Contact Lens Update
CLINICAL INSIGHTS BASED IN CURRENT RESEARCH

New technologies for assessing the contact lens wearing eye

March 7th, 2014

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New technologies for examination of the anterior eye in contact lens practice don't appear to have taken a huge leap in the past decade however there a several novel adaptations of existing technology worthy of note. In other areas of health we have self-diagnosis via smartphone or other gadgets adapted as medical devices. In practice and research in vitro and in vivo new adaptive technologies have expanded our capabilities in assessing the anterior eye, in particular corneal and conjunctival confocal microscopy.

Topography and tomography

Corneal shape and biomechanics are evaluated using slit-scanning and Scheimpflug imaging technologies, and when combined with a topographer has the advantage beyond a keratometer of not just measuring the anterior surface curvature but also measuring the elevation of all anterior segment structures and corneal thickness.

Anterior segment optical coherence tomography (OCT) utilises the Scheimflug imaging technology, ultrasound and optical coherence tomography combined and Placido disk technologies to evaluate the cornea and anterior segment by cross-sectional sections of anterior segment used in pre- and post-surgical evaluation (e.g. Visante® OCT from Zeiss). Corneal aberration evaluation assessed for custom ablation (e.g Keratron™ from Optikon) has been reported to have a high level of reproducibility[1]. Measuring corneal hysteresis (e.g the Ocular Response Analyzer® from Reichert) hasn't yet found a place in our consulting rooms and research labs, but does appear to be an effective yet expensive way of monitoring IOP in glaucoma patients[2].

Ocular wavefront sensors are now used clinically to assess aberrations and project vision loss caused by degradation of the pre-corneal tear film. Traditional tests such as tear film break-up time can also be estimated using wavefront sensors. OCT can provide high resolution (2-10 um) images of the anterior segment and also accurately measure tear film thickness over the cornea and at the upper and lower tear menisci[3].

Tear film meniscometry

A relatively new adaption of an established technique with a variety of potential applications is measuring tear film meniscus height with video-meniscometry. Yokoi and colleagues[4] have suggested the non-invasive technique of mensicometry will be useful in determining tear turnover, as an indication of dysfunction of the tear meniscus and for punctual plugs. Bandlitz et al.[5] demonstrated that the portable digital meniscometer was equivalent to the more expensive method of measuring tear meniscus volume than OCT.

Elipsometry & meibography

In contact lens and routine ophthalmic practice the assessment of the tear film lipid layer and meibiomian gland function is integral in dry eye diagnosis. Elipsometry, a technique used to measure thickness and refractive index of the lipid layer, can achieve measures at a resolution of approximately 100 nm using a modified wavefront sensor combined with placido disc[6]. This appears to be an advance on qualitative interferometry (colour assessment of the tear film by specular reflection) with cool light illumination systems such as the TearScope® by Keelor or the LipiView® Ocular Surface Interferometer by TearScience®.

A simple, handheld instrument has been invented to evaluate meibomian gland secretions during routine eye examination by applying consistent pressure to the outer skin of the lower eyelid. The Meibomian Gland Evaluator (MGE), attributed to Korb and Blackie[7], is used to express liquid from the meibomian gland orifices (visualized through old technology – a slit lamp biomicroscope), the presence of which indicates the meibomian gland is not obstructed. Following diagnosis, a new treatment applying an eyelid warming device (Blephasteam® from Théa) has been shown to be safe and effective at melting meibum. Additionally, application of this technique also appeared to reduce redness in those without meibomian gland dysfunction[8].

Laser meibometry, using ultra-high resolution OCT to produce morphological images of the tarsal area, may also have applications in clinical diagnosis of lid pathologies[9].

Non-contact corneal aesthesiometry

Corneal sensitivity measurement has progressed from a contact to a non-contact technique – the Cochet-Bonnet aesthesiometer and the cotton wisp test are relatively imprecise compared to non-contact corneal aesthesiometry[10,11]. Although non-contact aesthesiometry is well validated and used extensively in a research setting[10-18], we must currently build our own devices. Further, until these devices become automated and provide a clinical measure instantaneously, their value is limited in a clinical setting.

Ocular thermography

Ocular temperature has been measured using infrared thermometers for several years and a number of potential clinical ocular applications have been demonstrated, as well as a potential marker of carotid artery stenosis[19]. Anterior eye applications include the evaluation of tear film disorders[20,21], inflammatory conditions of the anterior eye, such as anterior uveitis[22], hordeolum, and acanthamoeba keratitis[23], scleritis and meibomian gland dysfunction[22], neurological disorders, such as Horner's syndrome in which anhydrosis is demonstrated on the forehead of the patient[23], and thermal consequences of photorefractive keratectomy[24,25] (Figure 1).

