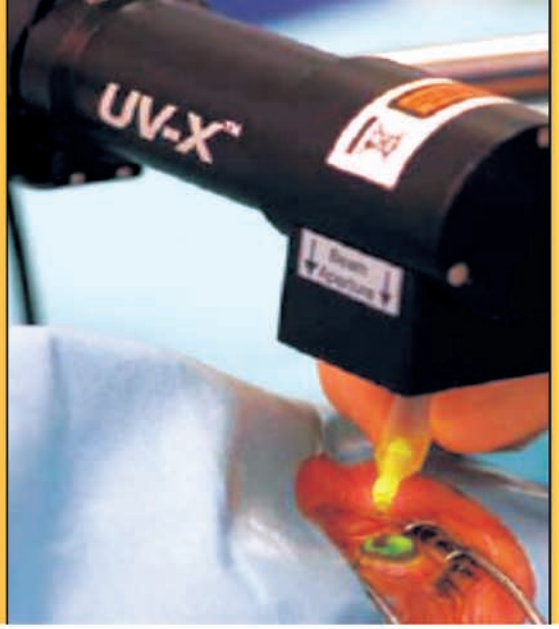

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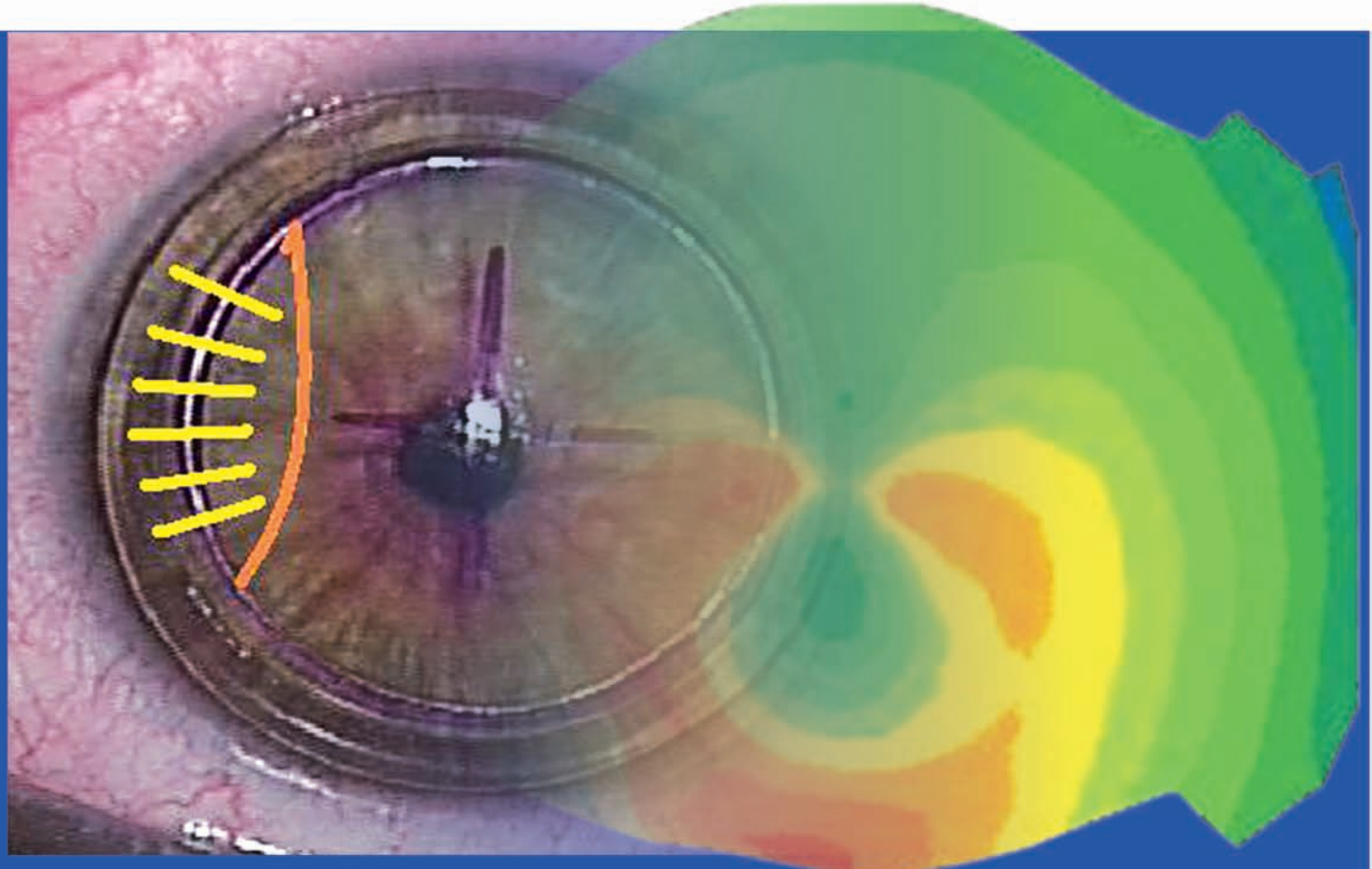
Antonio Leccisotti

KERATOCONUS SURGERY AND CROSS-LINKING



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Foreword
Stephen D Klyce

Keratoconus Surgery and Cross-linking

Keratoconus Surgery and Cross-linking

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Keratoconus Surgery and Cross-linking

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To

My wife Elena

and

My twins Chiara and Francesco

For their patience during the

time spent away from them

— Roberto Pinelli

To

My beloved ones

— Antonio Leccisotti

Foreword

I discovered many years ago that to truly understand a subject and to be able to distinguish between fact and conjecture, one has to read as many opinions on the subject as are available. What comes out as the distilled product is the knowledge that we all seek.

Dr Roberto Pinelli and Dr Antonio Leccisotti have assembled outstanding experts who have made recent major advances in the management and treatment of keratoconus. This is a disease that apparently affects only the cornea, yet is associated with so many other conditions. It is clear that keratoconus has a genetic basis and that a cure is not possible within current medical knowledge.

Corneal transplants have been very successful in the minority of cases requiring it, as many eyes with keratoconus stabilize at a stage where functional vision can be maintained with spectacles, and possibly with insert or contact lenses, although it is recognized that contact lenses can exacerbate progression or cause scarring. We need to find ways to predict the progression of keratoconus in the individual patient and to treat these before there is significant visual loss. So now there is the hope that keratoconus might be stabilized—even modestly regressed—with collagen cross-linking. Time will tell, but we have gone from guarded optimism to unbridled enthusiasm that collagen cross-linking may prove to be very effective in the management of ectasia, thanks to the pioneering work from Dresden!

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Preface

Many aspects contribute to the fact that keratoconus is an ideal link between refractive and corneal surgery. The expansion of the options for the visual rehabilitation in keratoconus has partly originated from the progress of diagnostic and therapeutical techniques in refractive surgery. Intrastromal rings and phakic IOLs, to mention a few, were conceived to correct myopia but have found a natural and successful application in keratoconic eyes. But some of the new techniques discussed in this book were expressly ideated to strengthen (collagen cross-linking) or to replace (lamellar keratoplasty) a weakened corneal stroma. The subject of the surgery of keratoconus has therefore become so wide that no single surgeon can exhaustively cover all its aspects.

With this in mind, we wanted to gather the experience of some of the most valuable keratoconus surgeons in the world in a comprehensive book. Some of the contributors are old friends who did not let us down in this daunting task, some are new friends who honoured us by believing in our project. Everyone is an outstanding surgeon and, above all, a brilliant medical writer, this latter quality being nowadays much rarer than the former. Thanks to such collaborations, the final result has reached the excellence we had in mind when the book was first planned.

We would like to thank the entire team of Istituto Laser Microchirurgia Oculare, Brescia—Italy and the Assistants of Dr Leccisotti for their blessings and motivation.

Roberto Pinelli
Antonio Leccisotti

Contents

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Detecting Corneal Ectasia

Michael J Endl
Stephen D Klyce

Introduction

Keratoconus, pellucid marginal degeneration, and iatrogenic ectasia all exhibit an irregular form of corneal 'bulging' secondary to progressive stromal thinning. These appear to be unrelated to any obvious inflammatory changes. The reported incidence of keratoconus among refractive surgical candidates when refractive surgery was first introduced was as high as 8 to 12 percent.[1] This number has dropped to closer to one percent as refractive practices have become more established.[2] Importantly, these percentages remain more than 10 times higher than the incidence of keratoconus in the general population (1.3-50 per 100,000 depending on ethnicity).[3,4] Most of these patients with asymmetrical corneas experience poor vision quality with spectacle correction or are experiencing a growing intolerance to ill-fitting contact lenses. For those reasons, patients with mild keratoconus tend to seek out other modalities for correction, and excimer laser treatments are novel and attractive alternatives. Thus, it is particularly important for all refractive surgical candidates to undergo careful screening which specifically includes bilateral corneal topography examinations.

As LASIK approaches 1.4 million procedures annually in the United States alone, it has become imperative that the modern day refractive surgeon possess an increasingly expert skill set for the detection of preoperative pathology such as keratoconus and pellucid marginal degeneration as well as the development of post-surgical corneal ectatic changes. Corneal topographers have been the standard of care for preoperative screening of refractive surgical candidates since the early 1990's.[5] In this chapter we will explore the basics of topographic pattern recognition essential to the detection of preoperative keratoconus as well as some of the advancing technologies that may complement our current knowledge base.

The mainstay for early detection, diagnosis and tracking of ectasia remains videokeratography, specifically the corneal topographic mapping of axial dioptric power with the color-coded contour map developed in the late 1980's.[6] Utilizing Placido-based maps provides the most sensitive and reproducible method for the detection of early ectasia. The amount of information displayed in these maps is determined in part by the topographic scale. However, without the use of a standardized or absolute scale,[7,8] certain irrelevant distortions can appear misleading or overemphasized **(Figure 1-1)**.

Although modern corneal mapping systems can display upwards of 22,000 data points on a single topographic map, a 1.5 D scale has sufficient resolution to detect all of the topographic characteristics necessary for diagnosing a variety of topographic abnormalities including: contact lens warpage, early and late keratoconus, penetrating keratoplasty, extracapsular cataract extraction, photorefractive keratotectomy, radial keratotomy, and epikeratophakia.[9]

Conversely, an ad hoc scale can cause the clinician to overlook early signs of irregular astigmatism or fail to detect progression of ectasia when following a keratoconus suspect. Such scales such as the normalized scale are self-adapting to the power range present in individual topography examinations. This technique can obscure important detail on highly irregular corneas and over emphasize topographic features irrelevant to diagnosis **(see Figure 1-1)**.

The hallmark of corneal ectasia remains an irregular astigmatism which can take several forms. The result is several patterns of irregular astigmatism with which the eye care professional must become familiar. Ectasia from keratoconus and ectasia following refractive surgery can be remarkably similar **(Figure 1-2)**. Keratoconus is most often associated with an inferior localized steepening as shown in **Figure 1-2**, although the cone can be present centrally or even superiorly.[10] However, keratoconus can also present as a central symmetric, but lopsided or 'lazy eight' bow tie

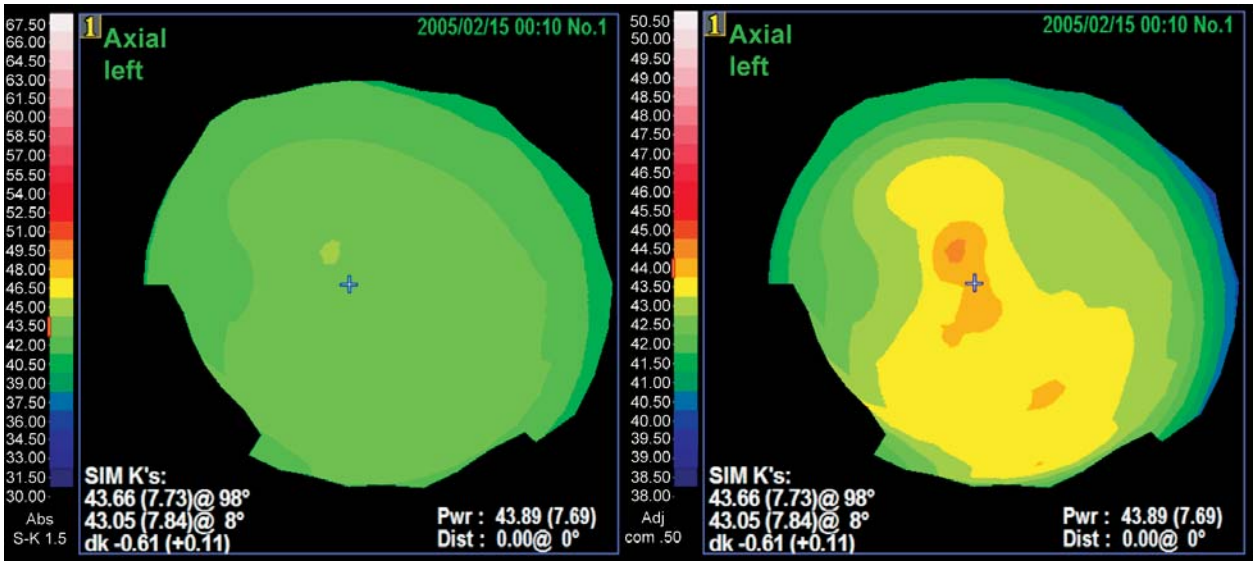


FIGURE 1-1: A fixed standard scale is essential for proper corneal topography interpretation. A single topography exam from a normal cornea is shown with two scales. The preferred 1.5 D interval scale used on the left panel leaves the correct impression that this cornea is regular with normal peripheral flattening. The right panel casts the same exam with a 0.5 D interval scale. The features that appear at this resolution are not of clinical significance, yet may give the incorrect clinical impression of irregular astigmatism.

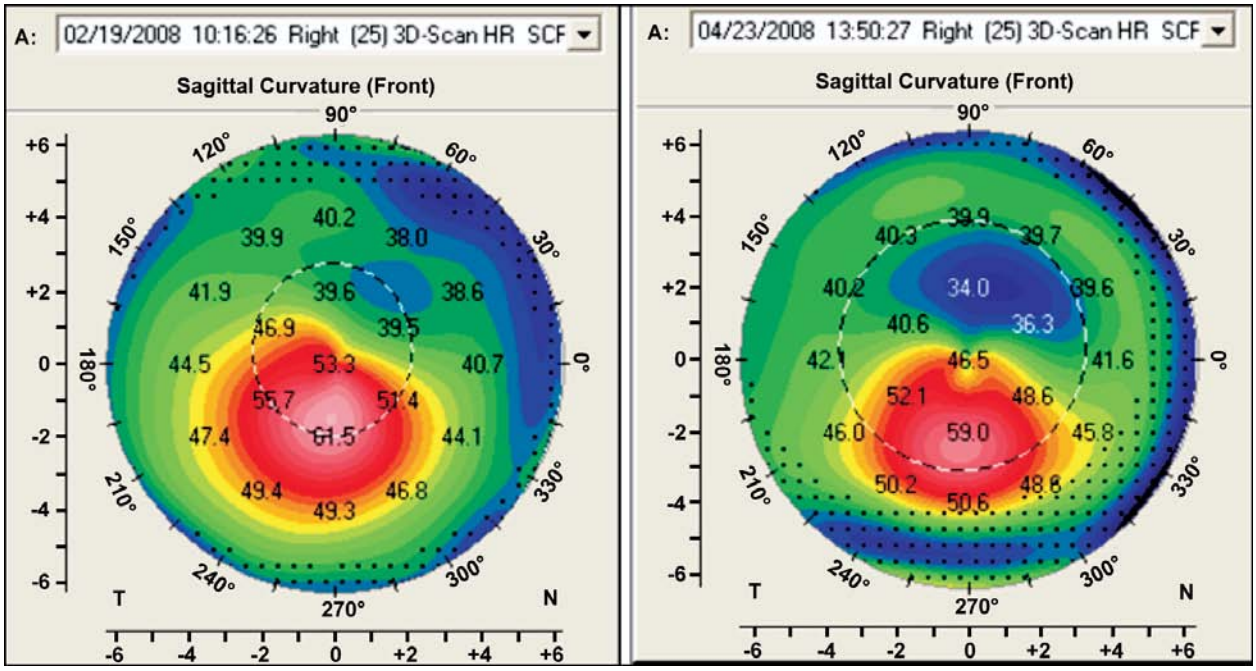


FIGURE 1-2: The topographic appearance of keratoconus (left panel) and iatrogenic ectasia (right panel) can be very similar.

(Figure 1-3) characterized by the skewed radial axes in the corneal topography recognized by Rabinowitz and Rasheed,[11] or as an asymmetric bow tie with or without skewing. A final characteristic of keratoconus topography is that its progression is usually uneven between the two eyes of a patient, and a small number of patients will appear to have unilateral keratoconus.[12] However, recognizing that keratoconus is a genetic disease, whose expression is variable between eyes, it is

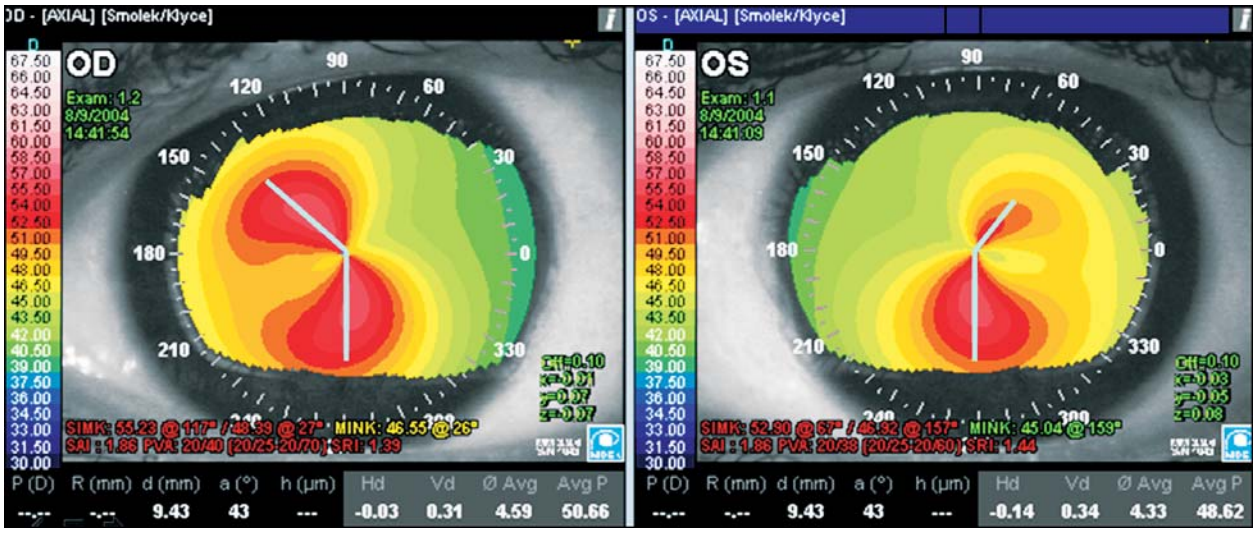


FIGURE 1-3: Keratoconus may present as a lazy eight bow tie. Note the skewing of the radial axes.

clear that if one eye of a patient exhibits keratoconus, the other eye will have the defect as well and be of similar risk for ectasia should it be treated with refractive surgery.

Another more rare form of naturally occurring progressive corneal ectasia and equally a risk factor for refractive surgical candidates is pellucid marginal degeneration.[13] Pellucid marginal degeneration involves an arcuate peri-limbal thinning which differentiates it from keratoconus in its more advanced stages. However, before stromal thinning can be measured, topographic signs emerge as the only detectable measure of a potential underlying pathology. The topographical pattern of pellucid marginal degeneration is typically a 'claw', or 'C' shape as seen in **Figure 1-4**. Note, however, if these topographic patterns occur without pachymetry, then the interpretation must be *topographic* pellucid marginal degeneration. This is because keratoconus can also exhibit the pellucid topographic pattern in some cases.

Other topographic signs of suspect keratoconus in addition to inferior steepening have been proposed. Levy, *et al* demonstrated that a 'J' pattern and an 'Inverted J' pattern in corneal topography

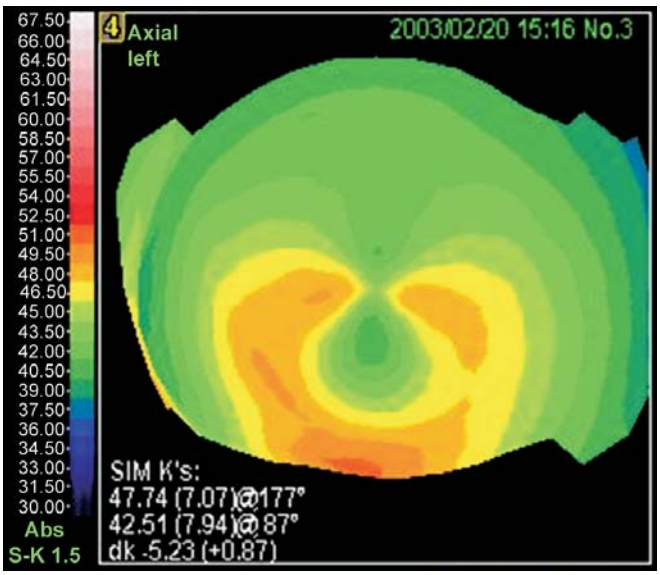


FIGURE 1-4: Pellucid marginal degeneration has a characteristic 'C' shape or claw shape on topography. Note the against the rule astigmatism frequently exhibited and the tear drop inferior depression. However, diagnosis of this cornea was only confirmed by slit lamp examination showing a peri-limbal inferior arcuate band of thinning, unique to this disorder.

were over represented in relatives of patients with clearly established Familial Keratoconus. These minimal images of the classic asymmetric bow tie with inferior steepening were not seen with statistical significance in their study's control population.[14] Other workers claim that the presence of a 'vertical D' pattern in corneal topography was a sign of keratoconus[15] and a risk factor for refractive surgery. Detected retrospectively in two patients who developed ectasia after LASIK, such abnormalities in preoperative corneal topography serve as a warning sign and potential exclusion criteria for refractive surgical candidates.

Differentiating these irregular patterns from dry eye, contact lens warpage or simply normal variants of regular astigmatism remains one of the more difficult and critical diagnostic dilemmas facing today's eye care professional. To better elucidate early ectatic or *forme fruste* corneal changes from more stable states, Maeda, *et al* demonstrated the benefits of incorporating an expert system that classified corneal maps based on discriminant analysis and a classification tree that considers eight different topographic indexes.[16] This method was shown to be more sensitive and specific to keratoconus detection than looking for elevated average Simulated Keratometry (Sim K) readings or previously utilized methods that relied on central corneal (K) power and Infero-Superior asymmetry (I-S) values.

Today this statistical approach has been extended through the use of neural networks to detect and interpret map patterns.[17] The Magellan Mapper from Nidek (Gamagori, Japan) features software that includes a neural network application capable of predicting various corneal diseases and possible post-surgical outcomes. This application of artificial intelligence utilizes a previously trained set of logic rules 'learned' from sets of abnormal and normal patient topographies. Unique to this system is the ability to differentiate between astigmatism, keratoconus suspects, true keratoconus, and pellucid marginal degeneration.[18] Furthermore, the Magellan is able to assign a percentage of probability, or grade, to these disease states. **Figure 1-5** illustrates a typical Magellan printout with a traditional axial map, a grouping of indices, and an easy to interpret bar graph that includes a percentage of each classification's probability. Other categories of potential classification by the neural network include: previous penetrating keratoplasty (PKP), myopic refractive surgery (MRS), hyperopic refractive surgery (HRS) and 'other' (OTH). This last designation is significant because the system has the ability to recognize and differentiate irregular patterns produced by early or *forme fruste* keratoconus suspect (KCS) from those asymmetries seen with dry eye or contact lens warpage.

However, it is important to note that like other clinical tests corneal topographer interpreters may not be 100% accurate. In some cases, contact lens warpage can produce inferior steepening that mimics keratoconus so closely that a false report of keratoconus can be given. The particulars related to contact lens wear should always be noted in the chart for patients being screened for refractive surgery. If there is inferior steepening, contact lens wear should be discontinued and a repeat topography taken after 2-3 weeks have passed to differentiate keratoconus and contact lens warpage. With keratoconus, the inferior steepening will tend to become more pronounced as contact lenses tend to press on the cone. If the inferior is due to contact lens warpage, the asymmetry should diminish.

Modern topographers can aid in the screening for early ectatic diseases and detect subtle irregularities such as those produced from over wear of contact lenses. For those patients going on to wavefront-guided excimer laser ablations, these findings may allow the surgeon to collect a more accurate portrait of patient wavefront information and thus produce better postoperative results.

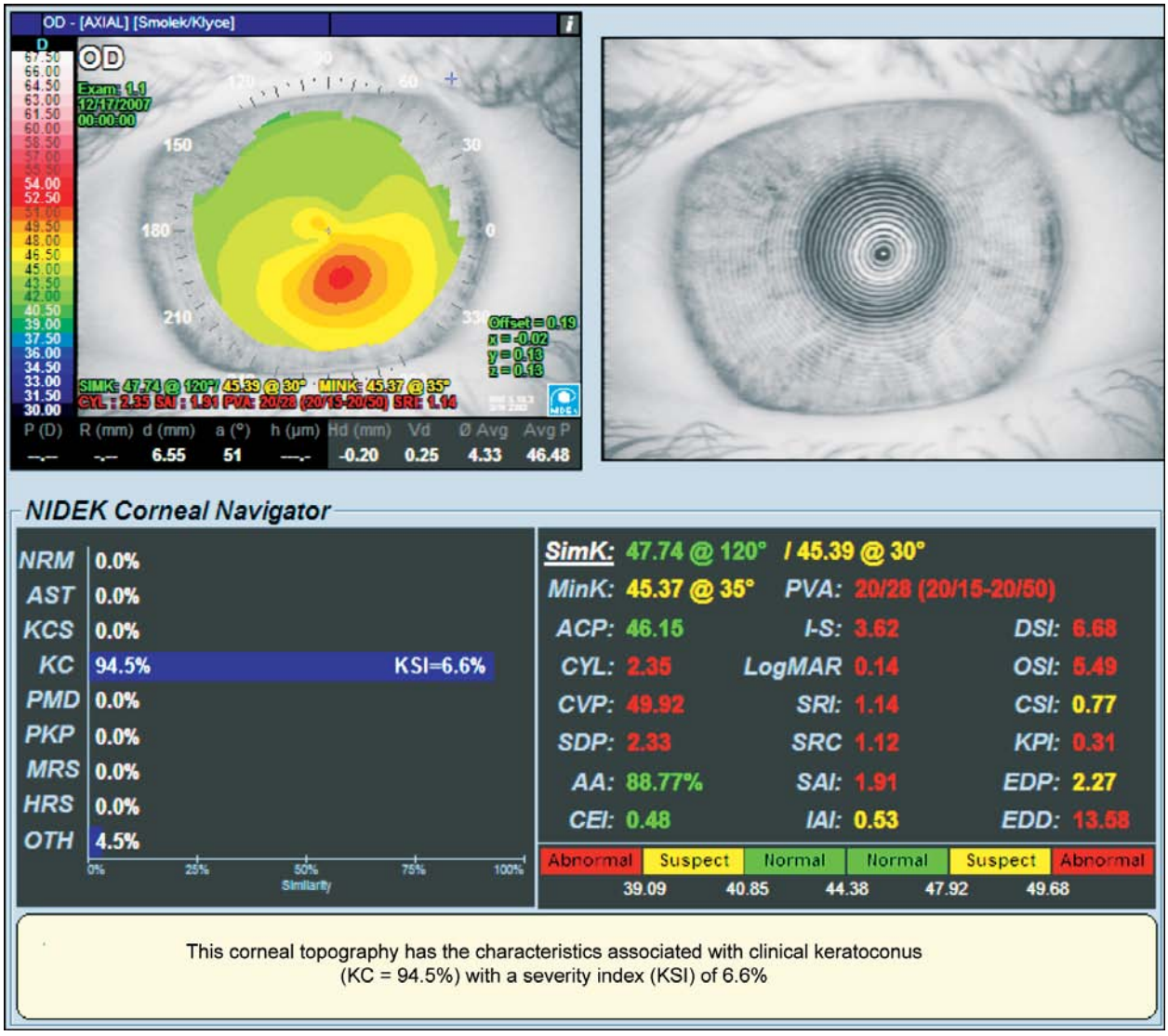


FIGURE 1-5: Screen shot of the NIDEK Corneal Navigator automatically interpreting keratoconus (KC) with a 94.5% likelihood that the topography matches keratoconus. The severity (Keratoconus Severity Index, KSI) is given as 6.6%.

The above discussion centers on the use of the axial power map for displaying corneal topography. It is noted that there are three other common topography displays on most corneal topographers. These include the tangential or instantaneous power map, the refractive power map, and a height or elevation map. The former two are in units of diopters while the latter is in units of mm or microns. The elevation maps are presented as the difference between a best fit sphere and the measured shape of a corneal surface. There are also scanning slit-based instruments (see below) that measure the position of the two corneal surfaces to yield pachymetry maps which are an important adjunct to corneal topography in the screening of patients for refractive surgery as well as differentiating keratoconus from pellucid marginal degeneration by the pattern of thinning.

Tangential power maps can be useful to show details of refractive surgery, in particular the characteristics of the transition zone after the correction of myopia. Abrupt transition between the optical zone and the peripheral corneal can produce symptoms of haloes and monocular polyopia. Refractive power maps present the true refractive power of the corneal surface, but are not generally

useful for clinical diagnosis. In fact, refractive power maps can obscure mild inferior keratoconus or pellucid marginal degeneration, since with the refractive power display, the algorithms used to calculate refractive power display a steepened peripheral cornea. The steep periphery in the refractive power map can mask the peripheral steepening characteristic of mild keratoconus.

Slit Scanning and Scheimpflug Imaging

By providing anterior and posterior corneal surface information, along with whole corneal pachymetry, the Orbscan (Bausch & Lomb, Rochester, NY), the Pentacam (Oculus, Inc., Lynnwood, Washington), and the Galilei™ Dual Scheimpflug Analyzer (Ziemer Ophthalmic Systems AG, Port, Switzerland) imaging systems can further aid in the detection and progression of corneal ectasia.

The Orbscan uses two scanning slit lamps to project a series of 40 slit beams on the anterior cornea, posterior cornea, anterior iris and anterior lens. This system is combined with a calibrated video and Placido disk imaging. **Figure 1-6** shows a typical Orbscan quad map. This provides elevation displays created as the difference between corneal surface elevation and the best fit sphere (the so-called anterior and posterior "float" displays). The Orbscan also displays the more clinically useful

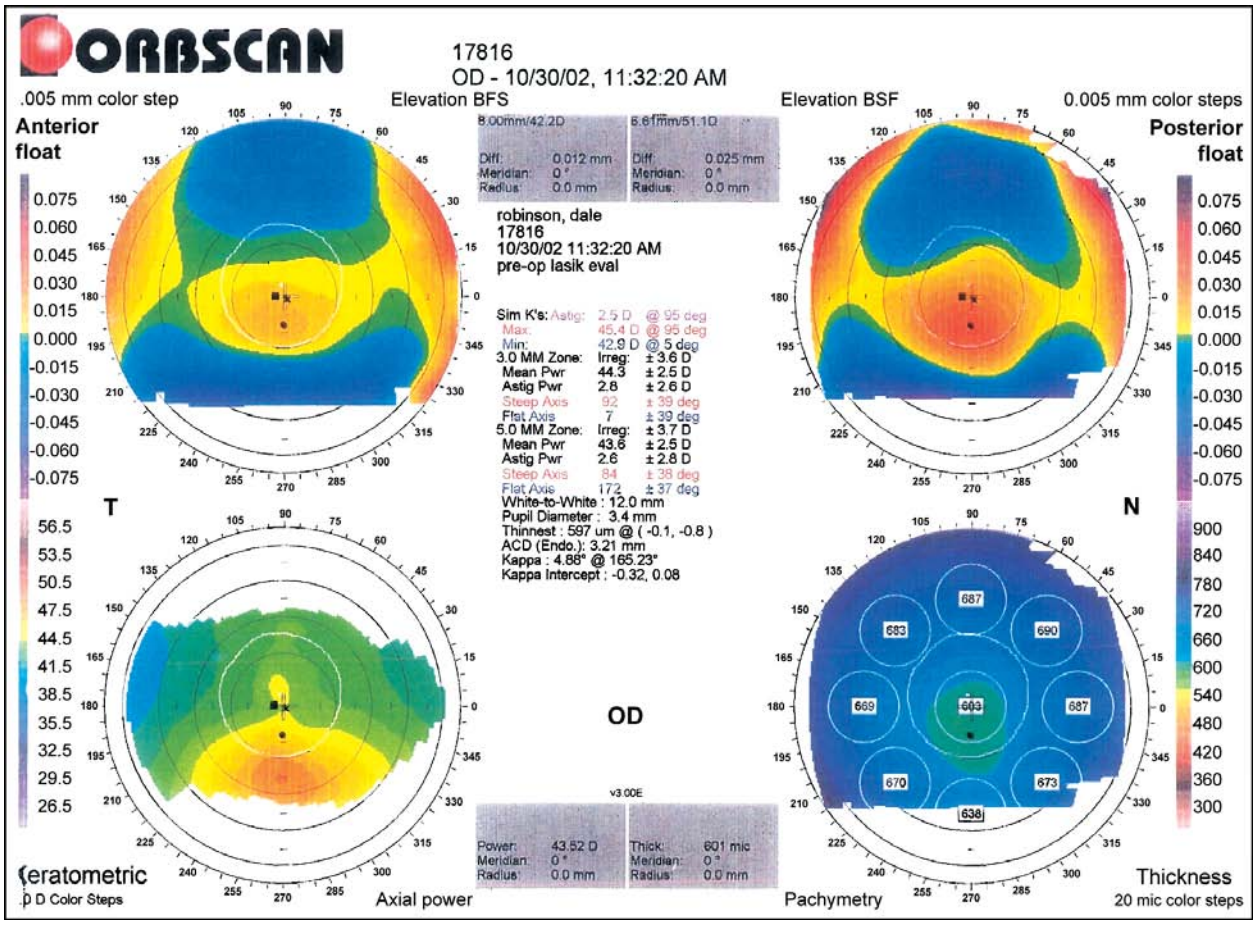


FIGURE 1-6: Keratoconus examination with the Orbscan II. Anterior (top left) and posterior (top right) floats provide the difference in elevation between the corneal surfaces and best fit spheres. Axial topography (bottom left) and pachymetry (bottom right) are shown. The thinnest point on this cornea is 597 microns illustrating the fact that keratoconus is not always associated with an abnormally thin cornea.

traditional Placido disk keratometric topography and full corneal thickness measurements over a broad area of the cornea.

When screening refractive surgery candidates, several 'red flags' or indices have been associated with possible signs of early ectasia.[19] With the Orbscan, these include: pachymetry readings with a thinnest point less than a certain threshold (470 - 500 microns), a minimum peripheral corneal thickness that is not at least 20 microns greater than the central cornea, posterior float greater than 50 microns,[20] high irregularity indices at the 3 mm and 5 mm zones, and the overall correlation of the highest/thinnest point coinciding on the anterior, posterior and pachymetry maps. Additional risk factors have been identified by Randleman and colleagues.[13] The strongest correlate was found to be abnormal topography, but other risk factors included high myopia, reduced preoperative corneal thickness, reduced residual stromal bed after refractive surgery, and age. Note that these indications are regarded as warning signs that have been correlated with keratoconus; the signs of keratoconus seen in the axial power map from the Placido topography remains the most sensitive and reliable clue to the presence of keratoconus. There are many reports of large series of refractive surgical patients who have had one or more of these warning signs (but with normal topography) and who have not developed iatrogenic ectasia. Again, apart from axial topography, none of these warning signs provide a strong indicator of *forme fruste* keratoconus by themselves. In addition, topographic irregularities at both the 3 mm and 5 mm zones may simply point to the presence of increased higher order aberrations without specific pathology. Further, the repeatability of peripheral slit-based pachymetry measurements is somewhat controversial compared to the more consistent central corneal thickness values.[21]

Note also, that corneas with scarring or moderate dry eye will frequently produce inaccurate pachymetry maps as the scarred or dry surface may be interpreted as the posterior corneal surface.

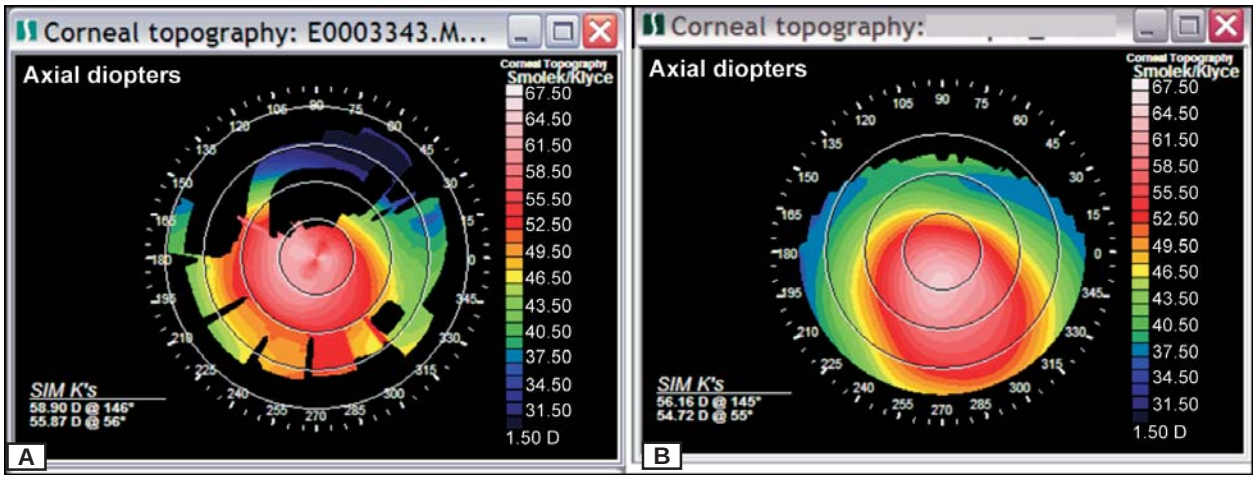
With the Pentacam, by orienting the camera lens and lens plane at intersecting angles, the Scheimpflug camera is able to record the corneal surfaces directly. Direct central recording is unavailable with the traditional Placido devices which places the viewing lens in the center of the Placido mires. Similar to the Orbscan, Pentacam slit images are gathered that image both surfaces of the cornea as well as the surface of the crystalline lens. Although slit-based corneal front surface data is not as high in resolution as Placido imagery, in cases of advanced ectasia, Placido mires become obscured while the slit images can be used to present topography **(Figure 1-7)**. This is a major advantage of slit-based topography.

For screening purposes, it is claimed that Pentacam anterior elevation values between +12 to +15 microns (above a reference sphere) are suspicious for ectasia and should prompt further investigation, whereas, a central deviation of the cornea's anterior elevation of more than +15 microns is indicative of keratoconus.[22] However, these guidelines have not received rigorous experimental proof.

The Ziemer Galilei is a dual Scheimpflug instrument that, like the Orbscan, has also a Placido function. This instrument combines slit and Placido data in displaying corneal topography.

Wavefront Sensing

It is becoming more apparent that wavefront data can further enhance our topographic diagnostic abilities. Maeda, *et al* showed that wavefront aberrometers may provide additional clues for the detection of early corneal ectasia.[23] The authors compared the total eye wavefront aberrations in normals to those in keratoconic eyes. An increase in the total higher order aberrations was noted in keratoconus and attributed to the corneal shape. Coma-like aberrations were dominant and increased



FIGURES 1-7A AND B: Comparison of the Humphrey map (A) with the Pentacam map (B) in the same eye of a keratoconus patient. With very steep corneas, the slit-based topography is able to track the surface, while Placido mires can merge with the loss of data. The data is compared with the same scales using VolPro software (Sarver and Associates, Carbondale, IL) (*Topography exams courtesy* of Renato Ambrósio, MD, PhD).

in the keratoconus eyes. Moreover, subsets of corneal ectasia have been shown to produce unique wavefront profiles. Pepose and Applegate demonstrated that patients with pellucid marginal degeneration could be differentiated from keratoconus based on wavefront data.[24] The patients with pellucid marginal degeneration were noted to possess higher amounts of peripheral aberrations (especially trefoil), whereas the keratoconus patients tended to show higher degrees of coma as in the Maeda study. An example of wavefront analysis of a keratoconus cornea is shown in **Figure 1-8**.

Corneal Hysteresis

To date, the bulk of our biomechanical corneal knowledge arises from the measurement of its geometrical aspects such as topography and pachymetry. When attempting to diagnose and treat a poorly understood corneal progressive thinning disease like keratoconus, any information regarding the biomechanical properties of the cornea would be welcome. The Reichert Ocular Response Analyzer (ORA; Reichert, Buffalo, NY) provides measurement of Corneal Hysteresis (CH) and the Corneal Resistance Factor (CRF) which are the result of viscous damping in the corneal tissue. The ORA utilizes a rapid pulse of air, and an advanced electro-optical system to record the displacement or deflection of the corneal surface before, during, and after the perturbation. The signal obtained during this process is shown in **Figure 1-9**. The response measured by the ORA is a complex combination of corneal and possibly other ocular biomechanical properties.

Importantly, the ORA provides a repeatable, Goldmann tonometer-correlated intraocular pressure (IOP) measurement. The additional parameters of Corneal Hysteresis and the Corneal Resistance Factor are being studied to determine whether they can be utilized for the detection of keratoconus. Early studies suggest a relationship between CH and the presence of keratoconus, although there is a great deal of overlap between normal corneas and those with keratoconus.[25-27] It is hoped that CH and CRF might be useful as diagnostic tools for determining who might be at risk for developing post-refractive ectasia.

