangential map (B) of the same eye. The cursor denotes the location of the corneal apex. Note the corneal apex on the axial map appears further from the centre of the cornea as compared to the tangential map. The tangential map reveals the curvature of the apex to be 7.47 mm which is steeper than that of the axial map (7.66 mm).

GUIDE

CORNEAL ECTATIC DISEASES AND THINNING DISORDERS PAGES 14-15

Early keratoconus and potential progression

Topography, traditional clinical techniques and adjunctive measures

Lindsay Moore

BOptom(Hons) BSc

Centre For Eye Health

KERATOCONUS is classified as a progressive, non-inflammatory disorder, involving corneal thinning and steepening, and is usually bilateral in nature. It has always been important to assess for risk factors and early signs of keratoconus in patients considering refractive surgery. Given the advent of crosslinking in particular, early diagnosis of keratoconus, especially in rapid progressors has become increasingly important; however, the literature on methods for early diagnosis as well as what constitutes progression is at times equivocal.

This article provides a brief overview of current knowledge in the field, focusing on early diagnostic methods as well as techniques for determining progression, while the accompanying chairside reference (Pages 14–15) aids in differentially diagnosing keratoconus from other mimicking conditions.

DIAGNOSIS OF EARLY KERATOCONUS

Historical associations

Keratoconus has been linked to atopy and repeated knuckle rubbing of the eye.[1]

Pre-Descemet's and posterior polymorphous corneal dystrophies have also been associated with keratoconic steepening,[2] while a number of eye and systemic conditions, such as Leber's congenital amaurosis as well as Down, Turner, Marfan and Ehlers-Danlos syndromes have an increased prevalence.[3]

Ethnicity can also guide diagnosis; persons of Asian, Arabian, Maori and Pacific Islander descent are more commonly affected.[3]

Functional markers of keratoconus are limited in the early stages but can include blurred vision, which is typically more evident in scotopic conditions, as well as decreased contrast sensitivity, glare, haloes, ghosting and monocular diplopia.[4]

Structural markers utilising standard optometric clinical equipment are characterised by an increase in astigmatism, scissors reflex on retinoscopy, oil droplet reflex on ophthalmoscopy, prominent corneal nerves, and abnormal or distorted keratometry readings.[5] On the contrary, Vogt striae, Fleischer's ring and Munson's sign as well as reduced corneal thickness are not typically present in early stages.[5]

Structural markers utilising imaging

Numerous imaging devices have been shown to detect changes in corneal properties with the aim of differentially diagnosing early keratoconus from an asymmetric normal eye; however, there are no specific, agreed-on instrumental values that define keratoconus. As a result, the initial diagnosis is often based on a combination of these results or alternatively a change in values signalling progression.

Corneal topography

A wide variety of corneal topographers are currently commercially available with a correspondingly large number of techniques and analyses aimed at the early diagnosis of keratoconus and the ability to quantify change. Elevation and sagittal maps are the most commonly utilised features, typically exhibiting an elevation of the anterior and posterior surfaces or an asymmetric 'bow tie' appearance, respectively[6] (Figure 1). It is typically more prominent on the posterior surface in early keratoconus. While this elevation is most commonly evident inferior to the visual axis, it can occur centrally and in other locations.

A wide variety of indices, such as the 'KISA% index,' are based on topographically-derived values and have been proposed in the literature to determine the likelihood of a cornea being keratoconic. To date, all of these markers have shown limited sensitivity and specificity.

Corneal pachymetry

As well as reduced values compared to expected norms, corneal thickness maps often show a decentration of the thinnest point inferior to the visual axis.[7] Epithelium thickness measurements, now commercially available with anterior optical coherence topographers (OCT) have been shown to demonstrate a relative thinning over the apex of

Continued page 16

Centre for Eye Health

Chair-side Reference

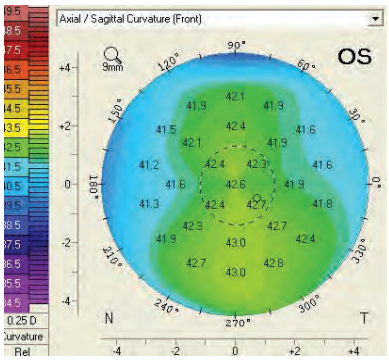
Corneal ectatic and thinning disorders can be sight threatening. The addition of imaging technologies, such as corneal topography and/or optical coherence tomography (OCT), enable earlier diagnosis and an improved ability to monitor progression.

Keratoconus

Age of onset: puberty. Progression typically occurs until 40 years of age. Bilateral, often asymmetric. Non-inflammatory, can be associated with systemic conditions including Down syndrome, Ehlers-Danlos syndrome, and osteogenesis imperfecta. There is also an association with Atopy and 'knuckle-rubbing'

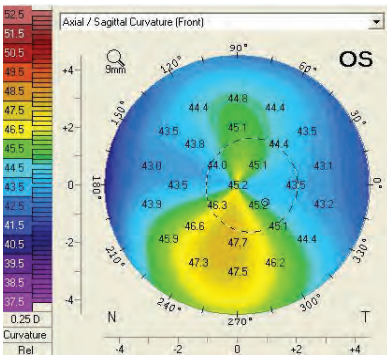
Sagittal front corneal topography	Anterior OCT and/or colour photography	Description

Forme Früste



- Typically refers to an 'incomplete form' of keratoconus
- The term can describe either of the following:
  1. Where the contralateral eye has keratoconus and the eye in question has:
     - Normal corneal topography
     - OCT findings are indistinguishable from a 'normal' cornea
  2. Some suspicious corneal topographical changes with no other clinical findings conclusive for a diagnosis of keratoconus
     - The term 'keratoconus suspect' is also used
     - In earlier research, this was also referred to as Forme Früste keratopathy

Early

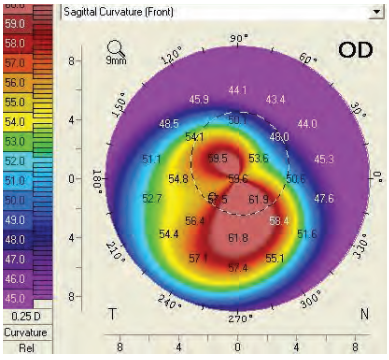


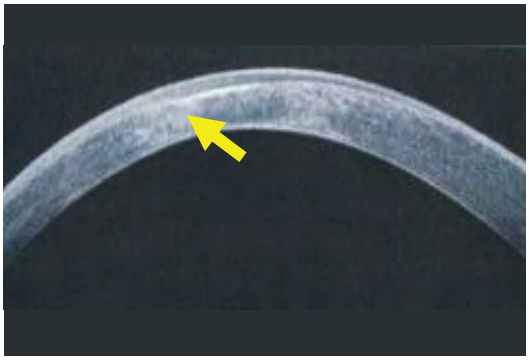
Slit lamp and OCT findings
- Subtle signs of corneal thinning

Topography
- Abnormal elevation (steepening) of the anterior and posterior surfaces often resulting in an asymmetric bow-tie appearance
  - Posterior changes can occur prior to anterior
  - Typically results in an increase in astigmatism

Pachymetry
- Abnormal corneal thickness distribution
- Apical corneal thinning
  - Thinning typically presents inferior to the visual axis although can be present in other corneal locations

Moderate to advanced keratoconus





Slit lamp findings
- Vogt's striae (identified by arrow in corneal photo)
- Fleischer's ring
- Corneal scarring at the conical apex (shown by arrow on OCT)

OCT findings
- Atypical corneal thinning and forward bowing
- Abnormal epithelial distribution

Topography
- Marked corneal elevation and steepening

Pachymetry
- Prominent corneal thinning
- Perforation or hydrops can occur

Keratoglobus (Imaging not available)

- Age of onset: Usually at birth
- Rare bilateral condition
- Some association with connective tissue disorders such as Ehlers-Danlos syndrome, Marfan syndrome and Rubenstein-Taybi syndrome
- Can occur in older patients following hydrops in those with keratoconus or PMD

Signs include
- Generalised thinning of the cornea, especially in the periphery
- Pachymetry reduced to up to one-fifth of normal corneal thickness
- Globular protrusion of the cornea
- High myopia with irregular astigmatism
- Perforation or rupture of cornea

Corneal ectatic diseases and thinning disorders

Optometry
NEW SOUTH WALES
AUSTRALIAN CAPITAL TERRITORY

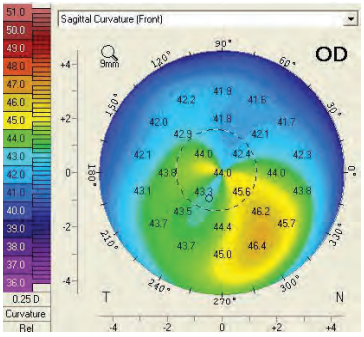
Grading scales exist for more common ectatic diseases such as keratoconus; however, there has not been consensus on a grading scale.

