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INVITED REVIEW

Optical coherence tomography imaging in keratoconus

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Harry Yip* MBBS
Elsie Chan† FRANZCO
*School of Medicine, Monash University, Melbourne, Victoria, Australia
†Ophthalmology, Royal Victorian Eye and Ear Hospital, Centre for Eye Research Australia, The University of Melbourne, Melbourne, Victoria, Australia
Email: elsie.chan@eyeandear.org.au

Optical coherence tomography (OCT) is being increasingly used as a tool in the diagnosis and management of keratoconus. While elevation-based topography remains essential, there is an expanding role for cross-sectional OCT imaging in the diagnosis of the disease. Images and measurements of corneal thickness, and in particular, epithelial thickness, may be important in diagnosing early cases, and following procedures such as intrastromal corneal ring segments, corneal transplants and corneal collagen cross-linking.

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Since its conception in the 1990s, optical coherence tomography (OCT) has become an important non-invasive, high resolution, imaging modality in the assessment of the cornea and anterior segment. In this review, we discuss uses of OCT in the diagnosis and management of keratoconus, including its utility in surgical treatments such as corneal collagen cross-linking (CXL), intrastromal corneal ring segments and corneal transplants.

Corneal topography

The current gold standard for the diagnosis of keratoconus and other corneal ectatic diseases is corneal topography.[1] There are several topography systems currently used in clinical practice. Placido disc systems (commonly referred to as topography, although they are not true topographers, as the curvature maps are derived), project concentric rings on the corneal surface, and algorithms are used to analyse the reflected image to derive anterior curvature measurements. Conversely, scanning slit devices (for example, Orbscan, Bausch & Lomb) and Scheimpflug imaging (for example, Pentacam, Oculus) measure both anterior and posterior elevation from which curvature is derived; the former uses a rapidly scanning slit beam and camera whereas the latter uses a rotating Scheimpflug camera to image the anterior and posterior corneal surfaces, iris and anterior lens surface. These devices enable 3-D reconstruction of the cornea using serial scans.

Elevation-based topography (tomography) systems are currently the most widely used systems in the diagnosis of keratoconus.[2] Some devices also include proprietary software to diagnose keratoconus and monitor its progression based on various anterior and posterior corneal indices and corneal thickness measurements (for example, the Belin-Ambrosio Enhanced Ectasia Display and the ABCD keratoconus grading system on the Pentacam [Oculus]).

The main disadvantage of topographical systems is that they are sensitive to a poor ocular surface (for example, dry eyes) and irregularities such as corneal scars. These can, in turn, make the diagnosis of keratoconus more challenging.[3] The image acquisition time is also relatively slow (for example, the Pentacam requires two seconds for 50 radial scans), increasing the risk of motion artefacts.[4,5] A third disadvantage of topography is its inability to provide visualisation of the individual corneal layers.

OCT

OCT technology overcomes some of the issues with topographical systems, allowing higher resolution, 3-D imaging of the cornea and anterior segment.[6,7] In addition, cross-sectional images of the anterior segment allow thickness maps to be generated of both the whole cornea and its individual layers, including the epithelium.[8–11] OCT can also measure anterior chamber depth, lens vault, pupil diameter, scleral spur angle and other anterior segment parameters.[12] The OCT is as reproducible and comparable to Scheimpflug imaging when measuring corneal thickness.[13,14]

More recently, swept-source/Fourier domain OCT devices (SS-OCT) have been introduced with higher speed and sensitivity allowing anterior and posterior corneal topography as well as cross-sectional corneal images (for example, Casia, Tomey).[15] Earlier OCT devices were limited by acquisition time and could not perform corneal topography. SS-OCT has been shown to be more repeatable than Scheimpflug and Placido-ring devices in keratoconus and following corneal transplantation in measuring keratometry values, elevation, anterior chamber depth and corneal thickness.[16,17]

This review focuses on the use of OCT in cross-sectional imaging of the anterior segment in keratoconus.