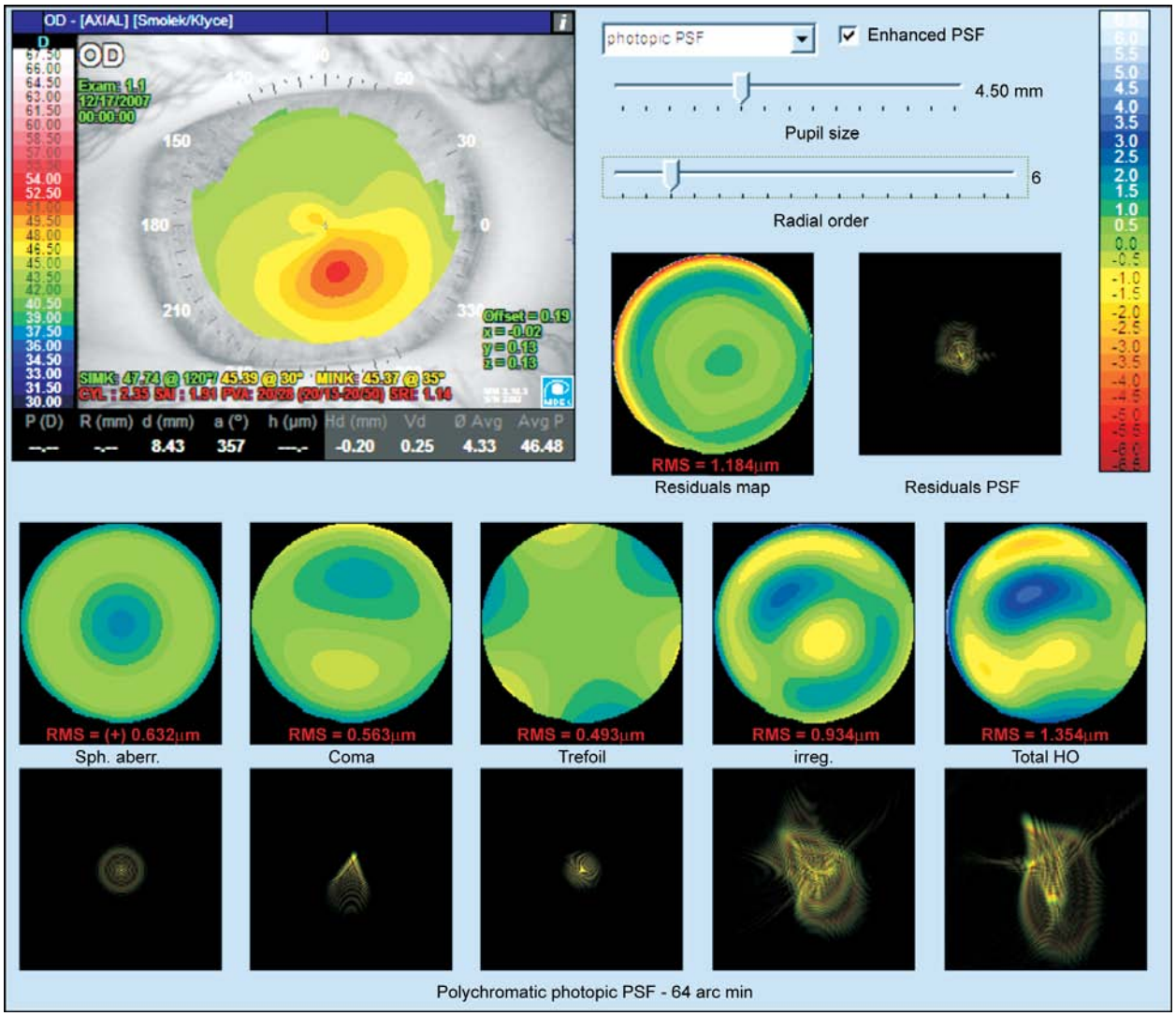


FIGURE 1-8: Wavefront analysis of keratoconus corneal topography using the Nidek Magellan topographer. With this cornea, there is a significant amount of spherical aberration, coma (usually a dominant aberration in keratoconus), and higher order aberrations. The residuals map shows the corneal wavefront that is not fit by the 6th order Zernike series.

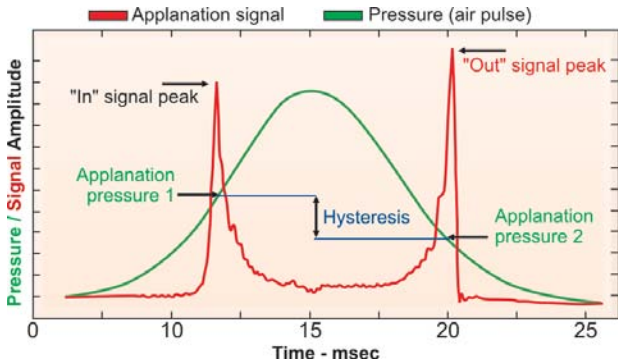
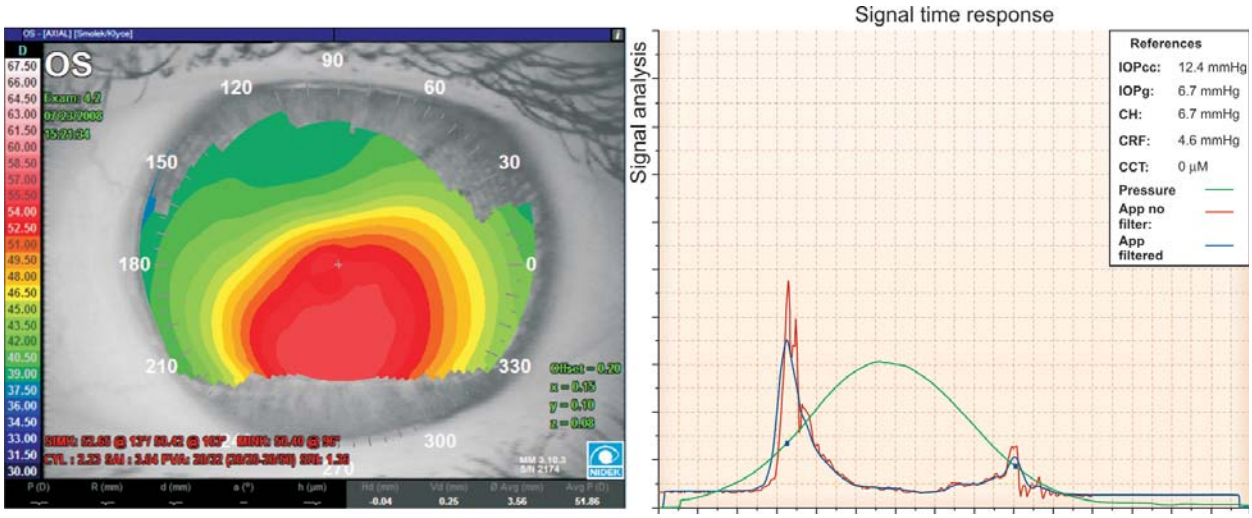


FIGURE 1-9: Optimal ORA response from a normal cornea (*Courtesy* of Reichert).

It should be noted that interpretation of CH and CRF is confounded by the fact that the entire globe and lamina cribosa are involved in the response to an air pulse delivered to the corneal surface. Hence, the characteristics of the response may not reflect only corneal biomechanics, but include those of other ocular components as well. Further, to date, no study has produced evidence that the early changes in the cornea associated with the *forme fruste* or mild stages of keratoconus can be detected with this approach.

In conjunction with CH and CRF, the other signal waveform characteristics may also yield clues to the presence of altered biomechanics as occurs in keratoconus. Signal analysis of a normal eye shows great symmetry and height between peak 1 and peak 2 and a smoother, less erratic waveform **(Figure 1-9)**. The signal waveform peaks of a keratoconic eye appears altered and CH and CRF can be lower than normal **(Figure 1-10)**. Current research is focusing on further analysis of the waveform characteristics to see if additional biomechanical properties can be gleaned, particularly from the earliest onset of pathology. Success may yield another test that can be used to assess risk factors associated with refractive surgery.



A B

FIGURES 1-10A AND B: Magellan corneal topography (A) of a keratoconus patient and the scan from the ORA (B). Note the reduction in amplitude of the second peak, and additional 'noise' on the raw signal.

Conclusion

In order to detect early ectatic disease, all refractive surgery candidates should have corneal topography examinations prior to any elective procedure. The Placido corneal topographer with its axial power map remains the most reliable method to screen for *forme fruste* keratoconus or *forme fruste* pellucid marginal degeneration. Contact lens history must be considered prior to conclusive diagnosis. Always use zonal pachymetry whether from multiple ultrasound readings (central, nasal, temporal, superior, and inferior) or from scanning slit or Scheimpflug map data. Although no one single diagnostic tool may yet provide the screening "crystal ball" desired to predict future disease in all cases, following the topographic guidelines outlined above will greatly enhance the ability to avoid potential postoperative complications

References

1. Kalin NS, Maeda N, Klyce SD, Hargrave S, Wilson SE. Automated topographic screening for keratoconus in refractive surgery candidates. CLAO J 1996;22:164-7.
2. Ambrósio R, Klyce SD, Wilson SE. Corneal topographic and pachymetric screening of refractive surgery patients. J Refractive Surg 2003;19:24-9.
3. Nielsen K, Hjortdal J, Aagaard Nohr E, Ehlers N. Incidence and prevalence of keratoconus in Denmark. Acta Ophthalmol Scand. 2007;85:890-2.
4. Assiri AA, Yousuf BI, Quantock AJ, Murphy PJ. Incidence and severity of keratoconus in Asir province, Saudi Arabia. Br J Ophthalmol 2005;89:1403-6.
5. Wilson SE, Klyce SD. Advances in the analysis of corneal topography. Surv Ophthalmol 1991;35:269-77.
6. Maguire LJ, Singer DE, Klyce SD. Graphic presentation of computer - analyzed keratoscope photographs. Arch Ophthalmol 1987;105:223-30.
7. Wilson SE, Klyce SD, Husseini ZM. Standardized color-coded maps for corneal topography. Ophthalmology 1993;100:1723-7.
8. Smolek MK, Klyce SD, Hovis JK. The universal standard scale: Proposed improvements to the ANSI standard corneal topography map. Ophthalmology 2002;109:361-9.
9. Oshika T, Klyce SD. Corneal topography: basic concepts. In FS Brightbill (Ed): Corneal Surgery: Theory, Technique, & Tissue. Part II. Testing and Measuring Corneal Function prior to Surgery (3rd edn). Mosby, Inc., St. Louis, 1999, 91-97, Color Plates 4-13.
10. Wilson SE, Lin DT, Klyce SD. The corneal topography of keratoconus. Cornea 1991;10:2-8.
11. Rabinowitz YS, Rasheed K. KISA% index: a quantitative videokeratography algorithm embodying minimal topographic criteria for diagnosing keratoconus. J Cataract Refract Surg 1999;25:1327-35.
12. Holland DR, Maeda N, Hannush SB, Riveroll LH, Green MT, Klyce SD, Wilson SE. Unilateral keratoconus. Incidence and quantitative topographic analysis. Ophthalmology 1997;104:1409-13.
13. Randleman JB. Ectatic disorders associated with a claw-shaped pattern on corneal topography. Am J Ophthalmol 2007;144:977-8.
14. Levy D, Hutchings H, Rouland JF, Guell J, Burillon C, Arné JL, Colin J, Laroche L, Montard M, Delbosc B, Aptel I, Ginisty H, Grandjean H, Malecaze F. Videokeratographic anomalies in familial keratoconus. Ophthalmology 2004;111:867-74.
15. Abad JC, Rubinfeld RS, Del Valle M, Belin MW, Kurstin JM. Vertical D: A novel topographic pattern in some keratoconus suspects. Ophthalmology 2007;114:1020-6.
16. Maeda N, Klyce SD, Smolek MK, Thompson HW. Automated keratoconus screening with corneal topography analysis. Invest Ophthalmol Vis Sci 1994;35:2749-57.
17. Maeda N, Klyce SD, Smolek MK. Application of neural networks to the classification of corneal topography: preliminary demonstration. Invest Ophthalmol Vis Sci 1995;36:1327-35.
18. Klyce SD, Karon MD, Smolek MK. Screening patients with the corneal navigator. J Refractive Surg 2005;21:S617-22.
19. Randleman JB, Trattler WB, Stulting RD. Validation of the ectasia risk score system for preoperative laser in situ keratomileusis screening. Am J Ophthalmol 2008;145:813-8.
20. Klein SR, Epstein RJ, Randleman JB, Stulting RD. Corneal ectasia after laser in situ keratomileusis in patients without apparent preoperative risk factors. Cornea 2006;25:388-403.
21. Cho P, Cheung SW. Repeatability of corneal thickness measurements made by a scanning slit topography system. Ophthalmic Physiol Opt 2002;22:505-10.
22. Maus M, Krober S, Swartz T, Belin MW, Michaelson M, Sutphin J, Wang M. Pentacam. In Wang M (Ed): Corneal Topography in the Wavefront Era, Chapter 24, Slack, Inc, Thorofare, NJ, 2006;281-93.
23. Maeda N, Fujikado T, Kuroda T, Mihashi T, Hirohara Y, Nishida K, Watanabe H, Tano Y. Wavefront aberrations measured with Hartmann-Shack sensor in patients with keratoconus. Ophthalmology 2002;109:1996-2003.
24. Pepose JS, Applegate RA. Making sense out of wavefront sensing. Am J Ophthalmol. 2005;139:335-43.
25. Luce DA. Determining in vivo biomechanical properties of the cornea with an ocular response analyzer. J Cataract Refract Surg 2005;31:156-62.
26. Kirwan C, O'Keefe M. Measurement of Intraocular Pressure in LASIK and LASEK patients using the Reichert Ocular Response Analyzer and Goldmann applanation tonometry. J Refract Surg 2008; 24: 366-70.
27. Ortiz D, Piñero D, Shabayek MH, Arnalich-Montiel F, Alió JL. Corneal biomechanical properties in normal, post-laser in situ keratomileusis, and keratoconic eyes. J Cataract Refract Surg 2007;33:1371-5.

2

Technique of Collagen Cross-linking with Riboflavin and UVA-light

Anne Hoyer
Frederik Raiskup-Wolf
Eberhard Spoerl

Please cite figure 2-2 in the text
and clear query on page 17

Introduction

The reduced mechanical stability of the cornea in keratoconus for example may be increased by photooxidative cross-linking of the corneal collagen.

Keratoconus is a corneal degeneration which often leads to a severe visual impairment due to an increasing corneal irregularity associated with a worsening of the optical abilities. The biomechanical characteristics of the cornea result from the collagen scaffold, the collagen compound and their bonding with the collagen fibrils. Even though the total amount of collagen lamellas is not significantly lower in keratoconic corneas[7] the stability is lowered by factor 0.7.[1] A decreased thickness[16] in addition to a modified configuration of the stromal collagen lamellas[5, 13, 15] are seen. Furthermore in keratoconic corneas twice as much hydroxyproline can be dissolved by pepsin.[1] Hydroxyproline stabilizes in a great amount the collagen's triplehelix. Moreover enzymatical alterations have been observed with an increased expression of lysosomal and proteolytic enzymes.[8, 16, 18, 35] as well as a decreased concentration of protease inhibitors.[8, 9] These facts indicate a disturbed cross-linking within or/and among the collagen molecules.

By photooxidative collagen cross-linking with riboflavin and ultraviolet (UV)-light additional covalent bindings between the collagen molecules can be achieved which consequently stabilize the collagen scaffold.

Photooxidative Collagen Cross-linking with Riboflavin and Ultraviolet (UV)-light

With the photooxidative collagen cross-linking with riboflavin and ultraviolet (UV)-light we are able to treat a limited area within a short time.

Riboflavin is a vitamin (vitamin B2), nontoxic and available as a drug. It has two important functions: the absorption of the UV-irradiation and as photosensitizer the generation of reactive oxygen species (singlet oxygen). In combination with UV-light, riboflavin creates free radicals which induce new chemical bonds. A significant increase in mechanical stiffness can be achieved through the cross-linking.

Because of the Riboflavin´s molecular weight (376 g/mol) an intact epithelium would be a diffusion barrier. Therefore only after removal of the epithelium the riboflavin can penetrate the stroma. The diffusion process of 0.1% riboflavin in the stroma can theoretically be described by the time-dependent one-dimensional diffusion equation assuming a diffusion coefficient of $D = 6.5 \times 10^7$ cm^2/s. The intrastromal distribution of riboflavin is shown in **Figure 2-1** varying in cornea´s depth and time. After 30 minutes in a 400 µm-thick cornea the concentration at the endothelium reaches a level where the absorption of the UV-light is high enough to protect endothelium and intraocular structures sufficiently according to the Lambert-Beer´s-law. If the stromal thickness is smaller than 400 µm, a hypoosmolalic riboflavin solution has to be used to swell the corneal thickness to 400 µm.

Riboflavin has two absorption maxima: 365 nm and 430 nm. According to the higher energy a greater cross-linking effect can be achieved when irradiated with 365 nm.[24] Therefore UVA-light of 370 nm wavelength is used for the irradiation. In this way approximately 90% of the UV-light is absorbed in a 400 µm thick deepithelialized cornea and thus there is no risk for endothelium, lens and retina to be damaged.

From investigations on the biomechanical effects with an irradiance of 3 mW/cm² an optimal irradiation time of 30 minutes was found.[2, 20] A significant increase in biomechanical stiffness starts after 15 minutes. An irradiation longer than 45 minutes shows no further stiffening.

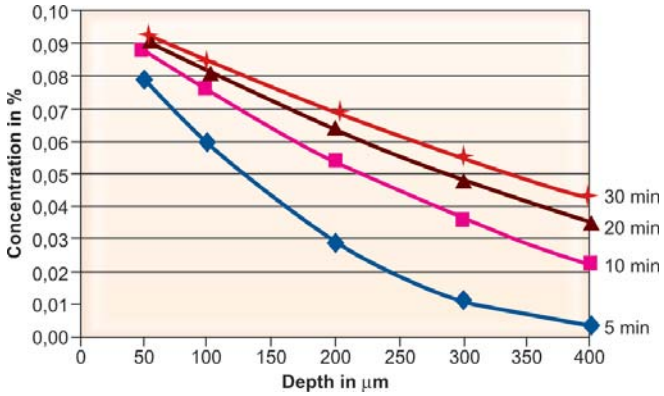


FIGURE 2-1: Intrastromal distribution of 0.1% Riboflavin in the corneal stroma at different times after riboflavin application at the surface.

Safety for Endothelium and Lens

According to industrial safety guidelines for an unprotected eye a daily UVA-irradiation of 1 mW/cm² without a photosensitizer is permitted.[23] 35% of this are absorbed in the cornea and the endothelium is strained with 0.65 mW/cm². For a 30 minutes irradiation without photosensitizer *in vivo* experiments showed a damage threshold for the endothelium of 4 mW/cm² .[30] By cross-linking with riboflavin and UV-light in a 400 µm cornea 94% of the UV-irradiation is absorbed and the endothelium gets only 0.18 mW/cm².[26] This value is below the determined damage threshold[30] and below the value from the industrial safety guidelines. Therefore there is no risk for lens and retina.

Another reason for its safety lies in the small distance between the irradiation source and eye and the irradiation´s divergency. Thus no UV-light is focussed on the retina.

Effect and Evidence of Cross-linking

Photochemical induced cross-linking cannot be visualized directly by staining or other microscopical techniques. However cross-linking causes modification of numerous physicochemical qualities of the stromal collagen which are indirect evidences for cross-linking. Below a few of these changes are pointed out.

INCREASE IN STIFFNESS AND BENDING STIFFNESS, INCREASE IN ELASTICITY MODULUS

The cross-linked cornea is stiffer by factor 1.8 than normal cornea. With it the reduced stability in a keratoconic cornea is compensated.[10, 24, 29] The stiffening effect is stronger in corneas with a higher amount of collagen respectively in elder corneas.[2, 29]

RAISING OF SHRINKING TEMPERATURE

The cornea´s shrinking temperature is raised from 63°C to 70°C. The shrinking temperature correlates positively with the degree of cross-linking.[27]

DECREASE OF SWELLING

Cross-linked collagen shows significantly less tendency for swelling.[25, 33]

INCREASED THICKNESS OF THE COLLAGEN LAMELLAS

The diameter of collagen lamellas increases by 12% in the anterior stroma and by 4.5% in the posterior.[32]

ENHANCED RESISTANCE AGAINST PROTEOLYTIC ENZYMES

In patients with keratoconus a higher expression of lysosomal and proteolytic enzymes as well as a decreased concentration of protease inhibitors was found in the lacrimal fluid.[8, 9, 12, 16, 18, 22, 35] These may account for the stromal thinning. The cross-linked cornea shows an enhanced resistance against proteolytic enzymes.[28] This decelerated degradation process also results in an extension of the collagen´s turn-over-time.

Stronger Cross-linking in the Anterior Stroma

The cross-linking effect is distributed inhomogeneous over the corneal depth. The stiffening effect is concentrated on the anterior 200 to 300 µm of the cornea.[10, 19] The UV-intensity is getting lower in deeper tissue due to its high absorbance. As a marginal increase of the collagen lamellas´ diameter,[30] an increased enzymatic degradation[28] and a stronger shrinking effect[27] were observed in the posterior stroma, a minor cross-linking effect can be assumed for the posterior parts.

This reduced cross-linking effect in deeper tissues can be explained by the above described intrastromal distribution of riboflavin **(Figures 2-1 and 2-2)** and by the exponentially declined UV-intensity according to the Lambert-Beer´s-law. 65% of the UV-light is absorbed in the anterior 200 µm, only 25 to 30% in the further 200 µm. Since the cross-linking effect predominantly depends on the UV-irradiance and not as much on the riboflavin concentration[20] the stiffening effect is strongest in the anterior 200 to 300 µm of the cornea.

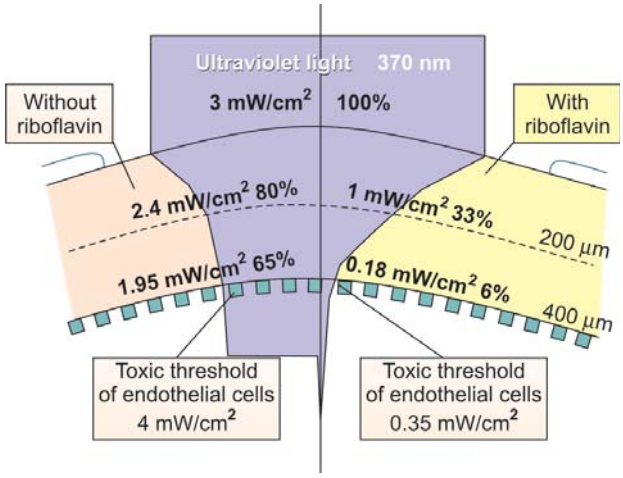


FIGURE 2-2: Decrease of UV-intensity by depth in a 400 µm cornea without (left) and with (right) riboflavin.

Treatment Procedure

The cross-linking is performed as an outpatient treatment.

The treatment parameter and protocol is shown in **Figure 2-3**.

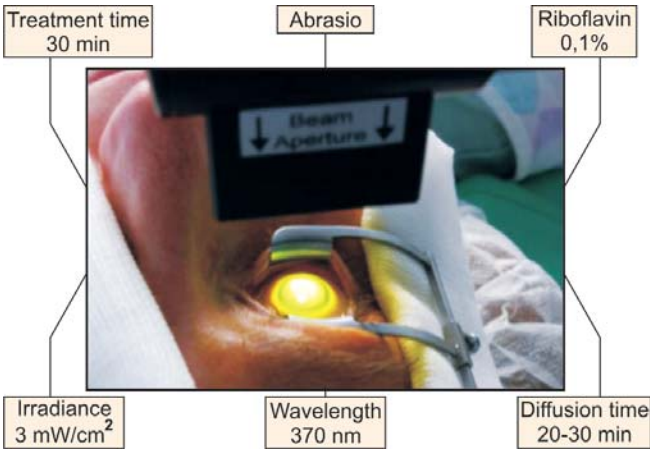


FIGURE 2-3: Treatment parameters.

After topical anesthesia, the epithelial tissue has to be removed maybe only partially in an area of 9 mm diameter. Since the intrastromal distribution of riboflavin takes time[26] it is necessary that 0.1% riboflavin solution is applied to the cornea 20 to 30 minutes before the irradiation. This time is necessary for a sufficient saturation of the stroma[22] to shield endothelium and lens.

As UVA-radiation source today radiator of different manufacturer such as the UV-X (Fa. Peschke) can be used **(Figure 2-4)**. It works with UVA-diodes and supplies a homogenous irradiance of 3 mW/cm² in a distance of 5 cm within a diameter of 8 mm of the central cornea. So local irradiation peaks, so called hot spots, which cause a local damage of the endothelium, are avoided. A homogeneous illumination of the cornea is essential for a safe treatment procedure. The irradiation area of 8 mm guarantees the cross-linking of only the central cornea, while the limbus, the sclera or the goblet cells are not.

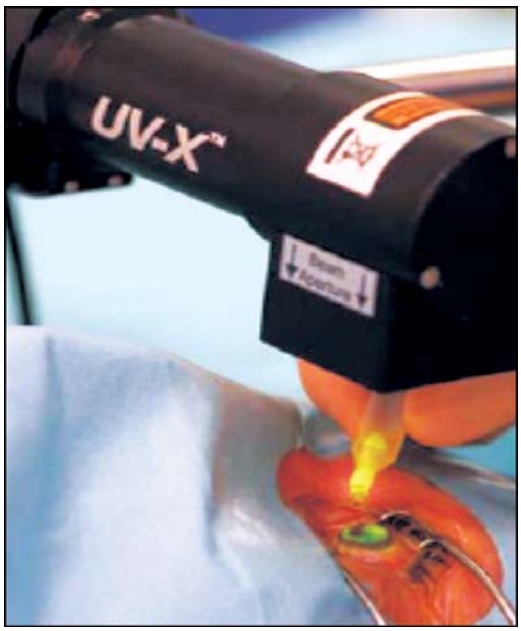


FIGURE 2-4: UV-X irradiation tool (Fa. Peschke).

During the 30 minutes of irradiation, drops of Riboflavin solution have to be applied to the cornea every 4-5 minutes. In this way, the necessary concentration of the riboflavin is sustained and desiccation of the cornea is avoided.

After Treatment

After cross-linking, antibiotic eye ointment and vitamin A eye ointment should be applied. Furthermore, analgesics can be prescribed. The ointments should be applied until complete reepithelialization of the cornea is achieved. If necessary, artificial tears and topical steroids can be prescribed.

After cross-linking the corneal curvature changes further by cellulary procedures. Therefore adjustment of new glasses or contact lenses should not be too soon. Apoptosis of keratocytes in the anterior stroma is seen after cross-linking.[4, 11, 31] 6 months after treatment no keratocytes are seen in the anterior stroma. Over the course of time new keratocytes move in from the limbus. This process is completed by approximately 4 months after cross-linking. This repopulation mechanism leads to a decrease of corneal curvature by approximately 2 diopters. The immigrated keratocytes respectively myofibroblasts´ contraction forces may be responsible.[3, 6, 14, 17, 34]

Due to the apoptosis and the repopulation of keratocytes the cornea of nearly all patients shows a slight haze of the anterior stroma within the first weeks. This haze can be seen in about 70% of the cornea´s depth and can be called as demarcation line between the mid and the posterior stroma.[21] The haze is certainly the reason for augmented glare. This phenomenon disappears normally 3 to 4 months after cross-linking. Sometimes though it can be seen still years after treatment.

Summary

By increasing the biomechanical stability of the cornea by riboflavin and UVA-induced collagen cross-linking it seems to be possible to stop the progression of keratoconus. Collagen cross-linking is a practical out-patient service, minimally invasive, cost-effective treatment with minimal strain for the persons treated. The knowledge and the observance of the biophysical basics of the photooxidative corneal collagen cross-linking account for a safe application of this therapeutical method.

References

1. Andreassen TT, Simonsen AH, Oxlund H. Biomechanical properties of keratoconus and normal corneas. Exp Eye Res 1980; 31:435-41.
2. Ahearne M, Yang Y, R´Then KY, et al. Non-destructive mechanical chracterization of UVA/riboflavin crosslinked collagen hydrogels. Br J Ophthalmol 2008 (in print).
3. Asaga H, Kikuchi S, Yoshizato K. Collagen gel contraction by firboblasts requires cellular fibronectin but no plasma fibronectin. Exp Cell Res 1991; 193:167-74.
4. Caporossi A, Baiocchi S, Mazzotta C, Traversi C, Caporossi T. Parasurgical therapy for keratoconus by riboflavin-ultraviolet type A rays induced cross-linking of corneal collagen: preliminary refractive results in an Italian study. J Cataract Refract Surg 2006;32:837-45.
5. Daxer A, Fratzl P. Collagen fibril orientation in the human corneal stroma and its implication in keratokonus. Invest Ophthalmol Vis Sci 1997; 38:121-9.
6. Guidry C, Grinnell F. Contraction of hydrated collagen gels by fibroblasts: evidence for two mechanisms by which collagen fibrils are stabilized. Coll Relat Res 1987; 6:515-29.

7. Ihme A, Krieg T; Müller RK, et al. Biochemical investigation of cells from keratoconus and normal corneas. Exp Eye Res 1983; 36:625-31.
8. Kao WWY, Vergnes JP, Ebert J, Sundar-Ray CV, Brown SI. Increased collagenase and gelatinase activities in keratoconus. Biochem Biophys Res Commun 1982; 107:929-36.
9. Kenney MC, Nesburn AB, Burgeson RE, Butkowski RJ, Ljubimov AV. Abnormalities of the extracellular matrix in keratoconus corneas. Cornea 1997; 16:345-51.
10. Kohlhaas M, Spoerl E, Schilde T, et al. Biomechanical evidence of the distribution of cross-links in corneas treated with riboflavin and ultraviolet A light. J Cataract Refract Surg 2006;32:279-83.
11. Mazzotta C, Balestrazzi A, Baiocchi S, et al. Stromal haze after combined riboflavin-UVA corneal cross-linking in keratoconus: in vivo confocal microscopic evaluation. Clin Exp Ophthalomol 2007; 35: 580-2.
12. Mackiewicz Z, Määttä M, Stenman M, et al. Collagenolytic proteinases in keratoconus. Cornea 2006; 25:603-10.
13. Meek KM, Tuft SJ, Huang Y. Changes in collagen orientation and distribution in keratoconuc corneas. Invest Ophthalmol Vis Sci 2005; 46:1948-56.
14. Netto MV, Mohan RR, Sinha S, et al. Stromal haze, myofibroblasts, and surface irregularity after PRK. Exp Eye Res 2006; 82:788-97.
15. Radner W, Zehetmayer M, Skorpik C, Mallinger R. Zur Anordnung der kollagenen Lamellen beim Keratokonus. Spektrum Augenheilkd 1996;10:156-60.
16. Rehany U, Lahav M, Shoshan S. Collagenolytic activity in keratoconus. Ann Ophthalmol 1982;107:1507-10.
17. Reichl S, Müller-Goymann CC. Entwicklung eines organtypischen Korneakonstrukts als ein in-vitro Modell für Permeationsstudien. Ophthalmologe 2001; 98:853-8.
18. Sawaguchi S, Yue BYJT, Sugar J, Gilboy J. Lysosomal enzyme activities in keratoconus. Arch Ophthalmol 1989;107:929-36.
19. Schilde T, Kohlhaas M, Spoerl E, et al. Enzymatischer Nachweis der Tiefenabhängigkeit der Vernetzungswirkung von Riboflavin/UVA an der Hornhaut. Ophthalmologe 2007 (in print).
20. Schreiber J. Verfestigung der Hornhaut durch UVA 365 nm und Riboflavin oder durch Glutaraldehyd. Dissertation Dresden: TU Dresden, 2003.
21. Seiler T, Hafezi F. Corneal cross-linking induced stromal demarcation line. Cornea 2006; 25: 1057-9.
22. Seppälä HP, Määttä M, Rautia M, et al. EMMPRIN and MMP-1 in keratoconus. Cornea 2006; 25: 325-30.
23. Sliney D, Aron-Rosa D, DeLori F, et al. Adjustment of guidelines for exposure of the eye to optical radiation from ocular instruments: Statement from a task group of the International Commission on Non-Ionizing Radiation Protection (ICNIRP). Applied Optics 2005; 44:2162-76.
24. Spoerl E, Huhle M, Seiler T. Induction of cross-links in corneal tissue, Exp Eye Res 1998; 66:97-103.
25. Spörl E, Huhle M, Seiler T. The swelling behaviour of the cornea after artificial cross-linking. Invest Ophthalmol Vis Sci 1997; 38: 507.
26. Spoerl E, Mrochen M, Sliney D, Trokel S, Seiler T. Safety of UVA-riboflavin cross-linking of the cornea. Cornea 2007; 26:385-9.
27. Spoerl E, Wollensak G, Dittert DD, et al. Thermomechanical behavior of collagen-crosslinked porcine cornea. Ophthalmologica 2004; 218:136-40.
28. Spoerl E, Wollensak G, Seiler T. Increased resistance of crosslinked cornea against enzymatic digestion. Curr Eye Res 2004: 29:35-40.
29. Wollensak G, Spoerl E, Seiler T. Riboflavin/ultraviolet-A-induced cross-linking for the treatment of keratoconus. Am J Ophthalmol 2003; 135:620-7.
30. Wollensak G, Spoerl E, Wilsch M, et al. Endothelial cell damage after riboflavin-ultraviolet-A-treatment in the rabbit. J Cataract Ref Surg 2003; 29: 1786-90.
31. Wollensak G, Spoerl E, Wilsch M, et al. Keratocyte apoptosis after corneal collagen cross-linking using riboflavin-UVA treatment. Cornea 2004; 23: 43-9.
32. Wollensak G, Wilsch M, Spoerl E. Collagen fiber diameter in the rabbit cornea after corneal cross-linking by riboflavin/UVA. Cornea 2004; 23: 503-7.
33. Wollensak G, Aurich H, Pham DT, et al. Hydration behaviour of porcine cornea crosslinked with riboflavin and ultraviolet A. J Cataract Refract Surg 2007; 33: 516-21.
34. Wollensak G, Iomdina E, Dittert DD, et al. Wound healing in the rabbit cornea after corneal cross-linking with riboflavin and UVA. Cornea 2007; 26: 600-5.
35. Zhou L, Sawaguchi S, Twining SS, et al. Expression of degradative enzymes and protease inhibitors in corneas with keratoconus. Invest Ophthalmol Vis Sci 1998; 39:1117-24.

3

Transepithelial Cross-linking for the Treatment of Keratoconus: Concepts

Roberto Pinelli

Introduction

Keratoconus is a non-inflammatory cone-like ectasia of the cornea, which is usually bilateral, that progresses over time, with consequent central or paracentral thinning of the stroma and irregular astigmatism.

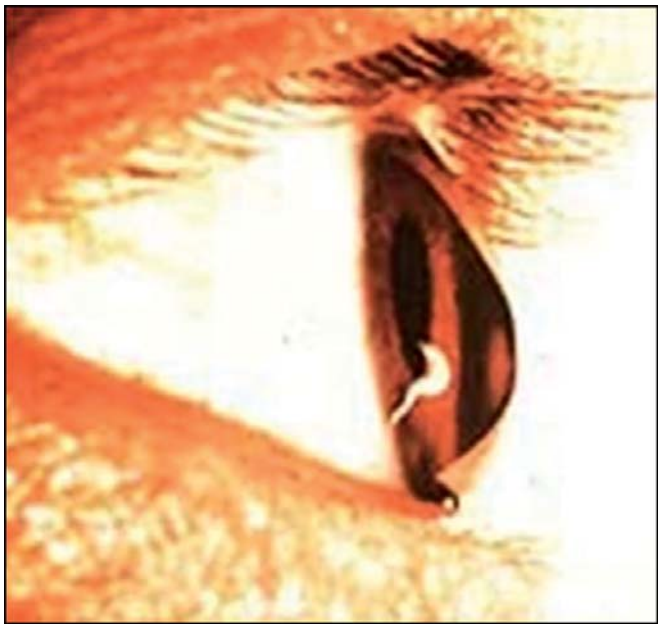


FIGURE 3-1: Keratoconus

The relevance of keratoconus in the general population seems to be relatively high, with approximately 1 in 2000,[1] even if the diffusion of new diagnostic means will permit to find prevalence rates certainly greater. In nearly all cases both eyes are affected, at least from a topographic point of view.

The cause of keratoconus is unknown, but it seems that enzymatic changes in corneal epithelium, such as decrease of the levels of the inhibitors of proteolytic enzymes and an increase of the lysosomal enzymes can be involved in the cornea degradation.

At the beginning, glasses are sufficient to correct myopia and astigmatism still regular or slightly irregular; successively, in cases of high astigmatism, it becomes necessary to apply hard contact lenses.

Epikeratoplasty is efficacious in patients which do not endure contact lenses and which do not show a significant central corneal opacity, but, due to its visual results not being perfect, this procedures was dropped.

Intracorneal rings also can be an option,[2] but all these described techniques unfortunately only correct refractive errors and do not treat the cause underlying the corneal ectasia and, therefore, they do not permit to stop the progression of keratoconus.

In 1996,[3] some theoretical studies started investigating more deeply the underlying causes of keratoconus and the possible parasurgical techniques to stop its progression. In all patients affected by keratoconus a reduced degree of cross-links in the corneal collagen fibers has been observed; that is, the aim of those studies was firstly to determine how to increase those cross-links to obtain an improved mechanical stability of the cornea and also to increase the resistance against enzymatic degradation.

Corneal Collagen Networks

Collagen is a structural protein organized in fibers. Those fibers are responsible of limiting the tissue deformation and preventing mechanical brakes. The collagen fibers are chemically stable and have high mechanical properties. Inside the connective tissue, fibroblasts synthesize tropocollagen molecules, the base blocks of collagen fibers. Those molecules have a typical weight of 300 kDa, a length of 280 nm with an average diameter of 1.5 nm. The molecule is composed by 3 helicoidal chains (alpha-chains) interlacing each other like a rope **(Figure 3-2)**.

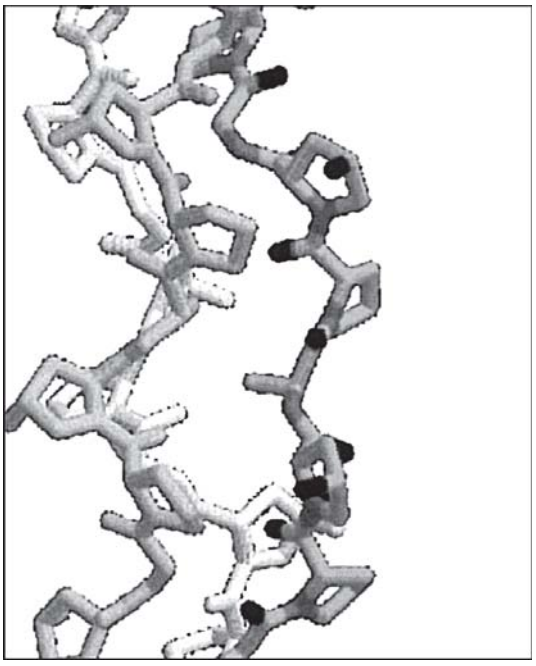


FIGURE 3-2: Collagen triple helicoidal chain

The factors of stabilization of those collagen molecules are related to the interactions between the 3 helics and are due to Hydrogen links, Ionic links and intra-chain reticulations (cross-links).

The stroma, composed mainly by collagen lamellae, gives the cornea 90% of its thickness. Between the lamellae, keratocytes can proliferate, migrate and turn into their activate state. Integrity of corneal epithelium for the switch of keratocytes (resting cells) in fibroblasts (active cells) is very important.

Keratansulphate type I is the most important mucopolysaccharide present in corneal stroma: it plays an important role for the orientation of collagen mashes and lamellae (corneal clarity, tensile strength) and for corneal hydration (corneal edema).

Photochemical Cross-linking

There are many different possibilities of cross-linking:[4]

- Lysyl oxidase (LOX) cross-links collagen enzymatically
- Transglutaminase (12h, pH=3)
- Sugar aldehydes (diabetes – Advanced Glycation End products—AGEs)
- Chemical cross-linking (glutaraldehyde, formaldehyde, DPPA)
- Photochemical cross-linking (UV, ionizating radiation)

The interaction between organic tissues and radiation depends on the type of radiation used. The ionizing radiation has enough energy to turn out electrons from the atoms of the tissues. Other types of radiation, i.e. UV radiation, have not enough energy to turn out electrons but to make them jump to higher energy levels (exciting radiation).

In the human biologic tissues, water molecules are present at a rate of 70 to 90%, so it is clearly the main target of radiation. During the water radiolysis process, the energy applied to water molecules ionizes them and generates free radicals. Free radicals are continuously produced in tissues and quickly inactivated by chemical or enzymatic transformation.

In the eye, ascorbic acid absorbs UV radiation (at cornea, lens and vitreous body areas); it is a cofactor of several enzymes, the best known of which are prolyne hydroxylase, enzymes involved in byosinthesis of collagen. In vitreous body, after cataract surgery (absence of glutathione), ascorbic acid (in ascorbate form) absorbs UV not stopped by the lens, resulting in the formation of free radicals, disaggregation of hyaluronic acid and increase in cross-linking of collagen fiber networks.

Riboflavin-UVA Treatment

A photo sensitizer is a substance which is activated by the absorption of light at a given wavelight and which can induce free radical reactions in its activate form. This substance can amplify light radiation effect on biologic tissues.

The basic mechanism of the photochemical treatment of keratoconus is to use Riboflavin as a photo sensitizer and apply on it UV irradiation at a determined wavelength to induce free radicals reactions and increase in this way the cross-links in the collagen fibers. Riboflavin has a high UV absorption between 360 and 450 nm; due to its additional shielding all structures behind the corneal stroma, including corneal endothelium, anterior chamber, iris, lens and retina, are exposed to a residual UV radiant exposure less than 1 J/cm^2 (in accordance with safety guidelines). The UV source is typically a group of 3 to 5 Light Emitting Diodes producing a radiation of 370 nm wavelength and 3 mW/cm^2 intensity **(Figure 3-3)**.

The cross-linking effect is obtained in 3 steps **(Figure 3-4)**.

FIGURE 3-3: UVA source (*Courtesy* of Peschke GmbH)

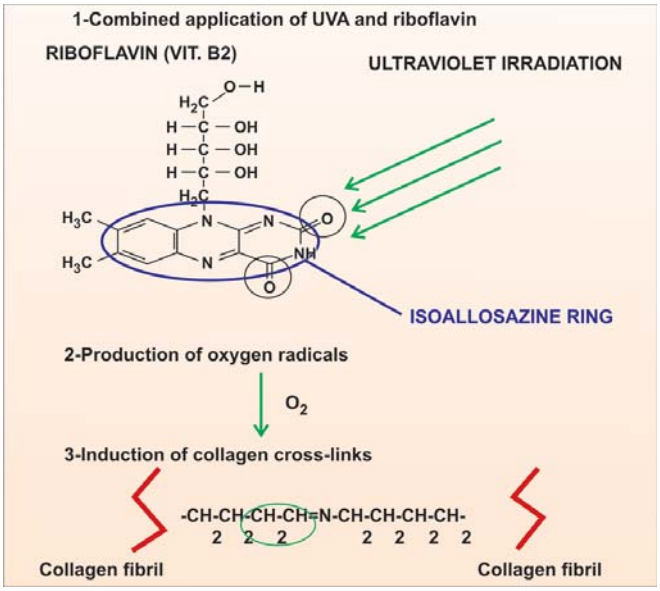


FIGURE 3-4: Photochemical induction of cross-links

Corneal Epithelium

The goal of the transepithelial treatment is to obtain mechanical X-Linking of collagen fiber networks of the corneal stroma without side effects (edema, demarcation lines in the anterior stroma of the cornea, phlogosis, etc).

The widespread technique of cross-linking is based on a central abrasion (with a diameter of 8 mm). This abrasion is made because the epithelium is believed to be a barrier to the correct diffusion of riboflavin so a possible factor of decreased effectiveness of the treatment.

What has been observed during the different studies[5,6] is that free radicals mediated by the riboflavin irradiated with UV light can create cell damage. Keratocytes showed (in both laboratory and clinical studies in epithelium-removed eyes) cells death up to a 350 nm depth. After 6 months the area is repopulated by keratocytes which, differently from corneal endothelium, can reproduce. To preserve the endothelium a minimum corneal thickness of 400 nm should be assured.