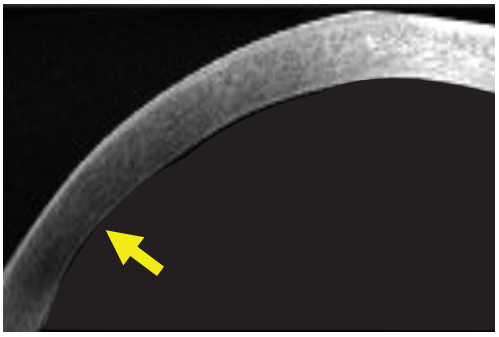
Pellucid marginal degeneration

Age of onset: 20-50 years, bilateral, non-inflammatory condition, male preponderance, presents with increasing against-the-rule astigmatism

Sagittal front corneal topography	Anterior OCT and/or colour photography	Description

Early





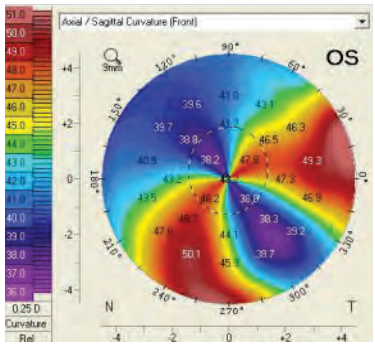
Spectacle visual acuity typically normal
- Difficult to distinguish from keratoconus

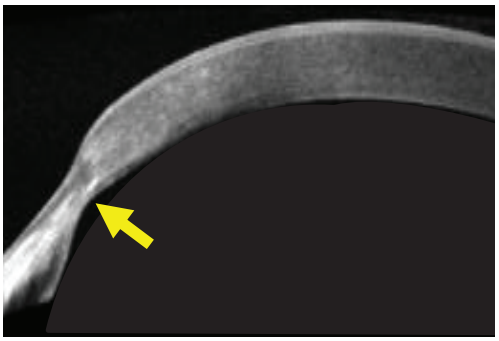
Slit lamp and OCT findings
- A 1-2 mm thick band of peripheral corneal thinning extending from 4 o'clock to 8 o'clock
- Cornea is clear at the area of thinning (yellow arrow)

Topography
- Inferior corneal thinning and steepening
- Superior corneal flattening along the vertical meridian
- 'Crab claw' pattern

Pachymetry
- Possible inferior thinning; however, typically minimal change in central corneal thickness

Advanced





Spectacle visual acuity is typically reduced but can remain normal with large cylindrical corrections

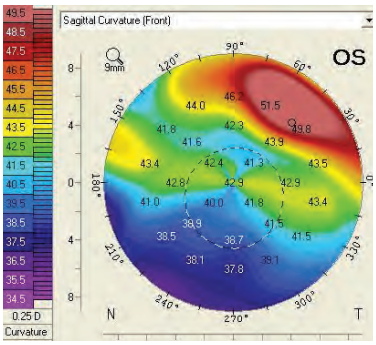
Slit lamp findings:
- Protrusion of the inferior cornea above the area of thinning
- Inferior peri-limbal striae

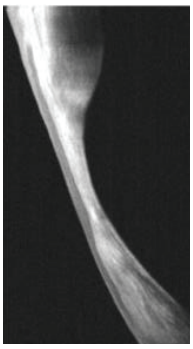
OCT findings
- Peripheral stromal thinning (yellow arrow)
- Epithelial changes overlying the area of thinning

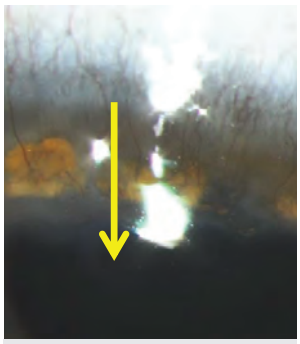
Topography
- Marked 'Crab claw' pattern
- Sometimes better appreicated on a Tangential map

Pachymetry
- Perforation or hydrops can occur

Terrien's marginal degeneration







OCT corresponds to the line shown on anterior eye image

Usually bilateral and symmetric, but may be asymmetric.
Males affected more than females
Can present in two forms:
Quiescent type
- Affects older individuals
- Asymptomatic during early stages

Inflammatory type
- Affects younger individuals between 20-30 years
- Can be associated with episcleritis or scleritis

OCT findings
- Thinning of the superior peripheral cornea (peripheral gutter)

Slit lamp findings
- Yellow-white punctate opacifications in the stroma (earlier)
- Lipid deposition along the anterior edge of the limbus (later)
- Pseudo-pterygia (20% of cases)

Topography
- Against-the-rule astigmatism
- Steepening of the superior peripheral cornea

Early keratoconus

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an impending cone prior to notable stromal thinning.[8]

Wavefront aberrometry

As early keratoconic corneas are typically asymmetric with an elevation inferior to the visual axis, higher order aberrations are often elevated above expected normal values and are predominated by coma.[9]

Corneal hysteresis

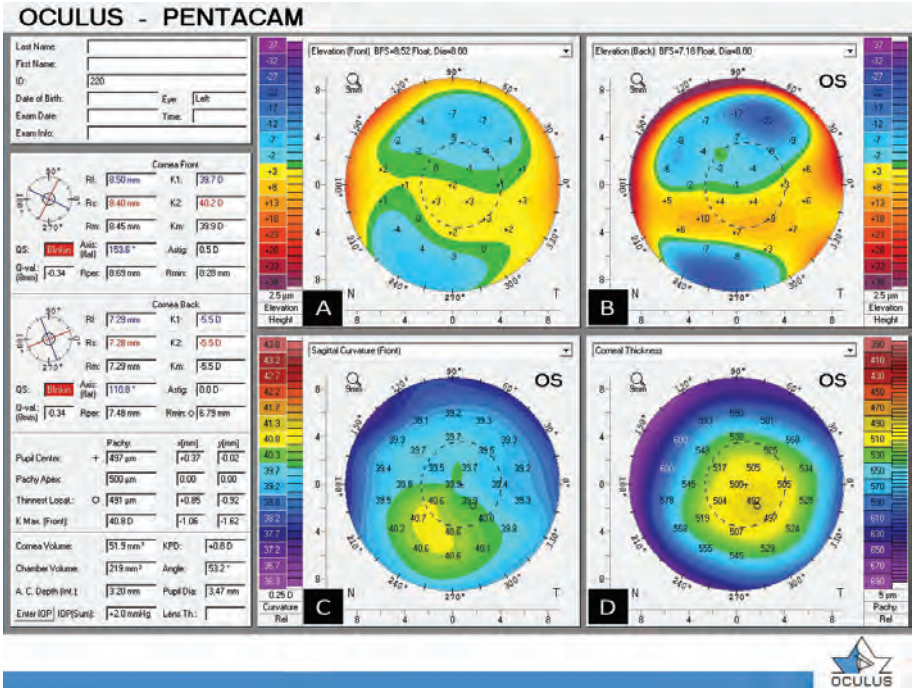
The Ocular Response Analyser, and more recently the Corvis, have been used to assess corneal resistance. Research has found the corneal resistance factor to be significantly lower in patients with early keratoconus.[7]

Determining progression

A large number of parameters have been proposed to determine whether keratoconus is progressive, including changes in each of the detection methods mentioned above. However, for most, longitudinal studies investigating the sensitivity and specificity and/or a definition of the degree of change signifying progression are still outstanding.

Proposed specific change criteria in the literature include: epithelial thinning by ≥ 2%, an increase in Kmax of ≥ 1.00 D, increased manifest cylinder of ≥ 1.00 D over 24 months and a change in radius of the back surface optic zone of a best fitting RGP lens ≥ 0.1 mm.[10]

In a recently published paper, 36 corneal specialists collaborated in an effort to standardise classification and management of keratoconus with regards to three topics: definition/diagnosis, non-surgical management and surgical treatment of keratoconus. Progressive keratoconus was defined as consistent change in two or more of the following variables with the value of the change more than the test-retest variation of the instruments:



▲ Figure 1. Topography of an early keratoconic eye: asymmetric corneal steepening is shown in the inferior anterior (A) and posterior (B) surfaces, and is more prominent in the posterior surface maps. An asymmetric bow-tie pattern is demonstrated on the axial curvature map (C) and minimum corneal thickness is located inferotemporal to the visual axis (D).