OCT changes in keratoconus

According to the Global Consensus on Keratoconus and Ectatic Diseases, keratoconus is characterised by posterior elevation and

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abnormal corneal thickness distribution, although the precise values for each depend on the type of imaging device used. Elevation-based topography (for example, with Scheimpflug or OCT) is currently considered the most appropriate device to detect early keratoconus.[2]

There has been increasing interest in using corneal thickness measurements to facilitate the diagnosis of keratoconus as it is less susceptible to other causes of surface distortion such as scarring, contact lens warpage and a poor tear film.[18,19] Focal and eccentric corneal thinning, asymmetric thinning between the inferior and superior quadrants, and between the inferotemporal and superonasal octants have been demonstrated on cross-sectional OCT (Figure 1). Such findings may provide a useful adjunct in cases where there is uncertainty following topographical imaging.[20] Changes in corneal thickness profiles over time may also provide information on disease progression.[2]

Corneal epithelial thickness mapping using OCT may also be useful for the early diagnosis of keratoconus.[11] Similar to total corneal thickness measurements, epithelial thickness maps have demonstrated that eyes with keratoconus have apical epithelial thinning, and in a typical inferotemporal cone, there is a corresponding thicker epithelial layer superonasally. This is in contrast to non-ectatic corneas, where the opposite applies: the corneal epithelium is thinner superiorly and thicker inferiorly.[21] Other epithelial thickness changes that have been reported are a decreased overall thickness, greater differences between the minimum and maximum epithelial thicknesses, and greater variability of the pattern standard deviation and map standard deviation compared with normal eyes.[11,22,23]

Epithelial thinning at the apex of the cone may be due to compensatory remodelling in response to the underlying stromal thinning and steepening to reduce anterior surface irregularity.[11,24] This may then lead to masking of the stromal thinning when measurements of the total corneal thickness are made, or cause topographic images to appear relatively normal, particularly in the early stages of keratoconus.[23,25] It is therefore important to consider analysis of the epithelium and stroma separately with OCT, which may allow more accurate diagnosis and assessment of keratoconus.[18,23] It could also be utilised to provide additional information in patients whose corneal topography is equivocal, especially in refractive surgery candidates.[26–28]

Despite the usefulness of cross-sectional OCT in measuring corneal and epithelial thickness, both parameters are insufficient as independent diagnostic parameters and should be used in combination with elevation-based corneal topography to diagnose keratoconus.[2,26]

Disadvantages of OCT

One of the disadvantages of using epithelial mapping in the diagnosis of keratoconus is the potential inaccuracy in the measurement of the corneal epithelium. This can occur if the tear film is not excluded from the measurement, or following eye rubbing and rigid gas permeable contact lens wear which may affect epithelial thickness and reflectivity.[11] In addition, fragmentation of Bowman's layer can occur in keratoconus,[29] resulting in an indistinct border between the epithelium and Bowman's layer on OCT.[11]

Corneal cross-linking

Corneal collagen cross-linking (CXL) is a treatment that slows or stops progression in keratoconus by strengthening the biomechanical and biochemical properties of the cornea. The procedure involves instillation of vitamin B_2 (riboflavin) drops, followed by exposure to ultraviolet A irradiation at 370 nm,[30] although many variations in the CXL treatment protocol exist.

The most widely reported change seen on cross-sectional OCT following CXL has been the appearance of a 'demarcation' line within the corneal stroma.[31–33] This line has been postulated to represent the depth of the CXL treatment, separating the treated anterior stroma and untreated posterior stroma.[34] The demarcation line is hyper-reflective when viewed with OCT, Scheimpflug imaging and on slitlamp biomicroscopy.[31,34] OCT provides the ability to measure the depth of the demarcation line[33,35,36] and has been used as an important outcome parameter when comparing various CXL protocols.[33,37,38] The demarcation line usually fades by three months and, in some corneas, is replaced with faint, irregular, hyper-reflective lines in the deep stroma.[39]

Other changes that can be noted on OCT images following CXL include increased reflectivity of the treated stroma, and the appearance of fainter, secondary stromal demarcation lines.[40] The hyper-reflective treated stroma has been correlated to confocal microscopy findings of increased extracellular matrix reflectivity and keratocyte hyperplasia.[41] The secondary stromal demarcation lines have been reported less frequently and appear at variable depths. These are thought to be related to differences in treatment depths and corneal thickness fluctuations during the irradiation stage of the CXL procedure.[40]

Epithelial mapping using OCT has also demonstrated notable post-operative changes. Compared to the epithelium in keratoconus, where there is apical epithelial thinning with a surrounding zone of thicker epithelium,[23] it has been shown that a more uniform epithelial thickness is observed in the early post-operative period after CXL. This could explain the observation that there is an increase in corneal curvature in the first few months after CXL,[25] whereby the more uniform thickness of the epithelium unmasks the underlying anterior stromal curvature.[25]

