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Featured Inside
Post-LASIK Ectasia



Progress is being made towards the prevention and treatment of post-LASIK ectasia

By Cheryl Guttman Krader

RECENT ISRS/AAO and ASCRS surveys of refractive surgeons suggest that the rate of new cases of post-LASIK ectasia is declining. However, even a low incidence of ectasia is worrying, considering the number of laser vision correction procedures performed each year and the devastating nature of this complication. Therefore, researchers continue to study the aetiology of post-LASIK ectasia, identify additional risk factors and screening methods, as well as to define the safety of surgical alternatives in at-risk eyes.

Theo Seiler MD, PhD, is credited with describing the first case of post-LASIK ectasia in 1996 and coined the term 'iatrogenic keratectasia'. Since then, various investigators have tried to determine the incidence of this complication, and while the estimates vary between series, the best available data suggest the rate is about one in 2500 procedures, said José Güell MD, PhD, who spoke on preventing corneal ectasia after refractive surgery during the 17th Congress of the European Society of Ophthalmology (SOE). The symposium was cosponsored by the ESCRS.

Almost half of cases occur within one year after surgery, but the corollary is that development is delayed in the other half. Therefore, the possibility of late post-LASIK ectasia should not be overlooked, noted Dr Güell, Universidad Autònoma de Barcelona, Spain.

Prevention strategies – the Ectasia Risk Score System

"As is always the case, prevention is the best management for post-LASIK ectasia, and today, there are certain 'laws' that surgeons need to adhere to in order to prevent ectasia. One is to always perform intraoperative pachymetry and the other is to avoid LASIK in high-risk eyes," Dr Güell said.

However, there is controversy regarding methods for identifying high-risk eyes. Using regression analyses to compare eyes with post-LASIK ectasia and those with a normal postoperative course, J Bradley Randleman MD, and colleagues at Emory Eye Centre, Atlanta, GA, developed the Ectasia Risk Score System (ERSS) as an easy-to-use tool for helping surgeons in their decision-making process. Age, manifest refraction SE, corneal thickness, placido disc topographic pattern, and residual stromal bed thickness are incorporated into the weighted scoring system, and the total score determines whether an individual is at low (score 0–2), moderate (3) or high risk (>4) for post-LASIK ectasia.

"In a follow-up study (*Am J Ophthalmol*. 2008 May) using an independent dataset, these researchers validated the ERSS and

determined it has sensitivity of 92 per cent and specificity of 94 per cent, which is quite good, if finally it would be accepted by all of us, considering its simplicity," Dr Güell said.

However, there are still eight per cent of the ectasia cases that were identified as a low risk based on the ERSS and there is no published data on the incidence of ectasia among eyes with different risk scores calculated using the ERSS, and its creators acknowledge the system is not perfect. Therefore, there is still a need for improvement in either sensitivity and specificity for screening refractive candidates, which will be refined and improved over time through the application of appropriate research and statistical methodology.

Other leading refractive surgeons also seem to agree the ERSS is an important step forward, but as expressed in "Letters to the Editor" [*Ophthalmology* 2008 115;849; *Ophthalmology* 2009;116:1014–5], some are waiting for further validation and raising questions about use of this theoretical tool as the sole screening method in clinical practice.

Perry S Binder MD, questions the appropriateness of applying the ERSS to today's refractive surgery candidate considering that the method was developed using data from eyes that were mostly operated on prior to 2002. He also has concerns about using a number from the ERSS to "draw a line in the sand" dividing eyes that can undergo LASIK from those that should be excluded.

"The ERSS may fail to identify some eyes that are truly at higher risk and inadvertently exclude those that are not," he said.

Improving safety with alternative techniques and technology

Research by John Marshall PhD, and others leading to improved understanding about the lamellar organisation of the corneal collagen fibrils, its relationship with corneal tensile strength and biomechanics, and how the latter is affected by LASIK flap creation and laser ablation has been the foundation for understanding why the risk of ectasia is lower after PRK versus LASIK as well as for the development of new LASIK techniques, eg, thin-flap LASIK and creation of flaps with an inverted side cut using the femtosecond laser, aiming to better preserve corneal biomechanical stability.

However, while iatrogenic ectasia appears to be far more common after LASIK than after PRK, the exact incidence of post-PRK ectasia is unknown, noted Dr Güell.