- steepening of the anterior corneal surface
- steepening of the posterior corneal surface
- corneal thinning[6]

It is important to note that while values for instrument variability have been shown to be small in normal eyes, variability markedly increases in pathological states.[11,12]

In summary, it is important to take into account historical risk factors as well as functional and structural markers when assessing a patient for early keratoconus and potential progression. Wavefront aberrometry, epithelial thickness measurements and corneal resistance measurements can be used as adjunctive measures to topography and traditional clinical techniques.

Acknowledgement

The author thanks Michael Yapp, Angelica Ly, Elizabeth Wong and Dr Barbara Zangerl for their input into this article. ▲

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Melbourne Rapid Fields

The suite of apps that transforms tablets into portable perimeters

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VISUAL FIELD examination is the premier vision test in the diagnosis and management of glaucoma and other ocular and brain disorders; however, perimetric equipment is expensive and bulky, making an in-office procedure unattainable in many small practices. Testing also requires routine clinical reviews, usually six-monthly, increasing the clinical burden of monitoring chronic eye disease. Overall, this leads to higher health-care costs and lengthy waiting lists that affect timely disease detection and patient management.

The lack of portability of bulky visual field devices also means that patients residing in aged-care centres or remote and rural areas may not receive the testing they need, compromising the detection or monitoring of their condition and delaying therapeutic intervention.

Melbourne Rapid Fields (MRF) is a suite of applications that allows visual field testing on a tablet or mobile device. MRF has been validated as a tangent perimeter and can produce reliable human visual field thresholds out to 30 degrees.[1] It is robust to blur, changes in ambient light and viewing distance, although glare or reflections off the screen can have an impact on thresholds.[1]

Tablets are low-cost, portable and ubiquitous within the Australian population where 79 per cent of those aged 65 years or older report that they access the internet with a tablet or mobile device.[2] This technology is therefore familiar to many patients who may develop chronic eye disease and it has the advantage that it can be used to self-monitor these conditions at home as well as by clinicians who need a portable perimeter.

The MRF apps are produced by a consortium that includes The University of Melbourne, The Royal Victorian Eye and Ear Hospital, glaucoma specialist and IT inventor Dr George Kong and optometrist and clinical scientist Professor Algis Vingrys.

The apps

Three apps of the MRF have been developed to target specific eye or brain conditions: MRF Glaucoma, MRF Macula and MRF Neural. (MRF Diabetes is planned for release soon). Each app has one or more near-acuity tests (Landolt C) and a visual field test grid tailored for the specific application. For example, although MRF Glaucoma and MRF Neural test the macula region, AMD is better detected and managed using the MRF Macula app which has been specifically designed for this purpose.

Acuity testing

To provide a full suite of vision assays, each MRF app contains a specially-designed acuity test (Figure 1). As this is achieved at near (33 cm) with normal reading spectacles (if any), it might have some limitations for returning precise acuity outcomes in myopes and younger adults, although testing in Africa reports accurate and reliable outcomes compared to an Early Treatment Diabetic Retinopathy Study chart in adults.[3]

Figure 1 is an example of the optotypes available for acuity testing in the MRF. These have been designed using the principles detailed by Westheimer[4] who found three discrete channels mediate acuity resolution: a high contrast size-dependent channel, which most clinicians are familiar with for detecting optical blur; a low contrast, low luminance channel that targets retinal and nerve dysfunction (note that amblyopes show little effect to this target); and an optotype shown in noise designed for higher order (brain) disorders.

Continued page 18

▲ Figure 1. Acuity targets used in the MRF applications target three discrete channels. A high-contrast target with contour interaction for standard acuity measures in the presence of optical blur; a low contrast, low luminance target to detect lower-order contrast processing deficits (retina, nerve); and an optotype in noise that can be used to detect integrative deficiencies (brain, for example: amblyopia).

Melbourne Rapid Fields

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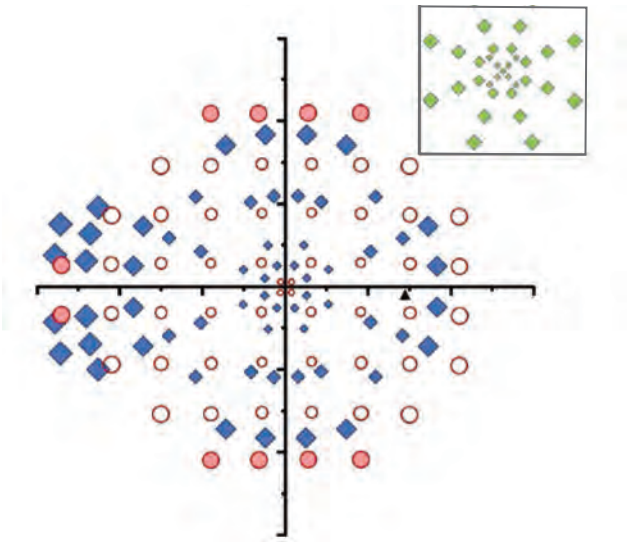


▲ Figure 2. Radial (blue diamonds) and extended 24-2 (red circles) test grids available in the MRF. MRF Neural does not test the far peripheral 24-2 locations (filled red circles). MRF Macula uses the grid shown in the inset (top right, green diamonds) with the box scaled to 20 degrees each side (10 degree eccentricity).

Visual field testing

A 30-degree field test is achieved by having the patient fixate on the corners of the tablet. Target size has been scaled (getting bigger) to give a constant threshold (30 dB) across the visual field. The test adopts a neighbourhood logic that checks points removed from the prediction of neighbouring locations. The test patterns are described next, including an expanding field that adds extra test points in regions of change to better define the edge of a scotoma.

MRF Glaucoma

This software has been designed to test the peripheral visual field out to 30 degrees by 24 degrees so it is ideal for glaucoma or any other condition needing peripheral visual field evaluation. Testing commences by thresholding a region out to 15 degrees by 12 degrees (9.7 inch screen tablet) then the test goes through a phase of moving the fixation point. This movement is to the four corners of the iPad, enabling the four quadrants of the peripheral field to be assayed (see below). The test grid is either a 66 point radial grid (Figure 2) optimised for glaucoma, neuropathy or macula defects or an extended 58 point 24-2 grid (Figure 2) with four extra points added in the fovea. Testing takes about four minutes per eye for the 9.7 inch screen or three minutes per eye for the large (12.9 inch) screen where fewer refixation movements are needed.

MRF Macula

This test was designed for macula conditions such as AMD or macula oedema. It is similar to the 10-2 pattern and evaluates the macula 10 degree region with a 33 point grid. It requires about 1.5 minutes per eye for testing. An example of a macula scotoma found with this test is shown in Figure 3.

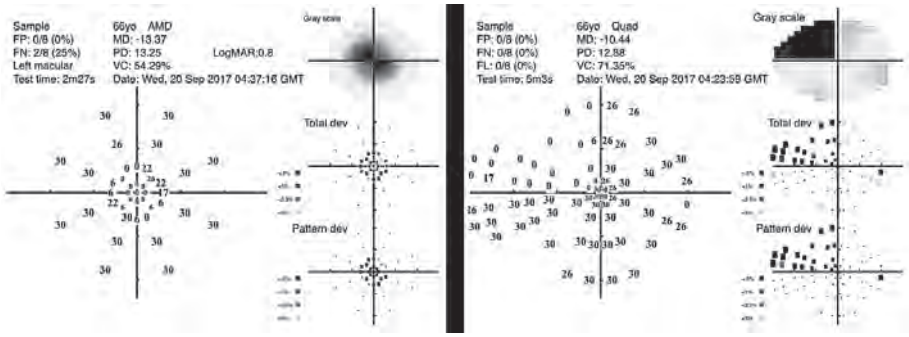
MRF Neural

This test was optimised for the large screen iPad Pro (12.9 inch) and neural conditions. It presents 46 points in a reduced 24-2 grid (21 degrees by 15 degrees, Figure 2) with four extra fovea points. The test is performed using central fixation only (no need for fixation changes) and requires about 2.2 minutes per eye for testing.

An Apple iPad generation 2 or newer device with a retina screen and iOS version 8 or higher is required to run the MRF software. An iPad mini (7.9 inch) or iPad3/4/Air (9.7 inch) may be used to run MRF Macula. MRF Glaucoma and MRF Neural require an iPad3/4/Air (9.7 inch) or the larger iPad Pro (12.9 inch) screen for testing.