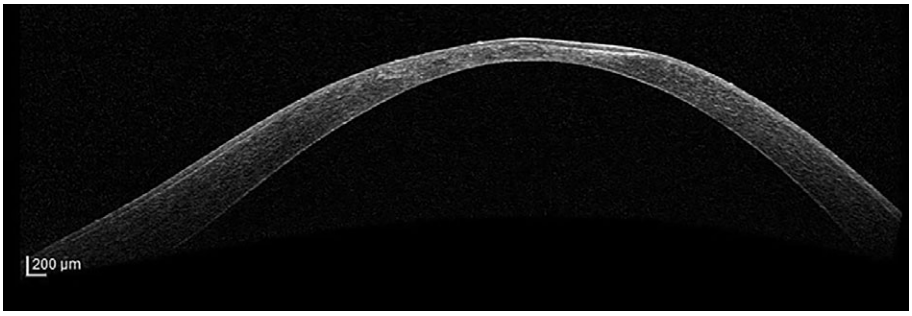


Figure 1. Apical thinning in keratoconus (Spectralis optical coherence tomography, Heidelberg Engineering)

Hydrops

Corneal hydrops is a rare complication of keratoconus which involves a break in

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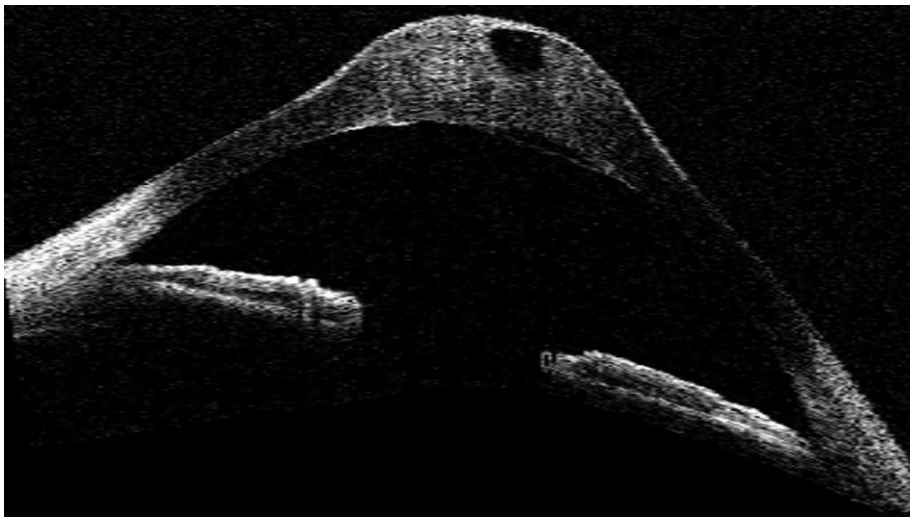


Figure 2. Corneal oedema secondary to hydrops (Visante anterior segment optical coherence tomography, Carl Zeiss Meditec)

Descemet's membrane and secondary stromal oedema from the leakage of aqueous humour into corneal stroma (Figure 2). Corneal hydrops generally resolves with a scar, but it can lead to corneal vascularisation, and rarely, bacterial keratitis, pseudocyst formation and corneal perforation.[42–45]

OCT is also useful following the occurrence of hydrops, as it can both assess the morphology of the hydrops as well as monitor healing and scar formation.[39,46]

Intrastromal corneal ring segments

Intrastromal corneal ring segments were developed to correct myopia,[47] and can also be used in keratoconus and other corneal ectatic diseases.[48] When placed within the mid-periphery of the cornea, the rings shorten the arc length of the anterior corneal surface, thereby inducing a flatter cornea.[49]

However, poor placement of rings can lead to complications.[50] When placed too deep within the stroma, there is an increased risk of perforation into the anterior chamber; whereas if they are placed too anteriorly, there is an increased risk of epithelial breakdown, extrusion and corneal melting.[50] Assessing the depth at which to place intrastromal rings by using the slitlamp alone may be less accurate, resulting in an increased risk of complications.[51]

OCT can help to accurately determine the thickness of the cornea at the site of ring placement pre-, intra- and post-operatively (Figure 3).[52] Pre-operatively, OCT can quantitatively and qualitatively evaluate the corneal stroma before implantation to ensure there is adequate depth for ring placement; intra-operatively, OCT can be used to assess manual or femtosecond laser created tunnels before implantation of the intrastromal ring.[53,54] Post-operatively, OCT can be used to monitor segment migration and depth so that complications can be more readily anticipated.[55]