The barrier-effect produced by the riboflavin, present at the level of the tear film and of the corneal epithelium, is one of the qualifying aspects of the transepithelial technique. Actually, this aspect makes the technique safer as far as the endothelial damage is concerned, especially in the thin corneas (400 microns), because most of the radiating energy emitted for the treatment, is blocked before entering the superficial layers of the corneal stroma. Moreover, a part of the energy reaches the superficial corneal stroma, where the riboflavin is located, even if in a small quantity, and then produces free radicals and cross-links between the collagen fibers.

The news in this treatment is represented by the possibility of realizing cross-linking keeping the epithelium unaltered. This natural barrier protects the cornea but it is not an impermeable stratus: it is an osmotic membrane through which the riboflavin can penetrate to the cornea. Of course, the riboflavin itself cannot penetrate easily so the question is, at this stage, about the real effectiveness of the treatment, compared with the traditional one. If we combine the riboflavin drops with a tension-active substance, we can have a more efficient penetration to the cornea. This substance acts

as a vector for riboflavin, with a double effect: reaching the cornea and filling the epithelium, contributing to its strengthening **(Figure 3-5)**.

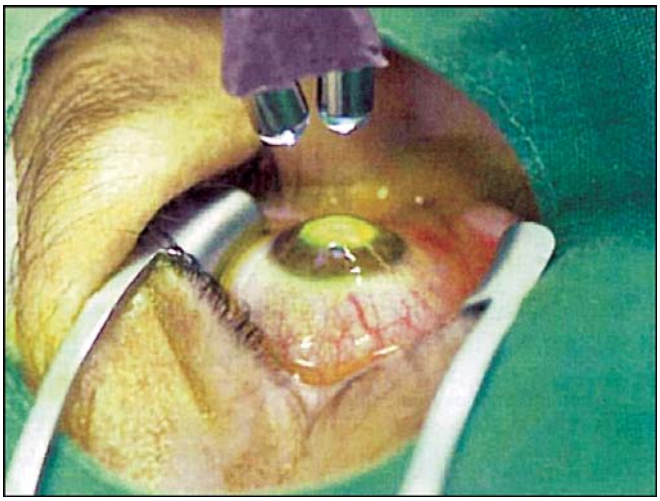


FIGURE 3-5: Patient eye under C3-R treatment.

The advantages of this particular technique is that all the macroscopic side effects related to the epithelium-removal technique are not present: no pain, no stromal edema (due to the abrasion) and, more important, the possibility to treat both eyes in the same session (85% of patients have bilateral keratoconus, so the treatment in most cases is necessary in both eyes).

Even if we assume that the riboflavin cannot penetrate efficiently the epithelium, we think that as the photo sensitizer is distributed homogeneously on the treated eye, we can at least obtain an increased rigidity of the corneal epithelium, thus a decreased instability in visual acuity of the patient.

The real question is about the effectiveness of the treatment, as the safety issues are not a worrisome with this technique: keeping the epithelium unaltered means reducing most of the side effects of the treatment (including the death rate of keratocites and the number of endothelial cells). We continue our studies in this way because we believe that the epithelium removal is something that could be avoided in the treatment and transepithelial technique will become the standard in cross-linking treatments.

References

1. Rabinowitz YS. Keratoconus. Surv Ophthalmol 1998;42:297-319.
2. Colin J, Cochener B, Savary G, Malet F. Correcting keratoconus with intracorneal rings. J Cataract Refract Surg 2000;26:1117-22.
3. Spoerl E, Huhle M, Seiler T. Induction of cross-links in corneal tissue. Exp Eye Res 1998;66:97-103.
4. Spoerl E. Physical background of the riboflavin/UV cross-linking of the cornea. World Vision Surgery Symposium, Sirmione, Italy, 22-23 June 2007.
5. Wollensak G, Spoerl E, Wilsch M, Seiler T. Keratocyte apoptosis after collagen cross-linking using riboflavin/UVA treatment. Cornea 2004;23:43-9.
6. Spoerl E, Mrochen M, Sliney D, Trokel S, Seiler T. Safety of UVA-riboflavin cross-linking of the cornea. Cornea 2007;26:385-9.

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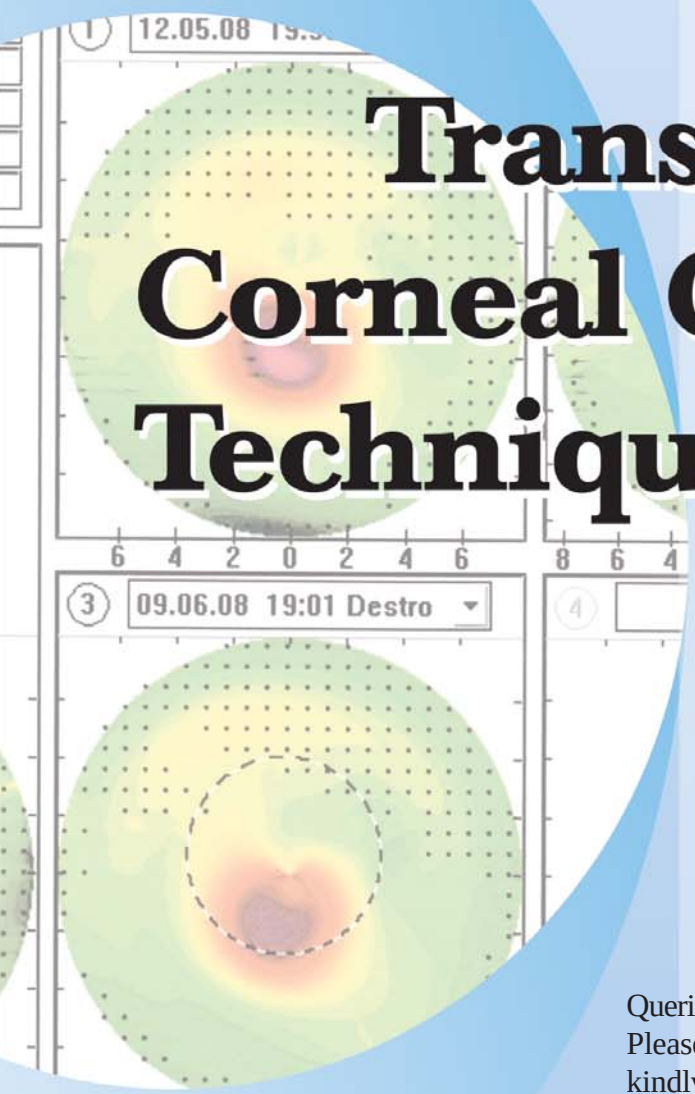

Transepithelial Corneal Cross-linking: Technique and Results

Roberto Pinelli
Antonio Leccisotti
Tarek El Beltagi

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Introduction

The term *cross-linking* indicates a medical intervention; it was originally used in specialties such as dentistry and orthopedics. Theo Seiler, MD, PhD, of Switzerland, was the first to suggest applying this principle to ophthalmology, more specifically cross-linking corneal collagen fibers.

After researching this idea, Professor Seiler and his colleagues studied the use of riboflavin (vitamin B2) and UVA irradiation, noting that the combination induced a strengthening of the corneal stroma. This effect was obtained by creating new bonds between the collagen fibers—where unstable riboflavin molecules produced these bonds after irradiation with UVA. This early research proved an effective treatment for keratoconus; however, one problem was standardizing the main parameters of the treatment, including riboflavin concentration and penetration, UV fluence, and time of exposure. This standardization was necessary to render the treatment safe and effective.

Present

The corneal collagen cross-linking (CXL) treatment initially required epithelial debridement to improve riboflavin penetration in the stroma; however, now the treatment may be performed with or without deepithelialization. There are different opinions regarding epithelial debridement, but we must remember that most complications of the procedure (infections, slow healing, subepithelial haze) arise from deepithelialization. Epithelial healing in keratoconic corneas is indeed much slower than in healthy corneas, and may take several weeks after CXL in some eyes (personal observation). Some surgeons argue that leaving the epithelium on the stroma is less efficacious because it slows the penetration of the riboflavin on the stroma; however, our experiences demonstrate the opposite.

Recently, Pinelli, *et al*[1] used fluoroscopy to observe the absorption of riboflavin in the absence of epithelial debridement **(Figure 4-1)**. Riboflavin 0.1% was applied to the cornea via a saturated Merocel sponge and left on the eye for 5 minutes before the start of UVA light administration. We repeated riboflavin applications every 3 minutes. After 6 minutes, the riboflavin penetrated under the epithelium; after 14 minutes, it penetrated the middle of the stroma; and after 30 minutes, we observes its full diffusion. Our research demonstrated that during CXL treatments, leaving the epithelium intact does not significantly limit the penetration of the riboflavin.

Personal Experience

Observing via fluoroscopy the riboflavin absorption without epithelial removal, we noticed that the epithelium does not restrict significantly the riboflavin penetration.

Riboflavin 0.1% (PriaLight®, PriaVision, Menlo Park, CA, USA) was applied on the cornea via a saturated Merocel sponge for 5 minutes before the start of UVA light administration. The riboflavin is then applied every 3 minutes during the whole procedure.

After 6 minutes the riboflavin penetrates under the epithelium; after 14 minutes it penetrates in the middle stroma and after 30 minutes we can observe its full diffusion **(Figure 4-1)**.

On this basis, we conducted a comparative study to evaluate the difference between C3-R with and without deepithelialization on patients affected by keratoconus.

They were divided into two groups (A and B) each was composed of five patients.

Group A was treated monocularly with CXL without deepithelialization; group B was treated monocularly with CXL with deepithelialization.

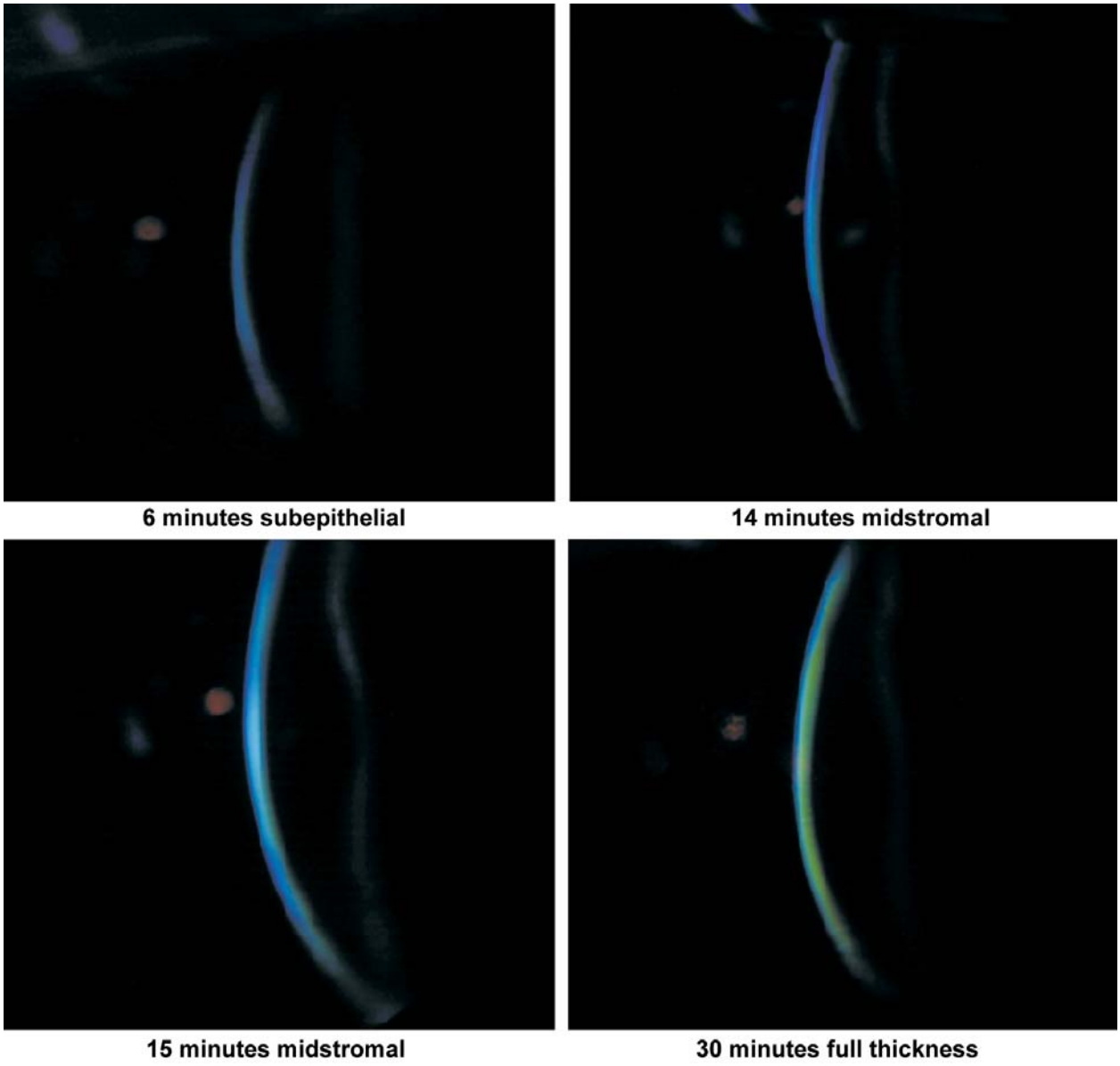


FIGURE 4-1: The penetration of riboflavin under the epithelium.

Before the treatment, all patients had an assessment of uncorrected visual acuity (UCVA), best spectacle-corrected visual acuity (BSCVA), manifest refraction spherical equivalent (MRSE), bio-microscope evaluation (corneal and lens transparency), intraocular pressure (IOP), corneal computerized topographic examination (Eyesys), linear scan optical tomography (Orbscan II), endothelial cell count and ultrasound pachymetry, and a satisfaction questionnaire was also administrated in order to monitor the level of satisfaction reached by the two different groups. All examinations were repeated at six and nine months after CXL treatment. Exclusion criteria included pachymetry thinner than 400 µm and aphakic eye.

Each eye was treated with proparacaine 0.5% for ≤ 30 minutes before exposure (i.e. approximately two drops every 5 minutes). Riboflavin was then applied on the cornea for ≤ 25 minutes before

irradiation and was then activated by a 30-minute exposure to the UVA light (i.e. 370 nm fluence at 3 mW/cm^2). Riboflavin solution was reapplied on the cornea every 3 minutes during the UVA irradiation.

Results

Before the treatment, UCVA ranged from 0.1 to 0.3, BSCVA from 0.4 to 0.7, medium K value ranged from 45 to 49 D, and corneal thickness from 432 to 463 microns.

At six and nine months postoperatively there were no significant differences in the analyzed parameters between the deepithelialized group and the non-deepithelialized one.

Mean K decreased, SE decreased, RMS error decreased **(Figure 4-2)**, gained lines in UCVA and BSCVA, pachymetry increased and no endothelial cells loss were observed in both groups **(Table 4-1)**. The only remarkable difference regarded discomfort evaluation and satisfaction questionnaire.

TABLE 4-1: Results of corneal cross-linking with and without de-epithelialization

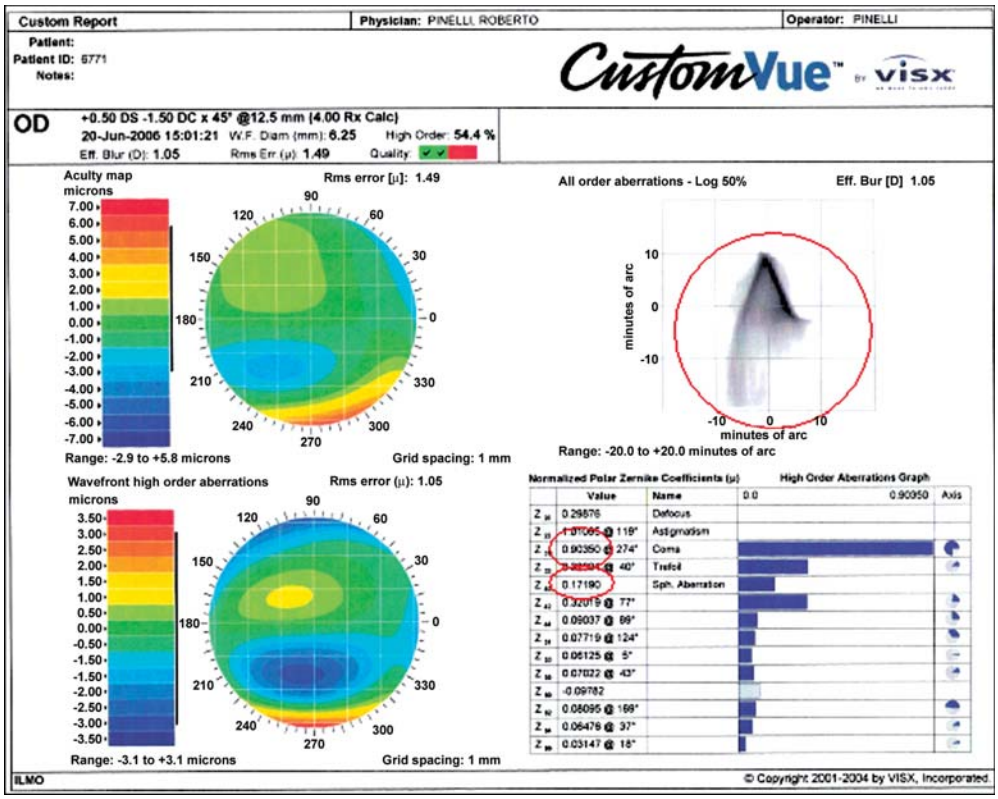
	A group (not deepithelialized)	B group (deepithelialized)
Gained Lines of UCVA	2	2
Gained Lines of BSCVA	1,6	1,8
Mean Pachymetry Increase	15 microns	13 microns
Mean K Decrease	-1,74 D	-1,92 D
Mean S.E. Decrease	-1,37	-1,75
Endothelial Cells Loss	NONE	NONE
Mean RMS Error Decrease	-2,21	-1,98
Discomfort Evaluation	1	4
Satisfaction Questionnaire	9	8

The deepithelialized group showed demarcation lines in the stroma (probably due to migration of keratocytes), that not necessarily represent a sign of cross-linking. According to our R&D department, signs of linking have to be demonstrated through direct and indirect analysis (direct: confocal microscopy and/or electronic microscopy; indirect through the study of the molecular properties of collagen). The non-deepithelialized group showed transparent cornea without any stromal abnormality.

The postoperative therapy for the first group was only artificial tears for one week, while the second group of patients needed topical steroids for two weeks.

At the Second International Corneal Cross-linking Congress 2006, in Zurich, Switzerland, Pinelli, *et al* reported results and characteristics of our CXL treatment protocol:[2]

- No epithelial debridement;
- Two drops of proparacaine 0.5% every 5 minutes for 15 minutes;
- A 5-minute presoak with riboflavin solution (0.1% riboflavin-5-phosphate and dextran);
- Up to 30 minutes of exposure to UVA light (370 nm fluence at 3 mW/cm^2) to the central 7 mm of the cornea (with the speculum in place);
- UVA light combined with reapplication of riboflavin solution every 3 minutes.



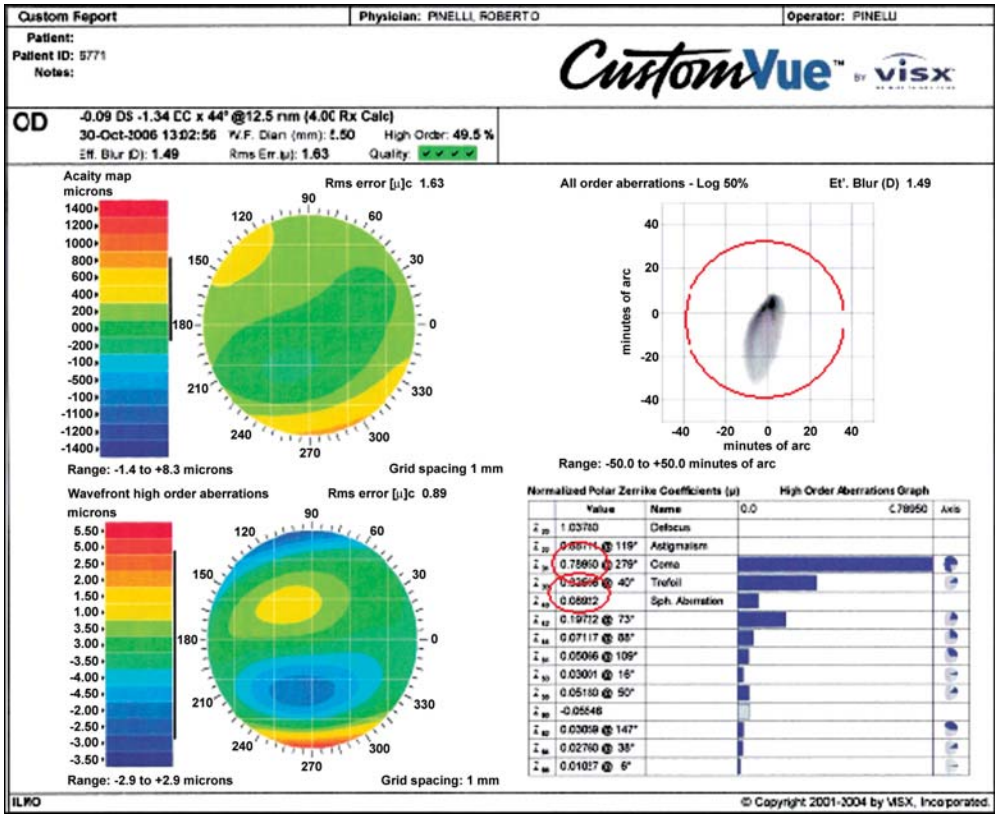


FIGURE 4-2: Aberrometry before and after corneal cross-linking without de-epithelialization

The penetration of riboflavin through intact epithelium can be enhanced by substances increasing its permeability, such as ethylenediaminetetraacetic acid (EDTA)[3] and topical gentamicin. Dr Leccisotti is currently pre-treating for 3 hours with these 2 components, all included in a standard topical gentamicin industrial preparation (Ribomicin eyedrops, Farmigea, Italy), then by topical anesthetic (oxybuprocaine) for 30 minutes, before instilling riboflavin and irradiating with UVA. His results at 6 months are encouraging, with BCVA unchanged in 21 eyes, improved in 11 eyes, worsened in 1 eye by 1 Snellen line. Mean BCVA improvement, in decimals, is 0.15. Mean curvature improvement is 1.3 diopters **(Figure 4-3)**. Endothelial safety was tested by specular microscopy, and cell density was unchanged at 1 month and 6 months. This is reassuring, and shows that UVA penetration is (as expected) under the threshold of endothelial damage.

Pinelli, *et al* have a patented a riboflavin formula (0,1% plus tensioactive) which is at the present time under investigation on rabbit eyes.

Drs. Pinelli and Leccisotti truly believe that in the near future the transepithelial procedure will be a new frontier of the treatment for keratoconus; the methods, epi-off and epi-on, can consist of different options for different cases. In the history of refractive surgery similar phenomenon are now routine for everybody (first step with PRK and then LASIK) and there is the firm belief that these two approaches to the cure of the keratoconus disease can cohabit in the near future.

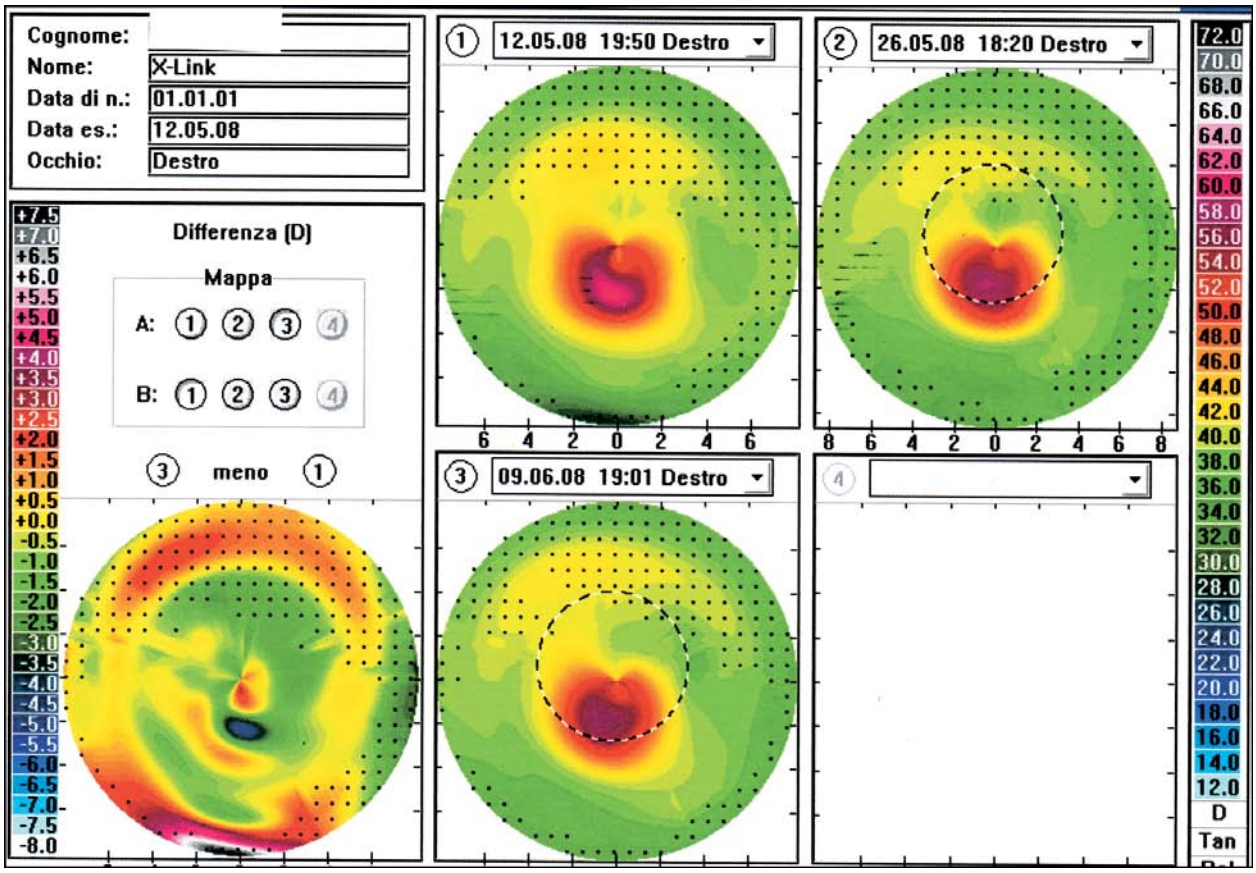


FIGURE 4-3: Changes of central curvature after corneal collagen cross-linking without deepithelialization at tangential videokeratography. Top center: preoperative. Top right: 1 week after treatment, showing initial improvement. Bottom center: 3 weeks after treatment, further improvement. Bottom left: differential map, showing a cone flattening of 4 diopters.

Future

Although ophthalmologists are still debating whether to remove or keep the epithelium intact before C3-R treatment, we prefer to avoid deepithelialization and its associated discomfort, especially until a scientific method or new technology *in vivo* will demonstrate the opposite.

In our opinion, the C3-R treatment in the future will be a less invasive, painless technique that does not require deepithelialization. A bilateral option may also be psychologically easier and more accepted by our patients. Thus far, C3-R treatments are effective, and results and follow-up are very encouraging. The numerous studies on C3-R and its impending CE mark demonstrate its safety.

References

1. Pinelli R. Corneal collagen cross-linking with riboflavin (C3-R) treatment opens new frontiers for keratoconus and corneal ectasia. Eyeworld, May 2007, Pages 34-40.
2. Pinelli R. The Italian Refractive Surgery Society (SICR) results using C3-R, paper presented at the Second International Congress of Corneal Cross Linking (CCL), Zurich, 2006.
3. Nakamura T, et al. Electrophysiological characterization of tight junctional pathway of rabbit cornea treated with ophthalmic ingredients. Biol Pharm Bull 2007;30:2360-4.

5

Surgical Treatment of Keratoconus: An Overview

Antonio Leccisotti
Roberto Pinelli

The authors have no financial or proprietary interest in any product or technique mentioned.

Please provide reference 19 and cite reference 20 in the text

Principles of Surgical Treatment of Keratoconus

The first consideration about keratoconus (KC) is that most keratoconic eyes do not need any surgical or parasurgical treatment, because of minimal deformation, of acceptable vision with contact lenses or even spectacles, and of stability.[1] However, the advent of collagen cross-linking has introduced an element of prevention of further corneal deformation even in those eyes in which no surgical treatment was considered in the past.[2] Therefore, we should clearly separate the indications to cross-linking from those to surgery. Cross-linking is indicated in earlier stages of keratoconus, showing progression, and with no scarring; we should not hope that this technique avoid surgery in eyes with advanced keratoconus and poor vision with contact lenses.

Surgical treatment of KC has several options: the simple correction of the associated refractive error without touching the cornea, by means of phakic or pseudophakic IOLs; the attempt to reshape the cornea, by insertion of intrastromal rings; the selective transplantation of the stroma, at different depths; finally, the full transplantation of the cornea.

Several techniques that have not passed the test of time or that are still under investigation will not be covered by this chapter. Procedures causing corneal weakening, such as excimer laser,[3] incisions and circular keratotomy[4] can have disastrous consequences and are therefore not advised on keratoconic eyes. Epikeratophakia, consisting in the application of a donor lenticule over the cornea[5] has been abandoned because of poor predictability and interface opacity.

Phakic IOLs

KC is often associated with a myopic refraction. When the cornea is not excessively irregular, the myopic error can be addressed by the implantation an phakic IOL,[6] with a toric component if the astigmatism is significant.[7] Since the same results can be achieved by refractive lens exchange (RLE), phakic IOLs are usually reserved to patients younger than 40, because their advantage over RLE is essentially the preservation of accommodation. Phakic IOLs do cause complications, may need explantation because of cataract or age-related shallowing of the anterior chamber (AC) and, when implanted in the AC, require a lifetime endothelial surveillance.

Several models of phakic IOLs are available, and their detailed description is beyond the purposes of this chapter. Angle-supported IOLs are currently falling out of favour, so the main phakic IOL models now in use are iris-fixated and posterior chamber. Iris-fixated IOLs have the advantage of rotational stability, and are therefore ideal toric IOLs. AC depth, lens rise (i.e. the convexity of the iris-lens plane) and endothelial status are of paramount importance in preoperative evaluation, as most complications are caused by the IOL contact with the iris (pigment dispersion, chronic iridocyclitis), the lens (cataract), and the endothelium (corneal decompensation).[8] Although the surgical maneuvers to implant a phakic IOL should disturb the vitreous less than those occurring during phacoemulsification, phakic IOLs are associated with retinal detachment, and this risk should be discussed with the patient. The difficulties in obtaining a reliable refraction, necessary to IOL power calculation, can explain some cases of significant overcorrection or undercorrection. In such cases, being unadvisable excimer laser fine-tuning, the phakic IOL should be exchanged.

Refractive Lens Exchange (RLE)

The indications of RLE are the same as phakic IOLs', but the loss of accommodation following RLE restricts this procedure to patients in the presbyopic age or younger patients that for some reason

may not undergo phakic IOL implantation. RLE is based upon phacoemulsification of the crystalline lens and implantation in the capsular bag of a pseudophakic IOL,[9] which may bear a toric component to correct corneal astigmatism.[10] Multifocal IOLs are obviously contraindicated in KC because corneal irregularity affects multifocality and cause aberrations and dysphotopsia.

The calculation of the IOL power is less reliable than in ordinary RLE; it has been advised to use videokeratographic K readings,[11] but the idea of using prepupillary corneal curvature appears more appropriate. If the cornea is not too irregular, intraoperative autorefraction can be helpful to directly calculate the IOL power (in highly myopic eyes) or to verify the power of a just implanted IOL.[9]

The main side effects of RLE in KC are under- or overcorrection, dysphotopsia, posterior capsule opacification, and vitreoretinal complications. Under- and over corrections can be treated by prompt IOL exchange (easier in the first postoperative weeks) or by piggyback implantation of a sulcus IOL (normally, for each diopter [D] of myopia the 1st IOL power should be reduced by 1 D, and for each D of hyperopia, the 1st IOL power should be augmented by 1.5 D). Dysphotopsia is generally well tolerated, because KC patients are used to glare and halos induced by KC itself or by contact lenses. Vitreoretinal complications include posterior vitreous detachment and retinal detachment, and are caused by the changes in the AC pressure during phacoemulsification.

Intrastromal Rings

Intrastromal ring segments reshape the keratoconic cornea by supporting the tissue and by shortening the corneal arc length.[12-14] Their implantation can be combined with cross-linking.[15] The indications to intrastromal rings are a clear cornea, contact lens intolerance, minimal central thickness of 400 micron. Their effect on refraction is a reduction of myopia and a regularization of astigmatism, but their predictability is limited in KC because of the variable tissue response. Two rings segments or a single segment can be implanted. Manual implantation is sometimes difficult; femtosecond laser is therefore often used to create the intrastromal tunnels.

The effects of intrastromal ring segments is reverted after explantation, and the cornea returns to the previous shape. The main drawbacks of intrastromal ring segments are poor predictability and initial irregular astigmatism.

Anterior Lamellar Keratoplasty

KC is essentially a stromal disease; therefore, partial or total replacement of the anterior central stroma (anterior lamellar keratoplasty—ALK) is theoretically its rational cure. Unfortunately, anterior lamellar keratoplasty often yields suboptimal visual results, and is therefore limited to cases in which contact lenses are not tolerated, spectacle-corrected visual acuity is not sufficient for the patient's activities, and the cornea is too thin or irregular for intrastromal rings (but several surgeons do not even consider the option of rings). The main drawback of anterior lamellar keratoplasty is astigmatism, which can be relevant and/or irregular. While mean astigmatism is 2.5 to 3 D in most series,[16] unexpected cases of frustrating high astigmatism may occur even after perfectly conducted surgery. The other complications include stromal rejection and suture-related inflammations, which can be however adequately tackled if early addressed, and intraoperative complications such as perforation, which can lead to penetrating keratoplasty (PKP).

Anterior lamellar keratoplasty is usually classified according to the depth of dissection. Some surgical techniques such as the big-bubble may bare the Descemet's membrane (total ALK or maximum depth ALK); in other cases, only 20-50 microns of stromal bed are left (deep ALK);[17] finally, in automated ALK, a microkeratome removes a 250 micron thick free corneal cap, replaced by an analogue but thicker donor flap (usually 350 micron thick). In all cases, the donor tissue is a central corneal button deprived of the endothelium and the Descemet's membrane, and of the same diameter of the excised host button (or 0.25 mm larger). The choice of the technique is essentially surgeon dependent; in general deeper dissections are technically more challenging but achieve best visual results because of no interface opacity.[18] Deep ALK is a good compromise between an acceptable intraoperative safety and a good final vision.

The advantages of ALK (especially of total and deep ALK) over PKP are enormous. The healthy perennial host endothelium is preserved; the endothelial rejection is impossible; surgery is not open sky; astigmatism is normally lower; finally, donor tissue is more readily available, because ALK does not need the endothelial standards required for PKP. Even the strongest advocates of PKP are progressively accepting the fact that visual acuity after ALK is comparable with PKP.[19]

Penetrating Keratoplasty

Currently, the indications for PKP in KC are rather restricted. Obviously, a previously failed PKP is the first indication. Unexpected perforation during ALK sometimes requires intraoperative conversion to PKP. Finally, extremely thin corneas are at high chance of intraoperative perforation during ALK, and therefore some surgeons directly perform PKP in such cases. We think that ALK should be attempted even in thin and protruding corneas, because the success rate is more than 50% in these cases; obviously, everything (adequate tissue included) should be ready for a PKP.

This said, we must remember that PKP has been the golden standard for advanced KC until recent years, and its merits are not questionable. The absence of donor-host interface, the fast learning curve, the manageability of rejection, its repeatability are well known.[20] Our main concerns with PKP are the duration of donor endothelium and open sky surgery, with the inherent risk of increased vitreous pressure.

Conclusion

The term KC entails a wide spectrum of corneal deformations: the approach to visual rehabilitation in KC is therefore based upon careful staging and realistic expectations. Contact lenses have a definite role in improving the quality of life and postponing or avoiding surgery in many keratoconic eyes. When corneal irregularity is limited, the spherical and astigmatic refractive error can be addressed by phakic or pseudophakic IOL implantation. Intrastromal ring segments can regularize the corneal shape in selected cases, and can be combined with IOL implantation. When corneal deformation is relevant, ALK in its variants is the most rational intervention, with most cases however resulting in a refractive error that will require spectacles, contact lenses or further surgical correction.

References

1. Rabinowitz YS. Keratoconus. Surv Ophthalmol 1998; 42:297-319.

2. Wollensak G, Spoerl E, Seiler T. Riboflavin/ultraviolet-A-induced collagen crosslinking for the treatment of keratoconus. Am J Ophthalmol 2003; 135:620-7.
3. Kremer I, Shochot Y, Kaplan A, Blumenthal M. Three year results of photoastigmatic refractive keratectomy for mild and atypical keratoconus. J Cataract Refract Surg 1998;24:1581-8.
4. Leccisotti A. Effect of circular keratotomy on keratoconus. J Cataract Refract Surg 2006;32:2139-41.
5. Halliday BL. Epikeratophakia for aphakia, keratoconus and myopia. Br J Ophthalmol 1990;74:66-72.
6. Leccisotti A, Fields SV. Angle-supported phakic intraocular lenses in myopia and keratoconus. J Cataract Refract Surg 2003;29:1530-6.
7. Budo C, Bartels MC, van Rij G. Implantation of Artisan toric phakic intraocular lenses for the correction of astigmatism and spherical errors in patients with keratoconus. J Refract Surg 2005;21:218-22.
8. Baikoff G, Bourgeon G, Jitsuo Jodai H, Fontaine A, Viera Lellis F, Trinquet L. Pigment dispersion and Artisan phakic intraocular lenses. Crystalline lens rise as a safety criterion. J Cataract Refract Surg 2005;31:674-80.
9. Leccisotti A. Refractive lens exchange in keratoconus. J Cataract Refract Surg 2006;32:742-6.
10. Sauder G, Jonas JB. Treatment of keratoconus by toric foldable intraocular lenses. Eur J Ophthalmol 2003;13:577-9.
11. Celikkol L, Ahn D, Celikkol G, Feldman ST. Calculating intraocular lens power in eyes with keratoconus using videokeratography. J Cataract Refract Surg 1996;22:497-500.
12. Kwitko S, Souto Severo N. Ferrara intracorneal ring segments for keratoconus. J Cataract Refract Surg 2004;30: 812-20.
13. Aliò JL, Artola A, Hassanein A, Haroun H, Galal A. One or 2 Intacs segments for the correction of keratoconus. J Cataract Refract Surg 2005;31:943-53.
14. Boxer Wachler BS, Christie JP, Chandra NS, Chou B, Korn T, Nepomuceno R. Intacs for keratoconus. Ophthalmology 2003; 110:1031-40.
15. Kamburoglu G, Ertan A. Intacs implantation with sequential collagen cross-linking treatment in post-operative LASIK ectasia. J Refract Surg 2008;24:S726-9.
16. Noble BA, Agrawal A, Collins C, Saldana M, Brogden PR, Zuberbuhler B. Deep Anterior Lamellar Keratoplasty (DALK): visual outcome and complications for a heterogeneous group of corneal pathologies. Cornea 2007;26: 59-64.
17. Anwar M, Teichmann KD. Deep lamellar keratoplasty. Surgical techniques for anterior lamellar keratoplasty with and without baring of Descemet's membrane. Cornea 2002;21:374-83.
18. Ardjomand N, Hau S, McAlister JC, et al. Quality of vision and graft thickness in deep anterior lamellar and penetrating keratoplasty. Am J Ophthalmol 2007;143:228-35.
19. Borderie VM, Werthel AL, Touzeau O, Allouch C, Boutboul S, Laroche L. Comparison of techniques used for removing the recipient stroma in anterior lamellar keratoplasty. Arch Ophthalmol 2008;126:31-7.
20. Muraine M, Sanchez C, Watt L, Retout A, Brasseur G. Long-term results of penetrating keratoplasty. A 10-year plus retrospective study. Graefes Arch Clin Exp Ophthalmol 2003;241:571-6.

6

Intrastromal Ring Segments: Manual Implantation

Ali A Mearza
Ioannis M Aslanides

Introduction

Intrastromal ring segments (ISRS) were originally developed to treat low levels of myopia in healthy eyes. By adding material to the peripheral cornea, they alter the curvature of the anterior cornea inducing a central flattening and thereby reducing myopia.

With increasing safety and accuracy of laser refractive surgery for vision correction, the use of ISRS for this indication has reduced dramatically in the last 10 years.

However, a new role for these segments in the treatment of corneal ectatic disorders has now been firmly established with numerous published articles to support their use.[1-13]

The purpose of this chapter is to provide an in-depth review of these ring segments for the treatment of keratoconus.

Although there are several types of ISRS, Intacs™ (Addition Technology, Inc, Fremont, California, USA) are the most commonly studied and used although implantation techniques and complications are similar between different types.

The implanted ring segments are two, clear, arcs of variable thickness up to 450 microns made of polymethylmethacrylate (PMMA), each with an arc length of 150 degrees. The outer diameter of each segment is 8.1 mm and the inner diameter measures 6.8 mm **(Figure 6-1)**.

The segments are implanted in the peripheral cornea at the 7 mm optical zone. The rationale for treatment of conditions such as keratoconus is that they regularize the corneal surface essentially by providing a scaffold for the cornea.

As the segments are inserted peripherally, they have the effect of flattening the central cornea with the effect proportional to the thickness of the segments. As such, they reduce the amount of astigmatism, regularize the anterior corneal surface and induce a hyperopic shift.

In many cases, they can delay or obviate the need for a corneal graft and can allow patients to resume contact lens wear where they were intolerant before.

Indications

Indications for the use of ICRS include keratoconus,[1-13] pellucid marginal degeneration[14-16] and other causes of corneal ectasia, e.g. refractive surgery induced.[17-20]

In keratoconus, ICRS are used in those patients intolerant to contact lenses, have a clear central cornea and who have a minimal central corneal thickness of at least 400 microns.

There are several algorithms available to determine where the initial incision should be and what thickness segment should be used. Ultimately, treatment is individualized to each patient based on their refraction, keratometry readings and their corneal topography.

Manual Implantation Technique

Surgery is performed either under topical anesthesia or general anesthesia according to patient and surgeon preference.

STEP-BY-STEP TECHNIQUE

1. The operative eye is prepped and draped in the usual fashion ensuring the lashes are well away from the surgical field.