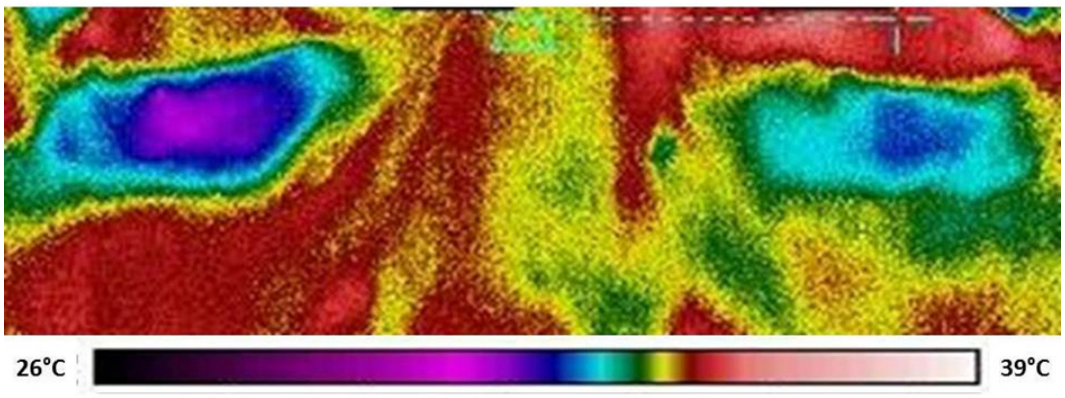

Figure 1. Thermograph of the ocular region of an individual with unilateral carotid artery stenosis (Courtesy: AM Shahidi)

In vivo confocal microscopy

Examination of the cornea has probably seen the most notable advances in technology as in vivo corneal confocal microscopy made its way from research into the clinical realm. Several research labs around the world are now using laser-scanning corneal confocal microscopy (such as the HRT3 with Cornea Rostock Module from Heidelberg), which represents a technological advance on the older, tandem- and slit-scanning devices.

As postulated by Chikama and colleagues in 2008[26], this technology is the closest we have to an 'in vivo biopsy". For the first time the anterior layers of cells can be appreciated at approximately 400-700x magnification with a quick, non-invasive technique, allowing new insights into form and function of the anterior ocular tissues.

At least three epithelial cells layers can be differentiated using confocal microscopy, as well as sub-basal and stromal nerves, stromal keratocytes and endothelium. The resolution of the instruments, however, does not permit the three membranes (Bowmans, Duas, Descemet's) to be easily appreciated. Quantification of the sub-layer thicknesses may eventuate with confocal microscopy and 3-D imaging[27].

Observation of pathology at the level of the membranes using confocal microscopy is a significant advancement to that afforded by the slit-lamp, and has improved our diagnostic capabilities in clinical practice. Confocal microscopy allows appreciation of acanthamoeba cysts[28], y-sutures and pigment epithelial cells on anterior lens surface[29] and endothelial dystrophy[30]. In our lab we've noted Hudson-Stahli lines appear as highly reflective material at the level of basal cell layer and Bowman's layer (Figure 2) and dystrophic or degenerative areas in otherwise healthy cornea (Figure 3).

Evaluation of the inflammatory status of the eye has included documentation of the number and type of presumed dendritic cells (possibly Langerhans cells) in the cornea (Figure 4) and conjunctiva (Figure 5)[31]. Increase in the number of these cells relative to healthy, quiet eye tissue is evident in contact lens wearers[32,33] and other inflammatory conditions[34], although their exact morphological identification in vivo has not been confirmed.

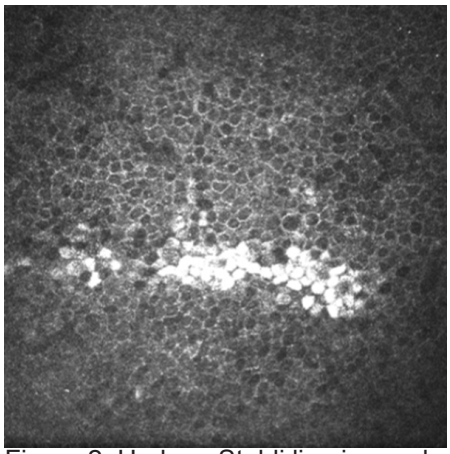

Figure 2: Hudson-Stahli line imaged with corneal confocal microscopy visible in basal epithelial layer (Courtesy N.Pritchard)