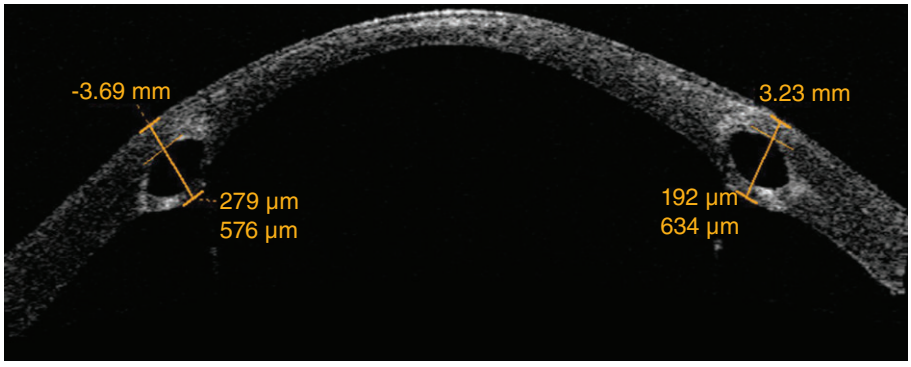


Figure 3. Intrastromal corneal ring segments (Visante anterior segment optical coherence tomography, Carl Zeiss Meditec)

Through its ability to precisely measure corneal parameters and the depth necessary for placement of intrastromal rings, OCT has become a useful tool in the management of keratoconic patients undergoing this procedure.[56]

Corneal transplants

In Australia, there are around 306 corneal transplants performed every year for keratoconus, with numbers remaining stable over the period 2000–2016.[57] Currently the two most common corneal graft procedures for the treatment of keratoconus are penetrating keratoplasty (PK) and deep anterior lamellar keratoplasty (DALK).[57] Both types of transplants have been shown to provide comparable visual outcomes.[58] DALK involves suturing a donor corneal button where Descemet's membrane and endothelium have been removed, onto the recipient's posterior cornea consisting of Descemet's membrane and endothelium, with or without a thin layer of posterior stroma (depending on whether there is baring of Descemet's membrane or not).[59] It has advantages over a PK in that it eliminates the risk of endothelial rejection, has increased wound strength and requires a shorter period of steroid drops post-operatively.[60] However, interface haze can lead to suboptimal visual outcomes if there is residual posterior stroma. PKs have an increased risk of endothelial rejection and graft dehiscence.[58,61] The decision on whether to proceed with a DALK or a PK is a balance between the increased risk of graft rejection and the necessity for replacement of the complete cornea for improved vision, for example, if there is a full thickness corneal scar.[60,62] This decision also depends on surgeon preference.

OCT has possible roles during the corneal transplant process. Pre-operatively, OCT can provide accurate measurements of the host corneal thickness.[52] In such cases, OCT has an advantage over other technologies in that it can provide both