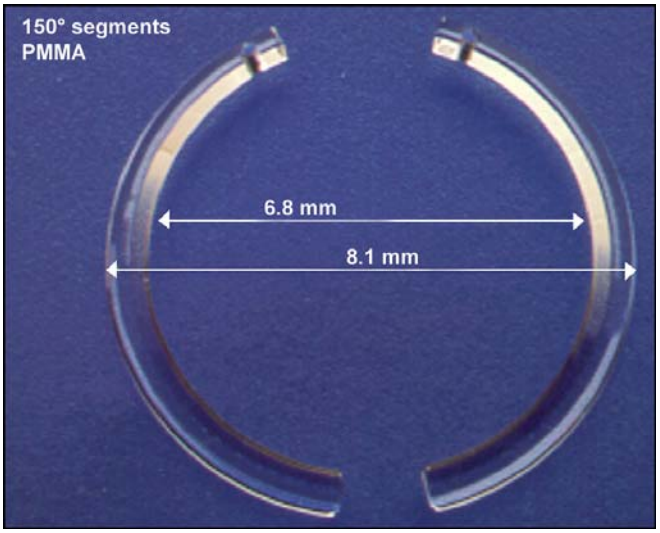


FIGURE 6-1: : Intrastromal ring segments
(*Courtesy* of Addition Technology, Inc, Fremont, California, USA.)

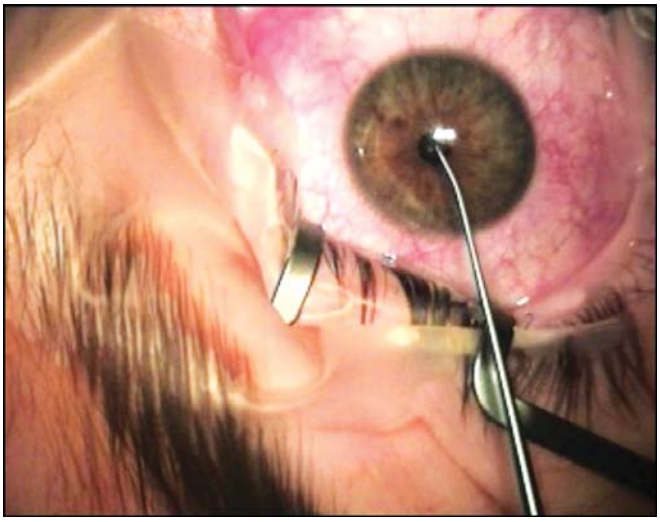


FIGURE 6-2: Marking of corneal centre

2. The geometric center of the cornea is marked with a Sinskey hook or marker **(Figure 6-2)**.
3. The ICRS marker which has previously been inked is then centered on the cornea with the incision site (arrowed on the marker) placed at the steep axis **(Figure 6-3)**.

   This provides a visual guide for the incision as well as placement of the segments themselves in the 7 mm optical zone **(Figure 6-4).**
4. A calibrated diamond knife set to 70% corneal depth is then used to make a 1.2 mm incision at the marked entry site in the peripheral cornea **(Figure 6-5)**.
5. A pocketing hook is then used to make a mini tunnel in either direction perpendicular to the main incision. It is important to ensure that the hook is inserted to the full depth of the incision **(Figure 6-6)**.
6. A modified corneal dissector is then used to extend the tunnel further on each side in preparation for manual dissection of the stromal channels **(Figure 6-7)**.

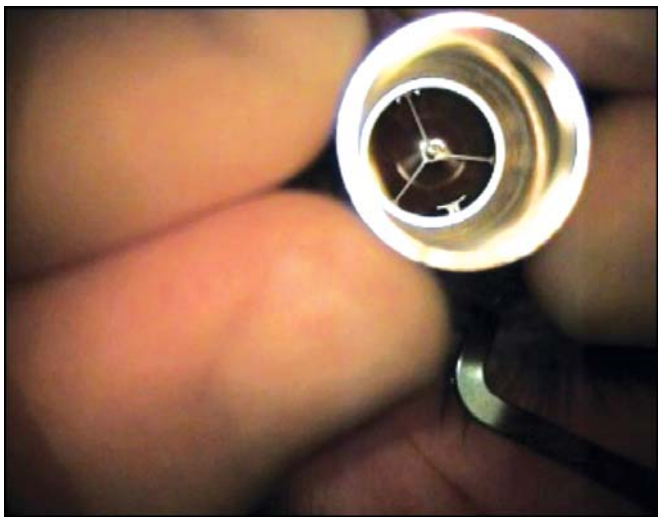


FIGURE 6-3: Placing of ICRS corneal marker

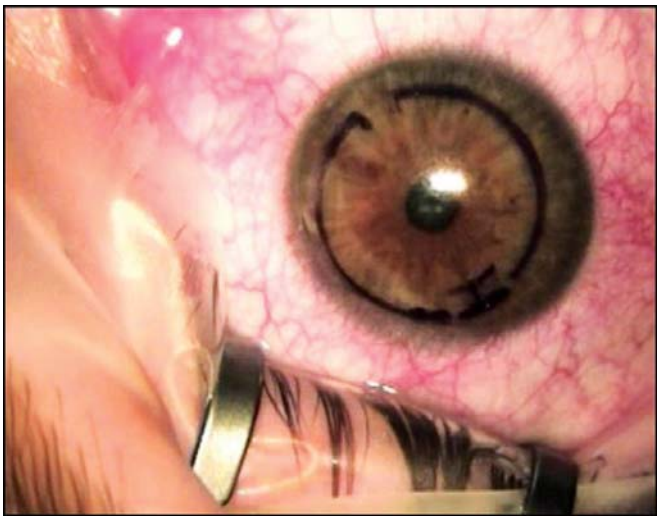


FIGURE 6-4: Resulting ink marking

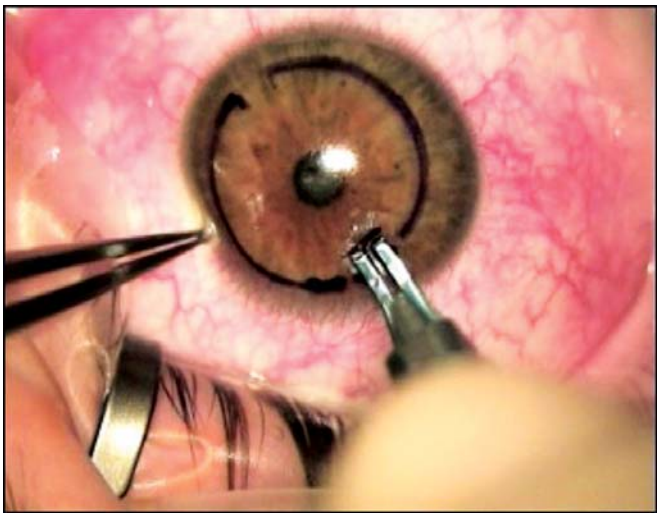


FIGURE 6-5: Incision at the tunnel entry

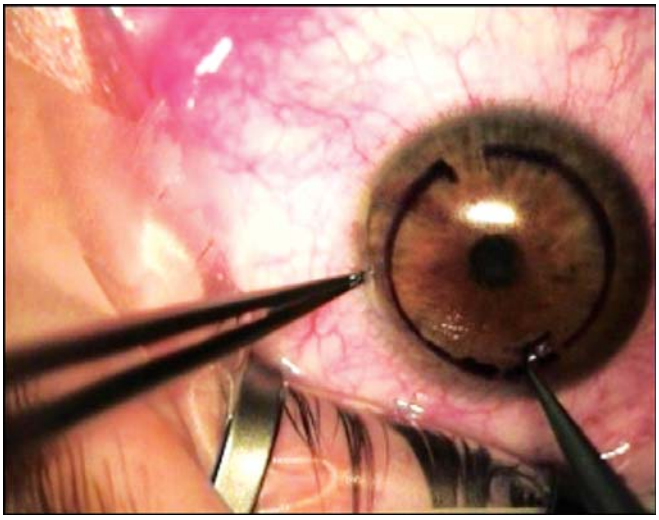


FIGURE 6-6: Mini tunnel by pocketing hook

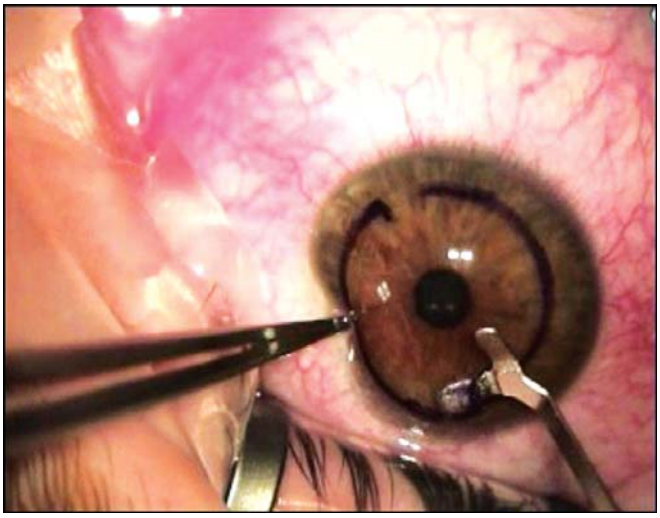


FIGURE 6-7: Extension of tunnel by dissector

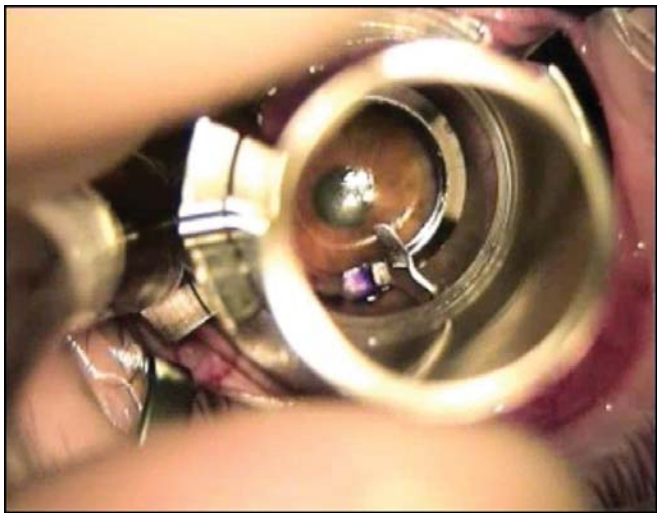


FIGURE 6-8: Suction ring is applied and lamellar dissection is started

FIGURE 6-9: Further lamellar dissection

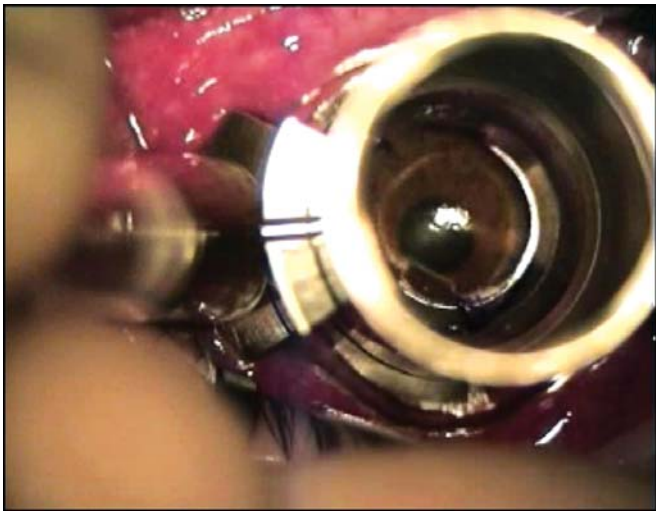


FIGURE 6-10: Completion of lamellar dissection

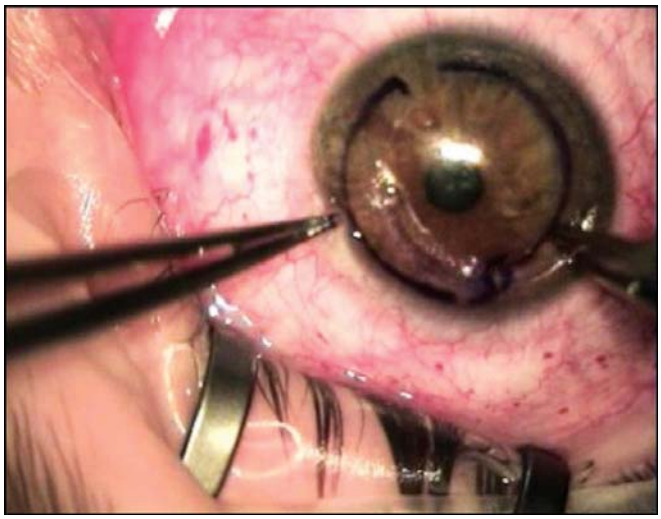


FIGURE 6-11: Insertion of ring segments

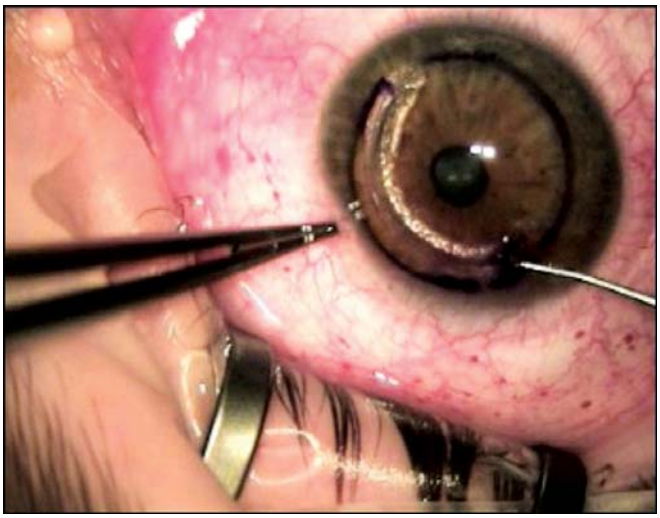


FIGURE 6-12: Segments pushed with a Sinskey hook

FIGURES 6-2 TO 6-12: (*Courtesy* of Ali Mearza)

7. A suction ring is then placed on the eye to stabilize the globe. Low suction is applied and centering is checked with the ICRS marker. If centering is incorrect, the vacuum is re-applied until accurate centering is achieved.
8. If centering is correct, high vacuum is then engaged and the stromal dissectors are used both clockwise and anticlockwise to create the stromal channels. The short lamellar dissector is used to facilitate entry of the stromal dissector channels **(Figures 6-8 to 6-10)**.
9. Once the channels are created, the segments are inserted clockwise and counter-clockwise after application of antibiotic eyedrops **(Figure 6-11)**.
10. The segments are pushed in beyond the initial incision with a Sinskey hook **(Figure 6-12)**.
11. The initial incision is sutured with 10-0 nylon.

Postoperative Management Regime

Postoperatively, patients are prescribed an antibiotic and steroid combination drop typically four times a day for 1 week, then twice a day for 1 week although protocols may vary between institutions.

Topical anesthetics and oral analgesics can be used in addition if there is pain in the immediate postoperative period. Alternatively, a bandage contact lens can be applied for short-term relief especially in the presence of an epithelial defect or significant pain.

Complications and Their Management

During surgery, reported complications include accidental perforation of the segments into the anterior chamber or extrusion of the segments anteriorly through the epithelium.[21]

In the case of perforation into the anterior chamber, the procedure should be aborted.

Anterior extrusion through the epithelium is secondary to superficial dissection. One approach to managing this is to repeat the initial incision and dissection ensuring the correct depth is obtained and then re-inserting the segments.

Other complications occurring at the time of surgery are relatively mild and resolve very quickly. These include epithelial defects, conjunctival chemosis and hemorrhage.

Perforation either anteriorly or posteriorly as well as ring decentration can all be prevented by meticulous surgical technique paying particular attention to centration and tunnel depth.

Wound complications include wound dehiscence with extrusion of the implants, epithelial ingrowth and new vessel formation.

With wound dehiscence and extrusion, the implant can be repositioned and the wound re-sutured. If there is new vessel formation, this is likely to progress and the implants should be removed.

Epithelial ingrowth is usually self limiting but if progressive, the implants may to be removed and the ingrowing epithelium debrided.

Deposits around the segments themselves are common and typically develop within the first six months of surgery. Their etiology is unclear but they typically have no effect on vision. If the deposits are marked, then removal of the segments are indicated.[22,23]

Infectious keratitis has also been reported with ICRS implantation and should be managed in the usual manner with a low threshold for segment removal. In some recalcitrant cases, penetrating keratoplasty has been required as a measure to control the infection.[24-28]

Glare and haloes have been reported and are sometimes debilitating enough to require segment removal. In one study[1] the ICRS had to removed in 12% of eyes because of visual symptoms.

Overall, complications are rare and as long as they are recognized and managed appropriately, there is minimal compromise to the patient's vision.

Clinical Results

There is now a wealth of published material on ICRS use for keratoconus and other causes of corneal ectasia.

Colin[1] in his landmark European clinical evaluation paper prospectively studied 57 keratoconic eyes who were contact lens intolerant and underwent ICRS implantation. At the 6 month time gate, 78% patients had an improvement in uncorrected visual acuity (UCVA) of 2 lines or more. Best corrected vision acuity (BCVA) improved from 53% of patients pre-operatively seeing 20/40 or better to 74% patients postoperatively. Keratometry readings were also reduced by a mean of 4.3 +/- 2.8 D. In 12% of eyes, the ICRS were removed because of visual complaints, typically glare and haloes but there were no complications associated with their removal.

Colin and Malet[2] recently published their 2 year prospective results in 100 keratoconic eyes. They found that the UCVA and BCVA improved in 80.5% and 68.3% of eyes at the 2 year time gate as well as a significant reduction in keratometry values. Overall, they concluded that significant and sustained improvements in vision occurred in most cases.

Other authors have also found significant improvements in keratoconic patients.

Aliò et al[3] looked at 3 year results in their small series of 13 eyes and found that mean BCVA increased from 20/50 preoperatively to 20/30 postoperatively at the 3 year time gate. They also noted decreased inferior-superior asymmetry by a mean of 2.81 Diopters which was sustained at the 3 year time gate.

Aliò's group[4] also published an interesting paper on potential factors that influenced whether the outcome was good or poor with ICRS implantation. They concluded that ICRS provided better results in those eyes with relatively low mean K values (less than or equal to 53 D) compared to eyes with advanced keratoconus with mean K's greater than or equal to 55 D.

The longest follow up data regarding the use of ICRS to date has been published by Kymionis *et al*.[5] They looked at 17 eyes with keratoconus in their 5 year retrospective study and found UCVA, BCVA and refraction was improved in the majority of patients (59%) with no evidence of progressive sight threatening complications.

Discussion

In patients with keratoconus, ICRS are a good stop gap prior to corneal grafting in contact lens intolerant patients. They not only improve UCVA and BCVA but also restore contact lens tolerance in the majority of patients.

Whereas in the past, the only option for contact lens intolerant patients with keratoconus was a corneal transplant procedure, there are now several modalities of treatment that can be employed prior to resorting to a corneal graft.

ICRS implantation is being made easier and more accurate with the use of the femtosecond laser to create the channels and the results have been shown to be comparable with the manual technique.[17,29,30]

In addition, ICRS can be combined with other modalities of treatment to further improve the visual outcome. There have been several published reports of ICRS combined with phakic intraocular lenses performed in a sequential manner to correct any residual refractive error with good results.[31,32]

The procedure has also been combined with the latest modality of treatment, collagen cross-linking in order to prevent further progression of keratoconus but published results on this combined approach are scarce at present.[33]

In the future, ICRS will be further refined to reliably predict the effect and outcome in keratoconic and other ectatic conditions. Addition Technology have already produced a new type of ICRS called Intacs SK™. This implant has been specifically designed to be used in severe keratoconic cases where the K's are extremely high and standard implants would be deemed ineffective.

The implants are elliptical in cross section and are designed to be inserted in the 6 mm optical zone, hence providing increased effect. Anecdotal evidence seems to show good results and further data is awaited with interest.[34]

Conclusions

Intracorneal ring segments are an important part of the surgical repertoire now available to treat keratoconus.

Patients no longer need to proceed automatically to a corneal graft procedure which involves a prolonged route to visual rehabilitation.

Intracorneal ring segments provide a safe and effective alternative in selected patients and are likely to become more efficacious in the future with continuing research and development.

References

1. Colin J. European clinical evaluation: use of Intacs for the treatment of keratoconus. J Cataract Refract Surg 2006;32:747-55.
2. Colin J, Malet FJ. Intacs for the correction of keratoconus: Two-year follow-up. J Cataract Refract Surg 2007;33:69-74.
3. Aliò JL, Shabayek MH, Artola A. Intracorneal ring segments for keratoconus correction: long term follow up. J Cataract Refract Surg 2006;32:978-85.

4. Aliò JL, Shabayek MH, Belda JI, Correas P, Feijoo ED. Analysis of results related to good and bad outcomes of Intacs implantation fro keratoconus correction. J Cataract Refract Surg 2006;32:756-61.
5. Kymionis GD, Siganos CS, Tsiklis NS, et al. Long-term follow-up of Intacs in keratoconus. Am J Ophthalmol 2007;143:236-44.
6. Levinger S, Pokroy R. Keratoconus managed by Intacs: one year results. Arch Ophthalmol 2005;123:1308-14.
7. Hellstedt T, Makela J, Uusitalo R, et al. Treating keratoconus with Intacs corneal ring segments. J Refract Surg 2005;21:236-46.
8. Boxer-Wachler BS, Christie JP, et al. Intacs for keratoconus. Ophthalmology 2003;110:1031-40.
9. Siganos CS, Kymionis GD, Kartakis N, et al. Management if keratoconus with Intacs. Am J Ophthalmol 2003;135:64-70.
10. Colin J, Cochener B, Savary G, et al. Intacs inserts for treating keratoconus: one year results. Ophthalmology 2001;108:1409-14.
11. Colin J, Cochener B, Savary G, et al. Correcting keratoconus with intracorneal rings. J Cataract Refract Surg 2000;26:1117-22.
12. Koch DD. Refractive surgery for keratoconus: a new approach. J Cataract Refract Surg 2000;26:1099-1100.
13. Siganos D, Ferrara P, Chatzinikolas K, et al. Intrastromal corneal rings for the correction of keratoconus. J Cataract Refract Surg 2002;28:1947-51.
14. Barbara A, Shehadeh-Masha'our R, Zvi F, et al. Management of pellucid marginal degeneration with intracorneal ring segments. J Refract Surg 2005;21(3):296-8.
15. Mularoni A, Torreggiani A, di Biase A, et al. Conservative treatment of early and moderate pellucid marginal degeneration: a new refractive approach with intracorneal rings. Ophthalmology 2005;112:660-6.
16. Kymionis GD, Aslanides IM, Siganos CS, et al. Intacs for early pellucid marginal degeneration. J Cataract Refract Surg 2004;30:230-3.
17. Carrasquillo KG, Rand J, Talamo JH. Intacs for keratoconus and post-LASIK ectasia:mechanical versus femtosecond laser-assisted channel creation. Cornea 2007;26:956-62.
18. Kymionis GD, Tsiklis NS, Pallikaris AI, et al. Long-term follow-up of Intacs for post-LASIK corneal ectasia. Ophthalmology 2006;113:1909-17.
19. Sharma M, Boxer Wachler BS. Comparison of single-segment and double-segment Intacs for keratoconus and post-LASIK ectasia. Am J Ophthalmol 2006;141:891-5.
20. Pokroy R, Levinger S, Hirsh A. Single Intacs segment for post-laser in situ keratomilieusis keratectasia. J Cataract Refract Surg 2004;30:1685-95.
21. Schanzlin DJ, Abbott RL, Asbell PA, et al. Two year outcomes of intrastromal corneal ring segments for the correction of myopia. Ophthalmology 2001;108:1688-94.
22. Fink AM, Gore C, Rosen ES. Corneal changes associated with intrastromal corneal ring segments. Arch Ophthalmol 1999;117:282.
23. Quantock AJ, Assil KK, Schanzlin DJ. Electron microscopic evaluation of intrastromal corneal rings explanted from nonfunctional human eyes. J Refract Corneal Surg 1994;10:142-8.
24. Hashemi H, Ghaffari R, Mohammadi M, et al. Microbial keratitis after INTACS implantation with loose suture. J Refract Surg 2008;24:551-2.
25. Slade DS, Johnson JT, Tabin G. Acanthamoeba and fungal keratitis in a woman with a history of Intacs corneal implants. Eye Contact Lens 2008;34:185-7.
26. Shehadeh-Masha'our R, Modi N, Barbara A, et al. Keratitis after implantation of intrastromal corneal segments. J Cataract Refract Surg 2004;30:1802-4.
27. Hofling-Lima AL, Branco BC, Romano AC, et al. Corneal infections after implantation of intracorneal ring segments. Cornea 2004;23:547-9.
28. Bourcier T, Borderie V, Laroche L. Late bacterial keratitis after implantation of intrastromal corneal ring segments. J Cataract Refract Surg 2003;29:407-9.
29. Rabinowitz YS. Intacs for keratoconus. Curr Opin Ophthalmol 2007;18:279-83.
30. Ertan A, Kamburoglu G, Bahadir M. Intacs insertion with the femtosecond laser for the management of keratoconus: one year results. J Cataract Refract Surg 2006;32:2039-42.
31. Coskunseven E, Onder M, Kymionis GD, et al. Combined Intacs and posterior chamber toric implantable collamer lens implantation for keratoconic patients with extreme myopia. Am J Ophthalmol 2007;144:387-9.
32. El-Raggal TM, Abdel Fattah AA. Sequential Intacs and Verisyse phakic intraocular lens for refractive improvement in keratoconic eyes. J Cataract Refract Surg 2007;33:966-70.
33. Chan CC, Sharma M, Wachler BS. Effect of inferior segment Intacs with and without C3-R on keratoconus. J Cataract Refract Surg 2007;33:75-80.
34. Personal Communication with Kestrel Ophthalmics LTD, Addition Technology distributors, UK.

7

Intrastromal Ring Segments: Implantation by Femtosecond Laser

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Colm McAlinden

Please cite reference 15 in the text and provide reference 16

Introduction

Keratoconus is a disease of unknown etiology or pathogenesis which results in progressive bilateral thinning and protrusion of the cornea. Various genetic factors have been implicated in its causation resulting in increased protease activity and possibly aberrant interleukin-1[1] expression resulting in both collagen loss or apoptosis of keratocytes.[2]

The initial mainstay of treatment consists of spectacles and then contact lens wear—progressing from soft contact lenses to hard. Once a person has become contact lens intolerant until recently the mainstay of treatment has been to carryout a penetrating keratoplasty (PKP). This is obviously an invasive treatment with both significant risks but also one requiring intensive follow-up with attention to suture removal, astigmatism management and anti-rejection treatment.

Where there is central opacification surgical intervention either in the form of PKP or lamellar surgery is a pre-requisite to clear the visual axis and rehabilitate the eyes visual function. Where the central cornea is transparent but the patient is intolerant of contact lens wear a variety of procedures are now becoming available to modify the corneal shape or otherwise improve visual function without the need for penetrating keratoplasty.

The ever expanding treatment options include:

1. Intacs™ (Addition Technology, Inc, Fremont, California, USA) corneal reshaping
2. Intacs™ plus cross-linking
3. Phototherapeutic keratectomy plus Intacs™ where there is central corneal scarring
4. Excimer laser plus corneal collagen cross-linking (with strict selection criteria)
5. Toric phakic intraocular lens (IOL)
6. Intacs™ plus toric phakic IOL
7. Cross-linking plus toric phakic IOL
8. Lamellar keratoplasty
9. Lamellar keratoplasty plus posterior cornea repositioning.

Intacs™ treatments were first instituted by Colin in 1997 on patients with keratoconus who had a central clear cornea but were contact lens intolerant. The aim of this treatment is to modify the shape of the cornea to improve vision rather than arresting the condition. These forms of treatment may be of particular interest in those patients where more invasive forms of management are more at risk such as in highly atopic individuals and in Down syndrome patients.

The treatment consists of inserting semicircular plastic rings within the peripheral corneal stroma in order to shorten the arc length of the anterior cornea and therefore force the anterior cornea to flatten. The usual treatment consists of either placing one or two Intacs™ within the cornea. Most commonly two Intacs™ are used and the thicker segment is placed inferiorly to thicken the degenerated area of cornea in an attempt to push the cone upwards. Increasingly often groups are placing only one inferior segment. Colin reported in the literature the first year results of Intacs™ treatment to manage keratoconus in 2000[3] where they described a flattening of overall cone reduction in astigmatism. In addition most patients reported improved uncorrected and best corrected visual acuity. Although Boxer Wachler has reported improvements in overall shape and visual acuity in patients with central scarring treated with Intacs™, most other studies have demonstrated improved clinical responses in those with no central scarring and only moderate keratoconic shape change.[4-6] Insertion of Intacs™ can be carried out by mechanical dissection or by femtosecond laser dissection.

Preoperative Evaluation

It is important to carry out a full ophthalmologic examination with uncorrected visual acuity and best corrected with both glasses and contact lenses. Slit-lamp examination indicating evidence and position of corneal opacities, folds and cone position. Corneal topography will provide detailed information on cone position and cone steepness. Corneal thickness can be determined with the Pentacam or Orbscan topographer or via ultrasonic pachymetry. An evaluation of contact lens fitting and tolerance is imperative.

Insertion of the Intacs™ by Femtosecond Laser Dissection

A femtosecond is equivalent to 10^{-15} of a second. The laser works in the infrared spectrum of electromagnetic radiation at wavelength 1053 nm. Unlike the excimer laser which exerts its energy on the surface of the cornea to ablate corneal tissue, the femtosecond is focussed at an exact predefined depth within the corneal tissue. Each tissue pulse causes plasma photodisruption to the precise area of corneal tissue upon which it is focussed. The tissue affected is vaporized and produces small bubbles within the corneal stroma which expand and cause a 5-12 µm microsplit in the corneal tissue at this point. Using thousands of these focussed spots it is possible to create three dimensional shapes within the corneal stroma. The bubbles of gas are gradually removed from the tissue by the endothelial cell pump.

The major advantages of the femtosecond laser are the ability to create the track from the inside out thus reducing the postoperative chances of infection. In addition, it provides the ability to make a consistent depth track at 70-80% of corneal thickness.

PRIOR TO INTRALASE DISSECTION OF INTACS™ TRACKS

1. Preoperative pachymetry, topography and refraction
2. Mark pupil center and center Intralase on that point
3. Decide on incision site (avoid superior as increased risk of neovascularization)
4. Choose thickness of Intacs™ based upon spherical equivalent
5. Often place two Intacs™ even if only one thought to be required—easy to remove one postoperatively.

Intacs™ are made of polymethylmethacrylate and have a crescent-shaped arc length of 150 degrees with an inner diameter of 6.8 mm and an outer diameter of 8.1 mm. The thickness ranges from 0.25 to 0.45 mm.

NOMOGRAMS

Various nomograms exist:[6-8] These are related to both the diameter of the tract and size of the Intacs™. Most groups vary between using an inner diameter of 6.6 mm minimum and a maximum outer diameter of 8.2 mm. The tighter the diameter of the track, the greater the effect gained from the procedure. Complications (peripheral haze, tract deposits and displacement of the Intacs™) however, have been increasingly found with tighter tracts compared to those which are wider. Though intuitive that adjustments should be made in the thickness of the tract to suit the thickness of the individual Intacs™ used. Most studies use one standard size of tract irrespective of the size of Intacs™—this may have an effect upon the efficacy of each treatment.

CHOICE OF SIZES

Oval cones: asymmetric segments
Nipple cone: symmetric segments
Mild cone: single segment

Increasingly one large segment is often used, i.e. 0.45 mm inferiorly—this has the function to thicken the thinned area of cornea and push the cone upwards. Various groups have published the benefits in improving postoperative vision by removing the superior segment in those cases with dual segment insertion. A recent report of two cases with Intacs™ placed in a vertical position rather than a horizontal position to thicken the temporally thinned cornea and displaced cone assisted in pushing the cone nasally. This also demonstrates the flexibility and ease of positioning of the implants using the femtosecond laser.[9]

Surgical Outcomes

Colin reported the results from a 100 cases of consecutive eyes at two years. 80.5% and 68.3% showed improvement in uncorrected and best corrected visual acuity respectively. Mean spherical equivalent improved from -6.9+/- 3.9 to -3.8 +/-2.7 D at year two.[10] A recent study of 118 eyes of 69 patients by Ertan demonstrated at one year 81% improvement in UCVA and 74% improvement in BCVA with mean spherical equivalent improved from -7.6 D to -3.7 D.[11] A head to head analysis of results from the mechanical compared to the femtosecond insertion of Intacs™ demonstrated better results using the femtosecond over the mechanical method, most of these benefits did not however reach statistical significance.[12]

Complications

UNDERCORRECTION

Induced regular astigmatism in early period which usually regresses by 6 months.

Residual myopia requiring CL fitting or possibly amenable to phakic IOL.

Surface laser ablation with or without cross-linking is a possible adjunctive therapy to those not tolerant of CL wear.

OVERCORRECTION

It is possible to induce astigmatism by a large superior segment causing over flattening to the superior segment. The easiest way to address this is to remove the superior segment.

NEOVASCULARIZATION

Limbal neovascularization is common in cases of chronic contact lens wear, this is often more apparent in the superior cornea **(Figure 7-1)**. It is best to avoid this region for insertion of the Intacs™ to avoid inducing inflammation in this point and possible subsequent neovascularization.

MIGRATION OF AN INTACS™ SEGMENT

Intacs™ can move particularly in the early period after insertion. It is important to ensure that the segment is moved adequately from the insertion site to prevent pouting of the wound and possible extrusion or induced inflammation.

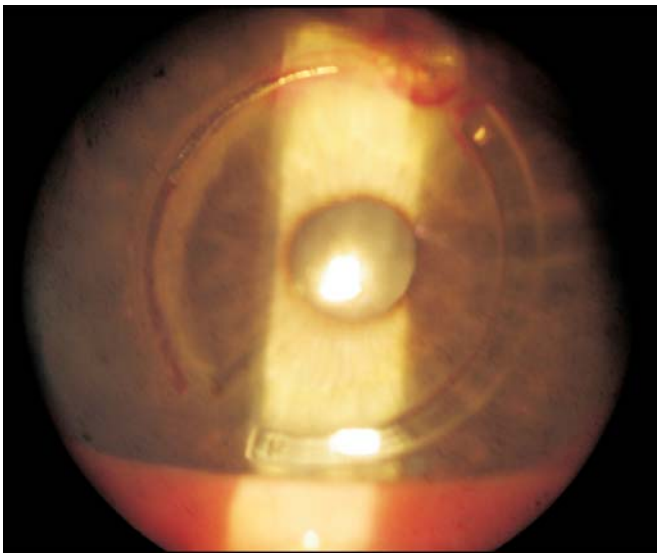

FIGURE 7-1: Neovascularization in an Intacs channel.

EXTRUSION

This can occur even many years after surgery, in a progressive condition such as keratoconus this is a more likely event. Infection can also result in extrusion and removal of the Intacs™ is advocated in most cases as part of the therapeutic intervention.[13]

OTHER COMPLICATIONS

A range of other less important complications can occur such as the development of deposits and epithelial plugs within and haze around the tunnels—these complications were found to be more common in where the channel was narrower with tighter fitting segments.[6, 11, 14, 15]

Predictability

The procedure is not as yet very predictable with similar treatments producing quite a varied range of results between patients. This may be related to both variation in each individual pathological eye and also implantation techniques and position. As the femtosecond laser tracks are highly reproducible variation is probably more related to the differences between each pathological eye.

Stability

Postoperatively there is often induced regular astigmatism caused by the implanted Intacs™ which gradually settles over the first 6 months. After 6 months, stability appears good however it is as yet unknown how keratoconus progression is affected in the long-term **(Figures 7-2A to C)**.

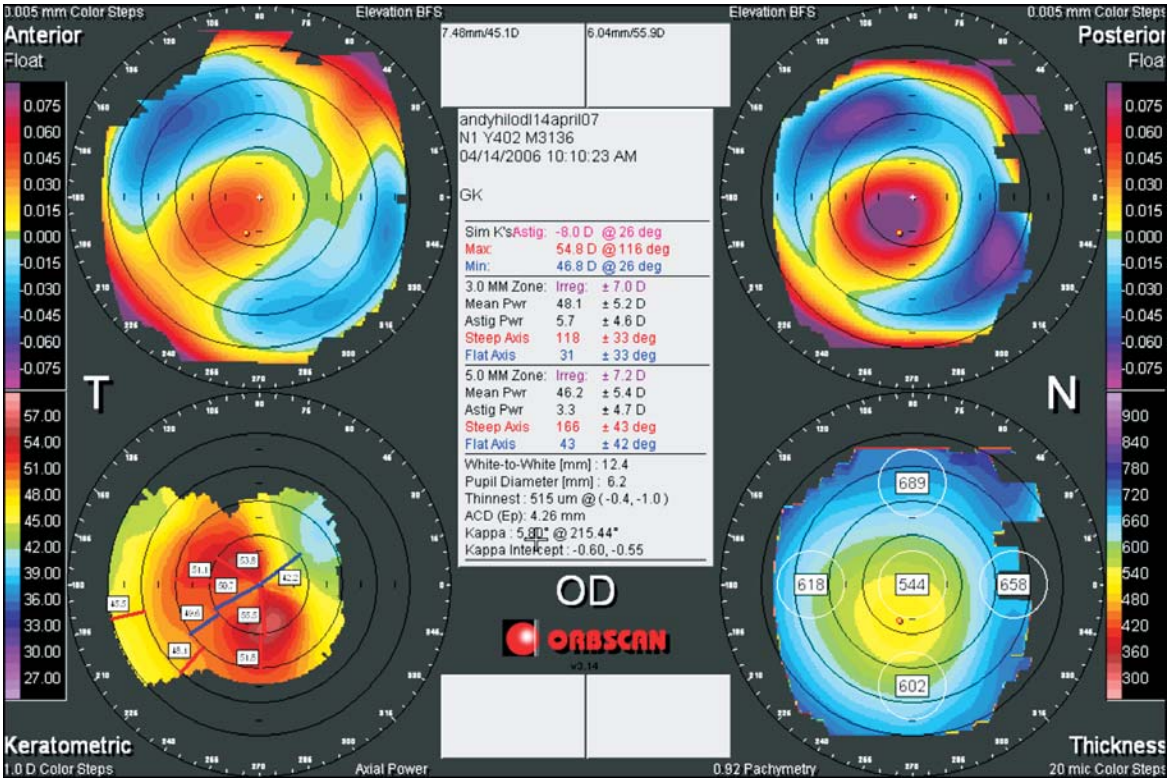

FIGURE 7-2A: Preoperative.

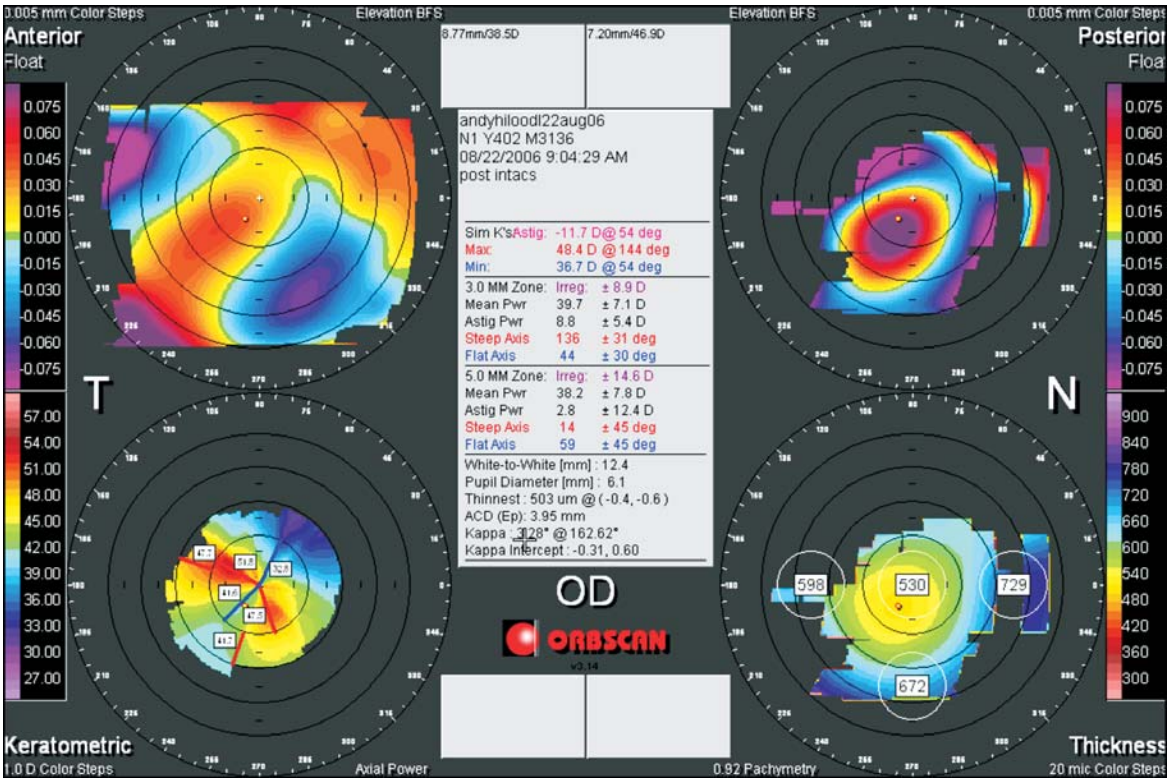

FIGURE 7-2B: 2 weeks post-Intacs™.

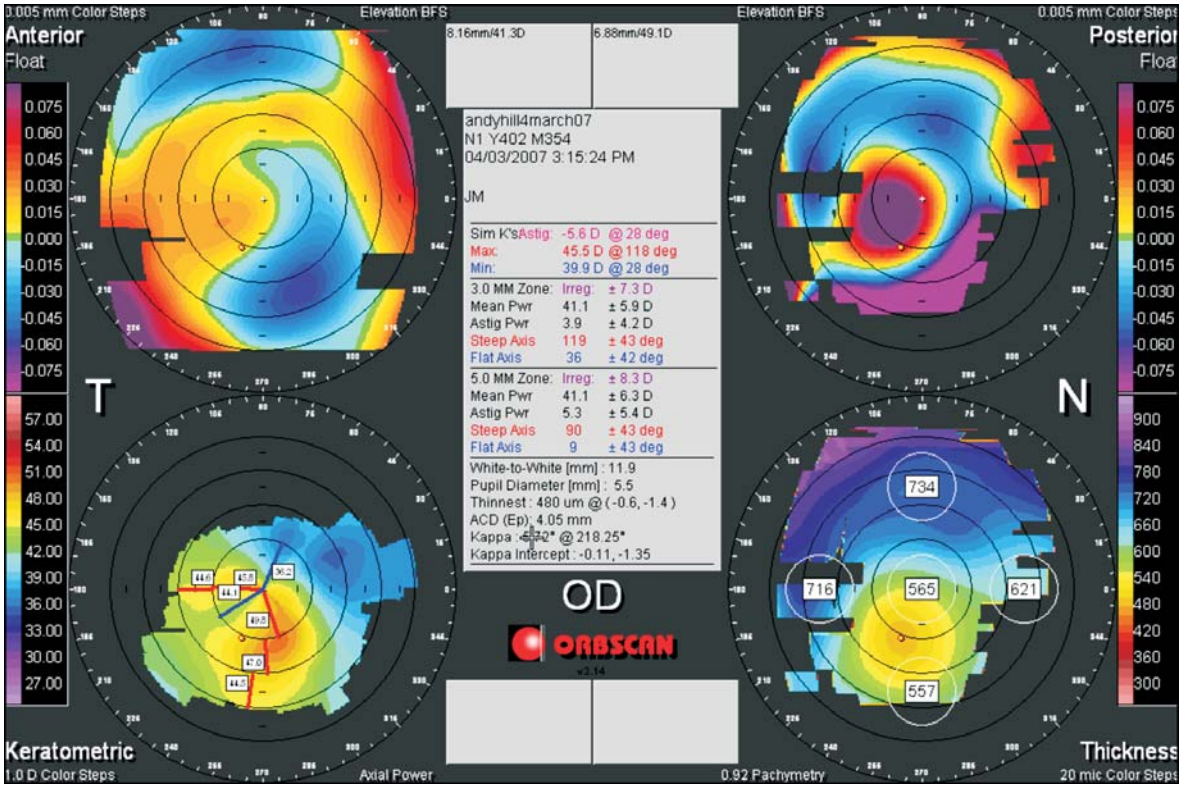

FIGURE 7-2C: 6 months post Intacs™.