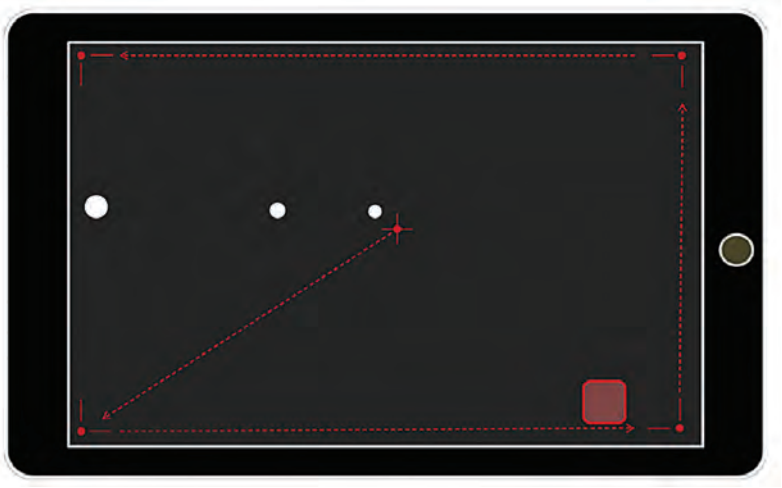
To perform an examination, the user is required to be seated in a dimly lit room free from reflections off the device's screen.[1] The patient's habitual reading correction should be worn and they must take care to ensure they are positioned approximately 33 cm from the screen. This is best checked with a calibrated string (a software process using the iPad camera is under development). Patching of the fellow eye can be achieved by covering with a hand or by draping a tissue over the spectacle lens, if spectacles are worn.

When a test is commenced, voice commands guide the patient through the examination. A red viewing cross appears in the centre of the screen as a fixation target on a background of 5

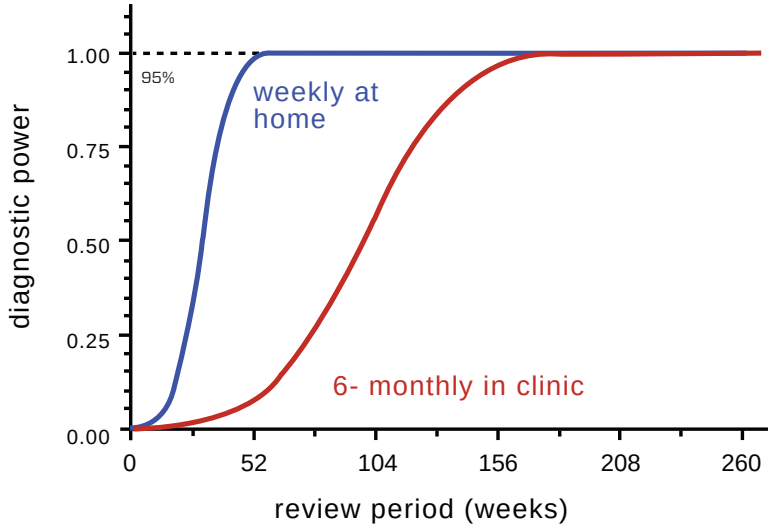


▲ Figure 3. Example field results in two patients tested with the 33-point MRF Macula grid (left) and 66-point MRF Glaucoma grid (right). As can be seen in the left panel, the MRF Macula test added eight extra test points to the grid shown in Figure 2 and required 2 minutes 27 seconds to define the central scotoma. On the right, the MRF Glaucoma test needed 5 minutes 3 seconds to define the left superior quadrantic loss in this patient.

cd/sqm. To respond to the stimulus, the user simply taps on the device screen to register that they have seen the spot. To avoid fingerprints on the screen and fingers from shielding a spot, a touch zone (red square) has been nominated (Figure 4). Stimulus responses may also be recorded by tapping the space bar of a Bluetooth keyboard if this is available. The keyboard is a recommended method of interfacing with the software and can be activated or deactivated by selection in the test menu. As the examination progresses, the fixation cross may move to each corner of the device to test peripheral locations of the visual field (Figure 4).



▲ Figure 4. A tablet showing the central fixation mark at the start of testing and the fixation pattern used during testing of peripheral locations. The response zone (red box) is shown in the lower right corner. Although the patient can respond by tapping the screen anywhere, they are encouraged to use the response zone to prevent the screen from becoming soiled and their fingers obscuring a spot location. The white spots on the screen show a schematic of the size scaling used in testing across the visual field.



▲ Figure 5. Predicted diagnostic power for weekly (at home) and six-monthly (in clinic) reviews for patients who have fast progression (-2 dB/year) in their visual field loss and comply with the requested test frequency.[6]

Thresholding takes place using a Bayes prediction that returns one of seven different outcomes (0-30 dB) after three presentations.[1] Reliability indices are assayed during the test (fixation loss, false positive, false negative) using a volley sampling method and patients who return error rates greater than 30 per cent should be considered as unreliable.

The results in Figure 3 are shown using familiar formats for the clinician: a grey scale plot, pointwise dB-plot, total deviation and pattern deviation plots with probability shading. The statistics that are calculated by the MRF are the mean defect (MD), the pattern defect (PD) and visual capacity (VC, is similar to Visual Field Index). A clinical trial has found very high concordance between the Humphrey Field Analyzer and the MRF MD indices (r = 0.91) despite the differences (test spot location, spot size, test procedure and background brightness) between these two devices.[5] This means that the results of the MRF can be confidently used in the management of glaucoma patients.

Once a test has been completed, results are stored via a cloud portal where artificial intelligence analyses the data and is able to detect changes in vision and alert the managing eye-care professional if these are present. This process needs five tests to define baseline threshold and variability and any changes are confirmed before any notification is made.

We routinely ask our patients to do MRF testing every day for the first week to establish baseline.

Given the lower cost and portability of these devices, patients now have the option to become involved in the management of their chronic vision loss by undertaking visual field examinations in the comfort of their own home. We have found that weekly home-monitoring by the patient has the capacity to detect progression in one-third of the time needed by regular six-monthly in-clinic reviews (Figure 5).[4] In addition, doctors practising in remote or rural locations can take advantage of the portability of the MRF and provide patients with an optimal standard of care.

Continued page 20

Melbourne Rapid Fields

From page 19

MRF is available to download from the Apple App Store. There is an initial download fee of $38 charged by the App Store, which allows six months use of the software as part of the download package. An on-going annual fee of $120 is charged for continued (12 months) use of the software. These fees go toward further software developments and in supporting community-based programs.

MRF comes in two forms: a regular and a 'lite' version. The lite versions have the same capacity as the regular versions but are free of charge and limited to eight saves only; they have been designed for practitioners or patients who want to gain familiarity with the software to see if it suits their purposes. ▲

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Relief for blepharitis and

Clinical strategies for

Dr Allan Ared

BOptom(Hons) GradCertOcTher(UNSW) FAAO

BLEPHARITIS and dry eye have for years been considered to be two separate diseases; however, courtesy of the extensive work undertaken by the Tear Film and Ocular Surface Society (TFOS)[1] we now readily accept that dry eye in both its evaporative and insufficiency forms is part of the natural sequelae from years of untreated lid disease.[2]

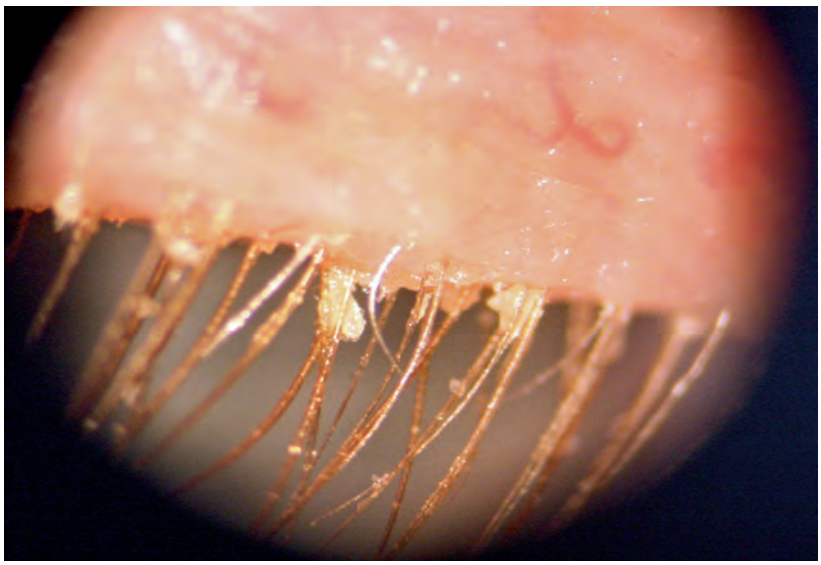
In other words, dry eye is simply the late manifestation of chronic blepharitis[3] and we as optometrists can do so much better in eye medicine by preventing damage to the lids in its early forms, instead of waiting to react to that damage once chronicity sets in.