"The only published literature consists of relatively few case reports, and most of those cases had identifiable, but undiagnosed risk factors, particularly significant inferior corneal steepening or frank keratoconus. In

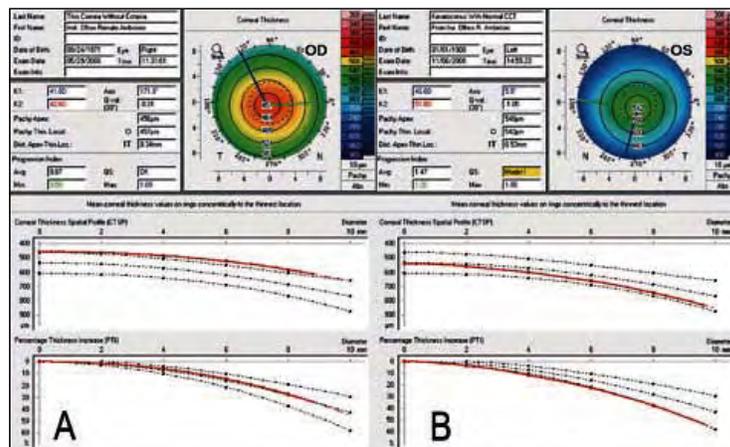


Figure 1: Thickness profile of a normal thin cornea with CCT 458 microns (A) and a Keratoconic cornea with CCT 548 microns (B)

other eyes, preoperative topography was not available," he explained.

"Therefore, for patients who are identified as a questionable candidate for LASIK, the safety of advanced surface ablation or sub-Bowman's keratomileusis (SBK, ie, thin-flap LASIK) remains to be defined."

In theory, use of the femtosecond laser for LASIK flap creation might reduce the risk for ectasia after refractive surgery via several mechanisms. Considering that residual stromal bed thickness is a risk factor for this complication a thin flap could afford biomechanical advantages; this suggests there is probably a benefit for using the femtosecond laser because it performs reliably in creating predictably thin flaps, said Rudy Nuijts MD, PhD.

The planar shape of the femtosecond laser flap versus the meniscus geometry of a mechanical microkeratome flap also contributes to less variation in flap thickness when using the former technique and is thought to be more beneficial for preserving corneal biomechanical stability. Moreover, the femtosecond laser enables creation of a flap with an inverted side cut that has been shown in animal and clinical studies to favour stronger flap adhesion due to increased healing.

In addition, results of a randomised, contralateral eye controlled study conducted by Drs Durrie and Slade and using the Ocular Response Analyzer (Reichert) to measure corneal hysteresis and corneal resistance factor provide evidence that the biomechanical properties of the cornea are similar after SBK compared with PRK.

"Still, while there are no published articles yet in the literature, it may be premature to conclude that SBK is immune from ectasia," said Dr Nuijts, Maastricht University, The Netherlands.

Prevention with intervention – corneal collagen crosslinking

Growing evidence of the success of corneal collagen crosslinking (CXL) for treating progressive keratoconus and post-LASIK ectasia has prompted interest in its use as a prophylactic technique in eyes at risk for post-LASIK ectasia. Both Theo Seiler MD, PhD, and A John Kanellopoulos MD, have experience combining CXL with laser vision correction in at-risk eyes, but they have different opinions on which procedure should be performed first and whether the two surgeries should be done simultaneously or in a staged approach.

Dr Seiler, Institute for Refractive and Ophthalmic Surgery, Zurich, Switzerland, told *EuroTimes* he has performed CXL and customised PRK simultaneously and stage in more than 20 eyes of patients with forme fruste keratoconus who have a strong desire for refractive surgery. Taking into account the viscoelastic properties of the cornea, he believes the outcomes are more predictable if the CXL is done before the surface ablation.

"Any biomechanical reaction to an external change to the cornea, such as ablation, consists of an immediate, elastic component and a delayed, creeping viscous component. If the PRK is done first, it creates an immediate elastic bulging out-effect that is frozen by CXL. To optimise outcome predictability, it makes much more sense to do the CXL first and freeze the cornea, followed six months later by the PRK. Don't forget some of these patients need more than a simple surface ablation but rather require a customised topography-guided treatment to correct the cone," he explained.