FIGURES 7-2A TO C: The three sets of Orbscan measurements above demonstrate the improvement in corneal topography possible through Intacs™ treatment. The initial change in corneal shape is most marked at two weeks, with almost 9 diopters present of with the rule astigmatism. This astigmatism reduces and stabilises over a 6 month period to 5 diopters of with-the-rule astigmatism.

References

1. Zhou L, Yue BY, Twining SS, Sugar J, Feder RS. Expression of wound healing and stress-related proteins in keratoconus corneas. Curr Eye Res 1996;15:1124-31.
2. Saghizadeh M, Chwa M, Aoki A, Lin B, Pirouzmanesh A, Brown DJ, Ljubimov AV, Kenney MC.Altered expression of growth factors and cytokines in keratoconus, bullous keratopathy and diabetic human corneas. Exp Eye Res 2001;73:179-89.
3. Colin J, Cochener B, Savary G, Malet F. Correcting keratoconus with intracorneal rings. J Cataract Refract Surg 2000; 26:1117-22.
4. Boxer Wachler BS, Christie JP, Chandra NS, Chou B, Korn T, Nepomuceno R. Intacs for keratoconus. Ophthalmology 2003;110:1031-40.
5. Alió J, Shabayek M, Belda J, Correas P, Feijoo E. Analysis of results related to good and bad outcomes of Intacs implantation for keratoconus correction. J Cataract Refract Surg 2006; 32:756-61.
6. Kanellopoulos AJ, Pe LH, Perry HD, Donnenfeld ED. Modified intracorneal ring segment implantations (INTACS) for the management of moderate to advanced keratoconus: efficacy and complications. Cornea 2006; 25: 29–33.
7. Alió JL, Artola A, Hassanein A, Haroun H, Galal A. One or 2 Intacs segments for the correction of keratoconus. J Cataract Refract Surg 2005;31:943-53.
8. Colin J, Cochener B, Savary G, Malet F, Holmes-Higgin D.INTACS inserts for treating keratoconus: one-year results. Ophthalmology 2001;108(8):1409-14.
9. Ertan A, Bahadir M. Topography-guided vertical implantation of INTACS using a femtosecond laser for the treatment of keratoconus. J Cataract Refract Surg 2007;33: 148-51.
10. Colin J, Malet FJ. Intacs for the correction of keratoconus: two-year follow-up. J Cataract Refract Surg 2007; 33: 69–74.

11. Ertan A, Kamburoðlu G, Akgün U. Comparison of outcomes of 2 channel sizes for intrastromal ring segment implantation with a femtosecond laser in eyes with keratoconus. J Cataract Refract Surg 2007; 33:648-53.
12. Rabinowitz YS, Li X, Ignacio TS, Maguen EJ. INTACS inserts using the femtosecond laser compared to the mechanical spreader in the treatment of keratoconus. J Refract Surg 2006;22:764-71.
13. Hashemi H, Ghaffari R, Mohammadi M, Moghimi S, Miraftaab M. Microbial keratitis after INTACS implantation with loose suture. J Refract Surg 2008;24:551-2.
14. Rodriguez-Prats J, Galal A, Garcia-Lledo M, De La Hoz F, Alió JL. Intracorneal rings for correction of pellucid marginal degeneration. J Cataract Refract Surg 2003; 29:1421-4.
15. Barbara A, Shehadeh-Masha'our R, Zvi F, Garzozi HJ. Management of pellucid marginal degeneration with intracorneal ring segments. J Refract Surg 2005; 21:296-8.

8

Toric Phakic Intraocular Lenses for the Correction of Refractive Errors in Keratoconus

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Merce Morral
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Introduction

Keratoconus is a non-inflammatory corneal disease that develops progressive thinning and anterior bulging of the cornea. Corneal ectasia frequently induces varied degrees of myopia and/or astigmatism.[1] In early stages, spectacles and contact lenses are the treatment of choice.[2-4] However, a considerable amount of patients with progressive keratoconus have not only reduced visual acuity with spectacles due to irregular astigmatism,[5,6] but also reduced tolerance to contact lenses.[7-10]

Before the advent of modern refractive surgery techniques, penetrating keratoplasty (PKP) or deep anterior lamellar keratoplasty (DALK) were the treatment of choice when a patient with keratoconus became contact lens intolerant or had poor best-spectacle corrected visual acuity (BSCVA). This is still true in advanced stages of the disease, where severe thinning and/or corneal scarring occurs. Because refractive anisometropia and high postoperative astigmatism are common problems after penetrating keratoplasty (PKP), visual rehabilitation and return to binocular function may be slow.[11-15] Moreover, complications related to corneal transplant surgery itself, such as endophthalmitis or rejection episodes, should also be taken into account.[16-21] Therefore, in early stages of keratoconus, when the central cornea remains clear, other options should be considered to avoid or delay keratoplasty.

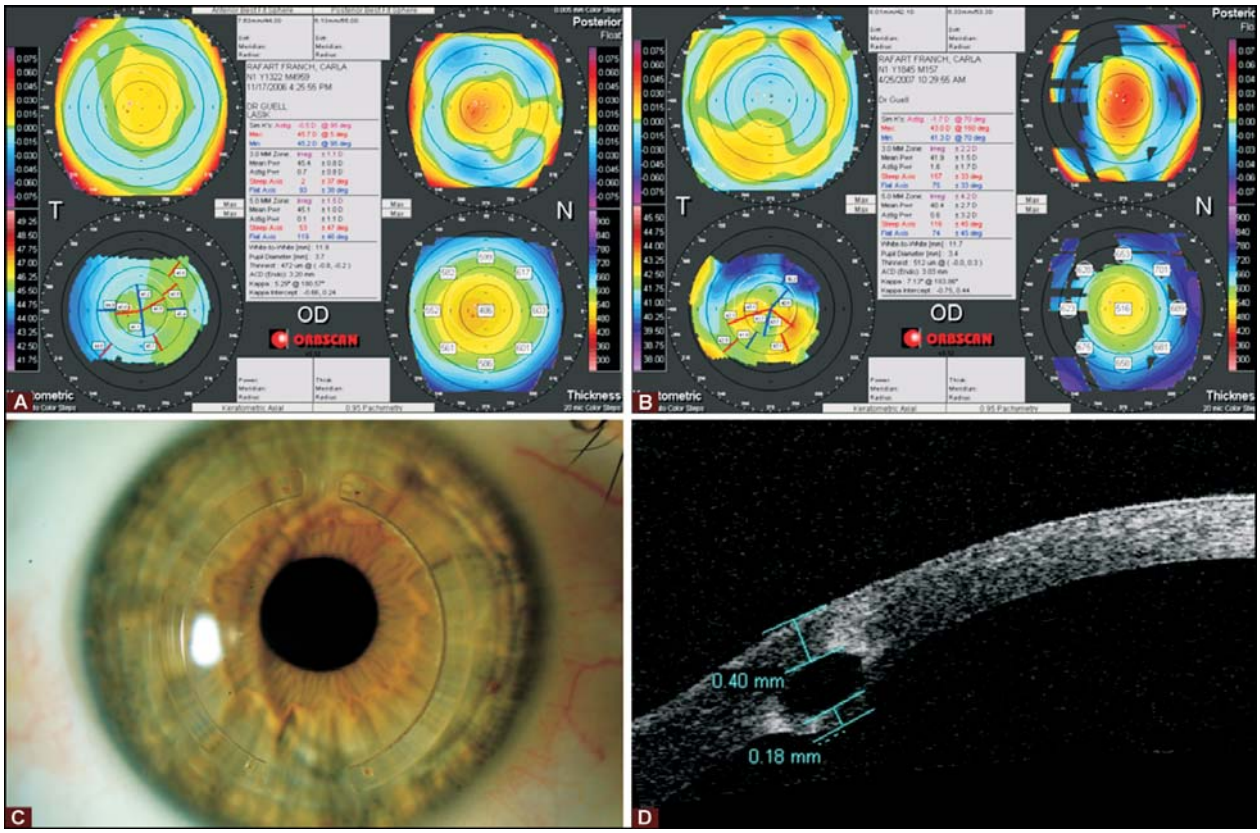
With the exception of some anecdotal reports, corneal incisional (radial keratotomy, or arquate keratotomy) and ablational refractive approaches such as PRK or LASIK are contraindicated in keratoconus, as they increase the risk of progressive, irreversible corneal ectasia.[22-25] Available refractive procedures include intrastromal corneal ring segments, and toric phakic intraocular lenses (TPIOLs). The main goal of these procedures is to provide enough BSCVA, and sometimes uncorrected visual acuity (UCVA), to postpone the need for a corneal transplantation.

Intracorneal rings provide structural reinforcement of the cornea, and reshape and center cornea's optical zone, improving topographic abnormalities (irregular astigmatism), quality of vision, and visual acuity **(Figure 8.1)**.[26-29] Intracorneal rings act as spacing elements that shorten the arc of length of the anterior corneal surface and flatten the central cornea, which reduce myopic spherical equivalent.[30-32] However, they only correct a limited range of myopia, and high refractive errors may remain. Residual refractive errors may be corrected with spectacles or soft contact lenses.[33] TPIOLs have also been implanted after ICRS.[34-36]

PIOLs have been used to correct moderate and high myopia, hyperopia and /or astigmatism. There are also a few reports on their use in patients with keratoconus.[37-39] The implantation of PIOLs has been reported to be a stable, predictable and safe refractive procedure.[40-50] This chapter deals with the use of TPIOLs for the correction of spherical errors (usually myopia) and astigmatism in patients with keratoconus.

Indications

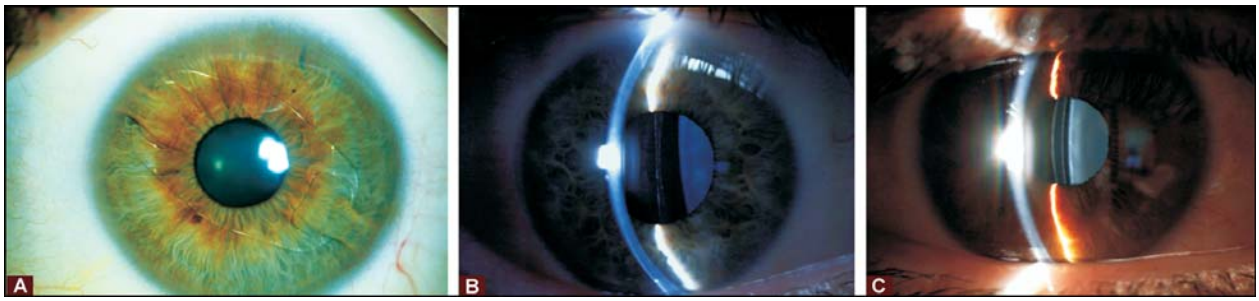
Recommended inclusion and exclusion criteria are summarized in **Table 8-1**. Being sure that keratoconus is stable is not an easy issue. Keratoconus is a progressive disease that starts around puberty, generally progresses slowly during early years, and usually stabilizes in the third and fourth decade of life.[1] However, it may move at any moment throughout life.[51] It has been generally accepted that a patient older than 25 years old who shows stability on keratometry and refraction for more than six months can be considered for PIOL implantation.[39] Moreover, if refraction changes in the future, PIOL might be exchanged for another one.



FIGURES 8-1A TO D: Patient seeking for refractive surgery that is diagnosed of keratoconus suspect. Preoperative BSCVA was 20/25 with -3.50 D. Ablational procedures are contraindicated and we decide to implant intrastromal corneal ring segments (ICRS) (Intacs, Contact Addition Technology, CA). (A) Preoperative Orbscan topography showing an increased posterior surface elevation, and a thin cornea. (B) Postoperative Orbscan topography showing the effect of flattening of the anterior surface of the cornea, thus decreasing the refractive power of the cornea. (C) Clinical photograph of the ICRS. UCVA was 20/25 and BSCVA was 20/27 with 85° -0.75 -0.25. (D) Anterior segment OCT image of the ICRS between the stromal collagen fibers of the cornea. Intacs should be implanted at 70% of the mid-periphery depth of the cornea.

TABLE 8-1: Generally recommended inclusion and exclusion criteria for implantation of phakic intraocular lenses

Inclusion criteria	Exclusion criteria
• Age > 21 years • BSCVA > 20/60[39] or 20/80 • Stability of refraction at least 1 year • Unsatisfactory vision with/intolerance of contact lenses or spectacles • Clear cornea • Irido-corneal angle ≥ 30° • cECC > 2300 cells/mm^2: (> 2500 cells/mm^2 if >21 years old, > 2000 if >40 years old) • No anomaly of the iris or pupil function • Scotopic pupil size < 5-6 mm • Toric PIOL if astigmatism > 2 D	• Background of active disease in the anterior segment • Recurrent or chronic uveitis • Any form of clinically significant cataract • Previous corneal or intraocular surgery (to be evaluated) • IOP > 21 mmHg or glaucoma • Preexisting macular degeneration or macular pathology • Abnormal retinal condition • Systemic diseases (e.g., autoimmune disorder, connective tissue disease, atopia, diabetes mellitus)



FIGURES 8-2A TO C: (A) Toric phakic Artisan/Verisyse phakic IOL implanted at 140°. (B) Slightly insufficient vaulting (< 250 µm) probably due to a too short ICL. (C) Excessive vaulting (> 750 µm) due to a too long ICL. However, both lenses are in the "safe" range of 90 µm to 1000 µm.

Some authors have proposed UV-A irradiation-induced corneal collagen cross-linking (CCL) as a first step to stop the progression of keratoconus.[52-56] Also, although the role of ICRS in stopping the progression of keratoconus is still controversial, some authors have implanted first the rings and then the TPIOL with a similar goal.

High astigmatism is frequently found in patients with keratoconus. Generally, if astigmatism is > 2 D a toric PIOL is recommended. Currently, there are two toric PIOLs available in the market: the anterior chamber iris-claw Artisan® (Ophtec B.V., Groningen, The Netherlands) – Verisyse® (AMO, Santa Ana, CA) toric PIOL **(Figure 8-2A)**, and the posterior chamber toric Implantable Contact Lens (ICL, STAAR Surgical AG, Monrovia, CA). The toric Artiflex (Ophtec, Groningen, The Netherlands) has undergone phase III clinical trials and will be available for use in the next few months. Iris-claw PIOLs' fixation system allows for unique rotational stability, and are our lenses of choice for the correction of astigmatism. Moreover, the "one-size-fits-all" overall diameter of 8.5 mm prevents complications due to sizing errors that may occur with angle-supported or sulcus-supported PIOLs. **Table 8-2** summarizes available powers of TPIOLs.

TABLE 8-2: Available powers of toric phakic intraocular lenses FDA approved and/or with CE mark

	Trademark	FDA/CE	Material	Power (D)	OD (mm)	TD (mm)
AC 'iris-claw'	**Verisyse/ Artisan**	+/+	PMMA	Sphere +12 to -23.5, Cyl +1 to +7	5	8.5
	Veriflex/ Artiflex	-/+	PMMA haptics Polysiloxane optic	Myopia – 2 to – 14.5 Cyl up to 5 D	6	8.5
PC	**ICL**	+/+	Collamer	Myopia – 3 to – 23.0, Cyl +1 to +6	4.65 to 5.5	11.5 to 13.0

OD = optic diameter; TD = total diameter; AC = anterior chamber; PC = posterior chamber; ICL = Implantable Collamer Lens; D = Diopters; Cyl = cylinder

LENS POWER CALCULATION AND CHOOSING THE DIAMETER OF THE LENS

TPIOL power calculations may be difficult in those cases that, due to the high refractive error and corneal irregularities, show low repeatability between preoperative keratometric and objective refraction measurements.[39,57] Moreover, if any refractive error remains after PIOL implantation, no further enhancement by excimer laser is possible. Thus, keratoconic patients need to be informed that, in case residual ametropia exists after PIOL surgery, spectacles might be needed postoperatively to perform some activities such as night driving.

For iris-claw PIOLs' power calculation, the Van der Heijde formula[58,59] is used, and includes patient's refraction, keratometry and adjusted ultrasound anterior chamber depth (ACD). Based on this formula, the manufacturers provide nomograms or software to calculate the PIOL required power. The iris-claw PIOL has an overall diameter of 8.5 mm.

For the calculation of the ICL power, the majority of users employ the formula proposed by Feingold and Olsen,[60,61] which uses patient's refraction from the 12 mm spectacle plane or the vertex refraction, keratometry, and adjusted ultrasound central ACD. Based on this formula, the manufacturers provide nomograms or softwares to calculate the PIOL required power at the ciliary sulcus plane.

The ICL's overall diameter depends on the ciliary sulcus diameter and the ACD, and should provide perfect stability with no excess of compression forces to the sulcus, and allow for a correct 'vaulting' **(Figures 8-2B and C)**. The 'vault' is the distance between the posterior surface of the ICL and the anterior surface of the cristaline lens, and should be > 100 µm and < 900 µm. An excessive vaulting (> 1000 µm) due to a too long ICL may cause angle-closure, pupil block glaucoma, or pigment dispersion glaucoma. On the other hand, insufficient vaulting (< 90-100 µm) due to a too short ICL increases the risk of cataractogenesis due to the contact between the posterior surface of the ICL and the anterior surface of the crystalline lens.[62-68] Before the development of ultrasound biomicroscopy (UBM) no system was available to determine the internal diameter of the ciliary sulcus. This evaluation was approximate and based on a white-to-white (WTW) measurement. ICL's diameter is oversized 0.5 mm from the WTW measurement in myopic eyes, and same-length in hyperopic eyes. However, recent studies demonstrate that there is no anatomical correspondence between external measurements and internal dimensions.[69-72] Therefore, WTW distance alone may not predict either angle or sulcus size, causing some of the problems observed with anterior chamber angle-supported or posterior chamber PIOLs.

Step-by-Step Surgical Technique

PMMA IRIS-CLAW TPIOLS

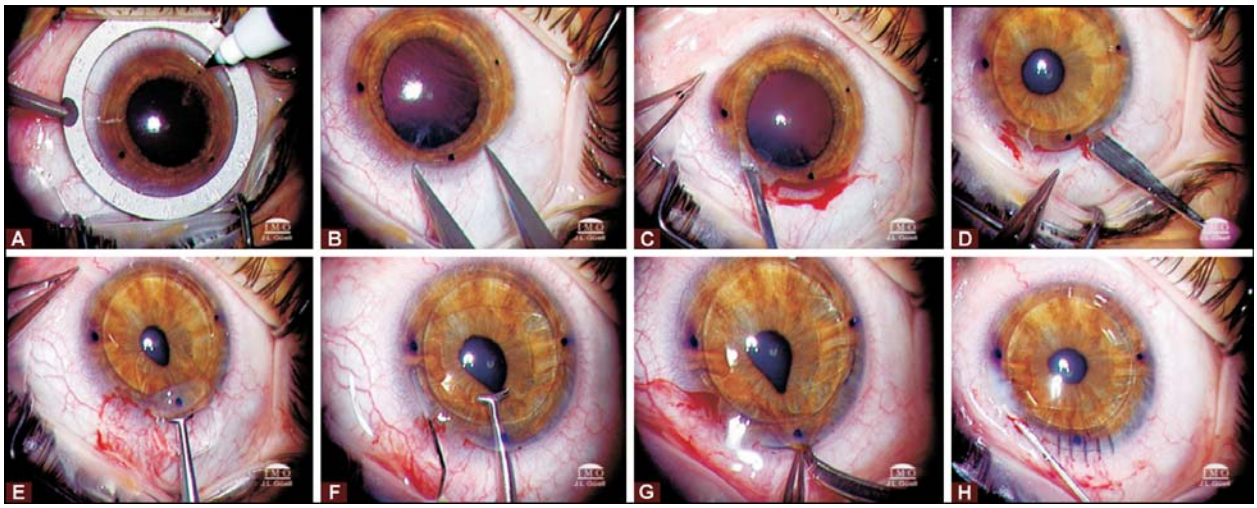
For the Artisan®-Verisyse® PIOL implantation procedure retrobulbar or peribulbar anesthesia is generally recommended, even though some surgeons prefer topical or general anesthesia. Toric Artisan®-Verisyse® implantation requires careful preoperative marcation of the axis of implantation. Marcation of the axis should be performed preoperatively at the slit lamp, with an ophthalmometer, or in the Argon laser, to avoid implantation errors due to cyclotorsion and/or position changes induced by the retro or peribulbar anesthesia injection. There are two models of Toric Artisan®-Verisyse®: one with the torus at 0°, and the other with the torus at 90°, so the implantation is always performed close to the horizontal or vertical axis, depending on surgeon's preference.

According to our recommended technique, a two-plane, 5.2 mm posterior corneal incision is centered 90° apart the axis of enclavation. Alternatively, a scleral incision may be used. Wound construction is important to minimize induced astigmatism or wound leaks. Two paracenteses are constructed directed vertically towards the area of enclavation. The pupil should be constricted so as to protect the crystalline lens from the contact with the PIOL or surgical instruments during the surgery. This can be achieved either instilling 1% pilocarpine preoperatively or injecting acetilcholine (Myochol, Ciba Vision) in the anterior chamber at the beginning of the procedure.

The center of the pupil should be marked so as to enable proper centration of the optic of the PIOL over the pupil. Pupil's marcation should be done before instilling 1% pilocarpine or injecting

acetilcholine in the anterior chamber, as pupil's decentration after pharmacologically induced myosis is not uncommon. After the anterior chamber is filled with a cohesive viscoelastic material, the lens is introduced and rotated 90 degrees up to the axis of enclavation. The TPIOL is fixed with an enclavation needle that pushes the iris into both claws. The needle is introduced through one of the paracentesis and holds the fold of iris while the lens is slightly depressed with the implantation forceps so that the claws will automatically grasp the iris. Then, hands are switched and the same maneuver is performed through the other paracentesis. Both the fixation of the iris claws and the proper centration and orientation of the PIOL over the pupil should be checked before the next step, which is one of the main advantages of this PIOL style. It is not unusual to have a mild ovalization of the pupil because of the effect of the miotic. If the lens is not well centered or oriented, the lens enclavation can be released by pushing in the central portion of the claw with the enclavation needle, reversing the previous steps.

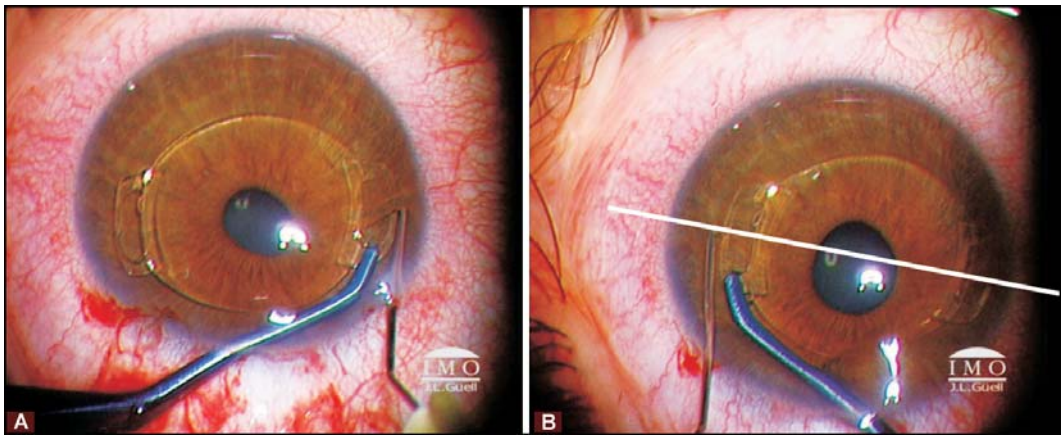
A peripheral iridectomy should always be performed to prevent pupillary block. Alternatively, Nd:YAG laser can be used preoperatively to create two small iridotomies 90° apart. The wound is then sutured with five interrupted 10-0 nylon stitches. The proper tension of the sutures may be checked with our standard qualitative Maloney keratoscope, or a quantitative projection keratometer installed at the operating microscope **(Figure 8-3)**. Beginning at week 4, and over a period of 3 months, sutures are selectively removed, depending on the patient's refractive and topographic astigmatism.



FIGURES 8-3A TO H: Toric Verisyse phakic IOL implantation (A) Preoperative marcation of the axis of implantation. (B) Surgical caliper measuring 5.2 mm incision. (C) Two vertical paracentesis directed towards the site of enclavation are performed. (D) A two-plane, 5.2 mm posterior corneal incision is centered 90° apart the axis of implantation. (E) Pupil constriction is achieved by injecting acetylcholine (Myochol, Ciba Vision) in the anterior chamber. The anterior chamber is filled with a cohesive viscoelastic material, the lens is introduced by means of a special forceps and rotated 90 degrees into a horizontal position. (F) Enclavation process. The enclavation needle is introduced through one of the paracentesis and holds the fold of iris and the claws automatically grasp the iris. (G) A peripheral iridectomy using scissors is performed to prevent pupil block. (H) The wound is then sutured with five interrupted 10-0 nylon stitches.

FOLDABLE IRIS-CLAW TPIOLS

Artiflex® TPIOL implantation may be performed under retrobulbar or topical anesthesia. As in all TPIOLs, Toric Artiflex® implantation requires careful preoperative marcation of the axis of implantation. A 3.1 mm incision is required, which corresponds to the width of the PMMA haptics



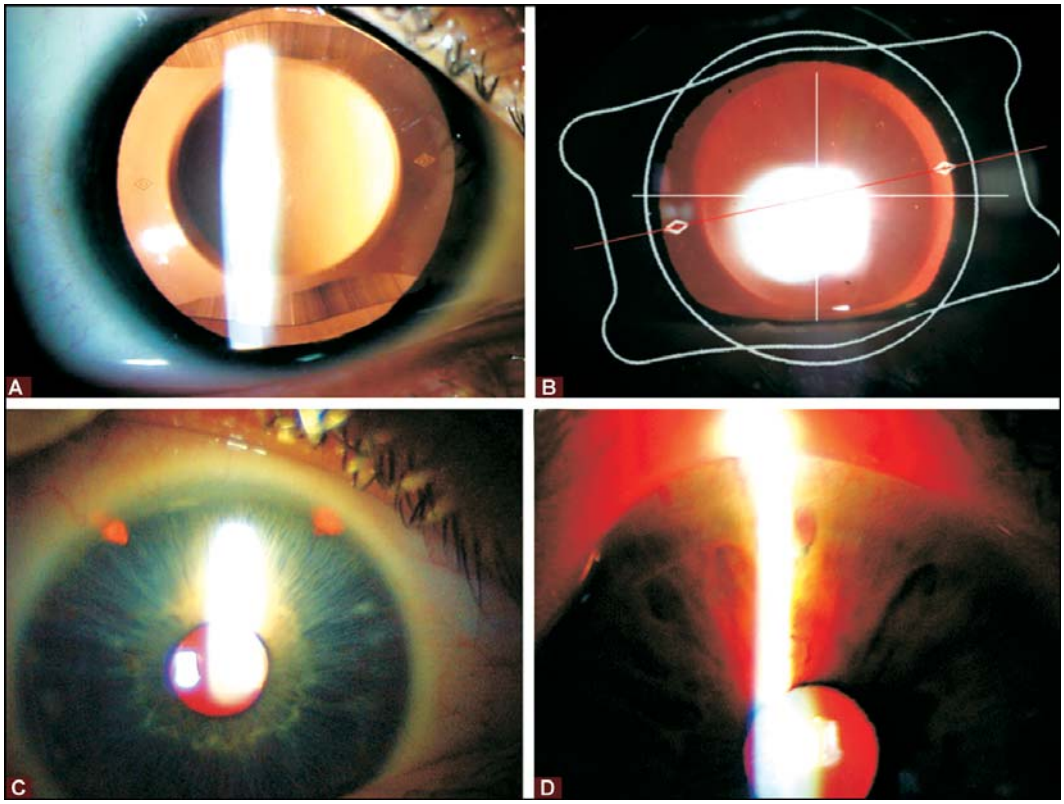
FIGURES 8-4A AND B: Enclavation process of the Artiflex/Veriflex phakic IOL. (A) The enclavation needle is introduced through one of the paracentesis and holds the fold of iris while the lens is grasped with the implantation forceps by the base of the haptic. (B) Hands are switched and the same maneuver is repeated to enclavate the other claw. The white line shows the axis of enclavation.

(3.0 mm). The incision is placed 90° apart the site of enclavation, and two vertical paracenteses are directed towards the area of enclavation. The Artiflex® lens is inserted using a specially designed spatula, and the process of enclavation is the same as for the PMMA lens. The only difference is that the lens is grasped with the implantation forceps by the base of the haptic instead of by the edge of the optic. Iridectomy should also be performed. The incision is usually water-tight, but we prefer to suture it with a 10/0 Nylon suture **(Figure 8-4)**.

IMPLANTABLE COLLAMER LENS

The correct loading of the ICL in the cartridge and the injector is essential for a correct and easy implantation. Using a modified McPherson forceps, or Aus der Ar coaxial forceps, with long, blunt, curved tips, the lens is carefully grasped and checked under the operating microscope. The ICL has two tiny holes on the footplates (distal-right and proximal-left) that allow correct anterior-posterior orientation of the lens. The cartridge is filled with viscoelastic material. The lens is loaded with the dome up, taking special care in correctly position the haptics so as not to rupture them during the injection. A piece of soft material, the Staar Foam-tip, is positioned to protect the ICL from contact with the plunger of the shooter. Additionally, some surgeons recommend inserting the tip of a wet surgical microsponge between the foam-tip and the ICL to further protect the optic and the haptics.

As with the other TPIOLs, Toric ICL implantation requires careful preoperative marcation of the axis of implantation **(Figure 8-5)**. Broad pharmacological mydriasis is essential for implantation. For Toric ICL's, a temporal sub-3.00 mm incision is preferred. One side-port incision of about 1 mm and separated 90° from the main incision is created. Some surgeons prefer two paracentesis to enable easier implantation of the haptics in the sulcus. The anterior chamber is filled with a cohesive, low-viscosity viscoelastic to protect the endothelium and the crystalline lens from surgical trauma, and to create enough space in the anterior chamber for surgical manipulation. The cartridge is inserted bevel-down, and the lens is then carefully injected. It is essential to control the unfolding of the lens, so as to twist the bevel right or left to assure the correct orientation of the lens. Finally, the haptics are gently pushed under the iris with a blunt spatula. When the correct centration of the ICL and the position of the haptics in the ciliary sulcus is checked, acetylcholine is injected in the anterior chamber



FIGURES 8-5A TO D: (A) The Toric ICL has two orientation marks that have to fit with the selected axis of implantation. (B) Clinical photograph of the toric ICL phakic IOL implanted at 15°. (C) Clinical photograph of the toric ICL phakic IOL. Notice the two superior Nd:YAG laser iridotomies 90° apart, to prevent pupillary block. (D) In this case, a superior iridectomy was surgically performed.

to constrict the pupil. Complete extraction of the viscoelastic, as in any intraocular surgery, is mandatory to avoid postoperative ocular hypertension **(Figure 8-6)**. A peripheral iridectomy should be performed to prevent pupil block, either with scissors or with a vitrector.[73] Alternatively, two Nd:YAG laser iridotomies are performed in the peripheral iris one week preoperatively (single burst, 3-10 mJ). These generally measure 250 to 500 µm and are located superiorly, 90° apart, thus being covered by the upper eyelid **(Figure 8-5)**. Finally, the incision is hydrated. Zaldivar, *et al* described the use of an argon-green laser prior to applying the Nd:YAG spots, in order to decrease iris bleeding and pigment deposition on the phakic IOL (50- µm spot size, 650 to 1000 mW power, 0.2-0.5 second duration).[74]

Results

Five-year follow-up data of implantation of Verysise™ TPIOLs in 30 eyes of 17 patients with moderate to high astigmatism who presented corneal topography (Orbscan topographer, Bausch and Lomb. Rochester, NY, USA) compatible with keratoconus or forme fruste keratoconus are reported herein. All patients were fully informed about the details and possible risks of the specific procedure, alternative refractive options and their respective benefits and risks. Written informed consent was

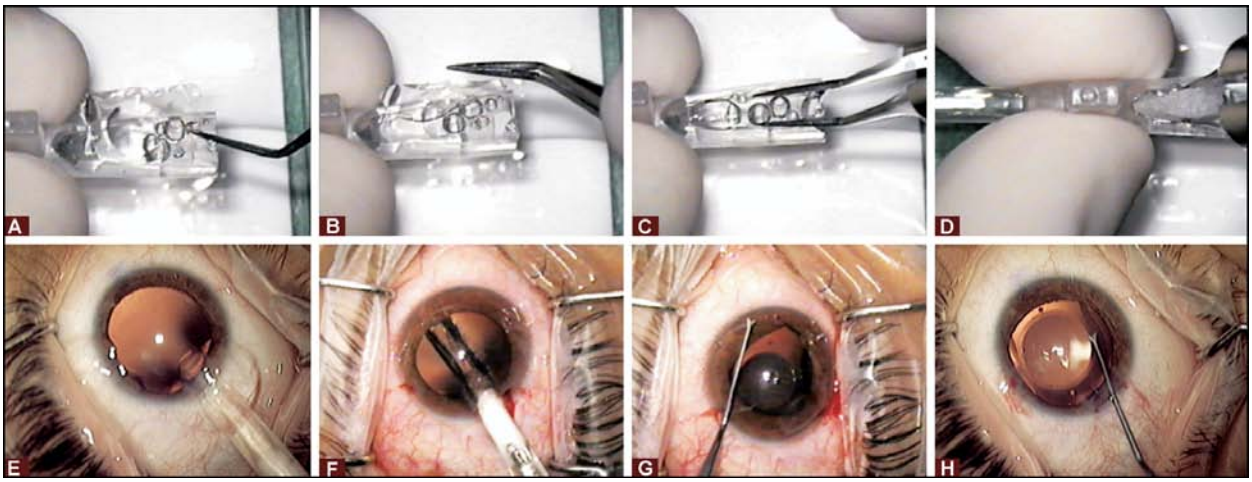


FIGURE 8-6: Implantation of the ICL. (A-D) Loading of the ICL in the cartridge. (A) Using a modified McPherson forceps, the lens is checked under the operating microscope. The two tiny holes on the footplates must be oriented distal-right and proximal-left. (B and C) The lens is loaded with the dome up. (D) A piece of soft material, the Staar Foam-tip, is positioned to protect the ICL from contact with the plunger of the shooter. (E) Broad pharmacological mydriasis is essential for implantation. The anterior chamber is filled with a cohesive viscoelastic, and the cartridge is inserted bevel-down. (F) The lens is carefully injected. (G and H) The haptics are gently pushed under the iris with a blunt spatula.

obtained from all patients before surgery in accordance with the tenets of the Declaration of Helsinki. All eyes were operated by the same surgeon (JLG). No intraoperative complications were encountered. **Table 8-3** shows baseline characteristics of this group of 30 keratoconic eyes.

REFRACTIVE OUTCOME

Mean (± standard deviation) spherical equivalent (SE) and cylinder before TPIOL surgery were -7.29 ± 7.82 D and -3.36 ± 1.02 D, respectively. After 5 years, they were -0.11 ± 0.22 D and -0.38 ± 0.42 D, respectively **(Figure 8-7)**. **Table 8-3** summarizes refractive data at baseline and at 5 years after surgery. Mean ± SD (*p* value resulting from Wilcoxon signed rank tests) are reported. Although keratoconus may be a progressive corneal ectasia and, as a result, refraction may change over time, SE and cylinder remained stable over the 5 years of follow-up in our group of keratoconic eyes (Wilcoxon signed rank tests; p>0.05). All the eyes were within 1 D of intended spherical equivalent, and 27 eyes (90%) were within 0.5 D of intended spherical equivalent.

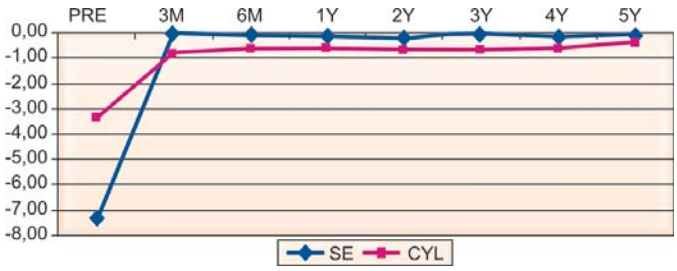


FIGURE 8-7: Stability of spherical equivalent and cylinder after TPIOL implantation throughout the 5-year follow-up period.

TABLE 8-3: Baseline characteristics and 5 years fter implantation of the toric Artisan-Verisyse PIOL.		
	Preop	**5 years postop**
Mean ± SD SE (D) (range)	-7.29 ± 7.82 (+9.5 to -22)	-0.11 ± 0.22 (+0.2 to -0.5)
Mean ± SD cylinder (D) (range)	-3.36 ± 1.02 (-1.25 to -6.0)	-0.38 ± 0.42 (0 to -1)
Mean UCVA (range)	< 20/400	20/27 (20/60 to 20/20)
Mean BSCVA (range)	20/30 (20/100 to 20/22)	20/25 (20/60 to 20/20)
Mean ± SD cECC (range) (cells/mm²)	2822 ± 393.33 (2071 to 3576)	2320 ± 299.34 (1962 to 2705)

SD = standard deviation; SE = Spherical equivalent; D = diopters; BSCVA= best spectacle-corrected visual acuity; cECC = central endotelial cell count.

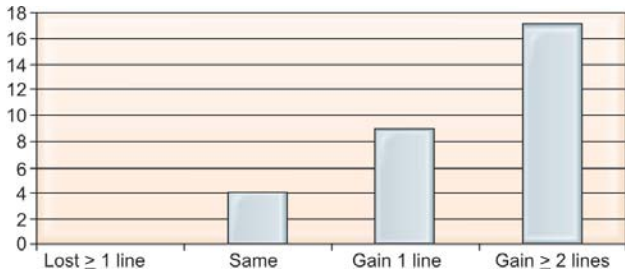


FIGURE 8-8: Number of eyes that gained or lost lines of best-spectacle corrected visual acuity.

VISUAL ACUITY, EFFICACY INDEX AND SAFETY INDEX

Table 8-3 summarizes mean UCVA and BSCVA at baseline and at 5 years after surgery. None of the eyes lost any line of BSCVA, and 26/30 (86.67%) gained at least one line of BSCVA **(Figure 8-8)**. Efficacy index (ratio between the mean postoperative UCVA and the mean preoperative BSCVA) was 1.17 and safety index (ratio between the mean postoperative BSCVA and the mean preoperative BSCVA) was 1.08.

ENDOTHELIAL CELL COUNTS

Endothelial cell count decreased from 2822 ± 393.33 cells/mm² to 2320 ± 299.34 cell/mm², which means a decrease of 8 ± 17% **(Figure 8-9)**. This decrease was statistically significant at each milestone of the follow up when compared to baseline (Wilcoxon signed rank tests; $p<0.05$), but showed no statistically significance when compared to the previous time point (Wilcoxon signed rank tests; $p>0.05$). **Table 8-4** shows preoperative cECC and at each interval of follow-up.

Discussion and Conclusions

This series of eyes shows that implantation of toric Artisan-Verisyse toric PIOLs is an effective and safe procedure for the correction of astigmatism in patients with keratoconic corneas. Although

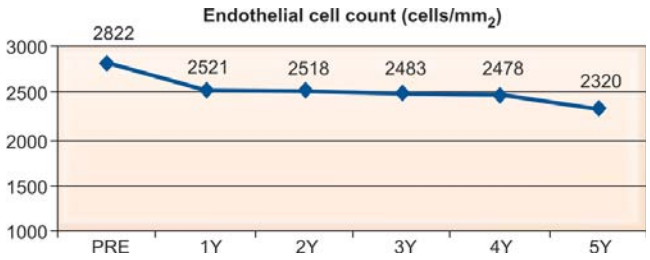


FIGURE 8-9: Endothelial cell count showed 8% decrease at 5 years.

TABLE 8-4: Preoperative and postoperative central endothelial cell count (cECC)

	Central endotelial cell count (cells/mm²) Mean ± Standard deviation
Preoperatively	2822 ± 393
1 year	2521 ± 390
2 years	2518 ± 337
3 years	2483 ± 573
4 years	2478 ± 354
5 years	2320 ± 299

keratoconus may be a progressive corneal ectasia and, as a result, refraction may change over time, SE and cylinder remained stable over the 5 years of follow-up in our group of keratoconic eyes. This may be explained by the fact that we usually perform this surgery in mild to moderate forms of KC, and once we have confirmed that the refraction is stable.

Most of our patients were seeking for refractive surgery, and the corneal abnormality was diagnosed when performing the Orbscan topography, which is part of the standard preoperative work-up. The rest were patients previously diagnosed of KC who were not satisfied with the visual acuity and optical quality achieved with spectacles and/or rigid gas-permeable contact lenses (RGPCL). It is well known that BSCVA with spectacles is often unsatisfactory in patients with KC, specially when anisometropia and high astigmatism is present.[6,75,76] RGPCL may provide better BSCVA even if significant irregular astigmatism is present.[77-79] However, 27% of chronic CL users become intolerant. When BSCVA is not adequate, or patients do not want to wear RGPCL, surgical intervention may be required to achieve optimal visual rehabilitation.[7-10] In our series, both UCVA and BSCVA improved after surgery.

The fact that the decrease in corneal endothelial cell count was only statistically significant when compared to baseline suggests that the endothelial cell loss observed is mostly related to the surgical procedure and not to the presence of the TPIOL in the anterior chamber. Nevertheless, longer follow-up is needed to clarify this later statement. Additionally, patients with keratoconus need to be advised against rubbing their eyes, as it is one of the factors for endothelial cell loss after anterior chamber phakic IOL implantation,[40] and it has also been related with progression of keratoconus.[80-82]

In conclusion, implantation of toric PIOLs is a safe procedure that provides excellent visual outcomes in patients with keratoconus, and enables the delay of keratoplasty.