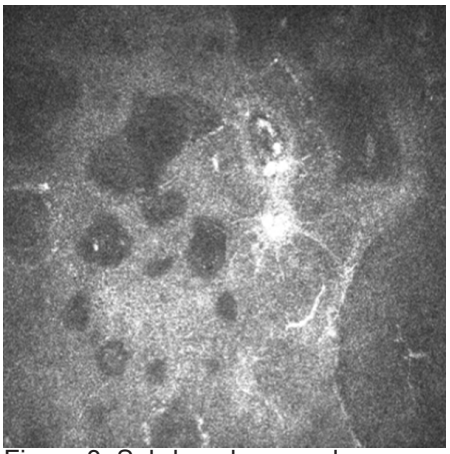

Figure 3: Sub-basal nerve plexus imaged with corneal confocal microscopy showing absence of typical nerve morphology in healthy 60 year old female (Courtesy: K Edwards)

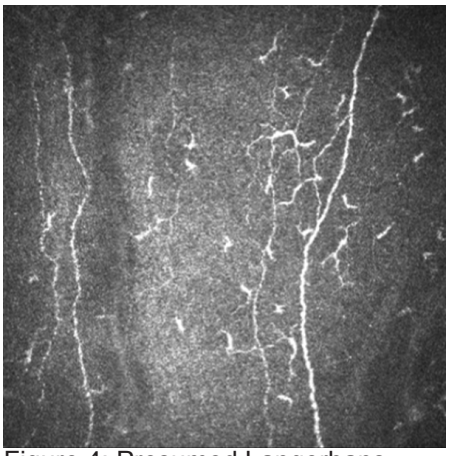

Figure 4: Presumed Langerhans cells in cornea imaged with corneal confocal microscopy (Courtesy: Y Alzarhani)

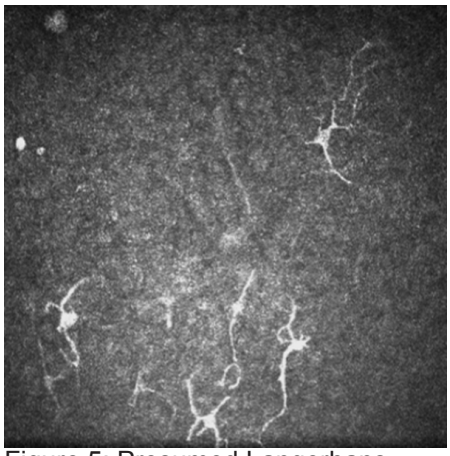

Figure 5: Presumed Langerhans cells in nasal conjunctival region of a healthy 31yo male imaged with corneal confocal microscopy. (Courtesy: Y Alzahrani)

The corneal sub-basal nerve plexus has been extensively explored in healthy and pathologic ocular tissue. New characteristics of this extensive plexus have been revealed by mapping together images captured by confocal microscopy to appreciate a large extent of the sub-basal nerves[35, 36], and more recently automatic wide-field mapping techniques have significantly reduced the time taken to perform such tasks[37, 38].

Corneal nerve morphology has been documented in a reasonable number of healthy eyes[36,39] as well as, for example, the corneal nerve deficits associated with diabetic neuropathy[40], vernal keratoconjunctivitis[41], herpes keratitis[42], keratoconus[43-45] and corneal transplantation[46].

Stromal keratocytes imaged by confocal microscopy are easily quantifiable, and recently automated detection and cell densities from ultra-high resolution optical coherence tomograms have been performed47. Quantification of stromal nerves using contact[29] and non-contact slit, tandem or laser scanning devices[48,49] has also been reported with a limited degree of agreement, suggesting that if the technique is to be used routinely, it requires some further validation.

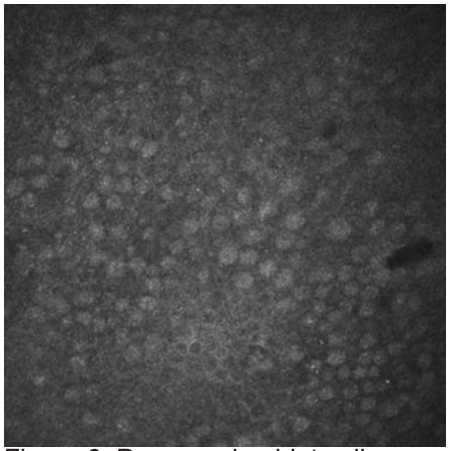

Figure 6: Presumed goblet cells nasal bulbar conjunctiva imaged with corneal confocal microscopy (Courtesy: M Aldossari)