To understand blepharitis correctly we must first understand the term blepharitis, which essentially means that we are dealing with an inflammatory eyelid condition. It is inflammatory due to the nature of the pathology, which often begins with bacterial colonisation of the lids followed by the formation of biofilms (Figure 1) then virulence factor production[4] before inflammatory inflicted lid damage.

MBE

Microblepharoexfoliation or MBE is a novel system for eliminating biofilm from the eyelid margins. Optometrists can easily perform this on patients as an in-office procedure by way of a patented instrument called BlephEx (BlephEx LLC).

BlephEx is a hand-held device that rotates a disposable, medical-grade water-soluble synthetic polymer-sponge which has been presoaked in a commercial eyelid-cleaning solution.



▲ Figure 1. Accumulation of biofilm in blepharitis

dry eye

maintaining a healthy ocular surface

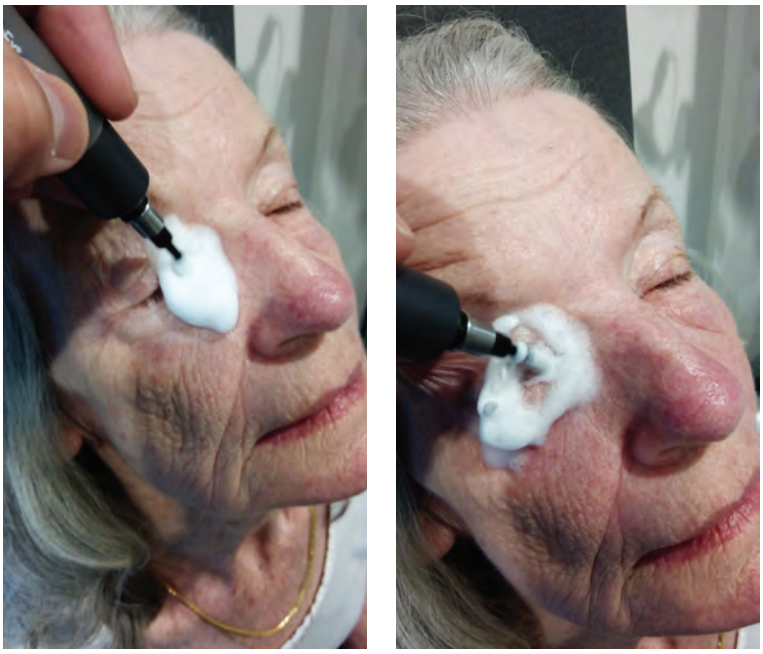
This micro-sponge tip spins at about 2000 rpm. This rotating action along with the lateral-medial-lateral motion of the tool by the operator provides detailed exfoliation to remove inflammatory biofilm and exotoxins, and debulks the bacterial overload. The procedure has also been reported to reduce the population of bacteria to below the quorum-sensing levels that induce virulence factor production.[3]

MBE is a simple procedure to master. Even after a few treatments, clinicians will have the expertise to handle the most difficult of blepharitis cases. The BlephEx device may be used with either hand and is held like a pen, supported between the thumb and the index finger. The disposable sponge tip needs to be presoaked in cleansing foam. I generally use Blephadex. After soaking, apply the spinning sponge onto the base of the lashes and with steady compression, move along the lid margin in small increments for roughly 25–30 seconds per lid.

The docking station of the BlephEx device has a built-in area for where the Blephadex foam is to be pumped. I have found it much easier to apply the foam over the patient's inner canthal area and to keep resoaking it from that canthal reservoir (Figure 2).

Both upper and lower lids are treated in a similar fashion and a new tip should be used for each eyelid to ensure elimination and disposal of the accumulated bacterial toxins.

Although the treatment is quick and relatively painless, most patients describe a tickling sensation or discomfort due to the quivering of the rotating tip. I use topical anaesthetic before the procedure and in cases of extreme sensitivity a topical anaesthetic gel along the base of the eyelids. After the lids have been meticulously cleaned, the excess foam is flushed out of the eye using a saline eye wash.



▲ Figure 2. Inner canthal area used as a foam reservoir of Blephadex

Topical therapeutic eye-drops, home lid remedies and over-the-counter artificial tears may only mask the symptoms of dry eye and blepharitis. Regular BlephEx treatment will clean the eyelid margins to eliminate the cause of irritation, offering the most effective results and immediate relief for both the clinical signs and symptoms of both dry eye and blepharitis. I tell patients that a BlephEx lid treatment is similar to a dentist tooth clean, far more effective than home brushing and vital for the effective long-term management and control. ▲

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Therapeutic NEWS of note

Associate Professor Mark Roth

BSc(Pharm) BAppSc(Optom) PGCertOcTher NEWENCO FAAO OAM

FDA approves new herpes zoster vaccine

GlaxoSmithKline's recombinant zoster vaccine Shingrix has been approved in the United States for the prevention of herpes zoster in adults aged 50 years and older.

The approval follows a unanimous vote by the Vaccines and Related Biological Products Advisory Committee of the US Food and Drug Administration that the vaccine is effective and safe for adults aged 50 years and older.

Shingrix combines an antigen, glycoprotein E, and an adjuvant system, AS01B, intended to generate a strong and long-lasting immune response that can help overcome the decline in immunity as people age, the company explained in a media release. Shingrix is given in two doses, with a two- to six-month interval between doses.

Shingrix was approved in Canada in October 2017 for the prevention of herpes zoster in people aged 50 years or older. Regulatory filings in the European Union, Australia and Japan are underway.

Nerf guns and serious ocular trauma

Nerf guns pose potential risks to the eyes of those who use them.

Researchers from the Accident & Emergency Department, Moorfields Eye Hospital NHS Foundation Trust, London, UK reported three unrelated patients presenting with pain and blurred vision following an injury caused by a Nerf gun.

Two of the patients were adults and one was a child, all of whom presented within a three-month period. All three cases were found to have ≥ 1mm of traumatic hyphaema, indicating significant ocular trauma. The two adult patients had formed hyphaema and uveitis. The 11-year-old child had formed hyphaema, corneal oedema, anterior uveitis, localised angle recession and commotio retinae, which further highlight the severity of the ocular trauma.

Although all three patients recovered their full vision, the study authors warned of potentially serious consequences from using the toy, noting: 'although Nerf guns are generally believed to be less harmful than pellet guns, this case series calls into consideration the need for protective eyewear with their use ... [and] calls for reconsideration of the safe age limits for Nerf gun use in children.'

BMJ Case Report. Sep 2017. doi: 10.1136/bcr-2017-220967.

OCT-A for corneal neovascularisation

Researchers demonstrated that optical coherence tomography angiography (OCT-A) can visualise corneal neovascularisation in patients with corneal diseases more clearly than slitlamp photography.

Five patients with five eyes showing partial or total limbal stem cell deficiency were involved in the evaluations. Three eyes had severe corneal scarring. Five 6 mm × 6 mm images (frontal, upper, lower, nasal and temporal) were obtained by OCT-A. Slitlamp photography was performed for all patients on the same day.

The results showed that OCT-A has two advantages over slitlamp photography for clear demonstration of corneal neovascularisation. OCT-A can show neovascularisation in cases with severe corneal opacification, and can detect not only large vessels but also small vessels that cannot be seen by slitlamp.

'OCT-A is a powerful tool for objective evaluation of vascularisation in the anterior and posterior segments of the eye,' the authors concluded.

Cornea. Sept 2017. 14. doi: 10.1097/ICO.0000000000001382.

Minor salivary gland transplantation for severe dry eyes

To evaluate the use of salivary glands as a source of lubrication to treat severe cases of dry eye, researchers at the Federal University of Sao Paulo, Brazil distributed symptoms questionnaires to patients who had undergone a specific procedure: minor salivary gland autotransplantation together with labial mucosa, used as a complex graft to the conjunctival fornix in severe dry eye.

The patients' responses revealed improvements in foreign body sensation, photophobia and pain. They also demonstrated significant improvements in best corrected visual acuity, Schirmer's test score, corneal transparency and neovascularisation after using this technique.

The authors wrote that their study demonstrated the viability of minor salivary glands transplanted into the fornix of patients with dry eye by performing immunohistochemistry on graft biopsies with antibodies against lactoferrin, lysozyme, MUC1 and MUC16.

Cornea. Nov 2017. doi: 10.1097/ICO.0000000000001358.

Delay between eye-drop instillations increases efficacy

Patients with chronic conditions requiring multiple, different eye-drops should wait five minutes between administration, according to a study in *Optometry and Vision Science.*

The authors designed their study to address a 'puzzling observation': patients are usually advised to wait five minutes between eye-drops to allow the first drop not to be washed out by the second one. However, in the only experimental study conducted in humans on the concurrent administration of two different eye-drops, the authors concluded that a 10-minute time interval between eye-drops did not increase their combined effect.