References

1. Rabinowitz YS. Keratoconus. Surv Ophthalmol 1998;42:297-319.
2. Riddle HK, Parker DA, Price FW. Management of postkeratoplasty astigmatism. Curr Opin Ophthalmol 1998;9:15-28.
3. Chastang PJ, Borderie VM, Carvajal-Gonzalez S, et al. Prediction of spectacle-corrected visual acuity using videokeratography. J Refract Surg 1999;15:572-9.
4. Speaker MG, Cohen EJ, Edelhauser HF, et al. Effect of gas-permeable contact lenses on the endothelium of corneal transplants. Arch Ophthalmol 1991;109:1703-6.
5. Busin M, Arffa RC, Zambiachi L, et al. Effect of hinged lamellar keratotomy on postkeratoplasty eyes. Ophthalmology 2001;108:1845-51; discussion 1851-2.
6. Vajpayee RB, Sharma N, Sinha R, et al. Laser in-situ keratomileusis after penetrating keratoplasty. Surv Ophthalmol 2003;48:503-14.
7. Lim N, Vogt U. Characteristics and functional outcomes of 130 patients with keratoconus attending specialist contact lens clinic. Eye 2002;16:54-9.
8. Geerards AJ, Vreugdebhil W, Khazen A. Incidence of rigid gas-permeable contact lens wear after keratoplasty for keratoconus. Eye Contact Lens 2006;32:207-10.
9. Espana EM, Tseng SC. Analysis of contact lens intolerance by exploring neuroanatomic integration of ocular surface defense. Cont Lens Anterior Eye 2003;26:131-7.
10. Glasson MJ, Stapleton F, Keay L, et al. Invest Ophthalmol Vis Sci 2003;44:5116-24.
11. Thompson RW Jr, Price MO, Bowers PJ, Price FW. Long-term graft survival after penetrating keratoplasty. Ophthalmology 2003;110:1396-1402.
12. Lim L, Pesudovs K, Coster DJ. Penetrating keratoplasty for keratoconus: visual outcome and success. Ophthalmology 2000;107:1125-31.
13. Brooks SF, Johnson D, Fischer N. Anisometropia and binocularity. Ophthalmology 1996;103(7):1139-43.
14. Perlman EM. An analysis and interpretation of refractive errors after penetrating keratoplasty. Ophthalmology 1981;88:39-45.
15. Perl T, Charlton KH, Binder PS. Disparate diameter grafting. Astigmatism, intraocular pressure, and visual acuity. Ophthalmology 1981;88:774-81.
16. Kruse FE, Cursiefen C. Surgery of the cornea: corneal, limbal stem cell and amniotic membrane transplantation. Dev Ophthalmol 2008;41:159-70.
17. Frost NA, Wu J, Lai TF, Coster DJ. A review of randomized controlled trials of penetrating keratoplasty techniques. Ophthalmology 2006;113(6):942-9.
18. Chang DH, Hardten DR. Refractive surgery after corneal transplantation. Curr Opin Ophthalmol 2005;16(4):251-5.
19. Taban M, Behrens A, Newcomb RL, et al. Incidence of acute endophthalmitis following penetrating keratoplasty: a systematic review. Arch Ophthalmol 2005;123(5):605-9.
20. Patel HY, Omonde S, Brookes NH, et al. The indications and outcome of paediatric corneal transplantation in New Zealand: 1991-2003. Br J Ophthalmol 2005;89(4):404-8.
21. Panda A, Vanathi M, Kumar A, et al. Corneal graft rejection. Surv Ophthalmol 2007;52(4):375-96.
22. Randleman JB, Woodward M, Lynn MJ, Stulting RD. Risk assessment for ectasia after corneal refractive surgery. Ophthalmology 2008;115:37-50.
23. Randleman JB, Russell B, Ward MA, et al. Risk factors and prognosis for corneal ectasia after LASIK. Ophthalmology 2003;110:267-75.
24. Randleman JB, Trattler WB, Stulting RD. Validation of the Ectasia Risk Score System for preoperative laser in situ keratomileusis screening. Am J Ophthalmol 2008;145:813-8.
25. Binder PS. Analysis of ectasia after laser in situ keratomileusis : risk factors. J Cataract Refract Surg 2007;33:1530-8.
26. Colin J. European clinical evaluation: use of Intacs for the treatment of keratoconus. J Cataract Refract Surg 2006;32:747-55.
27. Colin J, Cochener B, Savary G, Malet F. Correcting keratoconus with intracorneal rings. J Cataract Refract Surg 2000;26:1117-22.
28. Colin J, Cochener B, Savary G, et al. INTACS inserts for treating keratoconus; one-year results. Ophthalmology 2001;108:1409-14.
29. Siganos D, Ferrara P, Chatzinikolas K, et al. Ferrara intrastromal corneal rings for the correction of keratoconus. J Cataract Refract Surg 2002;28:1947-51.
30. Holmes-Higgin DK, Burris TE. Corneal surface topography and associated visual performance with Intacs for myopia: phase III clinical trials results. The Intacs Study Group. Ophthalmology 2000;107:2061-71.

31. Schanzlin DJ, Asbell PA, Burris TE, Durrie DS. The intrastromal corneal ring segments; phase II results for the correction of myopia. Ophthalmology 1997;104:1067-78.
32. Pokroy R, Levinger S. Intacs adjustment surgery for keratoconus. J Cataract Refract Surg 2006;32:986-92.
33. Ucakhan OO, Kanpolat A, Ozdemir O. Contact lens fitting for keratoconus after Intacs placement. Eye contact lens 2006;32:75-7.
34. Kamburoglu G, Etan A, Bahadir M. Implantation of Artisan toric phakic intraocular lens following Intacs in a patient with keratoconus. J Cataract Refract Surg 2007;33:528-30.
35. Colin J, Velou S. Implantation of Intacs and a refractive intraocular lens to correct keratoconus. J Cataract Refract Surg 2003;29:832-4.
36. Coskunseven E, Onder M, Kymionis GD, et al. Combined Intacs and posterior chamber toric implantable collamer lens implantation for keratoconic patients with extreme myopia. Am J Ophthalmol 2007;144:387-9.
37. Moshirfar M, Gregoire FJ, Mirzaian G, et al. Use of Verisyse iris-supported phakic intraocular lens for myopia in keratoconic patients. J Cataract Refract Surg 2006;32:1227-32.
38. Leccisotti A, Fields SV. Angle-supported phakic intraocular lenses in eyes with keratoconus and myopia. J Cataract Refract Surg 2003;29:1530-6.
39. Budo C, Bartels MC, van Rij G. Implantation of Artisan toric phakic intraocular lenses for the correction of astigmatism and spherical errors in patients with keratoconus. J Refract Surg 2005;21:218-22.
40. Güell JL, Morral M, Gris O, et al. Five-year follow-up of 399 phakic Artisan®-Verisyse® implantation for myopia, hyperopia and/or astigmatism. Ophthalmology 2008;115(6):1002-12.
41. Budo C, Hessloehl JC, Izak M, et al. Multicenter study of the Artisan phakic intraocular lens. J Cataract Refract Surg 2000;26(8):1163-71.
42. Stulting RD, John ME, Maloney RK. US Verisyse Study Group. Three-Year results of Artisan/Verisyse phakic intraocular lens implantation results of the United States Food and Drug Administration Clinical Trial. Ophthalmology 2008;115(3):464-72.
43. Pop M, Payette Y. Initial results of endothelial cell counts after Artisan lens for phakic eyes: an evaluation of the United States Food and Drug Administration Ophtec Study. Ophthalmology 2004;111(2):309-17.
44. Maloney RK, Nguyen LH, John ME. Artisan phakic intraocular lens for myopia: short-term results of a prospective, multicenter study. Ophthalmology 2002;109(9):1631-41.
45. Gimbel HV, Ziemba SL. Management of myopic astigmatism with phakic intraocular lens implantation. J Cataract Refract Surg 2002;28:883-6.
46. Uusitalo RJ, Aine E, Sen NH, et al. Implantable contact lens for high myopia. J Cataract Refract Surg 2002;28:29-36.
47. Pesando PM, Ghiringhello MP, Di Meglio G, Fanton G. Posterior chamber phakic intraocular lens (ICL) for hyperopia: ten-year follow-up. J Cataract Refract Surg. 2007;33(9):1579-84.
48. Sanders DR, Doney K, Poco M. United States Food and Drug Administration clinical trial of the Implantable Collamer Lens (ICL) for moderate to high myopia: three-year follow-up. Ophthalmology 2004;111:1683-92.
49. Zaldivar R, Davidorf JM, Oscherow S. Posterior chamber phakic intraocular lens for myopia of -8 to -19 diopters. J Refract Surg 1998;14:294-305.
50. Davidorf JM, Zaldivar R, Oscherow S. Posterior chamber phakic intraocular lens for hyperopia of +4 to +11 diopters. J Refract Surg 1998;14:306-11.
51. Tuft SJ, Moodaley LC, Gregory WM, et al. Prognostic factors for the progression of keratoconus. Ophthalmology 1994;101:439-47.
52. Wollensak G. Crosslinking treatment of progressive keratoconus: new hope. Curr Opin Ophthalmol 2006;17:356-60.
53. Wollensak G, Spoerl E, Seiler T. Riboflavin/ultraviolet-a-induced collagen crosslinking for the treatment of keratoconus. Am J Ophthalmol 2003;135:620-7.
54. Caporossi A, Baiocchi S, Mazzotta C, et al. Parasurgical therapy for keratoconus by riboflavin-ultraviolet type A rays induced cross-linking of corneal collagen: preliminary refractive results in an Italian study. J Cataract Refract Surg 2006;32:837-45.
55. Tan DT, Por YM. Current treatment options for corneal ectasia. Curr Opin Ophthalmol 2007;18:284-9.
56. Kanellopoulos AJ, Binder PS. Collagen cross-linking (CCL) with sequential topography-guided PRK: a temporizing alternative for keratoconus to penetrating keratoplasty. Cornea 2007;26:891-5.
57. Davis LJ, Schechtman KB, Begley CG, et al. Repeatability of refraction and corrected visual acuity in keratoconus. The CLEK Study Group. Collaborative Longitudinal Evaluation of Keratoconus. Optom Vis Sci 1998;75:887-96.
58. Van der Heijde GL. Some optical aspects of implantation of an intraocular lens in a myopia eye. Eur J Implant Refract Surg 1989;1:245-8.
59. Fechner PU, Van der Heijde GL, Worst JGF. The correction of myopia by lens implantation into phakic eyes. Am J Ophthalmol 1989;107:659-63.

60. Olsen T, Corydon L, Gimbel H. Intraocular lens power calculation with an improved anterior chamber depth prediction algorithm. J Cataract Refract Surg 1995;21:313-9.
61. Olsen T, Thim K, Corydon L. Accuracy of the newer generation intraocular lens power calculation formulas in long and short eyes. J Cataract Refract Surg 1995;17:187-93.
62. Lovisolo CF, Reinstein DZ. Phakic intraocular lenses. Surv Ophthalmol 2005;50(6):549-87.
63. Zaldivar R, Ricur G, Oscherow S. The phakic intraocular lens implant: in-depth focus on posterior chamber phakic IOLs. Curr Opin Ophthalmol 2000;11:22-34.
64. Smallman DS, Probst L, Rafuse PE. Pupil block glaucoma secondary to posterior chamber phakic intraocular lens implantation for high myopia. J Cataract Refract Surg 2004;30:905-7.
65. Sanders DR, Vukich JA. Incidence of lens opacities and clinically significant cataracts with the implantable contact lens: Comparison of two lens designs. J Refract Surg 2002;18:673-82.
66. Gonvers M, Bornet C, Othenin-Girard P. Implantable contact lens for moderate to high myopia: relationship of vaulting to cataract formation. J Cataract Refract Surg 2003;29:918-24.
67. Kohnen T, Kasper T, Buhren J, Fechner PU. Ten-year follow-up of a ciliary sulcus-fixated silicone phakic posterior chamber intraocular lens. J Cataract Refract Surg 2004;30: 2431-4.
68. Sanders DR, Vukich JA, Doney K, Gaston M. US Food and Drug Administration clinical trial of the Implantable Contact Lens for moderate to high myopia. Ophthalmology 2003;110:255-66.
69. Apple DJ, Werner L. Complications of cataract and refractive surgery: a clinicopathological documentation. Trans Am Ophthalmol Soc 2001;99:95-107; discussion 107-9.
70. Werner L, Apple DJ, Pandey SK, et al. Phakic posterior chamber intraocular lenses. Int Ophthalmol Clin 2001;41(3): 153-74.
71. Werner L, Izak AM, Pandey SK, Apple DJ, Trivedi RH, Schmidbauer JM. Correlation between different measurements within the eye relative to phakic intraocular lens implantation. J Cataract Refract Surg 2004;30: 1982-8.
72. Pop M, Payette Y, Mansour M. Predicting sulcus size using ocular measurements. J Cataract Refrat Surg 2001;27: 1033-8.
73. Davidorf JM, Zaldivar R, Oscherow S. Posterior chamber phakic intraocular lens for hyperopia of +4 to +11 diopters. J Refract Surg 1998;14:306-11.
74. Zaldivar R, Davidorf JM, Oscherow S. The intraocular contact lens. In: Buratto L, Brint SF (Eds). LASIK. Principles and Techniques. Thorofare, NJ: Slack 1997;401-13.
75. Pesudovs K, Garamendi E, Elliott DB. A quality of life comparison of people wearing spectacles or contact lenses or having undergone refractive surgery. J Refract Surg 2006;22(1):19-27.
76. Wietharn BE, Driebe WT Jr. Fitting contact lenses for visual rehabilitation after penetrating keratoplasty. Eye Contact Lens 2004;30(1):31-3.
77. Riddle HK, Parker DA, Price FW. Management of postkeratoplasty astigmatism. Curr Opin Ophthalmol 1998;9:15-28.
78. Chastang PJ, Borderie VM, Carvajal-Gonzalez S, et al. Prediction of spectacle-corrected visual acuity using videokeratography. J Refract Surg 1999;15:572-9.
79. Speaker MG, Cohen EJ, Edelhauser HF, et al. Effect of gas-permeable contact lenses on the endothelium of corneal transplants. Arch Ophthalmol 1991;109:1703-6.
80. McMonnies CW. Abnormal rubbing and keratectasia. Eye Contact Lens 2007;33(6 Pt 1):265-71.
81. McMonnies CW. The biomechanics of keratoconus and rigid contact lenses. Eye Contact Lens 2005;31(2):80-92.
82. Krachmer JH, Feder RS, Belin MW. Keratoconus and related noninflammatory corneal thinning disorders. Surv Ophthalmol 1984;28(4):293-322.

9

Our Experience with Toric Phakic IOLs in Keratoconus

H Burkhard Dick
Fritz Hengerer

Introduction

Keratoconus, which is marked by the presence of ectasia and thinning of the cornea, induces myopia and astigmatism. Treatments are available to correct these aberrations, including contact lenses and spectacles in the early stages of the disease and penetrating keratoplasty (PK) or lamellar keratoplasty (LK) once the disease progresses to contact lens intolerance. However, the visual outcome after PK is often limited by high residual astigmatism, sometimes reaching 4.00 to 5.00 D.[1-6] Additionally, keratoplasty requires a long visual recovery time and frequent postoperative follow-up. Other refractive methods of treatment include arcuate keratotomy, PRK, and LASIK.[7]

Many surgeons are also exploring the option of using phakic intraocular lenses (IOLs) as an alternative treatment for keratoconus. These IOLs better treat the keratoplasty-associated astigmatism left behind with more conservative treatment approaches. Moreover, this IOL modality preserves accommodation compared to a refractive lens exchange. Recently, I started to implant the Verisyse toric phakic IOL (Advanced Medical Optics, Santa Ana, CA, USA; also known as Artisan by Ophtec BV, Groningen, the Netherlands) to correct corneal astigmatism in phakic eyes. This modality of treatment tends to delay—or possibly even avoid—the need for PK in patients with clear corneas who are contact lens intolerant. Although contact lenses may be effective in as many as 80% of patients,[8] patients who previously underwent keratoplasty often have topographical abnormalities, blepharitis, dry eye, and poor manual dexterity. In this population, other solutions are necessary to treat keratoconus.

The Verisyse toric phakic IOL, with an overall diameter of 8.5 mm and an optical zone diameter of 5 mm, is an iris-fixated anterior chamber lens with ultraviolet filtration. There are two models available—in the first, the axis runs through the claws at 0° and in the other, the axis is perpendicular to the claws at 90°. This provides surgeons with the option to implant the IOL through a superior incision, allowing optimal implantation in the correct axis. Additionally, its cylindrical power goes up to 7.00 D, and the spherical power ranges from -3.00 to -23.50 D for myopia and 1.00 to 12.00 D for hyperopia.[1]

Case Report

In 1997, a 27-year-old female underwent PK for the treatment of a decompensated keratoconus. Her BCVA was 20/32, and a high corneal astigmatism (7.60 D) related to the keratoplasty was unsuccessfully treated with contact lenses or spectacles. We proceeded with implantation of the Verisyse toric IOL with a power of -3 - 7 × 0° (individually manufactured). The lens was implanted into the anterior chamber using a sclerocorneal tunnel incision. We noted postoperatively that the Verisyse was well centered and stable. At 3 months, her UCVA was 20/25; at 6 months, her UCVA was 20/20, and the IOL remained well centered. This is a typical example of my results with phakic IOLs, and the literature has also shown that the Verisyse toric phakic IOL provides a stable and predictable refractive outcome, correcting high ametropia and astigmatism within one single surgical session.[1,8,9]

Budo, *et al* implanted the iris-fixated toric phakic IOL in six eyes (three patients) with keratoconus, a clear central cornea, and contact lens intolerance.[9] Investigators noted that the reduction in spherical equivalent refraction was significant, with four of the six eyes within ±1.00 D of emmetropia postoperatively. Additionally, the majority of eyes experienced an improvement in visual acuity compared with preoperative levels. Tahzib, *et al* [8] studied toric phakic IOL implantation in 36 eyes

(35 patients) with contact lens intolerance. In their study, despite two patients with irreversible graft rejections and one with gradual endothelial decompensation, the vast majority of patients experienced a reduction of refractive astigmatism (88.8% ± 29.5%) and ametropia (77.8% ± 19.3%). On a scale of zero to 10, patient satisfaction increased from 3.6 preoperatively to 8.0 postoperatively.

Although we do not expect patients' refraction to remain stable after phakic IOL implantation, the need for PK is delayed. Additionally, the use of a phakic IOL, including a toric model, does not hinder the results of the eventual need for PK or LK for those patients with keratoconus and contact lens intolerance.[10-12]

Limitations

The use of a toric phakic IOL for the treatment of keratoconus does have its limitations. For instance, if a patient has high myopia, use of a toric phakic IOL may induce halos and glare when the patient is confronted with dim-light conditions.[1] Additionally, Budo, *et al*[9] concluded that although the predictability for spherical errors is high, the predictability for astigmatic errors is only moderate. Endothelial cell count is also a concern when implanting a toric phakic IOL. We choose not to implant this lens in patients whose endothelial cell count is below 2000 mm^2.

Another drawback to use the toric phakic IOL is incision size. The IOL only fits through an incision of at least 5.5 mm, which may induce astigmatism. My colleagues and I were able to show that the surgically induced astigmatism after toric phakic IOL implantation in nondiseased eyes was 0.53 D.[9]

I would suggest only using this method of treatment in an eye with stable keratometry and subjective refraction. If the patient does not meet these requirements, such as patients with recently diagnosed keratoconus or those with progressive keratoconus, consider other options for the treatment of keratoconus, including LASIK,[13] intracorneal rings and segments,[14] epikeratoplasty,[15] and lamellar keratoplasty.[16] Be aware, however, that keratoconus is a contraindication of LASIK and, therefore, its use for this purpose is limited. Furthermore, although intracorneal rings or segments reduce astigmatism, the marked reduction is not as great as what toric phakic IOLs offer.[1]

Conclusion

In some cases, patients may benefit from the use of spectacles or contact lenses to correct astigmatism; however, when patients become contact lens intolerant, I frequently use the iris-fixated toric phakic IOL (Verisyse) as an alternative treatment. In my experience, this IOL reduces the patient's refractive error and astigmatism to a more manageable level and provides patients with a speedy visual rehabilitation.

In conclusion, I believe that toric phakic Verisyse implantation is the natural first step to the treatment of keratoconus and should be done before performing PK, especially in patients with associated myopia. The risk of endothelial cell loss should not be taken lightly, however, and long-term follow-up is necessary for patients.

References

1. Budo C, Bartels MC, van Rij G. Implantation of Artisan toric phakic intraocular lenses for the correction of astigmatism and spherical errors in patients with keratoconus. J Refract Surg 2005;21:218-22.

2. Lim L, Pesudovs K, Coster DJ. Penetrating keratoplasty for keratoconus: visual outcome and success. Ophthalmology 2000;107:1125-31.
3. Webber SK, Lawless MA, Sutton GL, Rogers CM. LASIK for post penetrating keratoplasty astigmatism and myopia. Br J Ophthalmol. 1999;83:1013-8.
4. Troutman RC, Lawless MA. Penetrating keratoplasty for keratoconus. Cornea 1987;6:298-305.
5. Binder PS. The effect of suture removal on postkeratoplasty astigmatism. Am J Ophthalmol 1988;106:507.
6. Seitz B, Langenbucher A, Jus MM, et al. Nonmechanical corneal trephination with the excimer laser improves outcome after penetrating keratoplasty. Ophthalmology 1999;106:1156-64.
7. Tehrani M, Dick HB. Implantation of an Artisan toric phakic intraocular lens to correct high astigmatism after penetrating keratoplasty. Klin Monatsbl Augenheilkd 2002;219:159-63.
8. Tahzib NG, Cheng YYY, Nuijts RMMA. Three-year follow-up analysis of Artisan toric lens implantation for correction of postkeratoplasty ametropia in phakic and pseudophakic eyes. Ophthalmology 2006;113:976-84.
9. Dick HB, Alio J, Bianchetti M, Budo C, Christiaans BJ, El-Danasoury MA, Güell JL, Krumeich J, Landesz M, Loureiro F, Luyten GP, Marinho A, Rahhal SM, Schwenn O, Spirig R, Thomann U, Venter J. Toric phakic intraocular lens: European multicenter study. Ophthalmology 2003;110:150-62.
10. Brierly SC, Izquierdo L Jr, Mannis MJ. Penetrating keratoplasty for keratoconus. Cornea 2000;19:329-32.
11. Kirkness CM, Ficker LA, Steele AD, Rice NS. The success of penetrating keratoplasty for I-III stage-specific surgical treatment of keratoconus. Klin Monatsbl Augenheilkd 1997;211:94-100.
12. Buzard KA, Tuengler A, Febbraro JL. Treatment of mild to moderate keratoconus with laser in situ keratomileusis. J Cataract Refract Surg 1999;25:1600-09.
13. Colin J, Cochener B, Savary G, Malet F, Holmes-Higgin D. Intacs inserts for treating keratoconus: one-year results. Ophthalmology 2001;108:1409-14.
14. Siganos D, Ferrara P, Chatzinikolas K, Bessis N, Papastergiou G. Ferrara intrastromal corneal rings for the correction of keratoconus. J Cataract Refract Surg 2002;28:1947-51.
15. Wagoner MD, Smith SD, Rademaker WJ, Mahmood MA. Penetrating keratoplasty vs epikeratoplasty for the surgical treatment of keratoconus. J Refract Surg 2001;17:138-46.
16. Richard JM, Paton D, Gasset AR. A comparison of penetrating keratoplasty and lamellar keratoplasty in the surgical management of keratoconus. Am J Ophthalmol 1978;86:807-11.

10

Refractive Lens Exchange in Keratoconus and after Keratoplasty

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The authors have no financial or proprietary interest in any material or method mentioned.

Introduction

Refractive lens exchange (RLE) entails phacoemulsification of a clear crystalline lens and implantation in the capsular bag of a pseudophakic intraocular lens (IOL), with the purpose of correcting a refractive error.[1] This technique is currently used when less invasive techniques (i.e. corneal refractive procedures) are contraindicated because of a high refractive error or to because of a thin or pathologic cornea. The myopia associated with keratoconus (KC) is therefore an indication to RLE, especially in the presbyopic age, because RLE causes loss of accommodation.[2, 3] Apart from age, the indications are the same as those for phakic IOLs in KC. Another indication is a high spherical error after penetrating keratoplasty (PKP) or anterior lamellar keratoplasty (ALK).

The advantages of RLE over phakic IOLs are several:

1. The IOL is implanted in its physiologic place, has no contact with uveal and corneal structures, does not cause pigment dispersion, inflammation, pupil deformation;
2. The technology is readily available to any cataract surgeon;
3. There is no need for frequent endothelial follow-up as with phakic IOLs;
4. Surgery is definitive and not temporary as with phakic IOLs, which will ultimately need removal because of age and cataract.

The disadvantages include:

1. Loss of accommodation, which cannot be compensated by a multifocal IOL, which is strongly contraindicated in KC because of an unbearable summation of aberration;
2. A possible increase of vitreoretinal complications, despite recent optimistic long-term reports.[4] We must remember, however, that retinal detachment rate is not very different after phakic IOL implantation;[5]
3. With phakic IOLs the IOL power is determined by refraction, whereas with RLE it is determined by axial length transformed in diopters (D);
4. Posterior capsule opacification is unavoidable in a number of patients, requiring Nd:YAG laser capsulotomy.

Indications

RLE in myopia and KC is only indicated when corneal astigmatism is not excessively irregular (stages I – II). Ideally, the patient should have a best-spectacle corrected visual acuity (BSCVA) better than 0.5, which will be obviously improved by the magnifying effect of the elimination of myopia. High astigmatism (which is never regular in KC) is not a contraindication, but we must remember that biometry in KC is less than accurate and laser enhancement is not possible: therefore, even if we implant a toric pseudophakic IOL, we must be prepared to refractive surprises that may impair its final refractive effect.

In normal myopia, RLE is preferred over phakic IOL over the age of 40, but in KC some considerations are necessary. Toric phakic IOLs, especially if iris-fixated, are rotationally stable and predictable, whereas RLE in KC has a less precise outcome, and in-the-bag toric IOLs are less stable. Therefore, phakic IOLs tend to have a better refractive outcome but have a slightly worse safety profile, especially as for the anterior chamber. We prefer RLE in eyes in which phakic IOLs are contraindicated for anatomical reasons, eyes showing early lens changes, eyes with refractive astigmatism <3 D. Refractive and KC stability are required, but are normally present in patients in the presbyopic age.

RLE after PKP and ALK has less limitations. A higher degree of astigmatism is not an absolute contraindication, because laser enhancement or even incisional surgery (astigmatic keratotomy) is possible after both PKP and ALK. A toric IOL can be used in these cases as well, but most cases of post-keratoplasty astigmatisms have an irregular component: therefore, biometry and calculation of the toric component are surely less accurate than in regular corneas.

Preoperative Work-up

Corneal topography is of paramount importance, because it help assessing KC stability and grade. In addition, an endothelial cell count by means of specular microscopy is mandatory, as KC patients may have contact-lens induced polymegatism, and post-keratoplasty eyes (even after ALK) may have a low cell count, discouraging any surgery in the anterior chamber (AC). An altered endothelial status requires some additional intraoperative attentions, such as protection with an adhesive ophthalmic viscosurgical device (OVD), but an endothelial cell count with less than 1300-1400 cell/mm² (especially after PKP in a young patient) is an absolute contraindication to RLE.

IOL power calculation can be carried out by ultrasound biometry, by partial coherence interferometry (IOL Master, Zeiss Humphrey, USA), or by intraoperative autorefraction. In the 2 first options, the value of keratometry is a vexed question, and it has been proposed to use sim-K from videokeratography[6] or pre-pupillary curvature.

Intraoperative autorefraction is indicated in high myopia, where it yields the best results.[7] It is performed just after the cortical cleaning of the capsular bag, with the anterior chamber reformed with balanced salt solution (BSS) **(Figure 10-1)**. The value of aphakic spherical equivalent (x) is directly transformed into the IOL power for emmetropia (y) by the parabolic relation

$$y = 0.07\ x^2 + 1.27\ x + 1.22$$

as simplified by **Table 10-1.**[7]

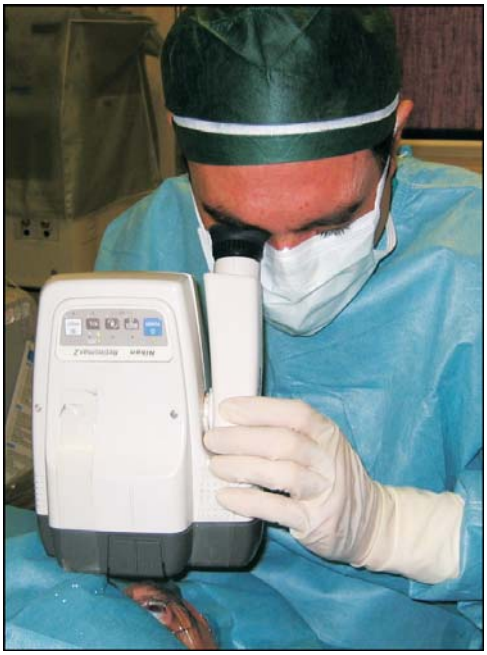


FIGURE 10-1: Intraoperative autorefraction.

TABLE 10-1: Spherical equivalent (SE) at intraoperative aphakic autorefraction (in dioptres) and suggested intraocular lens (IOL) power to be implanted in the capsular bag of myopic eyes. The IOL A-constant is 118.2

Autorefraction	IOL for emmetropia
–4	–2.5
–3	–1.5
–2	–1
–1	0
0	+1.5
+1	+2.5
+2	+4.5
+3	+5.5
+4	+7
+5	+8.5
+6	+12
+7	+14
+8	+16
+9	+18
+10	+20

Intraoperative autorefraction does not require K readings, but is not very accurate in irregular corneas and is only recommended in myopia greater than -10 D. In all cases, however, standard biometry should be performed, in the case intraoperative autorefraction should result impossible because of vitreous pressure, eyelid squeezing, etc.

A personalized informed consent is crucial. Dissatisfaction usually arises from the comparison with previous vision with rigid gas-permeable (RGP) contact lenses. Patients should understand that residual irregular astigmatism can be partially corrected by spectacles, but some activities may require RGP contact lenses again. The purpose of RLE in KC is ultimately to reduce dependence from contact lenses and from thick spectacles; in some cases, a useful unaided vision is obtained. Normally, an idea of the final result can be anticipated to the patient (and to the surgeon) by placing in a trial frame only spherical lenses, until the best spectacle-corrected visual acuity (BSCVA) is obtained.

Surgical Technique

Refractive lens exchange is performed by standard phacoemulsification with few modifications, due to the soft nucleus. Topical anesthesia is in our opinion warranted in calm patients who, during preoperative examinations, allow eye contact and manipulation without squeezing their eyelids; peribulbar anesthesia is advised in all other cases. Intravenous sedation is sometimes administered in anxious patients.

The prevention of endophthalmitis, very rare in young and healthy patients with short surgery, is based upon complete eyelid and cilia isolation by the plastic drape, by 5% povidone-iodine instilled in the conjunctival sac 5 minutes before incision, and by avoiding a clear cornea incision; a limbal incision has the only drawback of some bleeding. The effect of incision location is minimal in modern phacoemulsification. Theoretically, it should be placed on the steepest meridian derived from subjective refraction, which in keratoconic eyes does not always correspond to the steepest meridian on topography. This makes the final effect on refraction quite unpredictable **(Figure 10-2)**.

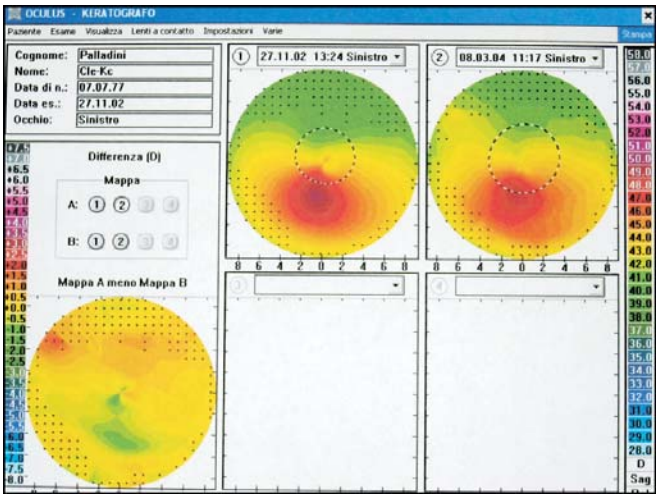


FIGURE 10-2: Partial cone flattening after a 5.5 mm limbal incision on the steepest meridian for phakic IOL implantation.

A sclero-corneal tunnel is made, anterior chamber filled with a cohesive OVD (sodium hyaluronate [Provisc®]), continuous curvilinear capsulorrhexis performed by forceps, and, after hydrodissection, the lens nucleus is emulsified with high vacuum and the cortex aspirated. The temptation of using hydrodissection to push the soft nucleus in the anterior chamber should be resisted, because this maneuver leads to phacoemulsification in the AC, too near the endothelium, and because (especially with a small capsulorrhexis) it can cause sudden rupture of the posterior capsule, with dropping of the nucleus in the vitreous.

When the IOL power is to be decided by intraoperative autorefraction, the AC is reformed with BSS and autorefraction performed by a hand-held instrument (Nikon Retinomax 2®, Tokio, Japan), with the patient on the operating bed and the eyelid speculum on. OVD is then introduced in the AC and the desired IOL is inserted by an injector.

The most common complications of RLE in KC are undercorrection and overcorrection. These occurrences should be addressed soon, because laser fine-tuning is not recommended in keratoconic eyes, and IOL exchange is best performed when the capsular bag is not fibrotic yet. A few months after surgery, IOL exchange can become dangerous in terms of capsular damage and vitreous loss, and a piggyback implantation of a second IOL in the ciliary sulcus is the safest option. The calculation of the IOL to be implanted can be simplified by the following rule (valid both for IOL exchange and for piggyback):[8]

if a positive error is found, increase IOL power of +1.5 D for every D; if a negative error is found, decrease IOL power of the same amount (1D for each D).

A sulcus piggyback must have an overall diameter = or > 13 mm for good centration. Piggybacking with both IOLs in the capsular bag must be avoided, as it may induce interlenticular opacification. Before IOL exchange, the endothelial status should be checked, and in case of damage from previous RLE, piggyback should be preferred to IOL exchange.

Results

In a published series of ours, RLE with implantation of a non-toric IOL was performed in 34 eyes of 20 keratoconic patients.[3] Mean age was 56.7 years ±10.4 (standard deviation), range 45 to 76 years. Twenty eyes had keratoconus stage I, and 14 eyes stage II.

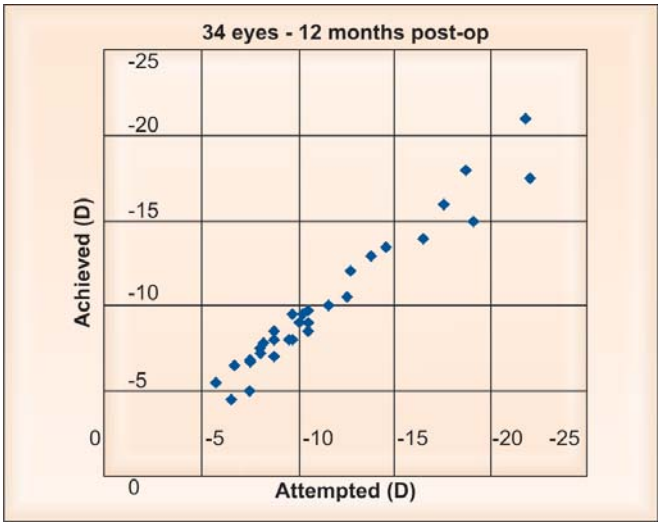


FIGURE 10-3: Scattergram of attempted vs. achieved correction (spherical equivalent) 12 months after myopic refractive lens exchange in 34 keratoconic eyes.

Surgery was uneventful in all cases. Preoperative mean spherical equivalent (SE) was –11.0 D (±4.65 [standard deviation], range -5.75 to –22), at 12 months –1.31 D (±1.08, range –0.25 to –4.5); the difference is statistically significant (95% CI for the mean of the differences of paired data –8.26 to –11.18 D) **(Figure 10-3)**.

Preoperative mean defocus equivalent was 12.0 D (±4.64, range 6.50 to 23), at 12 months 1.94 D (±1.57, range 0.25 to 5.5); the difference is statistically significant (95% CI for the mean of the differences of paired data 8.63 to 11.46 D). Twenty-two/34 eyes (65%) were within ±2 D of defocus equivalent; 16/34 (47%) were within ±1 D; 3/34 eyes (9%) were within ±0.5 D.

Preoperative mean refractive cylinder was 1.86 D (±1.39, range 0.5 to 5), at 12 months 1.22 D (±1.37, range 0 to 4); the difference significant with 95%CI for the mean of the differences of paired data (0.4 to 0.9 D). Mean surgically induced astigmatism, calculated by vector analysis, was 0.54 D (±0.43, range 0 to 1.80 D).

Preoperative mean BSCVA was 0.55 (±0.20, range 0.2 to 0.9), at 12 months 0.76 (±0.23, range 0.4 to 1.0); the difference is statistically significant (95%CI for the mean of the differences of paired data 0.19 to 0.25) **(Figure 10-4)**. Mean uncorrected visual acuity (UCVA) at 12 months was 0.48 (±0.25, range 0.1 to 0.9) **(Figure 10-5)**. Safety index was 1.38; efficacy index was 0.87.

Stability was evaluated by paired comparison of mean defocus equivalent at 3 months (1.78 D) and at 12 months after surgery (1.95 D). The variation is not statistically significant (95% CI for the difference between means for paired data: –0.51 to 0.20 D).

Posterior capsule opacification occurred in 6 eyes (17.6%) of 4 patients; Nd:YAG laser was performed in all cases with full functional recovery.

Dysphotic phenomena were reported by 3/20 patients (15%), consisting especially of light reflections caused by lateral lights; however patients favorably compared dysphotopsia with halos generated by rigid gas-permeable contact lenses.

Conclusion

RLE in KC and after keratoplasty is indicated for presbyopic patients with higher spherical errors; the astigmatism can be addresses either by a toric IOL or, in KC, by intracorneal rings (in this case,

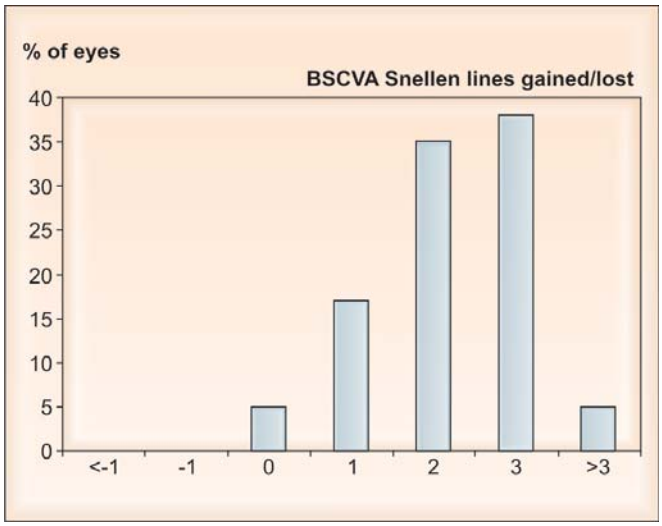


FIGURE 10-4: Changes in best-spectacle corrected visual acuity (BSCVA) 12 months after myopic refractive lens exchange in 34 keratoconic eyes.

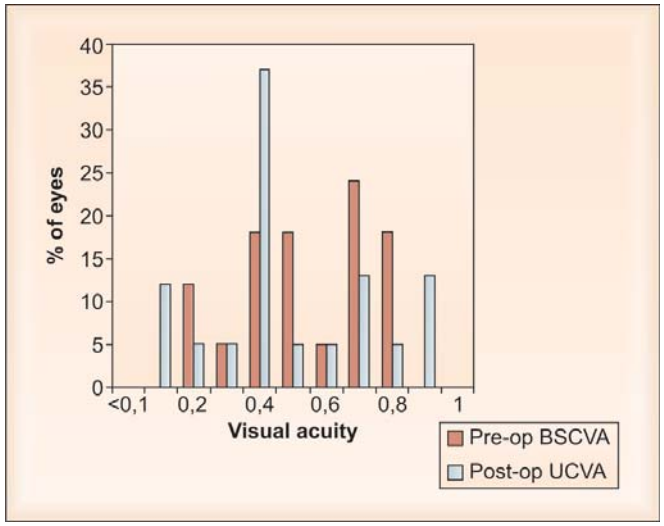


FIGURE 10-5: Efficacy of myopic refractive lens exchange in 34 keratoconic eyes, 12 months after surgery. Red columns: pre-operative best spectacle-corrected visual acuity (BSCVA). Blue columns: post-operative uncorrected visual acuity (UCVA).

ring implantation should precede CLE for a better IOL calculation). Toric IOLs in keratoconus have, as main disadvantage, the difficulty in determining axis and power of preoperative astigmatism. On the contrary, RLE after keratoplasty can be enhanced by excimer laser (LASIK or PRK with mitomycin-C).

When RLE is considered, keratoconus stability is important to maintain long-term refractive results (as progression would lead to increased corneal myopia), and to reduce the risk of a future keratoplasty (causing a hyperopic shift by means of a flatter cornea). In both cases, further adjustment can be achieved by the implantation in the ciliary sulcus of a second (piggyback) IOL. Prolonged contact lens use can reduce corneal endothelial cell density,[9] therefore patient selection must be accurate, as intraoperative or postoperative IOL exchange may further affect the endothelium.

References

1. Fernàndez-Vega L, Alfonso JF, Villacampa T. Clear lens extraction for the correction of high myopia. Ophthalmology 2003;110:2349-54.

2. Sauder G, Jonas JB. Treatment of keratoconus by toric foldable intraocular lenses. Eur J Ophthalmol 2003;13: 577-9.
3. Leccisotti A. Refractive lens exchange in keratoconus. J Cataract Refract Surg 2006;32:742-6.
4. Neuhann IM, et al. Retinal detachment after phacoemulsification in high myopia: analysis of 2356 cases. J Cataract Refract Surg 2008;34:1644-57.
5. Ongucci T, Kojima T, Azar DT. 10-year review of the literature on complications of incisional, thermal, and lenticular refractive procedures. In Aliò LJ, Azar DT (Eds). Management of Complications in Refractive Surgery. Springer: Berlin, 2008;339-50.
6. Celikkol L, Ahn D, Celikkol G, Feldman ST. Calculating intraocular lens power in eyes with keratoconus using videokeratography. J Cataract Refract Surg 1996;22:497-500.
7. Leccisotti A. Intraocular lens calculation by intraoperative autorefraction in myopic eyes. Graefes Archive Clin Exp Ophthalmol 2008;246:729-33.
8. Holladay JT. Piggyback intraocular lenses. Ann Ophthalmol 1998;30:203-4.
9. Esgin H, Erda N. Corneal endothelial polymegethism and pleomorphism induced by daily-wear rigid gas-permeable contact lenses. CLAO J 2002;28:40-3.

11

Automated Lamellar Therapeutic Keratoplasty in Keratoconus

Chitra Sambare
Sunil Shah

Introduction

The advent of automated lamellar therapeutic keratoplasty (ALTK) using an automated microkeratome and artificial anterior chamber to obtain lamellar cuts of repeatable quality and thickness has changed lamellar corneal transplantation completely. In addition, the recent introduction of femtosecond lasers for the creation of lamellar cuts has offered further opportunities.Lamellar surgery has been practiced in various forms for many years, however ALTK has reduced the dependence on individual surgeon expertise and has made lamellar keratoplasty more available.