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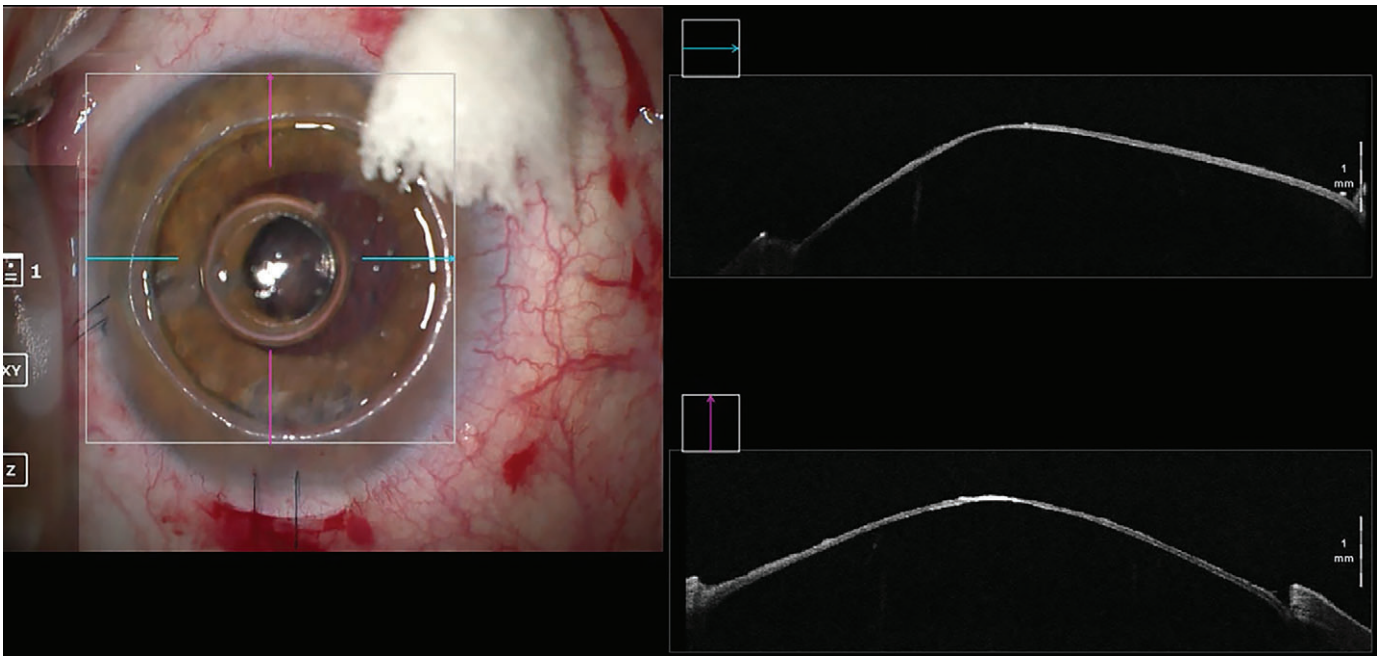


Figure 4. Intraoperative image following donor stroma removal during a manual deep anterior lamellar keratoplasty procedure. The surgical microscope view is shown on the left, and the optical coherence tomography (OCT) image is shown on the right. The OCT shows the thin, residual stromal bed, consisting of posterior stroma, Descemet's membrane and endothelium. (Rescan 700, Carl Zeiss Meditec.)

pachymetry measurements in the presence of corneal scarring as well as being able to measure the depth of scars.[63] This is particularly relevant when assessing the likelihood of success in performing a Descemet's-baring DALK using the big-bubble technique, where the presence of a full thickness corneal scar would preclude successful bubble formation.[64]

OCT can also be used to image donor corneas,[65] to reduce the risk of transplanting donor tissue with undiagnosed pathologies such as keratoconus or corneas that have previously undergone laser refractive procedures which were not reported by donors' families.[66,67]

More recently, OCT has been used intraoperatively as a novel tool.[68] In particular, it can be useful in DALK procedures where a manual technique is used to dissect the stromal bed to ensure a minimum amount of residual stromal material (Figure 4). A residual stromal thickness of less than 65 µm in a non-Descemet's membrane-baring DALK procedure can result in visual outcomes comparable to a PK.[58] It can also be helpful in cases where there is a small Descemet's perforation, to confirm the absence of interface fluid (between the donor cornea and host posterior stroma/Descemet's membrane) before completing the surgery.

Post-operatively, OCT is useful in the documentation and follow-up of corneal transplants to assess for complications such a double anterior chamber (if a Descemet's membrane perforation occurred during DALK) (Figure 5).[39,69] In PK, the OCT allows analysis of the graft position, thickness, curvature and apposition to the recipient peripheral rim,[39] which is particularly useful in cases of subsequent graft failure, when an endothelial keratoplasty can be considered. OCT has led to the diagnosis of late Descemet's membrane detachment many years after a PK for keratoconus, in cases presenting with sudden onset of corneal oedema which may mistakenly be diagnosed as endothelial rejection or graft failure. In such cases, rebubbling of the Descemet's membrane



Figure 5. Double anterior chamber following deep anterior lamellar keratoplasty. A focal perforation in the host Descemet's membrane resulted in aqueous in the interface between Descemet's membrane (arrow) and the donor cornea. (Visante anterior segment optical coherence tomography, Carl Zeiss Meditec.)

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with air in the anterior chamber can lead to clearing of the cornea without the need for a further transplant.[70,71]

Conclusion

By being able to assess parameters that previous imaging modalities could not evaluate as reliably or accurately, the use of OCT in keratoconus has improved a clinician's ability to diagnose and manage the disease. Its role may become even greater with increased resolution and more advanced imaging techniques.

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