Dr Seiler acknowledges there are advantages to same session surgery – it is more efficient than a staged approach and minimises patient exposure to



Theo Seiler José Güell Perry S Binder Rudy Nuijts A John Kanellopoulos Renato Ambrósio Jr Ioannis Pallikaris

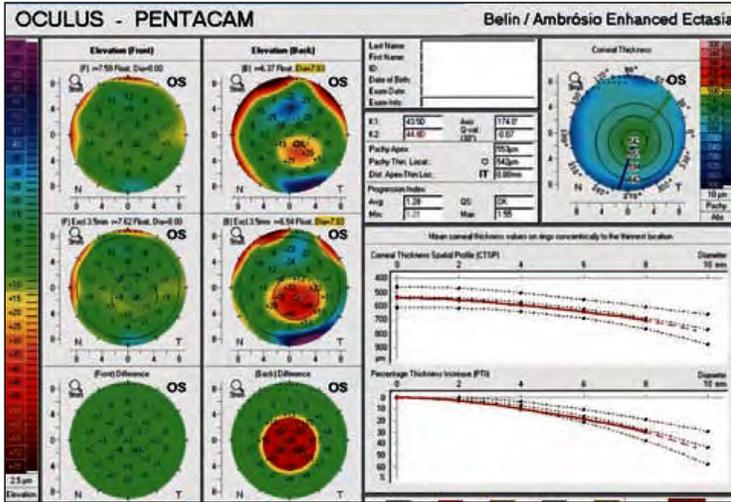


Figure 2: BAD from the contralateral eye with normal front surface curvature map of a patient with very asymmetric (not unilateral) keratoconus. This eye, if evaluated independently from the right eye, would have been considered as a low risk for ectasia based on the ERSS

postoperative morbidity. While he has done both simultaneous and sequential procedures, depending in part on patient preference, he favours waiting six months between procedures with the goal of enhancing predictability.

Over the last five years, Dr Kanellopoulos, Laservision Institute, Athens, Greece, has performed topography-guided PRK followed immediately by CXL to treat over 600 eyes with progressive keratoconus or post-LASIK ectasia. The simultaneous procedure affords the benefit of single session convenience and he believes there are multiple advantages for performing the surface ablation procedure prior to CXL.

Dr Kanellopoulos explained to *EuroTimes*, "By exposing cornea stroma, the partial PRK facilitates the diffusion of the topically applied, large riboflavin molecule, and so may increase the efficacy of the CXL. In addition, the PRK redistributes the strain from the cone apex in a larger area. This normalisation of the ectatic cornea prior to the CXL appears to create more biomechanical stability so that the tissue may better resist blinking and eye rubbing."

"Furthermore, this protocol avoids removal of cross-linked tissue by the PRK and seems to reduce PRK-related scarring. The simultaneous combined technique also appears to have synergistic efficacy compared to when crosslinking is done first and the partial topo-guided PRK later."

We have recently published a large comparison case series. In this study of about 400 cases we compared CXL first followed at least six months later with a partial PRK, to combining topo-guided PRK and CXL immediately after. In almost all the parameters studied the same day combined:

topo-guided PRK and CXL group did better, suggesting a synergistic effect. (*Kanellopoulos AJ, JRS Sept 2009.*)

About four years ago, Dr Kanellopoulos began performing CXL prophylactically at the completion of the laser vision correction procedure in eyes at risk for ectasia. He has combined it with both PRK and thin flap LASIK, choosing between these procedures primarily by considering patient age and thinnest cornea pachymetry – PRK is performed when the cornea is less than 480 microns and usually if the patient is less than 30 years old. Based on his experience, CXL prophylaxis appears to be safe and effective.

"I have observed no adverse effects on healing after surface ablation, refractive outcomes are as expected without any need for nomogram adjustment, and no eyes have developed ectasia with follow-up ranging up to four years," Dr Kanellopoulos said.

He added, "I also feel this combined technique may have wider application in all LASIK cases in the future as it may not just reverse some of the negative corneal biomechanical changes induced by LASIK, but also provide a 'suturing' effect of the flap to the stroma through CXL-promoted interlinking of collagen fibres."