The benefits of lamellar corneal surgery are well recognized and include reduced rejection rates, increased speed of rehabilitation, reduced suture related problems, reduced postoperative astigmatism and higher wound tensile strength.

ALTK is relatively simple, reversible, extraocular surgery and has reduced risks of immunologic reaction. The visual results of lamellar surgery in the form of epikeratophakia have been reported to be nearly equal or often superior to those of penetrating keratoplasty (PKP).[1,2] However, there are a sparsity of reports on ALTK.

Most techniques involving lamellar surgery for keratoconus involve using manual dissection. They include Anwar's big bubble technique,[3-6] viscoelastic separation of lamellae[7] and Melles' technique.[8] However, all of these techniques have the drawback of an irregular interface (except with good baring of Descemet in the big bubble technique) and the risk of perforation. An irregular interface can result in visual compromise. All of these procedures are dependant on the skill of the surgeon. Even in the hands of experienced surgeons, these procedures can be complicated by micro or macro perforation in a relatively high number of cases (up to 1 in 3) – which can make conversion to a PKP necessary.

ALTK triumphs over all these methods in this respect. It is useful for superficial scars, epithelial and stromal dystrophies. However, it suffers from the need for relatively expensive instrumentation. However, this instrumentation is becoming cheaper and more available because of its use for posterior automated lamellar transplantation (Descemet stripping automated endothelial keratoplasty).

ALTK can be used to produce a lenticule similar to that from epikeratophakia but has many of the same problems as epikeratophakia such as interface haze, melting and suture related problems, etc.

In ALTK for keratoconus, the interface remains clear if there was no scarring preoperatively, although, it is difficult to produce adequate flattening of the ectasia without suturing tightly. Whilst this can give good results, there is also a fairly high incidence of peripheral corneal melting related to the tight sutures. The addition of tissue to the ectatic cornea hence has the ability to thicken the cornea, add some rigidity and flatten the cornea.

Massimo Busin has used this technique for keratoconus and modified it further to obtain desirable visual outcome in advanced keratoconus.[10] According to him, microkeratome-assisted lamellar keratoplasty for keratoconus has the advantage of being a standardized, technically easy procedure, which yields smooth dissected surfaces compatible with 20/20 vision. He has modified the original technique of just adding tissue by perforating the residual base after the microkeratome cut in a circular fashion but just leaving 3 bridging points to hold the tissue in place. This technique has the advantage of allowing increased flattening of the ectatic area. He has reported ALTK in patients with keratoconus with an average keratometry reading of up to 57 D.

Instrumentation and Procedure

A number of ALTK systems are available and include Gebauer (Neuhausen, Germany http://www.gebauer-sl.com/dsaek_alk.htm) and Moria (Antony, France http://www.moria-surgical.com/). This is used to cut both donor and recipient lamellae of the desired thickness and diameter.

The systems consists of a motor unit, an artificial anterior chamber, microkeratome with variable plate sizes from 120 microns to 450 microns, suction rings, and applanation lenses **(Figure 11-1)**.

The desired attributes of any microkeratome system include consistency of flap thickness and minimal rate of flap complications, including epithelial defects, buttonholes, free caps and flap irregularities as well as fixed depth plate adaptability to deep set and small eyes.

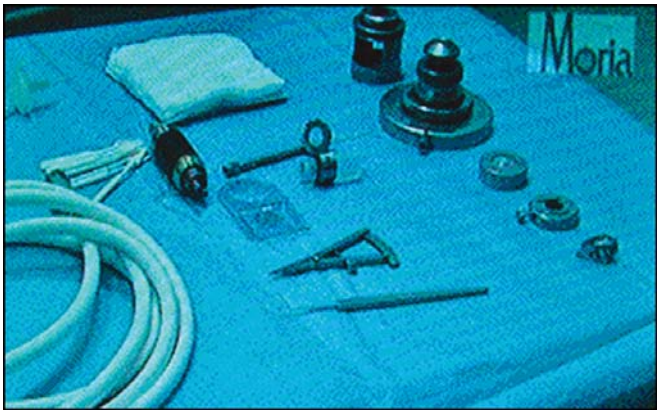


FIGURE 11-1: ALTK assembly.

Preparation of the Recipient Bed

Accurate ultrasonic pachymetry or anterior segment imaging of the recipient's cornea at different points, particularly at the apex of the cone is ideal. A typical microkeratome cut is approximately 250 micron thick and 9 mm in diameter so as to encompass whole of the cone. It has to be remembered that a nominal 250 micron head will not even cut 250 microns on average. The actual average will be different from 250 microns even in normal corneas with a standard deviation of about 30 microns. There is little information about what these nominal heads actually cut in ectatic corneas. It is important be aware of this difference in between the nominal depth plate and the actual cut achieved especially in abnormal corneas and hence there is a period of trial with any new system.

It may not always be possible to perform a lamellar cut of the whole of the ectatic area but the significance of this is unknown. In PKP, it is however well recognized that there is an incidence of ectasia outside the graft host interface causing problems. The irregular rim left behind at the periphery in case of such cones, may occasionally give rise to an irregular profile of the cornea after surgery.

Consideration should be given to under sizing donor grafts by 0.25 to 0.50 mm. It is easy to punch the correct graft size just as one would do in a full thickness cornea. The graft should be thicker than the recipient cut. The recipient cut will vary in thickness depending on the thickness of the recipient cornea - thinner corneas will need thinner cuts.

It is important to ensure that the electrical connections, plugs and the voltage are checked beforehand and are ready for use. The motor and the suction foot pedals should be securely connected to the main control unit. To test the motor the foot pedal is depressed and the voltage checked on the display for both forward and backward directions.

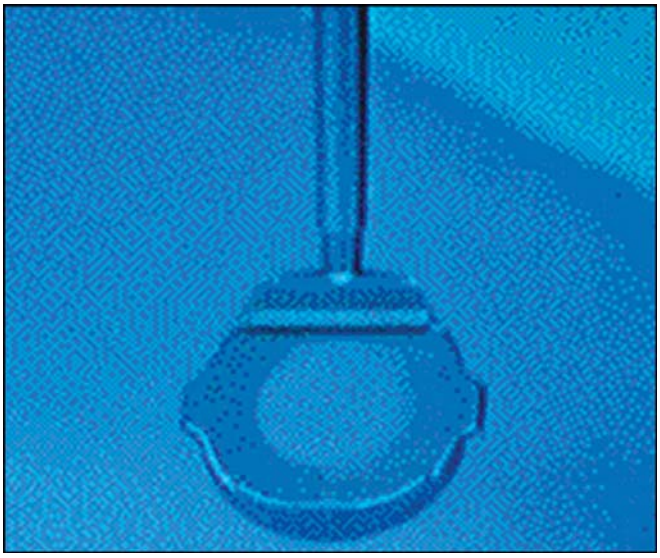


FIGURE 11-2: Suction ring.

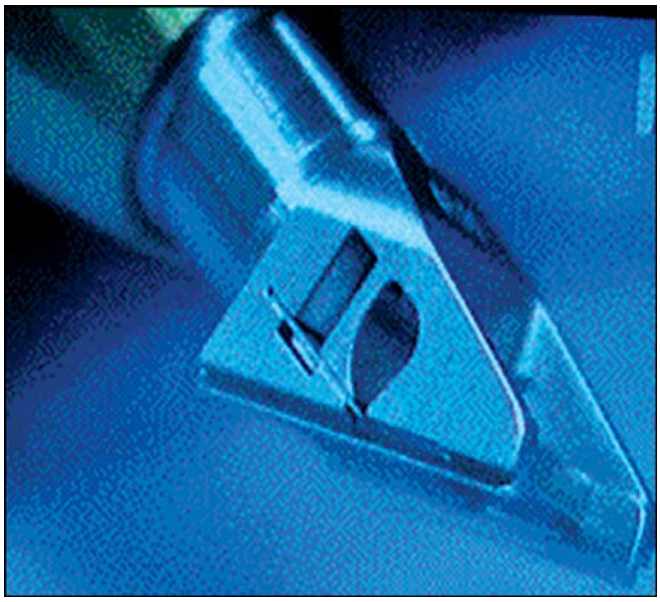


FIGURE 11-3: Microkeratome.

Generally, the recipient button is cut first **(Figures 11-2 to 11-4)** so as to safeguard the donor button for a full thickness graft if there is failure to obtain the desired flap. The suction ring is selected depending on the radius of curvature of the patient's cornea (depending on the system used). A reference chart enables us to select the ring diameter and/or characteristics. The suction ring is tightly connected to the handle, which in turn is connected to the vacuum machine. Once the suction is activated, the value of the vacuum may be displayed, on the machine or alternatively audible signals indicating good vacuum may be made. Prior to use, the vacuum is checked by occluding the orifices on the suction ring or by kinking the vacuum tubing.

The microkeratome unit has a unique sound or pitch that may be altered if the microkeratome is not working properly. Listening to this sound in the forward and the backward directions can help

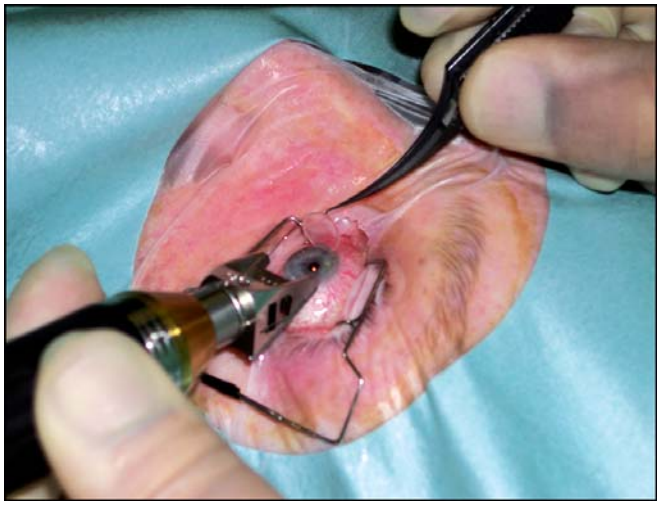


FIGURE 11-4: Obtaining recipient corneal button.

detect problems if any. The microkeratome blade should be checked under the microscope for any irregularities. The gap between the depth blade and the plate is also checked under the microscope as is the smoothness of the track of the microkeratome.

The microkeratome is inserted into the suction ring and the foot pedal is depressed in forward and reverse directions to ensure smooth movement of the microkeratome on the suction ring. Once it is made sure that the system is ready for use patient is prepared for surgery.

Topical anesthetic drops, such as proxymetacaine are instilled in the patient's eye (this has the benefit of having some lubricating properties). Anesthesia in the form of topical, peribulbar or subtenon anesthesia or general anesthetic is given. If local anesthetic is used, then extreme care should be made to avoid chemosis as this will prevent adequate suction being achieved (or pseudo suction where the suction ring orifices are blocked but the eye is not held). The eyelashes and fornices are cleaned thoroughly. The eye is draped taking care of the lashes and meiobomian glands. The drape must not be in a position to block suction or the movement of the keratome. A locking eyelid speculum is placed on the eye to obtain adequate exposure.

Once everything is clear from the operating field, the suction ring is applied to the eye. Making sure that the fornices are clear, the vacuum is activated. The eyelid speculum is slightly depressed. The patient is warned of the slight feeling of pressure and discomfort. If the position is adequate the suction pressure is activated and the patient is warned that the vision may go dark. Four helpful signs assure surgeon that adequate suction has been obtained.[11] These are:

1. The suction ring can be lifted towards the ceiling slightly and the eye should come up with it.
2. The pupil will dilate slightly.
3. The patient will confirm that everything has gone dark.
4. The eye will feel firm to palpation or to the Barraquer tonometer (If the surgeon visualizes a fluid meniscus smaller than the ring of the tonometer this confirms an intraocular pressure of over 65 mmHg).

If adequate suction is not obtained the vacuum pressure should be released and the suction ring reapplied. This pseudosuction is caused by conjunctiva being pulled into the ring orifices preventing suction on the globe.

With an adequate suction and good position, the microkeratome pass is initiated. Different systems have manual (e.g. Moria LSK1 and C-B varieties) or automated passes of the microkeratome head (e.g. Gebauer). A free cap is achieved and the cut free cap is saved until the end of the procedure. A stop ring is not used as we want free flap.

Preparation of the Donor Button

A corneal button with a good scleral rim is necessary for ALTK **(Figure 11-5)**, so that it can be secured on the artificial anterior chamber. The artificial anterior chamber is connected to the hydrostatic system, maintaining required pressure during lenticule removal. The corneal button is placed on the top of the artificial anterior chamber. The cornea is sealed and made leak proof using the locking screw. The applanation lens may help select the diameter of the cornea using the adjustable screw prior to making dissection. The applanation lens has pre-calibrated circular marks to enable the diameter of donor cornea to be calibrated in order to match the corneal button taken from recipient irrespective of its original radius of curvature. The microkeratome guide rests on the top of the artificial anterior chamber maintainer. Once the whole system is assembled and ready, the microkeratome is moved through the guide creating a free flap **(Figures 11-6 to 11-9).**

The donor graft is usually planned at least 100 µm thicker than the recipient lamellar cut. The ideal difference in thickness is not known.

Suturing of the Graft

The donor button thus obtained, is then sutured onto the recipient bed under tension **(Figure 11-10)**. The cone is flattened and a normal corneal shape is restored. Generally 10-0 ethilon interrupted sutures are employed although mixed continuous and interrupted sutures can be used. Interrupted sutures are preferred as the main aim being to achieve a flattening of the cone.

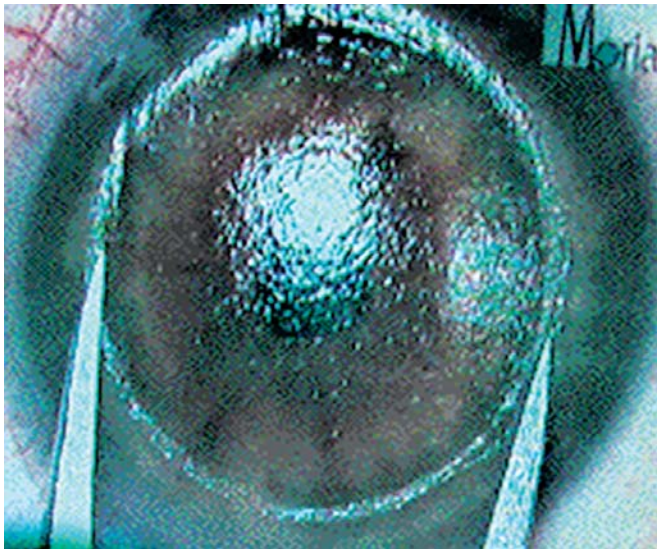


FIGURE 11-5: Measuring exact dimensions.

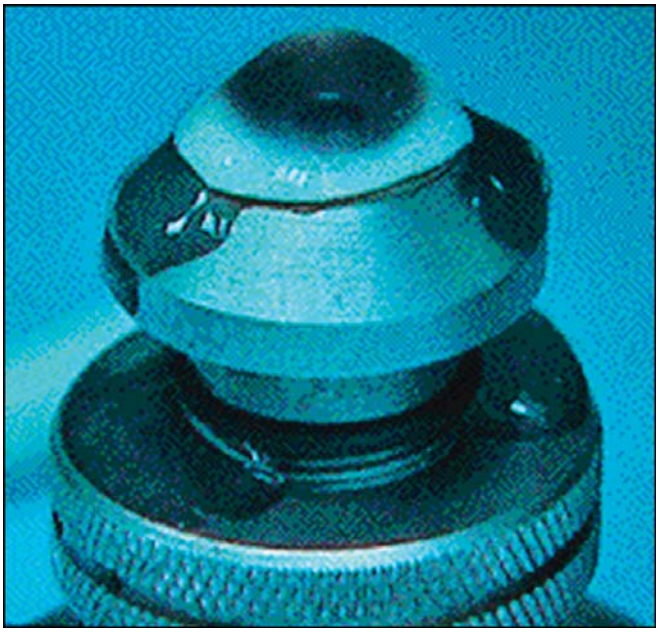


FIGURE 11-6: Corneo-scleral rim mounted on artificial anterior chamber.

FIGURE 11-7: Watertight artificial anterior chamber.

In cases of advanced keratoconus, folds in the recipient bed may result from excessive flattening of the ectatic recipient bed. These folds usually disappear after surgery.

Once sutures are removed, a considerable amount of tension in the corneal structure is released thereby reducing the flattening effect with suture removal. This may even lead to myopic shift.

FIGURE 11-8: Applanation tonometry.

FIGURE 11-9: Obtaining donor corneal button.

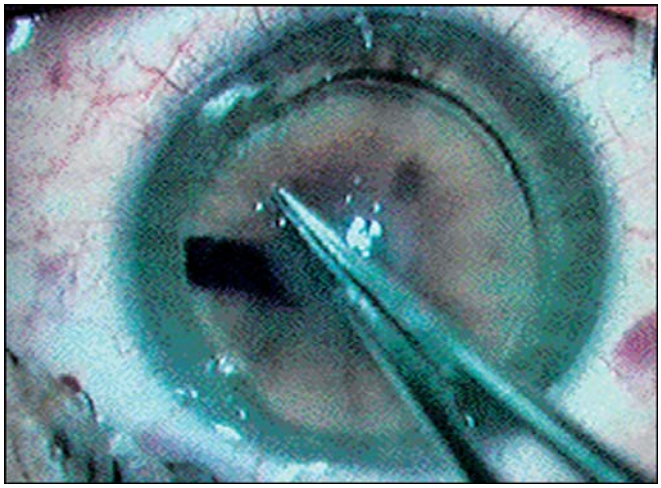


FIGURE 11-10: Apposing corneal graft.

Busin's Technique of Cone Collapse for Moderate to Advanced Keratoconus

Busin has modified the ALTK technique further for the management of more advanced keratoconus.[12,13] The theory is that the residual ectatic lamella of the recipient bed, which resists the flattening action of the donor button is attributable to the recipient bed's "keratoconus memory". If sutures are applied under tension, folds can be produced in the recipient's cornea and can be responsible for an irregular corneal surface postoperatively. To overcome this problem, the technique of cone collapse has proved to very useful.

Once the anterior lamella from the host cornea has been removed, a partial trephination of the recipient bed with typically a 6.5 mm trephine is performed. The trephination is made full thickness in a trefoil pattern, leaving 3 thin tissue bridges at the 4, 8 and 12 o'clock position. As a result, the recipient endothelium attached to a lamella of deep stroma floats freely other than the tissue bridges. The cone in the recipient bed collapses fully and with ease without pushing against the overlying lamellar graft. It simply attaches to it, and no significant tension is required while suturing because no mechanical flattening against a "resistant" ectatic recipient bed is necessary. Under sizing of the donor button is therefore not necessary and usually a 9 mm button in a 9 mm recipient bed is used.

The difference in tissue thickness is maintained, the donor graft being cut at least 100 µm thicker than the excised corneal lamella.

The creation of a 6.5 mm circular vertical incision in the recipient bed, inevitably leaves a scar, which binds together the donor graft and host cornea at the site of trephination. This scar further stabilizes the structure of the cornea.

In a series of patients operated by Busin, 10 out of 11 patients gained visual acuity more than 20/40, with a refractive astigmatism within 4 D. The mean keratometry readings decreased from 61.12 D preoperatively to 42.76 D, one month after surgery.

Advantages of ALTK

The visual recovery time is very rapid (may be days in case of overlay sutures used for opacities) and as the cut made by microkeratome is regular and homogenous, there is less postoperative irregular astigmatism.[9] The interface between the donor graft and recipient bed is completely clear and barely visible even at high magnification of the slit-lamp.

The optical quality of vision is probably better than standard penetrating keratoplasty as there is little irregular astigmatism. The best-spectacle corrected visual acuity (BSCVA) is 20/40 or better in nearly all patients and refractive astigmatism is within 4 D in most cases. It is important to note that the majority of these patients have good BSCVA rather than the need for contact lenses. Given that a number of these patients are intolerant of contact lenses, this is an important benefit.

On the other hand, the equipment is expensive and there is a steep learning curve. There is also a lack of predictability in matching the thickness of recipient and donor corneal buttons.[14] However, the relevance for this when treating keratoconus is unknown because a significant flattening of the cone is achieved.

From the surgeon's perspective, it is an easy procedure to learn especially if they are experienced LASIK surgeon. Reduced interface haze and crisp vision, quick recovery and fast rehabilitation are definite motivating factors for corneal surgeons to adapt to these procedures.[15,16] It is standardized, easy, time-sparing and most importantly eliminates the risk of endothelial rejection.

Epikeratophakia

Epikeratophakia for keratoconus was first introduced in 1982 by Werblin and Kaufman.[17] This was followed by a number of studies including a nationwide study by MacDonald, *et al*.[18,19] It is a simple, reversible, extraocular surgery and has a reduced risk of immunologic reactions. Epikeratophakia has a wide range of possible refractive correction (up to about 30D of hyperopia or myopia). The visual results for epikeratophakia have been reported to be nearly equal or often superior to those of PKP.[20] It has some similarity to ALTK.

TECHNIQUE

The procedure uses a donor human corneal lenticule lathed to the shape of lens using a cryolathe. The lenticules were made in different diameters and power models for aphakia, myopia and keratoconus.[11] The tissue lenses are made in 4 steps consisting of pressing, freezing, lathing and lyophilizing donor corneal tissue followed by storage in a vacuum sealed container. A typical epikeratophakia lens has a central optical zone and a thin peripheral wing which is sutured to hold the lens in place. Most of the lenses were made with a specially developed cryolathe which has a facility for automatically making a smooth transition between the radius of cut used for the optical zone and the radius used for the wing. Alternatively, lenses are made with a single radius of cut, so that the optical zone in these extended to the edge of the lens.

A vacuum sealed vial containing the lyophilized tissue lens is opened and the tissue lens is rehydrated for 20 minutes in BSS with 100 micrograms of gentamicin per millilitre. During rehydration, the green dye that provided visibility during lathing diffuses away and the tissue lens becomes softer and more translucent.

PREPARATION OF THE PATIENT

The visual axis is marked on the cornea. 2% pilocarpine drops are instilled to ensure that the visual axis mark lies over the pupil. The basic technique of epikeratophakia consists of initially removing corneal epithelium, then dissecting a peripheral pocket for the wing of the lens, which is then sutured in place. Thorough removal of corneal epithelium is necessary so that there is no subsequent cellular proliferation at the interface between the epikeratophakia lens and host cornea. Epithelium peripheral to the lens should be left intact, as it is from this peripheral cornea that epithelial regeneration covers the epikeratophakia lens.

Failure of prompt re-epithelialization may be associated with melting of the lens and infective keratitis.

Following de-epithelialization, the next step in the operation is to create a pocket for the insertion of the wing of the lens. A 7 or 7.5 mm diameter Hessburg-Baron suction trephine or manual if preferred is used to make a partial thickness trephination to a depth of about 180 microns. A 21 gauge needle, bent to 90 degrees 2 mm from the end, is used to dissect a pocket, parallel to the corneal surface. Ideally, a 0.5 mm wide and 0.3 mm deep annular keratectomy is performed. Alternatively, pocketing knives are available.

The tissue lens soaked, rehydrated is placed on a Teflon cutting block and punched at 8.5 mm. Since the diameter of the tissue lens is 8.5 mm and diameter of the trephine is 7 mm the tissue lens appears oversized. The excess tissue is required so that the wing of the tissue lens can be placed beneath the corneal surface. For keratoconus tight sutures are tied while an assistant pressed firmly to reduce the ectatic cornea. It is important to take deep tissue bites 0.7 to 1 mm long to hold sutures

tight. The wing of the tissue lens is pushed below the recipient lip so that it lies in the peripheral lamellar keratectomy created by the lamellar dissector. The sutures are left in place unless they became loose or are inducing astigmatism in case of keratoconus.

COMPLICATIONS

The major complications of epikeratophakia are related to delay in epithelialization. With a compromised epithelium and nonviable donor cap, patients are at risk of developing infections, and poor epithelialization can lead to melting of the tissue. Persistent refractive errors and infiltrates at the recipient-lenticule interface are other important issues. A rare complication is dehiscence of the graft. Persistent haze is another postoperative issue.

In a series of patients at Moorfields Eye Hospital,[21] patients who were intolerant to contact lenses underwent epikeratophakia, six out of seven patients (86%) with more than two months' follow-up achieved a good result with BSCVA of 6/9 or better. The remaining patient achieved 6/12 but with a very high cylinder and required penetrating keratoplasty. Results of 1-year follow-up findings on 42 of the first epikeratophakia procedures performed for keratoconus at the Helsinki University Central Hospital showed encouraging results.[22] The mean flattening by keratometry readings was 9.8 diopters (D) and the mean decrease in myopia in terms of spherical equivalent was 5.3 D. The degree of irregular astigmatism was measured in five cases showed that the mean preoperative irregular astigmatism of 3.9 D was reduced to 1.3 D in the long-term analysis.

The noninvasive nature of epikeratophakia makes it a safe and desirable option for the treatment of keratoconus.[23] In properly selected patients, epikeratophakia can effectively be used to treat keratoconus and thus avoid potential intraocular surgical complications and immunogenic phenomena. However, ALTK has overshadowed this technique because the availability of the lamellar graft is much simpler.

Femtosecond Laser

The femtosecond laser is possibly the single biggest innovation in corneal surgery in the past thirty years.[24-28] The main principle of femtosecond is the use of ultrashort infrared laser pulses causing intrastromal microdissection without ablation. Femtosecond employs a solid state laser with a 1053 nm wavelength and uses brief pulses to cause disruption in the lamellar plane. Examples of femtosecond include

Intralase (AMO Santa Ana, USA http://www.amo-inc.com/products/refractive/ilasik/intralase-fs-laser),

Femtec (20/10 Perfect Vision, Heidelberg, Germany http://www.2010pv.com/2010-pv/products/femtec-femtosecond-laser-workstation_100003_0.html),

Visumax (Carl Zeiss Meidtec http://www.meditec.zeiss.com/visumax) and

FemtoLDV (Zeimer, Port, Switzerland http://www.ziemergroup.ch/?id=33).

As the lamellar cut is controlled by software, a variety of shape and configuration of incisions may be easily programmed and can enable us improve indications in corneal surgery. The advantages of femtosecond laser corneal dissection include:

1. Precise cuts
2. Improved mechanical stability
3. Better wound healing
4. Early suture removal
5. Reduced astigmatism due to better apposition.

Different geometric patterns have been used by different surgeons across the world to obtain perfect apposition of the graft in PKP and in lamellar corneal surgery. Angled incision edge facilitates stromal excision with scissors. Interlocking wound configuration facilitates matching anterior donor and recipient surfaces.

Anterior Lamellar Keratoplasty has been performed by Sheraz Daya in an initial series of fourteen patients using zigzag incisions within seventy microns of Descemet's membrane.

Whilst the technology is available to perform lamellar transplants for keratoconus, this is not in routine use as yet.

References

1. Tan D, Ang LPK. Automated lamellar therapeutic keratoplasty for post-PRK corneal scarring and thinning. Am J Ophthalmol 2004; 138: 1067-9.
2. Jimenez-Alfaro I, Perez-Santonja. Therapeutic lamellar keratoplasty with an automated microkeratome. J Cataract Refract Surg 2001;27:1161–5.
3. Anwar M. Dissection technique in lamellar keratoplasty. Br J Ophthalmol 1972;56:711-3.
4. Anwar M. Techniques in lamellar keratoplasty. Trans Ophthalmol Soc UK 1974; 94:163-71.
5. Archila EA. Deep lamellar keratoplasty dissection of host tissue with intrastromal air injection. Cornea 1984/85;3:217-8.
6. Price FW Jr. Air lamellar keratoplasty. Refract Corneal Surg 1989;5:240-3.
7. Manche EE, Holland GN, Maloney RK. Deep lamellar keratoplasty using viscoelastic dissection. Arch Ophthalmol 1999;117:1561-5.
8. Melles GRJ, Lander F, Rietveld FJR, Remeijer L, Beekhuis WH, Binder PS. A new surgical technique for deep, anterior lamellar keratoplasty. Br J Ophthalmol 1999;83:327-33.
9. Vajpayee RB. Automated lamellar therapeutic keratoplasty (ALTK) the treatment of anterior to mid-stromal corneal pathologies. Acta Ophthalmol Scand 2006;84:771-3.
10. Busin M, Zambianchi L, Arffa RC. Microkeratome-assisted lamellar keratoplasty for the surgical treatment of keratoconus. Ophthalmology 2005;112:987-97.
11. Agarwal S, Agarwal A, Apple DJ, Buratto L, Aliò JL, Pandey SK, Agarwal A. Textbook of Ophthalmology, vol 2. Lippincott: Philadelphia, 2002.
12. Busin M. New techniques for the surgical treatment of keratoconus. Ophthalmology Times Europe, January 2005.
13. Tan DT, Ang LP. Modified automated lamellar therapeutic keratoplasty for keratoconus: a new technique. Cornea 2006;25:1217-9.
14. Giaconi JA, Culbertson W. Predictability of donor lamellar graft dimensions in an artificial anterior chamber system with the Moria ALTK microkeratome. Invest Ophthalmol Vis Sci 2003;44: E-Abstract 4682.
15. Tan DT, Mehta JS. Future directions in lamellar corneal transplantation. Cornea 2007;26:S21-S28.
16. Busin M, Arffa RC. Atlas of Microkeratome Assisted Lamellar Keratoplasty. Slack: Thorofare (USA), 2006.
17. Tamaki K, Yamaguchi T, McDonald MB, Kaufman HE. Epikeratophakia for aphakia, keratoconus, and myopia. Br J Ophthalmol 1990;74:67–72.
18. McDonald MB, Kaufman HE, Aquavella JV, et al. The nationwide study of epikeratophakia for myopia. Am J Ophthalmol 1987; 103:375-83.
19. McDonald MB, Kaufman HE, Durrie DS. Epikeratophakia for keratoconus, the nationwide study. Arch Ophthalmol 1986;104:1294-300.
20. Busin M, Bechrakis-Böker I, Denninger U. Surgical therapy of keratoconus. Epikeratophakia versus penetrating keratoplasty. Fortschr Ophthalmol 1991;88:794-6.
21. Halliday BL. Epikeratophakia for aphakia, keratoconus, and myopia. Br J Ophthalmol 1990;74: 67–72.
22. Spitznas M, Eckert J, Frising M, Eter N. Long-term functional and topographic results seven years after epikeratophakia for keratoconus. Graefes Arch Clin Exp Ophthalmol 2002;240:639-43.
23. Dietze TR, Durrie DS. Indications and treatment of keratoconus using epikeratophakia. Ophthalmology 1988;95: 236-46.
24. Sarayba MA, Maguen E, Salz J, Rabinowitz Y, Ignacio TS. Femtosecond laser keratome creation of partial thickness donor corneal buttons for lamellar keratoplasty. J Refract Surg 2007;23:58-65.

25. Jones YJ, Goins KM, Sutphin JE, Mullins R, Skeie JM. Comparison of the femtosecond laser (IntraLase) versus manual microkeratome (Moria ALTK) in dissection of the donor in endothelial keratoplasty: initial study in eye bank eyes. J Fr Ophtalmol 2007;30:689-94.
26. Hoffart L, Proust H, Matonti F, Ridings B, Conrath J. Short-term results of penetrating keratoplasty performed with the Femtec femtosecond laser. Am J Ophthalmol 2008;146:50-55.
27. Mehta JS, Por YM, Cajucom-Uy H, Parthasarathy A, Tan DT. Femtosecond laser for endothelial keratoplasty. J Cataract Refract Surg 2007;33:1141.
28. Suwan-Apichon O, Reyes JM, Griffin NB, Barker J, Gore P, Chuck RS. Microkeratome versus femtosecond laser predissection of corneal grafts for anterior and posterior lamellar keratoplasty. Cornea 2006;25:966-8.

12

Near-Descemetic Deep Anterior Lamellar Keratoplasty (DALK)

Antonio Leccisotti

The author has no financial or proprietary interest in any product or technique mentioned.

Why Near-Descemetic?

Deep Anterior Lamellar Keratoplasty (DALK) has only recently become the standard of care for advanced keratoconus (KC). This is surprising, because we already had the technology for modern DALK at least 20 years ago, and because the many advantages of DALK over penetrating keratoplasty (PKP) in keratoconus are obvious: preserved endothelium, rejection virtually absent, no opening of the anterior chamber (AC), better control of astigmatism. What has really changed is the surgeon's mindset, together with the observation that the 'Holy Grail' of Descemet's membrane baring is not necessary to achieve a good visual result.

Two myths have indeed delayed (and still hamper) the diffusion of DALK as the rational substitute of PKP in KC: the first is that PKP yields better visual results, the second is that DALK is a difficult procedure, reserved to few excellent surgeons, because, without the exposure of Descemet's membrane, the interface recipient stroma/donor stroma would become hazy and cause visual aberrations. Fortunately, both prejudices have been demolished by studies demonstrating that DALK can achieve the same visual results as PKP[1] and that avoidance of Descemet's membrane baring does not affect final visual acuity.[1-3]

Several techniques have been proposed for DALK, using air, viscoelastic, hydration to help dissection.[4-7] One of the most interesting and popular method is the Big-Bubble technique,[8, 9] in which, after partial trephination, air is forcefully injected into the stroma by a needle, to create a big air bubble separating the posterior stroma from the Descemet's membrane. After the excision of most of the stromal tissue, the bubble is anteriorly perforated, and the residual stroma is removed. The Big-Bubble technique has some drawbacks:

1. The big bubble does not occur in 20-50% of cases, depending on surgeons experience, depth of trephination, etc.
2. The last phase of Descemet's membrane exposure carries a high risk of perforation.

The same authors have described an alternative technique ("near-Descemetic" DALK) to use when a big bubble did not form or in the presence of a damaged Descemet's membrane:[10] with this method, after partial trephination and intrastromal air injection, stromal emphysema is used to help manual deep dissection only to a pre-Descemetic stromal plane. This variant is safer and technically easier than Big-Bubble, and has become my preferred technique for DALK in KC.

Indications

DALK is indicated in all cases of KC in which best-corrected visual acuity by spectacles or contact lenses is not satisfactory, and cannot be improved by less invasive surgical techniques. When the cornea is not particularly deformed, myopia associated with KC can be corrected by phakic intraocular lenses (IOLs) in younger patients,[11] and by refractive lens exchange in the presbyopic age;[12] the advent of toric IOLs has improved the visual prognosis of these techniques. Corneal collagen cross-linking by ultraviolet and riboflavin has recently emerged as a para-surgical technique that can improve earlier stages of KC.[13] Intrastromal ring segments do not involve tissue transplantation, can be implanted with femtosecond laser, are reversible and have few complications.[14]

I generally consider DALK when contact lens cannot be worn or yield a corrected visual acuity <0.5, *and* best-spectacle corrected visual acuity is <0.5. Endothelial cell count is not relevant, as long as the stroma is transparent. The status of Descemet's membrane is equally not significant if we adopt a near-Descemetic approach. Corneal thickness is important but does not preclude DALK,

because when facing a thin cornea, we should prepare (surgeon, instruments and tissue) for PKP, but we should first attempt DALK.

Stromal scars, especially at the cone apex, do not represent an absolute contraindication to DALK, especially if superficial (contact lens induced).

Preoperative Work-up

If a correct preoperative assessment is the key for all surgery, this is even more true for DALK in KC. Poor results and dissatisfaction often stem from poor preoperative evaluation, poor planning, poor communication with the patient.

History is mandatory. Amblyopia is not rare in keratoconic eyes, which sometimes start as astigmatic eyes. Best corrected visual acuity with contact lenses, spectacles, and pin-hole (which will often indicate the achievable postoperative visual acuity) are obviously needed before any decision. Undilated and dilated anterior segment slit-lamp examination, intraocular pressure (IOP) measurement and dilated funduscopy should be performed in all cases.

The evaluation of keratoconus is best carried out by corneal topography (videokeratography). Orbscan and Pentacam can be helpful to assess the posterior surface and to obtain a pachymetry map in suspect KC, but in advanced KC these techniques are highly unreliable. Therefore, Placido-based topography remains the golden standard to assess the corneal deformation, the KC stage, and the variations over time. Usually, axial topography gives an overall impression of the KC, tangential topography should be used in contact lens warpage and post-surgical ectasia, and the altitudinal map help localizing the cone apex. When the cornea is so altered that no color coded image is possible, an image of Placido rings should be enclosed in the patient chart.

Corneal thickness is of paramount importance, and should be measured by ultrasounds. Ultrasound pachymetry is fast, inexpensive and highly reliable in all kind of corneas (scarred, edematous, thin); the best pachymetry map is obtained checking at the slit-lamp the position of the probe tip. The important points to measure are the corneal geometrical center, the presumed apex, and the 4 cardinal points at 4 mm from the center, where the trephination will take place. In lid squeezers or in poorly collaborating patients, pachymetry should be repeated in the operating theatre after the induction of anesthesia.

The evaluation of corneal endothelium by specular microscopy should be done, but in my experience is of a limited value, apart from the rare association keratoconus/endothelial dystrophy,[15] in which the endothelial cell density can be so poor that a PKP is directly planned. In such cases, the endothelium has the classical beaten silver appearance at slit-lamp, and specular microscopy will confirm the finding by showing dark rounded areas (corresponding to guttae) circumscribed by a thin brighter net **(Figure 12-1)**. In plain KC, dark or defocused images can result from severely deformed corneas **(Figure 12-2)**, but, as long as the stroma is transparent, a near-Descemetic DALK can be performed, even in the presence of Descemet's ruptures, despite a sub-normal endothelial cell density. A DALK with a postoperative cell density of 1200 cell/mm^2 is always better than any PKP, and, should such a cornea decompensate, a PKP can be performed later with the same success rate and at an elder age.

Ultrasound biometry can be used to predict, with a large approximation, the postoperative spherical equivalent (SE). Eyes with a normal axial length normally end between -1 and -3 diopters (D) SE. In eyes with long axial length a myopic outcome should be anticipated to the patient, thus helping him/her to understand the need for postoperative spectacles and contact lenses.

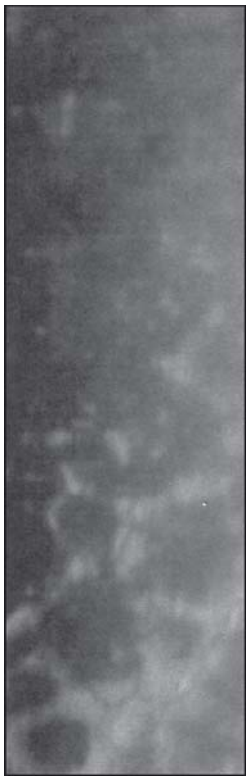


FIGURE 12-1: Endothelial specular microscopy in endothelial dystrophy associated with keratoconus. Darker areas correspond to guttae.

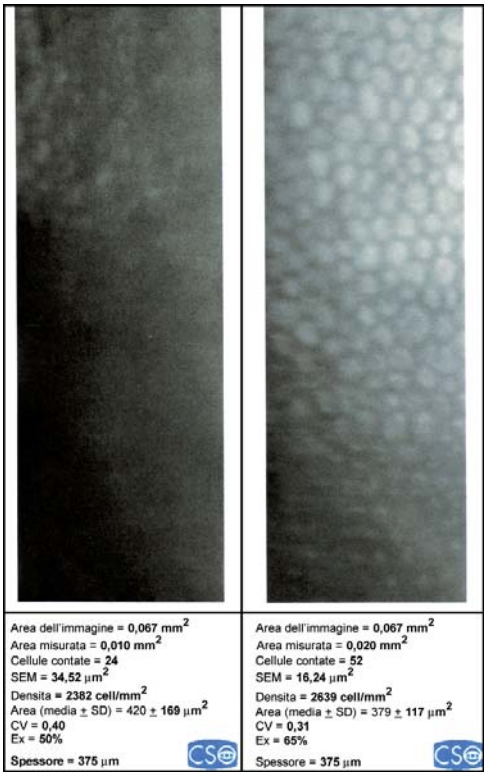


FIGURE 12-2: Endothelial specular microscopy in advanced keratoconus. Inferiorly, the darker, defocused area corresponds to the protrusion.

Informed Consent

KC, and even only the diagnosis itself of KC, has a very negative impact on the quality of life. The young age, the progression of disease, possible heredity, the lack of a cure, the belief that a transplantation will be ultimately needed, the fear of blindness, of surgery, of pain, of rejection: in this scenario, informed consent cannot be a bunch of papers to sign. A long explanation of the disease and of all the possibilities of treatment in the specific case must be presented. All irrational fears must be washed away, one by one. Optimism is the final message, because we are offering the patients a real solution of their visual impairment, but we should not induce exaggerated expectations.

A balanced preoperative discussion will mention the following points:

a. DALK can intraoperatively become a PKP. This is rather likely in thin corneas (<300 micron) and at the beginning of the surgeon's learning curve, but is rare in thicker corneas. I generally tell patients that the chance of conversion to PKP is 1/20, but that PKP, despite being more invasive, will solve their problem as well.
b. After DALK, glasses, contact lenses or refractive surgery are needed. Emmetropia is indeed exceedingly rare, and a variable amount of astigmatism should be expected. Provisional glasses and contact lenses can be prescribed after 2-3 months, when some tightest sutures can be safely removed. Refractive surgery (by excimer laser, phakic IOLs or refractive lens exchange) will only be possible 2 months after removal of all sutures (i.e. approximately 14 months after surgery).
c. Major complications, such as infections, rejection, graft opacity are very rare and are generally well managed by topical treatment or repeat DALK.

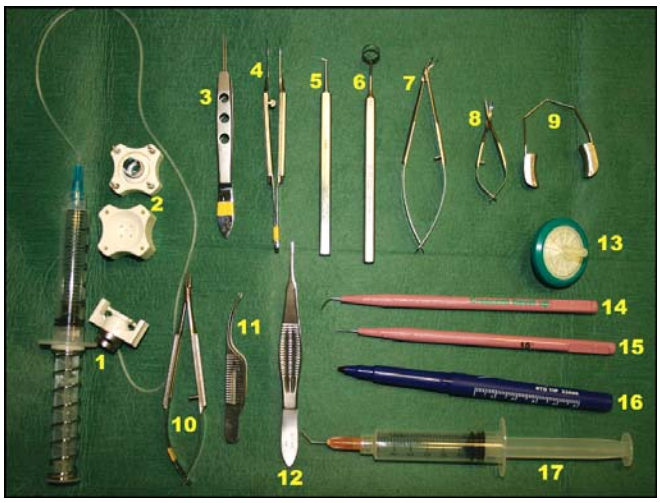


FIGURE 12-3: Main instrumentation for DALK. 1) Hessburg-Barron trephine, 2) Barron Punch, 3) straight tying forceps, 4) curved tying forceps, 5) 0.5 mm gauge, 6) 8 mm marker, 7) curved corneal scissors, 8) blunt Vannas scissors, 9) solid blade speculum, 10) needle holder, 11) small forceps, 12) bigger forceps, 13) air filter, 14) crescent bevel up blade, 15) 15° blade, 16) violet gentian felt tip pen, 17) luer-lock syringe with bent 25-gauge needle.