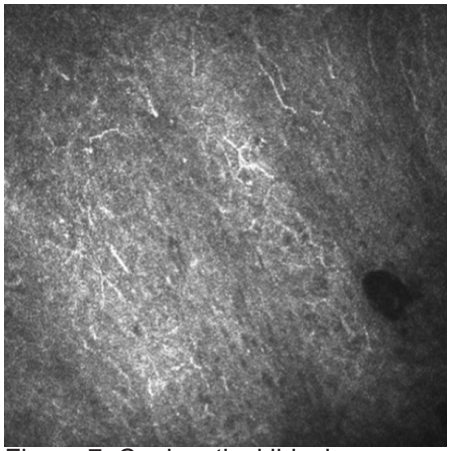

Figure 7: Conjunctival lid-wiper region a healthy 31yo male imaged with corneal confocal microscopy (Courtesy: Y Alzahrani)

The *'in vivo* biopsy' of the conjunctiva is an exciting adventure, and the structural detail is far from the traditional text description of the tarsal papillae, crypts and cellular features[50,51]. Figure 6 shows presumed goblet cells in the nasal bulbar conjunctiva and the lid margin or lid-wiper region examined by confocal microscopy may inform new perspectives in dry eye (Figure 7).

Using confocal microscopy to observe cells in conjunctival vessels has been used as an indicator of sub-clinical inflammation – the less the cells roll (or the more they stick), the more inflamed the eye is52, and less conjunctival blood flow was observed in contact lens wearers compared to non-contact lens wearers when measured using a modified Heidelberg Retinal Flowmeter[53].

Tear film thickness and integrity has been explored by in vivo confocal microscopy. The Heidelberg instrument with Tomocap readily reveals dry spots[29]. More recently using a non-contact objective attached to the Heidelberg instrument, we were unable to image the anterior cellular layers of the cornea but dynamic tear film evaluation was possible[49], shown in Figure 9.

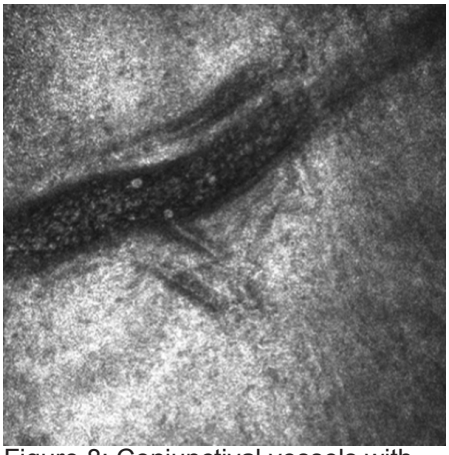

Figure 8: Conjunctival vessels with prominent red blood cells and leucocytes imaged with corneal confocal microscopy (Courtesy: M Aldossari)

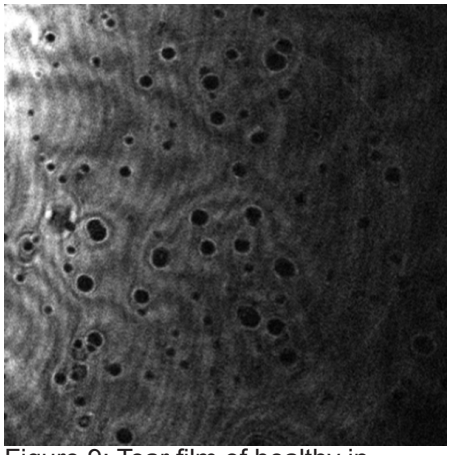

Figure 9: Tear film of healthy individuals imaged using confocal microscopy fitted with a non-contact objective lens. (Courtesy N Pritchard & K Edwards)

Conclusions

In the future, the electronic contact lens promises bionic capabilities for everyone. There are already apps to assist reading urine strips, monitor heart rate and blood glucose level. A group in London is developing a portable eye examination kit to assist in performing visual acuity and contrast sensitivity, colour vision, visual field, lens and retinal imaging in remote populations.

A great deal of cooperation between funders, biotech, clinicians and researchers is required. Bringing established technologies to developing countries will hopefully help to reduce preventable blindness in prone populations. Reducing invasiveness of procedures will also pose a challenge. For example, the equivalence of contact vs. non-contact instrumentation in diagnosis of corneal and conjunctival anomalies and pathology should be an attainable goal, and technological cooperation is necessary to make this happen.

No app currently exists for monitoring the contact lens wearing eye, however relatively sophisticated technology and the ability to monitor parameters such as cell counts and tissue thickness is becoming routine and these new technologies tend to redefine standard of care. Automation is a critical factor if these tools are to be useful in situations where information is needed immediately, such as in clinical practice. It is hoped that automation tasks

will push forward rapidly in the near future, enhancing our technological capabilities, hence patients' well-being in all parts of the globe.

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