Using digital photographs shot in photopic conditions in 40 eyes of 20 healthy volunteers, researchers compared relative pupil surface before

and after the administration of one drop of 10% phenylephrine and one drop of 0.5% tropicamide either immediately or after a five-minute time interval.

One hundred and sixty pupil and iris surface images were anonymised and randomly arranged before being presented to two independent observers. The researchers found that waiting five minutes between two different eye-drops significantly increased their combined effect, contrary to previous conclusions made by other studies.

They propose that if two drops of different drugs are administered separately, with too small an interval between them, dilution limits the extent of absorption of both drugs compared with a combined drug solution.

Optom Vis Sci. Aug 2017. doi: 10.1097/OPX.0000000000001104.

Is aspirin safe for AMD patients?

The answer, according to a review published in *Retina,* is a qualified yes.

Researchers reviewed the current literature of the benefits that aspirin provides for patients' cardiovascular health compared to the risk of AMD worsening. Six cardiovascular and four ophthalmological trials on the risks and benefits of aspirin use were analysed.

The reviewed meta-analysis literature demonstrated a statistically significant 32 per cent reduction in the risk of nonfatal stroke with regular aspirin users. The study also documented that aspirin users decreased the risk of fatal vascular deaths by 15 per cent. Of the three ophthalmological studies highlighting the adverse affects of aspirin association with AMD, all suggested an exacerbation of AMD without statistical significance and broad confidence bands.

The authors concluded that the number, size and quality of the cardiovascular studies recommending aspirin use were far superior to the fewer, smaller and conflicting studies suggesting a possible adverse effect of aspirin use in relation to AMD.

'The benefits of aspirin usage include preserving the duration and quality of life by decreasing stroke and heart attack risk,' the authors wrote. 'These benefits seem to far outweigh the theoretical risks of possibly exacerbating wet AMD, which can be reasonably controlled with anti-VEGF therapy.'

Retina. Sept 2017. doi: 10.1097/IAE.0000000000001475

CoQ10 in retinal diseases

In a review published in *Current Medicinal Chemistry*, authors proposed that coenzyme Q10 (CoQ10) could have therapeutic potential for various retinal diseases.

CoQ10 plays a critical role in mitochondrial oxidative phosphorylation by serving as an electron carrier in the respiratory electron transport chain. CoQ10 also functions as a lipid-soluble antioxidant by protecting lipids, proteins and DNA damaged by oxidative stress.

The authors explained that CoQ10 deficiency had been associated with a number of human diseases including mitochondrial diseases, neurodegenerative disorders, cardiovascular diseases, diabetes and cancer, along with the ageing process. In many of these conditions CoQ10 supplementation therapy had been effective in slowing or reversing pathological changes, the authors noted. Oxidative stress is also a major contributory factor in the process of retinal degeneration.

The authors also discussed the use of CoQ10 in the treatment of age-related macular degeneration and glaucoma, and suggested that CoQ10 could have therapeutic potential for other retinal diseases in light of current data.

Curr Med Chem. Aug 2017. doi: 10.2174/0929867324666170801100516. [Epub ahead of print]

Topical tacrolimus for SEIs

Topical tacrolimus, compounded in the pharmacy, appears to be an effective and safe alternative for the treatment of corneal subepithelial infiltrates (SEIs) secondary to adenovirus keratoconjunctivitis.

To determine the efficacy and safety of topical tacrolimus for the treatment of SEIs secondary to adenoviral keratoconjunctivitis, researchers conducted a retrospective study of patients who had been dispensed topical tacrolimus for the condition during the previous year.

Fifty-five patients (85 eyes) were included, 54.5 per cent with bilateral involvement. A total of 31 (36.5 per cent) eyes were treated with tacrolimus ointment and 54 eyes (63.5 per cent) with tacrolimus eye-drops. The median length of treatment was 185 days and the mean follow-up duration was 363 days.

In 62.35 per cent of the eyes, the SEIs were reduced in number and size, and in 31.76 per cent, they were eliminated. The patients had better visual acuity after treatment with highly statistically-significant differences. Tolerance was good overall, being better in the eye-drops group.

Cornea. Sept 2017. doi: 10.1097/ICO.0000000000001279.

Low-dose atropine safer

A meta-analysis of published studies has found that low-dose atropine is equally effective in slowing myopia progression in children and has fewer side-effects than higher doses.

Researchers conducted a meta-analysis of published studies in PubMed, EMBASE and the Cochrane Central Register for Controlled Trials.

The data showed significantly less progression of myopia with all doses of atropine compared with control groups, but no correlation was found between dose and treatment effect. Ethnicity also had no impact on the effect of treatment.

A total of 308 adverse effect events occurred in 2,425 patients in the atropine groups (12.7 per cent). The difference with control groups was statistically significant. The most common effects were photophobia, poor vision at near and allergy, and their incidence significantly increased with dose escalation.

The authors recommended the use of the lowest dose of atropine (0.01%) for therapy, but cautioned that more clinical trials with this dose were needed.

JAMA Ophthalmol. Jun 2017. doi: 10.1001/jamaophthalmol.2017.1091

Assessing artificial tears

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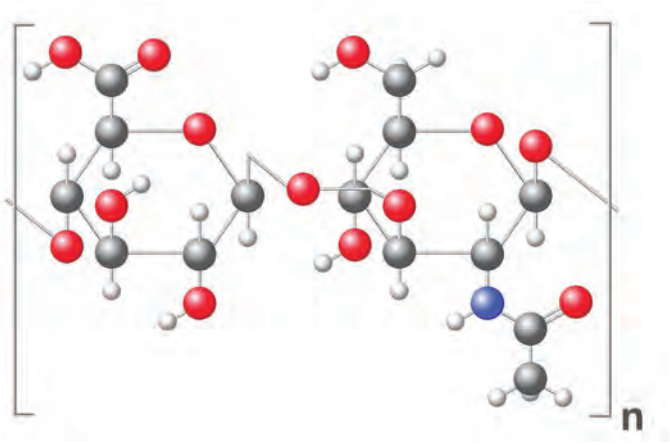

WHAT MAKES a good artificial tear (AT)? It's hard to answer this question as most of us who treat dry eye are aware that no single AT is effective for all patients. Many patients appear refractory to all ATs. In some cases, ATs worsen dry eye symptoms.

Comparative studies of ATs are somewhat futile in this context too, as it is difficult to predict how a patient will respond to a given product with variations in their disease severity over time. Successive meta-analyses are also inconclusive on this point,[1,2] as is DEWS II (2017 international dry eye workshop) which acknowledged that no two dry eye patients are alike and that no single treatment plan can be effective for all patients.[3]

In this article, we select one class of pharmaceutical used in the treatment of dry eye: hyaluronic acid (HA), highlighting some of its potential advantages.

Historically, artificial tears (ATs) act as a first-line topical treatment in dry eye. ATs mainly comprise three classes of pharmaceutical: natural cellulose derivatives, (such as carboxymethylcellulose), synthetic polymers (such as PVA and HP-guar) and hyaluronic acid. In their own way, ATs can have a role to play in reducing ocular surface inflammation.

Carboxymethylcellulose (CMC) and hyaluronic acid (HA) are two of the most commonly prescribed and used artificial tears.[4] CMC's anionic cellulose polymer with substituted carboxyl group makes it 'sticky' to the ocular surface, enabling greater bio-adhesion and increased tear retention time. In comparison, HA is a glycosaminoglycan with repeating alternating N-acetylglucosamine and glucuronate sequences in linear chains. This structure is viscoelastic and binds water molecules,[5] helping to reduce surface dehydration and shear forces during blinking,[6,7] effects that indirectly help lessen surface inflammation.

What is hyaluronic acid?