Alternative screening criteria

While Placido disc-based corneal topography is one of the most important components of refractive surgery patient screening, limitations of this methodology are prompting investigation of alternative techniques. Some of these were presented at the 2009 annual meeting of the American Society of Cataract & Refractive Surgery.

For example, researchers at Emory Eye Centre evaluated the role of Orbscan II (Bausch & Lomb) slit beam-based indices, but found that this information did not improve the identification of abnormal corneas beyond use of Placido-based imaging alone, reported J Bradley Randleman MD, Emory Eye Centre.

However, novel methods for interpreting Corneal Topography (CTm) should be considered, so that the more detailed 3D corneal architecture data would provide clues to identify ectasia risk. Methods for characterising pachymetric distribution have been developed by Renato Ambrósio Jr MD, PhD, and colleagues from the Rio de Janeiro Corneal Tomography and Biomechanics Study Group in Brazil since 2003, using different systems. The concept of corneal thickness spatial profile (CTSP) is based on the rate of increase in thickness from the thinnest point out to the periphery. The averages of values on circle lines centred on the thinnest point with increase in diameters are calculated along with the percentage thickness increase (PTI) at each diameter. This concept was implemented and further refined on the Pentacam software since 2004.

Graphics are presented containing the mean and 95 per cent confidence interval of a normal population for the CTSP and the PTI, along with pachymetric indexes. The comprehensive analysis beyond central corneal thickness (CCT) enables characterisation of patients with very thin normal corneas without ectasia (Figure 1A), and cases with keratoconus and relatively normal CCT (Figure 1B).

The sensitivity of the thickness profile for screening ectasia risk or susceptibility has been demonstrated in a study comprising 53 patients with very asymmetric keratoconus, in which one eye had a normal topography that was presented by Marcella Salomão MD from the Rio de Janeiro Corneal Tomography and Biomechanics Study Group at the ESCRS in 2008. The combination of CTSP and PTI data along with enhanced elevation analysis with a new best-fit sphere to the peripheral cornea, as proposed by Michael W Belin MD, FACS (Tucson, Arizona), identified abnormalities in 94 per cent of cases despite a normal surface curvature map (Figure 2).

The improvement in sensitivity was also demonstrated in another study by Allan Luz MD from the Rio de Janeiro Corneal Tomography and Biomechanics Study Group. Data from four cases with ectasia after Intralase-LASIK, despite having low-risk ERSS score and normal preoperative Orbscan interpretation was provided by Dr Colin Chan MD from Australia. The CTSP and PTI graphs were calculated from the numeric

pachymetric maps from the Orbscan. The vertical pachymetric asymmetry (VAP), another method described by Canrobert Oliveira MD from Brasilia's Eye Hospital (HOB), was also applied. All cases have abnormalities identified on the comprehensive pachymetric analysis. "The opportunity to identify preoperative corneal abnormalities in eyes that had post-LASIK ectasia with unrecognized risk factors is a strong evidence of the enhanced sensitivity of this approach. In addition, we have also collected cases that had LASIK with stable outcomes, in which there was a retrospective identification of high-risk ERSS scores. Such cases have typically normal pachymetric distribution, which suggest this approach also enhances specificity. However, we still need to expand these studies to definitively validate this approach," concludes Dr Ambrósio.

David Huang MD, PhD, and colleagues at University of Southern California, Los Angeles, are developing a method using optical coherence tomography-derived pachymetry maps to capture the focal thinning that is characteristic of keratoconus. Dr Huang's group has developed a system to detect focal thinning and asymmetric thinning that he believes will complement topographic detection of keratoconus. An even newer approach based on fitting the data to a Gaussian waveform also shows promise.

Expanding the etiologic view

During the SOE symposium, Ioannis Pallikaris MD, PhD, University of Crete, suggested that researchers focusing entirely on the cornea may be pursuing the wrong path in trying to understand the aetiology of ectasia refractive surgery. Recognising the cornea as being only part of the "system", it is important to consider the bigger picture that is the whole globe, he said.

Dr Pallikaris has been studying how corneal shape may be influenced by other ocular factors, including ocular rigidity (a parameter expressing the elastic properties of the globe) and intraocular hydrodynamics (blood circulation and aqueous flow). His research includes developing methods to measure these factors so that he can investigate their interactions.

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Courtesy of Renato Ambrósio Jr MD