Sodium hyaluronate is a naturally-occurring molecule of the human body, but sodium hyaluronate and hyaluronic acid are different chemicals; the former is a water-soluble salt form of the latter. Although about half the HA in our bodies is found in skin, it was first discovered by Karl Meyer and John Palmer in human vitreous.[8] Synthetic HA was patented in 1942 by Endre Balazs for commercial use in baking products, and was originally intended for use as a substitute for egg white.[9]

The name 'Healon' (a highly purified form of HA) was trademarked in 1970 and first used medically in ophthalmic surgery. Today HA has become widely used in ophthalmic surgery, dry eye care and cosmetic medicine to improve skin texture and hydration.[10]

HA is one of several viscosity enhancers used in ATs. Its ability to retain a significant volume of water[11] and its visco-elasticity helps it to maintain corneal surface wettability, reduce tear osmolarity and reduce shear forces associated with blinking and air flow. HA has been shown to improve corneal density of all five layers,[12] and suppress specific inflammatory mediators, while up-regulating other protective mediators.[13] It is also associated with protection of goblet cell density and a reduction of dry eye associated squamous metaplasia, two characteristics of dry eye.[14] Collectively, these properties appear to have stabilising effects on the ocular surface, preventing disease and enhancing epithelial repair processes.[15,16]

BENEFITS OF HYALURONIC ACID

Tear osmolarity

Excessive tear evaporation and reduced aqueous volume can lead to hyperosmolar tears. These changes cause stress on the ocular surface with resultant corneal and conjunctival cell death, tissue inflammation and a destructive cycle of events.[17]

Tear osmolarity's predictive value for dry eye disease was conceptualised from indecision regarding diagnostic criteria for Sjögren's syndrome, but its experimental origins date from almost 50 years ago. In animal studies, hypo-osmolar electrolyte solutions appear best suited to reducing the effects of dry eye,[18] while hypotonic HA is effective in human trials[2,19] and may be more effective in lowering tear film osmolarity than carboxymethylcellulose and HP-guar.[20]

pH balance and phosphate free

The pH of normal tears is 7.4 (tolerance: 6.6–7.8). AT complexity revolves around buffer maintenance of this criterion while ensuring good wettability, lubricity and retention time

on the ocular surface. While some ATs use phosphate as a buffer, the use of citrate has been found to be desirable.

Although phosphate buffers in eye-drops are effective, innate corneal calcium can react with phosphate to form calcium phosphate crystals. These have been shown to cause corneal calcification: an accumulation of the insoluble crystals, particularly in severe dry eye and already compromised corneas. In one study, 26 of 59 eye-drops tested had phosphate levels above physiological levels, with very high concentrations being found in three products.[21] In some reported cases, affected patients have required corneal transplants.[22] Fortunately, the incidence of this adverse response is low; however, given a choice, phosphate-free is more prudent.

Preservative free

Many eye-drops contain the preservative benzalkonium chloride (BAK), a cationic surfactant which disrupts the lipid layer on contact with the eye. It also penetrates the epithelial cell microvilli and goblet cells with consequential cell death. Without clearance of the BAK, cell death allows release of the BAK to affect neighbouring cells;[23,24] a single drop of 0.01% BAK is detectable in the epithelial cell layer for up to seven days.[25] In addition to cell toxicity, the use of preserved ATs is also associated with allergies in some patients.[26] Newer ATs contain neutralising or less-invasive preservatives; however, some of these are also associated with adverse ocular surface effects.[27]

There are many unpreserved ATs on the market, but only two main delivery systems. Individual-use vials are most common. These are typically used once, prior to disposal.

The alternative is a multi-dose system such as the one used by AFT pharmaceuticals for Hylo-Forte. The 'COMOD' (COntinuous MOno Dose multidose) system comprises a pump in a bottle; the solution is contained within the bottle in a sterile flexible bag. By pressing the pump, a drop is expelled from the bag onto the eye. When the pump is released, air pressure is restored in the bottle via a ventilation duct, but not into the bag. The contents of the bag therefore remain sterile.

The active ingredient in Hylo-Forte may also prove useful in patients who use BAK-containing medications for other purposes such as glaucoma treatment, as HA may reduce the toxic effect of benzalkonium chloride.[28]

Conclusion

Hylo-Forte is one of a number of dry eye products that contribute some significant features and benefits to the choice of AT for our dry eye patients. Apart from the active ingredient 0.2% sodium hyaluronate, the other Hylo-Forte components are citric acid, sodium citrate dehydrate and sorbitol. While we cannot entirely predict the outcome of a treatment, informed choice can help to prevent prescribing errors.

Disclosure

This article was written with the financial support of AFT Pharmaceuticals. ▲

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PBS list of medicines prescribed by optometrists

Revised November 2017

By writing a PBS prescription for an antiglaucoma agent, the prescriber is certifying that the criteria set out in the PBS guidelines are satisfied

	Product	Max qty	Repeats
ANTI-GLAUCOMA PREPARATIONS			
Betaxolol eye-drops, suspension, 2.5 mg (as hydrochloride)/mL, (0.25%), 5 mL	Betoptic S	1	5
Betaxolol eye-drops, solution, 5 mg (as hydrochloride)/mL, (0.5%), 5 mL	Betoptic, BetoQuin	1	5
Bimatoprost eye-drops 300 mcg/mL (0.03%), 3 mL	Lumigan	1	5
Bimatoprost eye-drops 300 mcg/mL (0.03%) 30 x 0.4 mL unit doses	Lumigan	1	5
Bimatoprost with timolol eye-drops containing bimatoprost 300 mcg/mL (0.03%) with timolol 5 mg (as maleate)/mL (0.5%), 3 mL	Ganfort 0.3/5	1	5
Bimatoprost with timolol eye-drops containing bimatoprost 300 mcg/mL (0.03%) with timolol 5 mg (as maleate)/mL (0.5%), 30 x 0.4 mL unit doses	Ganfort PF 0.3/5	1	5
Brimonidine tartrate eye-drops 1.5 mg/mL (0.15%), 5 mL	Alphagan P 1.5	1	5
Brimonidine tartrate eye-drops 2.0 mg/mL (0.2%), 5 mL	Alphagan P 2.0	1	5
Brimonidine with timolol eye-drops containing brimonidine tartrate 2 mg/mL (0.2%) with timolol 5 mg (as maleate)/mL (0.5%), 5 mL	Combigan	1	5
Brinzolamide eye-drops 10 mg/mL (1%), 5 mL	Azopt, BrinzoQuin	1	5
Brinzolamide 10 mg/mL (1%) eye-drops containing brimonidine tartrate 2 mg/mL (0.2%), 5 mL	Alphagan, Enidin	1	5
Brinzolamide with timolol eye-drops containing brinzolamide 10 mg/mL (1%) with timolol 5 mg (as maleate)/mL (0.5%) 5 mL	Azarga	1	5
Dorzolamide eye-drops 20 mg (as hydrochloride)/mL (2%), 5 mL	Trusopt, Trusamide	1	5
Dorzolamide with timolol eye-drops containing dorzolamide 20 mg (as hydrochloride)/mL (2%) with timolol 5 mg (as maleate)/mL (0.5%), 5 mL	Cosopt, Cosdor, Dorzolamide/ Timolol Sandoz 20/5	1	5
Latanoprost eye-drops 50 mcg/mL (0.005%), 2.5 mL	Latanaprost, Xalaprost, Xalatan	1	5
Latanoprost with timolol eye-drops containing latanoprost 50 mcg/mL (0.005%) with timolol 5 mg (as maleate)/mL (0.5%), 2.5 mL	Xalacom, Latanocom, Xalamol 50/5, Latanaprost/Timolol Sandoz 50/5	1	5
Pilocarpine eye-drops containing pilocarpine hydrochloride 10 mg/mL (1%), 15 mL	Isopto Carpine	1	5
Pilocarpine eye-drops containing pilocarpine hydrochloride 20 mg/mL (2%), 15 mL	Isopto Carpine	1	5
Pilocarpine eye-drops containing pilocarpine hydrochloride 40 mg/mL (4%), 15 mL	Isopto Carpine	1	5
Timolol eye-drops 5 mg (as maleate)/mL (0.5%), 5 mL	Tenopt, Timoptol	1	5
Timolol eye-drops (gellan gum solution) 2.5 mg (as maleate)/mL (0.25%), 2.5 mL	Timoptol XE	1	5
Timolol eye-drops (gellan gum solution) 5 mg (as maleate)/mL (0.5%), 2.5 mL	Timoptol XE	1	5
Timolol eye gel 1 mg (as maleate)/g (0.1%), 5 g	Nyogel	1	5
Travoprost eye-drops 40 mcg/mL (0.004%), 2.5 mL	Travatan	1	5
Travoprost with timolol eye-drops containing travoprost 40 mcg/mL (0.004%) with timolol 5 mg (as maleate)/mL (0.5%), 2.5 mL	Duotrav	1	5

NOTE: Antiglaucoma preparation Tafluprost eye-drops 15 mcg/mL (0.0015%) single dose units 0.3 mL x 30 is PBS listed for optometric prescribing. At this time it is not included on the Optometry Board of Australia approved list of drugs that optometrists are authorised to prescribe. As a result, optometrists cannot currently prescribe Tafluprost eye-drops.

	Product	Restriction	Max qty	Repeats
ANTI-VIRAL EYE PREPARATIONS				
		Restricted:		
Aciclovir eye ointment 30 mg/g (3%), 4.5 g	Zovirax	Herpes simplex keratitis	1	0

PBS list of medicines prescribed by optometrists (continued)

	Product	Restriction	Max qty	Repeats
ANTIBIOTICS				
Chloramphenicol eye-drops 5 mg/mL (0.5%), 10 mL	Chlorsig	Restricted: For treatment of patients identifying as Aboriginal or Torres Strait Islander	1	2
Ciprofloxacin eye-drops 3 mg /mL (0.3%), 5 mL	CiloQuin, Ciloxan	Authority required: bacterial keratitis	2	0
Framycetin sulfate eye-drops 5 mg/mL (0.5%), 8 mL	Soframycin		1	2
Gentamicin eye-drops 3 mg/mL (0.3%), 5 mL	Genoptic	Restricted: Suspected pseudomonal eye infection	1	2
Ofloxacin eye-drops 3 mg/mL (0.3%), 5 mL	Ocuflox	Authority required: bacterial keratitis	2	0
Tobramycin eye-drops 3 mg/mL (0.3%), 5 mL	Tobrex	Restricted: Suspected pseudomonal eye infection	1	2
Tobramycin eye ointment 3 mg/g (0.3%), 3.5 g	Tobrex	Restricted: Suspected pseudomonal eye infection	1	0
ANTI-INFLAMMATORY AGENTS				
Dexamethasone eye-drops 1 mg /mL (0.1%), 5 mL	Maxidex	Applications for increased maximum quantities and/or repeats will not be authorised.	1	0
Fluorometholone eye-drops 1 mg/mL (0.1%), 5 mL	Flucon, FML Liquifilm		1	0
Fluorometholone acetate eye-drops 1 mg/mL (0.1%), 5 mL	Flarex		1	0
Hydrocortisone acetate eye ointment 10 mg/g (1%), 5 g	Hycor		1	0
Prednisolone acetate with phenylephrine hydrochloride eye-drops 10 mg-1.2 mg/mL (1%-0.12%), 10 mL	Prednefrin Forte	Restriction: Uveitis. Applications for increased maximum quantities and/or repeats will not be authorised.	1	0
ANTI-ALLERGY AGENTS		Restricted:		
Sodium cromoglycate eye-drops 20 mg/mL (2%), 10 mL	Opticrom	Vernal keratoconjunctivitis	1	5
TEAR SUPPLEMENTS		Restricted: Severe dry eye including Sjögren's syndrome		
Carbomer 980 eye gel 2 mg/g (0.2%), 10 g	Optifresh eye gel	As above	1	5
	PAA	As above	1	5
	Viscotears	As above	1	5
Carmellose sodium 5mg/mL (0.5%) with glycerol 9 mg/mL (0.9%) eye-drops, 15 mL	Optive	As above	1	3
Carmellose sodium eye-drops 10 mg/mL (1%), 15 mL	Refresh Liquigel	As above	1	5
Carmellose sodium eye-drops 5 mg/mL (0.5%), 15 ml	Refresh Tears plus	As above	1	5
Hypromellose eye-drops 3 mg/mL (0.3%), 15 mL (contains sodium perborate)	In a Wink Moist'ing Genteal	As above	1	5
Hypromellose eye-drops 5 mg/mL (0.5%), 15 mL	Methopt	As above	1	5
Hypromellose 3 mg/mL (0.3%) with carbomer 980 2 mg/g (0.2%) ocular lubricating gel, 10 g	HPMC PAA Genteal gel	As above	1	5

PBS list of medicines prescribed by optometrists (continued)

	Product	Restriction	Max qty	Repeats
TEAR SUPPLEMENTS		Restricted: Severe dry eye including Sjögren's syndrome		
Hypromellose 3 mg/mL (0.3%) with dextran eye-drops 1 mg/mL (0.1%), 15 mL	Poly-Tears, Tears Naturale	As above	1	5
Polyethylene glycol 400 mg/mL (0.4%) with propylene glycol 3 mg/mL (0.3%) eye-drops, 15 mL	Systane	As above	1	5
Polyvinyl alcohol eye-drops 14 mg/mL (1.4%), 15 mL	PVA Tears, Liquifilm Tears	As above	1	5
Polyvinyl alcohol eye-drops 14 mg/mL (1.4%), 15 mL (contains sodium chorite/hydrogen peroxide as preservative)	Vistil	As above	1	5
Polyvinyl alcohol eye-drops 30 mg/mL (3%), 15 mL (contains sodium chorite/hydrogen peroxide as preservative)	Vistil Forte	As above	1	5
UNPRESERVED TEAR SUPPLEMENTS		Authority required:		
Carbomer 974 ocular lubricating gel 3 mg/g (0.3%), single dose units 0.5 g x 30	Poly Gel	Severe dry eye syndrome in patients sensitive to preservatives in multi-dose eye-drops	3	5
Carbomer 980 eye gel 2 mg/g (0.2%), single dose units 0.6 mL x 30	Viscotears Gel PF	As above	3	5
Carmellose sodium eye-drops 5 mg/mL (0.5%), single dose units 0.4 mL x 30	Cellufresh Optifresh Tears	As above	3	5
Carmellose sodium eye-drops 10 mg/mL (1%) , single dose units 0.4 mL x 30	Celluvisc Optifresh Plus	As above	3	5
Carmellose sodium eye-drops 2.5 mg/mL (0.25%), single dose units, 0.6 mL x 24	TheraTears	As above	4	5
Carmellose sodium ocular lubricating gel 10 mg/mL (1%), single dose units 0.6 mL x 28	TheraTears	As above	3	5
Hypromellose 3 mg/ mL (0.3%) with dextran eye-drops 1 mg/mL (0.1%), single dose units 0.4 mL x 28	Bion Tears	As above	3	5
Polyethylene glycol 400, 4 mg/mL (0.4%) with propylene glycol 3 mg/mL (0.3%) eye-drops, single dose units 0.8 mL x 28	Systane	As above	2	5
Sodium Hyaluronate sodium hyaluronate eye-drops 1 mg/mL (0.1%), 10 mL	Hylo-Fresh	As above	1	5
Sodium Hyaluronate sodium hyaluronate eye-drops 2 mg/mL (0.2%), 10 mL	Hylo-Forte	As above	1	5
Soy Lecithin 1% + tocopherol 0.002% + vitamin A palmitate 0.025% eye spray, 100 actuations	Tears again	As above	2	5
TOPICAL OCULAR LUBRICANT OINTMENTS				
Paraffin 1 g/g compound eye ointment 3.5 g	Polyvisc, Duratears		2	5
Paraffin 1 g/g pack containing 2 tubes compound eye ointment 3.5 g	Polyvisc (2 pack), Ircal (2 pack), Refresh Night Time (2 pack)		1	5
Paraffin paraffin + retinol palmitate 138 mcg/g (0.0138%) (equivalent to 250 units/g vitamin A) eye ointment, 5 g	VitA-POS		2	5

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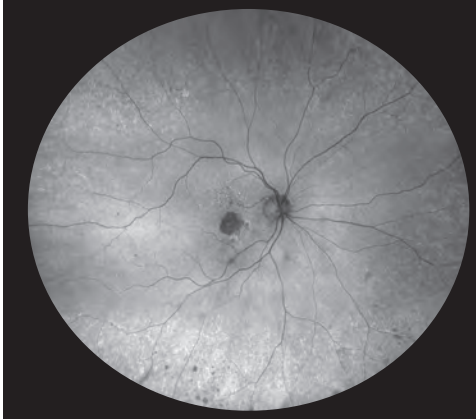

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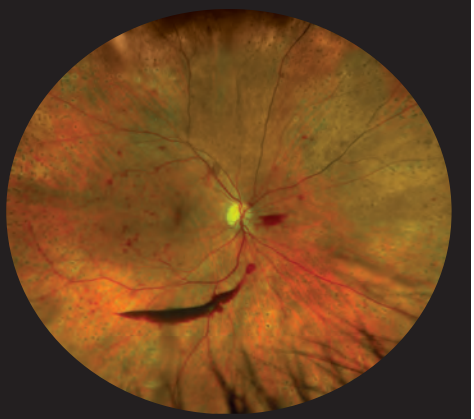

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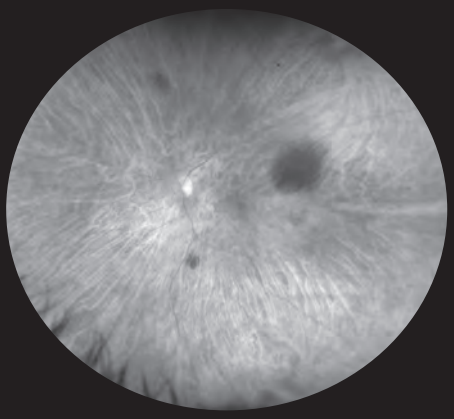

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