Instrumentation

Near-Descemetic DALK requires a simple set of instruments, by which the eventuality of PKP can be addressed as well **(Figure 12-3)**:

- disposable Hessburg-Barron trephine (Altomed, Tyne & Wear, England), 8 mm diameter
- disposable Barron punch (Altomed, Tyne & Wear, England), 8.25 mm diameter
- a Barraquer solid blade eyelid speculum (Sir, Italy, E-10011)
- a bevel-up crescent knife (Alcon)
- a 15° blade for possible paracentesis
- a needle-holder with curved head for 10-0 sutures
- 2 tying forceps (1 straight, 1 curved) of excellent quality
- a smaller and a larger straight forceps
- an 8 mm round corneal marker with central cross
- a violet gentian felt tip pen
- a straight Vannas scissor with blunt tip (of excellent quality, to be checked at microscope)
- 2 curved scissors for corneal transplantation (1 right, 1 left), with lower blade internal and upper blade external (in case of PKP, the lower blade will only damage the endothelium that is removed) (e.g. Sir, Italy, C928)
- a 5 cc syringe with luer-lock connection, and a 30-gauge needle
- an air filter
- ophthalmic cohesive viscoelastic (such as Pro-Visc, Alcon), only needed for PKP
- a guarded diamond blade, only needed in case of shallow trephination
- 10-0 nylon suture with curved needle
- a 0.5 mm gauge (PMS, Germany, E15-225)
- Maloney surgical keratometer
- Merocell sponges
- balanced salt solution (BSS) for irrigation and anterior chamber reformation in case of perforation
- an AC cannula.

Donor Tissue

One of the main advantages of DALK is tissue availability. Donor tissue with endothelium that is unusable for PKP can be safely destined to DALK. The problem at the beginning of the surgeon's learning curve is the possibility of conversion to PKP. The suggestion of planning in the same session a DALK and a PKP is highly unpractical, especially because PKPs will hopefully decline in the future. It is therefore necessary, at least for the first cases, to use a donor tissue with an endothelial status also appropriate for PKP.

The donor age is, in any case, not relevant.

Anesthesia

Excluding as absolutely inappropriate topical anesthesia, the choice is between general and infiltrative anesthesia. The surgical procedure is particularly long in the first cases (my first DALK lasted 3 hours), becoming only a little faster with experience (never less than 1 hour). In addition, eye and head movements should be avoided by all means in many delicate phases. The preference goes therefore to general anesthesia, which reduces patient's and surgeon anxiety. A peribulbar block can still be employed in selected cases: expert surgeon *and* very calm patient, or contraindications to general anesthesia.

Surgical Technique

1. The periocular skin is cleaned with 10% povidone iodine, and 2 drops of 5% povidone iodine are instilled in the conjunctival sac and over the cornea. The eyelids and cilia are isolated by the surgical adhesive drape and by adjunctive adhesive strips. The cornea should be well exposed and in a vertical gaze position.
2. An 8 mm circular marker tinted with gentian violet is centered on the geometrical center of the cornea and applied to the epithelium **(Figure 12-4)**.
3. The Hessburg-Barron trephine is inspected under the microscope, and its blade (inner metal circle) is aligned with the suction ring (intermediate metal circle) **(Figure 12-5)**, and then turned back (anti-clockwise) of a full turn, to avoid immediate contact of the blade with the cornea.
4. The syringe connected to the trephine is held by the assistant, air is expelled and the plunger is kept pushed. The cornea must be not too wet, nor too dry.
5. The surgeon puts the trephine on the cornea, holding it vertical with the thumb and the forefinger of the non-dominant hand, checking its centration with the ink marks under the microscope **(Figure 12-6)**.
6. The assistant releases the plunger and suction is checked by slow movements of the trephine. If centration is incorrect or suction is not valid, steps 4 and 5 must be repeated.
7. With the forefinger of the dominant hand, the trephine is slowly turned clockwise. The first full turn will bring the blade in contact with the cornea, then each subsequent full turn will produce a circular cut of the depth of 250 micron. With a peripheral thickness of 500 micron, a full turn and a half (approximately 400 micron) are advised. The center of the cornea is constantly checked, and if a drop of fluid (aqueous) is unexpectedly seen, the suction is immediately released.
8. After completing the partial trephination, suction is released, and the depth of trephination is checked by a blunt instrument, such as a large cyclodialysis spatula or a 0.5 mm gauge. If the cut

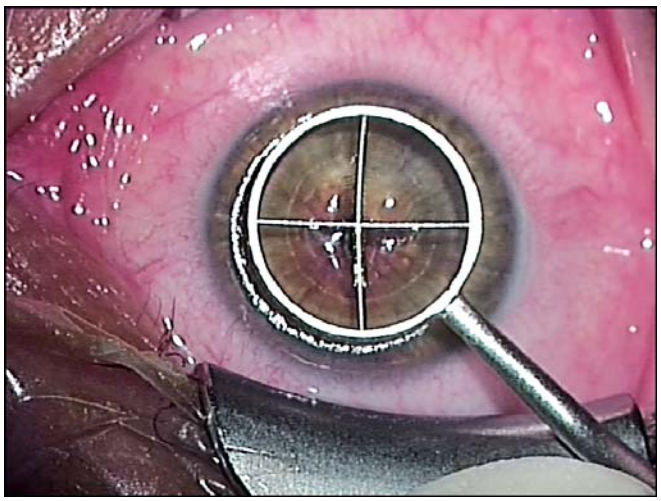


FIGURE 12-4: Marking of corneal geometrical center and of 8 mm.

FIGURE 12-5: Alignment of the trephine blade (yellow) with the internal edge of suction (pink).

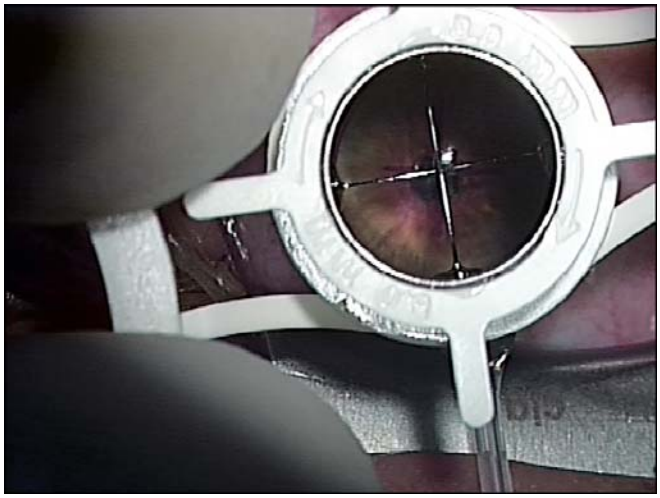


FIGURE 12-6: Host trephination to 400 microns.

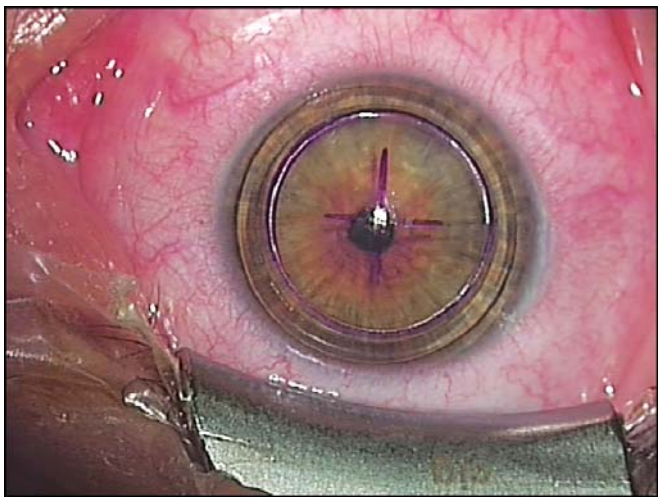


FIGURE 12-7: Completed partial trephination.

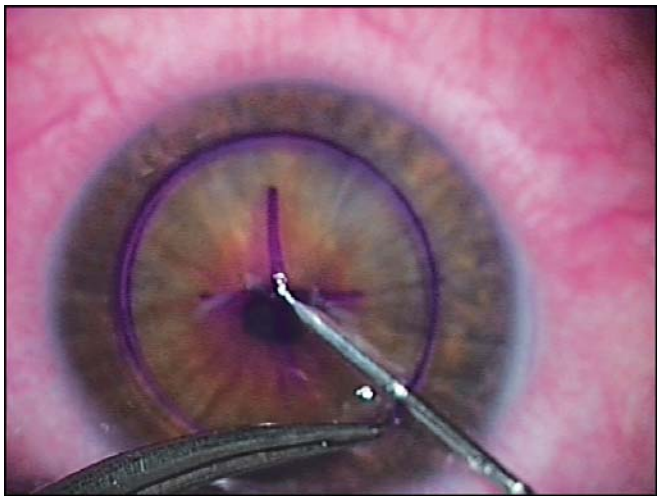


FIGURE 12-8: Insertion of the bent 25-gauge needle at approximately 2/3 of stromal thickness.

is unduly shallow (because of bad suction or wrong calculation of trephination), it should be deepened by a guarded diamond blade, set at 400 micron (or less, in case of thinner cornea). It is important that, at least superiorly, the cut is deep enough for needle insertion and for the first dissection **(Figure 12-7)**.

9. A 5 cc syringe is filled with sterile air and is locked to a 30 gauge needle, which is bent under the microscope by a needle-holder at approximately 8 mm from the tip, forming a 100°-110° angle, with the bevel down. I prefer a large diameter such as 30 gauge to achieve easier penetration along the corneal planes, and to have a more efficient air penetration in the stroma.
10. The needle is inserted at 2/3 of stromal thickness in the stroma, usually at 10 or 11 o'clock for right handed surgeons, holding the central corneal button with a forceps. The needle is advanced slowly but firmly, following a corneal plane, reaching the corneal geometrical center, but avoiding the cone if possible **(Figure 12-8)**.
11. The syringe plunger is pushed with a constant pressure to inject intrastromal air. The stroma will whiten only after 2-3 cc of air have been injected. Usually, the center will whiten first, then air will find its way to the rest of the cornea in a very irregular and variable pattern, often

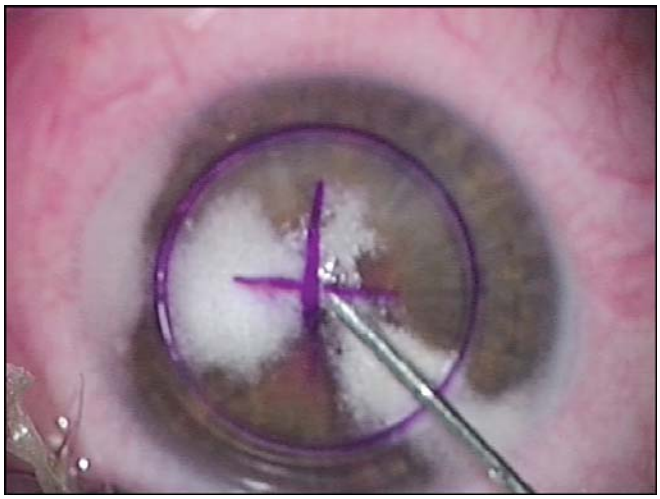


FIGURE 12-9: Intrastromal air injection.

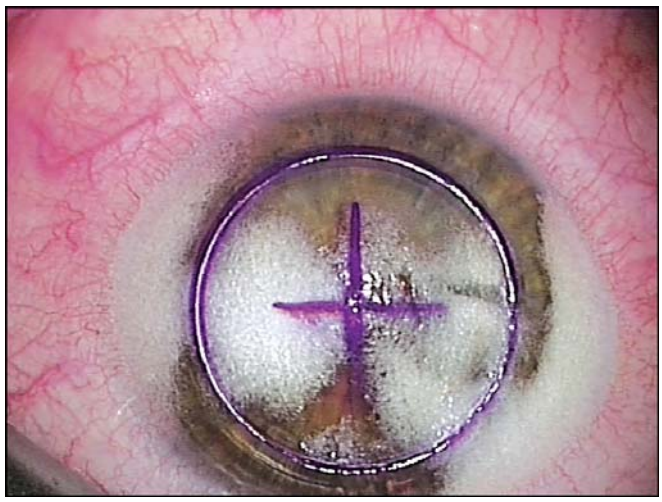


FIGURE 12-10: Stromal emphysema.

escaping through the trephination, and when the cut is shallow, reaching the limbus **(Figures 12-9 and 12-10)**. It is best to stop air injection if the limbus starts to whiten, otherwise air will reach the anterior chamber through the trabecular meshwork in the form of small bubbles. These bubbles are not dangerous, but may impair the vision of the last corneal layers in the ultimate phases of stromal dissection. If the cornea has only partially whitened, the needle can be retracted and air injected in the remaining part, but this maneuver is not needed if the central cornea is emphysematous. It is important not to insist with air injection when the central cornea has whitened, to avoid the creation of a big collection of air beneath the stroma (the Big Bubble).

12. The needle is retracted, and the excision of the anterior stroma is performed with a bevel up crescent blade. In this phase a rather thick portion of stroma should be removed, to speed the procedure. The blade is inserted superiorly at approximately ¾ of the stromal depth and maintained at the same level all over **(Figures 12-11 and 12-12)**, sliding safely within a same stromal plane. When reaching the trephination, the blade should undermine for 1-2 mm its external edge, to allow good external apposition of the sutured margins despite their different thickness **(Figure 12-13)**. The button is peripherally excised by corneal round scissors **(Figure 12-14)**.

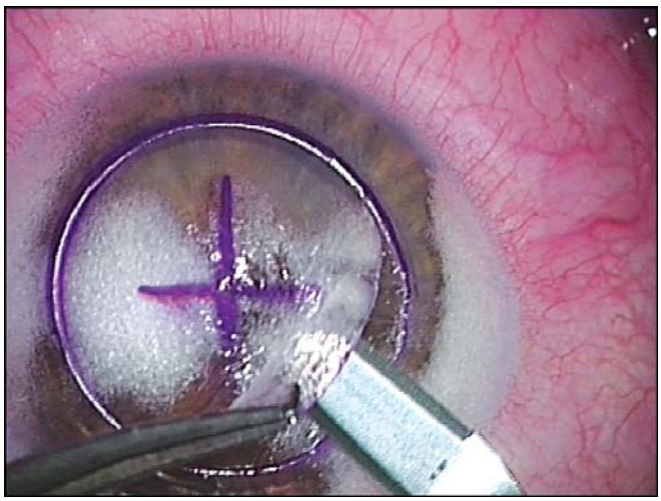


FIGURE 12-11: Beginning of anterior stromal dissection by a crescent blade.

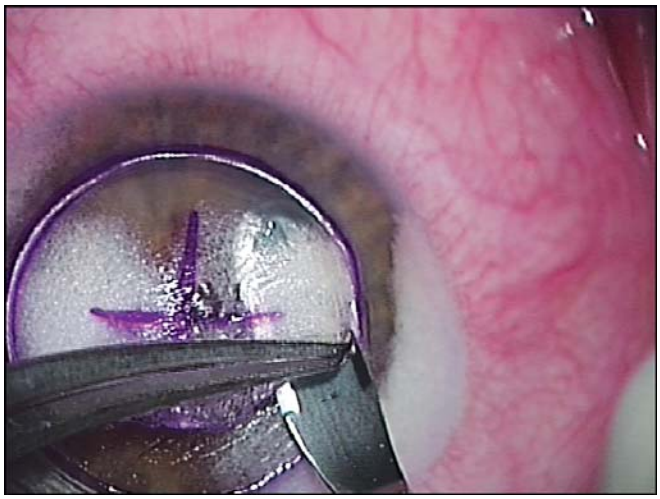


FIGURE 12-12: Anterior stromal dissection by a crescent blade.

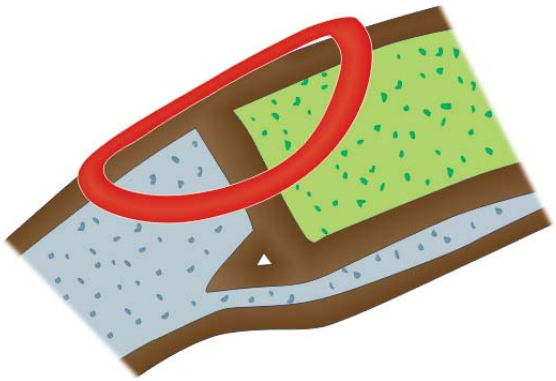


FIGURE 12-13: Undermining the anterior dissection allows good alignment of the external surfaces.

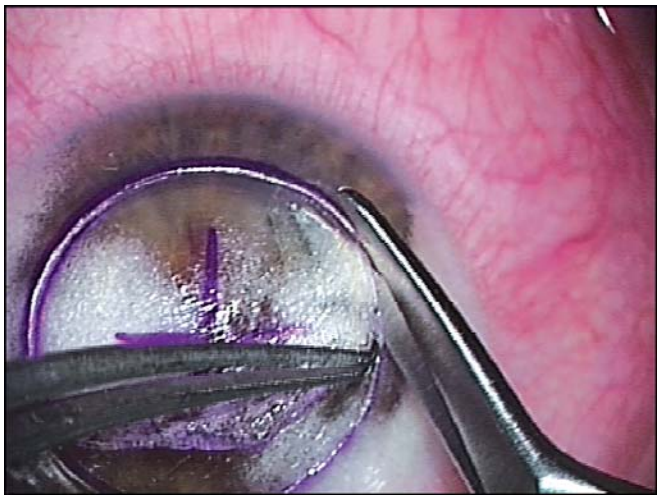


FIGURE 12-14: Anterior stromal dissection: excision by scissors.

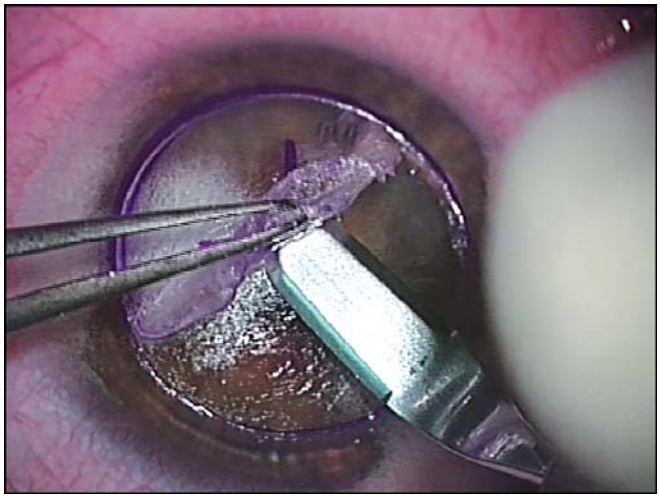


FIGURE 12-15: Anterior stromal dissection in the center.

13. After the thicker stromal button is excised **(Figure 12-15)**, a more delicate excision of one or two additional thin stromal layers is performed. It is easier to start this dissection superiorly, where the first dissection was begun: there, the stromal bed is normally thick enough to grasp it with delicate forceps and partially penetrate it with the bevel up blade **(Figures 12-16 to 12-18)**, this time only dissecting the central 6-7 mm **(Figure 12-19)**. A more peripheral dissection is only needed if we realize that the first dissection was too shallow by indirect clues, e.g. the stromal bed is still white from emphysema or is still thick at the edge of trephination. With experience, it is possible to have an idea of the depth of excision, but it is not particularly important (and is much less safe) to reach the Descemet's membrane.
14. The donor button is laid upon the cutting block of the Barron punch with the endothelium up, and is centered under the microscope. The punch is then gently applied, and the position of the donor cornea checked again. The punch is finally pressed uniformly with both thumbs and forefingers **(Figure 12-20)**, until a characteristic crunching noise is heard. The punch is pressed again in each of its quarters, and is finally removed, leaving the cut donor button on the cutting block. If the corneal rim is still attached in some part to the central button, the cut should be completed by corneal scissors.

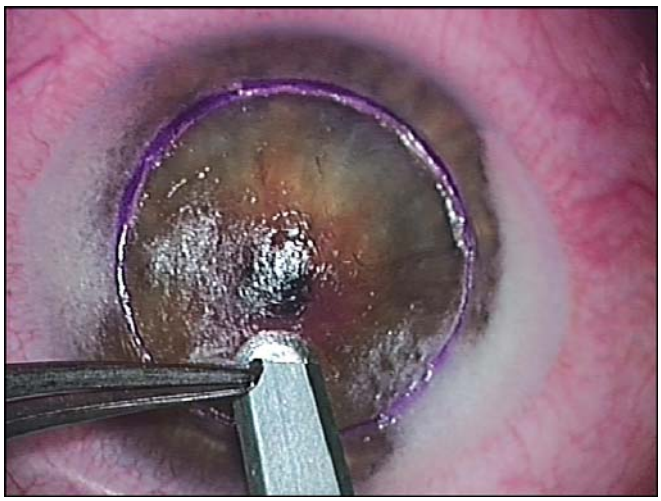


FIGURE 12-16: Beginning of deeper stromal dissection by a crescent blade.

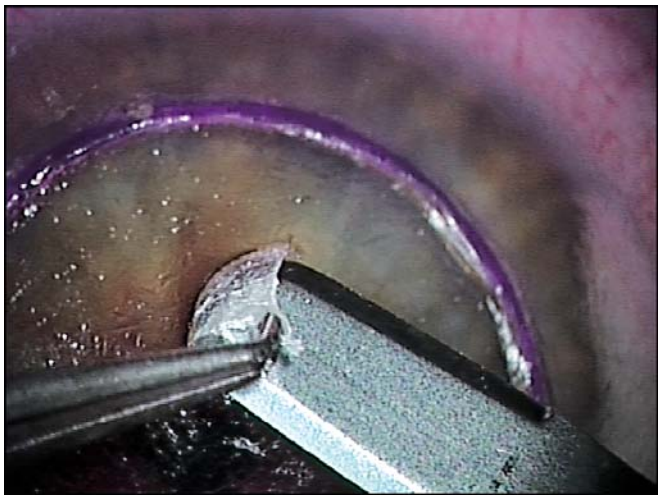


FIGURE 12-17: Deeper stromal dissection in the center.

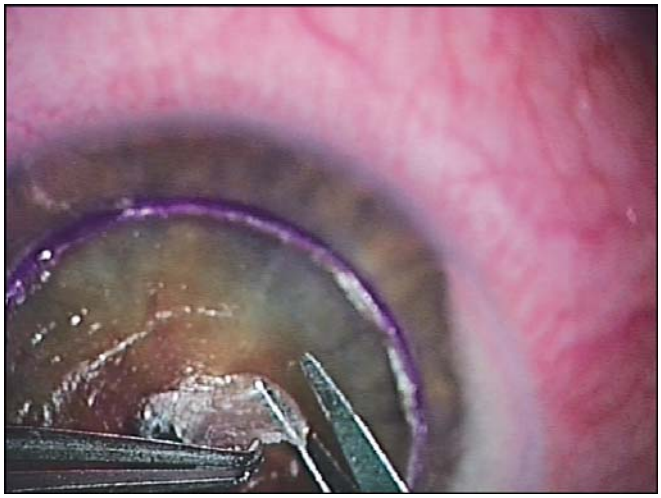


FIGURE 12-18: Deeper stromal dissection: excision by scissors.

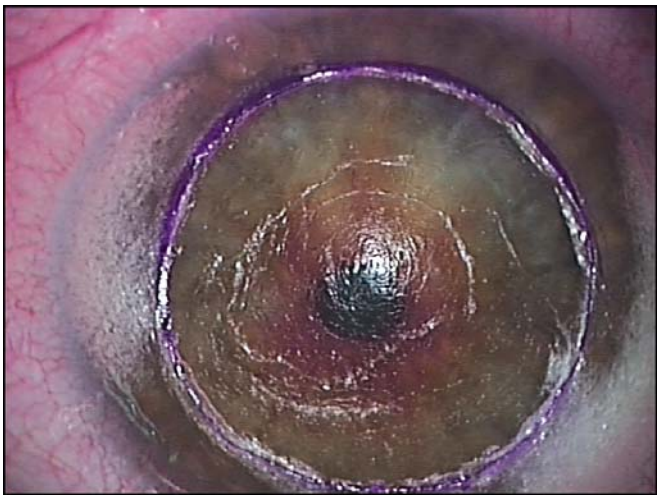


FIGURE 12-19: Completion of deeper stromal dissection in the central 5-6 mm.

FIGURE 12-20: Punching of donor cornea.

15. The endothelial side of the donor button, still on the cutting block, is gently dried with a Merocell sponge and the endothelium marked with small dots of the felt tip pen, to help its full removal **(Figure 12-21)**. The cutting block is held firmly on a steady surface by the assistant, and, under the microscope, the surgeon holds the edge of the stroma with larger forceps, and pinches the central Descemet's membrane with delicate forceps. It is much easier to start this maneuver from the center, as only the Descemet's membrane will be caught by the forceps **(Figure 12-22)**. On the contrary, when peeling is started from the button's edge, it is not uncommon to pinch stromal tissue as well. The Descemet's membrane is peeled away, usually in a piecemeal fashion, more rarely as a whole, because its fragility and its stromal attachments are rather variable **(Figure 12-23)**.
16. The prepared donor button retains its convexity and it is therefore easily laid upon the stromal bed. Suturing is best done by sixteen 10-0 nylon interrupted sutures. The needle is first passed in the donor, not at full thickness, and then in the recipient, as deep as possible to avoid a protruding edge **(Figure 12-24 to 12-26)**. Usually, the knot is 3:1:1. There is no need for excessively tight sutures; the suture must approximate well margins and not be loose by all means, but

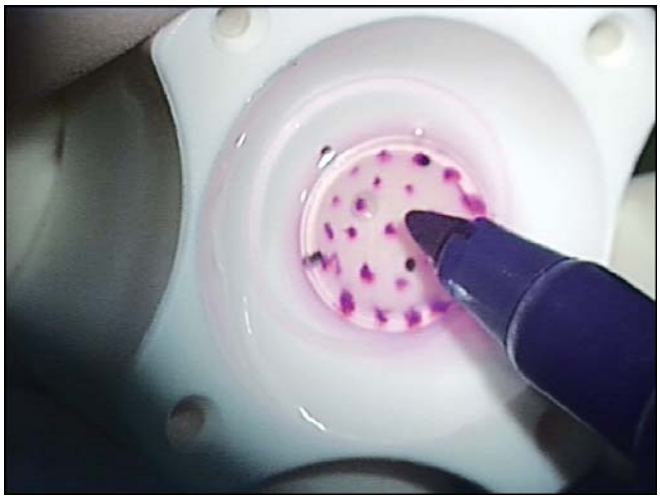


FIGURE 12-21: Painting of donor endothelium.

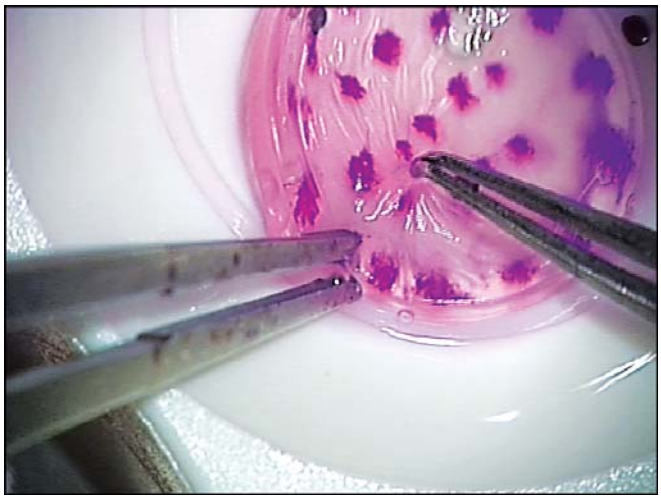


FIGURE 12-22: Beginning from the center of the peeling of donor endothelium and Descemet's membrane.

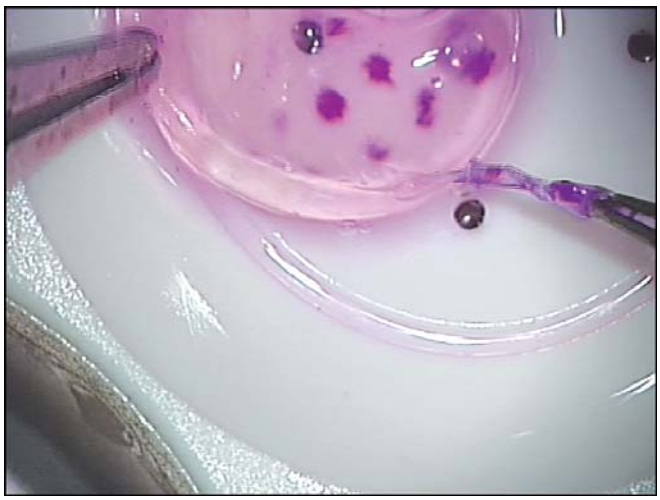


FIGURE 12-23: Completion of the peeling of donor endothelium and Descemet's membrane.

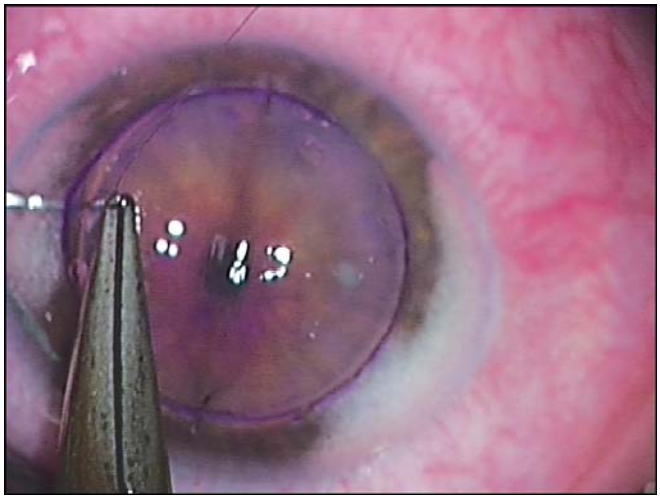


FIGURE 12-24: Host-donor suturing.

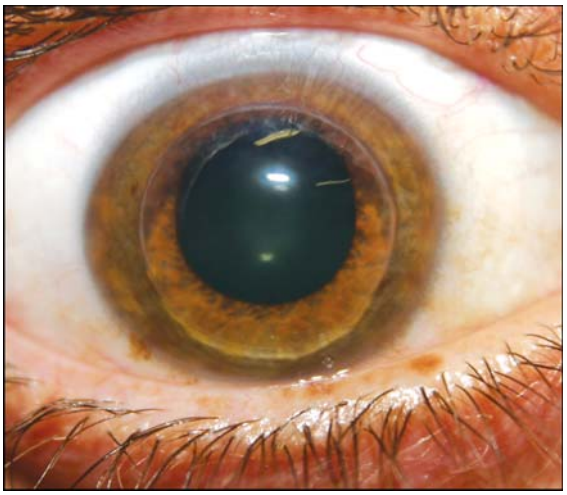


FIGURE 12-25: Prominent edge of donor button, due to poor alignment of margins.

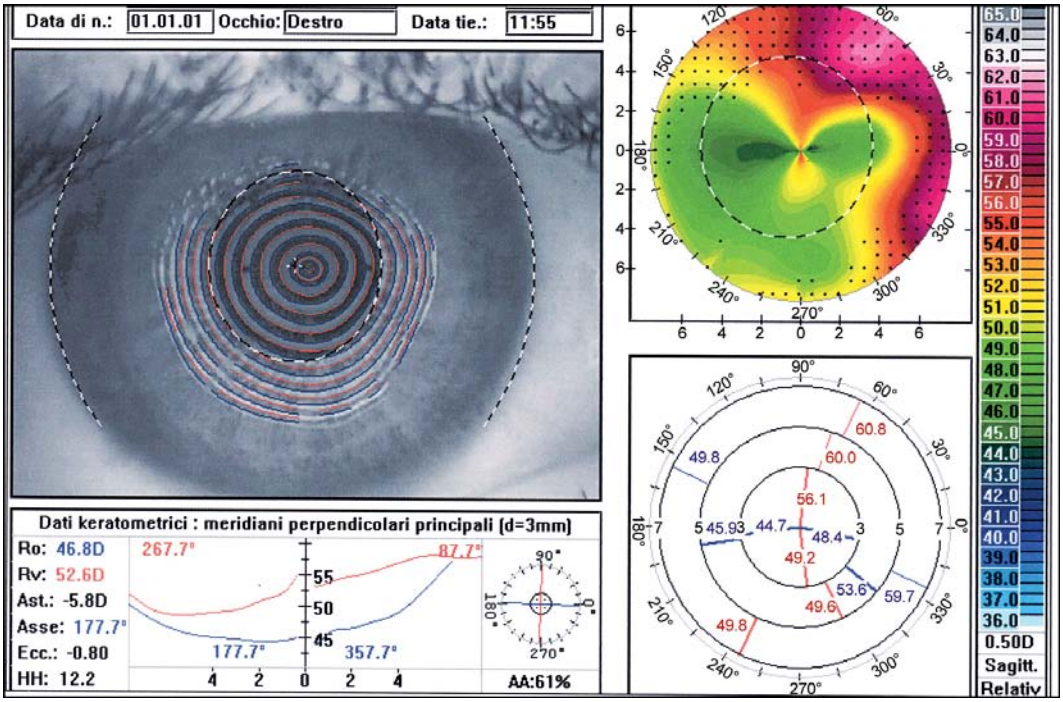


FIGURE 12-26: Axial topography revealing irregular astigmatism (case of Figure 12-25).

should not create excess tension. The 2 first sutures are of paramount importance, as they should perfectly align the button. At the end of suturing, a Maloney keratometer can reveal excessively tight sutures by indentation of circles towards the corneal center **(Figure 12-27)**. However, it is generally unnecessary to repeat sutures; tight sutures can be more precisely addressed in the postoperative period. Suture ends are buried in the recipient side of the cornea, to help later safe removal at slit-lamp **(Figure 12-28)**.

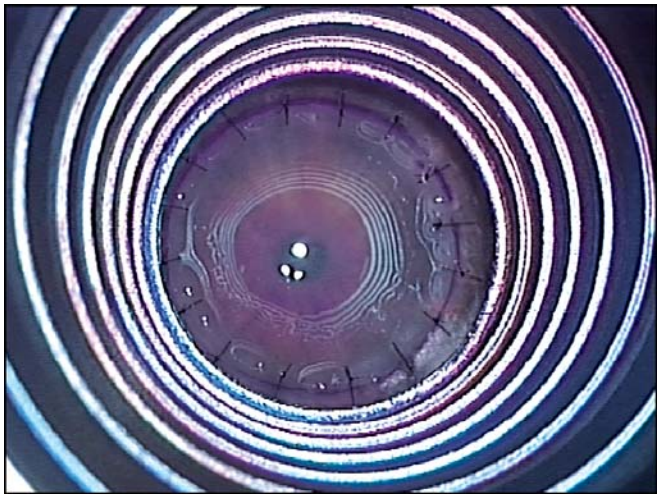


FIGURE 12-27: Intraoperative check of astigmatism by Maloney keratometer.

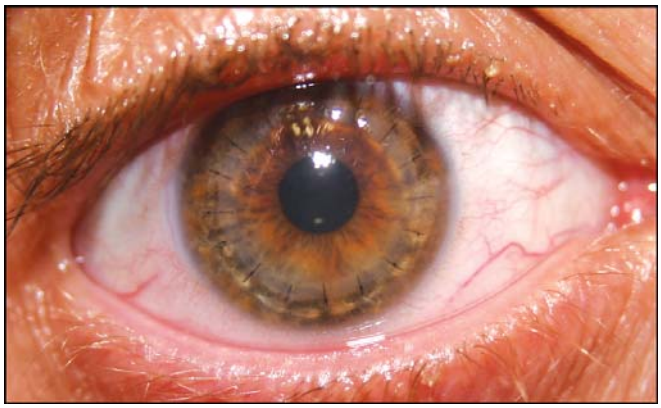


FIGURE 12-28: Five days after DALK. The suture knots are buried in the host cornea.

Postoperative Care

The first postoperative week is characterized by re-epithelialization of the donor button. The donor epithelium is often gradually replaced by the overriding recipient epithelium, but sometimes, when the donor epithelium has a weak adhesion, large epithelial defects are slowly covered by the advancing recipient epithelium. This process is normally easy and uneventful, but it must be frequently checked and facilitated by frequent (every 2 hours when awake) lubrication with a preservative-free gel and topical preservative-free antibiotics and steroids. Our preference goes to unpreserved netilmicin and dexamethasone, 5 times daily until full reformation of a transparent epithelial layer. Should epithelialization be delayed, a softer unpreserved steroid such as fluorometholone can be temporarily used. A bandage contact lens is usually unnecessary and carries an increased risk of infections.

After full epithelialization, topical dexamethasone or betamethasone should be used 4 times daily for 2 to 3 months, then treatment can be switched to loteprednol, 4 times daily for 3 to 4 months. I usually continue with fluorometholone, 3 times daily, until the 9-10th month.

The follow-up of uncomplicated DALK, apart from suture management, is usually simple and with no surprises. The advised schedule is day 1, day 5, month 1, 2 , 4, 6, 8, 10, 12 (suture removal), 14, and then twice a year. The patient must be instructed to call at once in case of redness, pain, blurred vision: these are 99% of times symptoms of a loose suture, which must be removed at once.

When a significant refractive error exists, temporary spectacles can be prescribed as soon as the tightest sutures are removed, i.e. 1-2 months. Rigid gas permeable and even soft contact lenses can be prescribed at 3-4 months, with the usual attention to avoid suture exposure.

Management and Complications of Sutures

The rules with DALK sutures are few but mandatory.

a. *Remove at once all loose sutures*, at any moment. Loose suture do not serve their purpose, collect mucus, may cause inflammation, rejection, neovascularization, and ultimately corneal melting **(Figures 12-29 to 12-31)**. Be prepared to do this in the office, by always keeping a sterile good tying forceps (the suture can be cut by the tip of a sterile needle, any size).

b. *After 1-2 months, excessively tight sutures can be gradually removed,* to improve astigmatism. It is uncertain whether timely addressing tight sutures will change the final astigmatism, but it surely has an immediate visual and psychological benefit for the patient. Tight sutures are recognized at topography by a red area overlying the suture itself **(Figures 12-32 and 12.33)**. It is not wise to remove 2 adjacent sutures before the 3rd month, to avoid the risk of wound dehiscence.

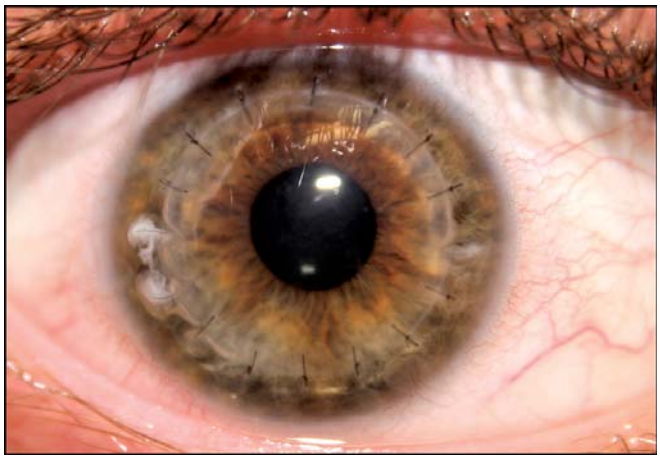


FIGURE 12-29: Loose and exposed sutures at 3 and 9 o'clock. At 9 o'clock, moderate peripheral melting is seen.

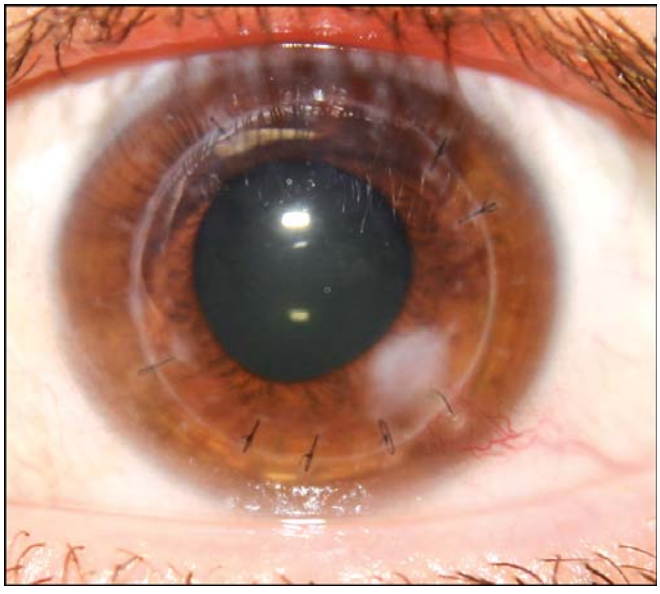


FIGURE 12-30: Donor button abscess and corresponding peripheral neovascularization caused by a loose suture at 4 o'clock.

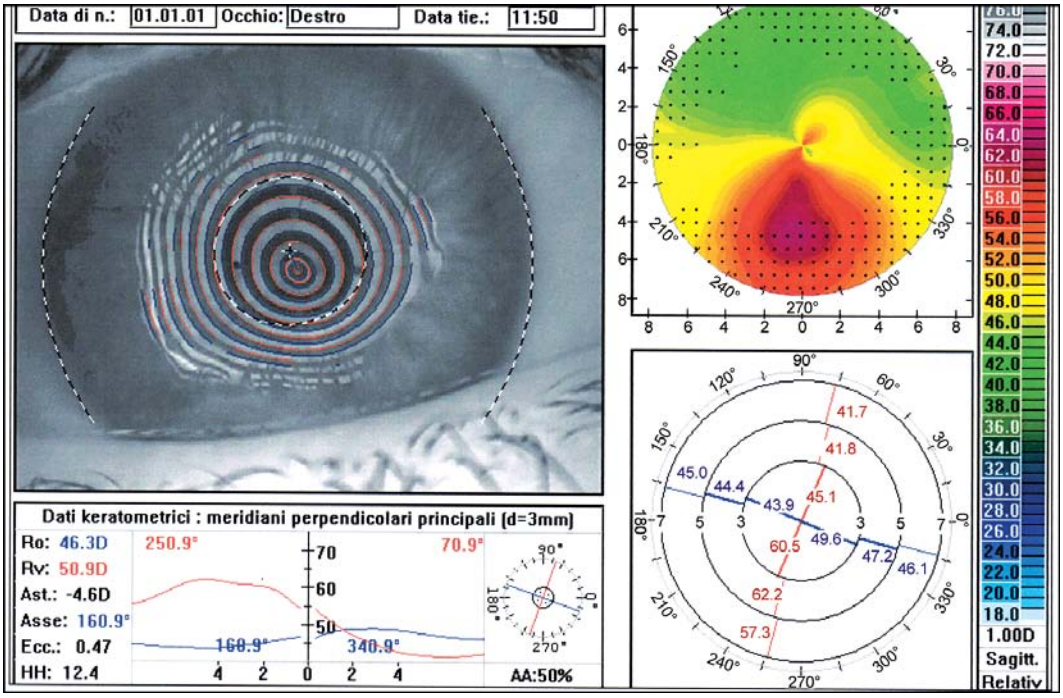


FIGURE 12-31: Effect of a localized donor melting on an axial map, resembling to recurrent keratoconus.

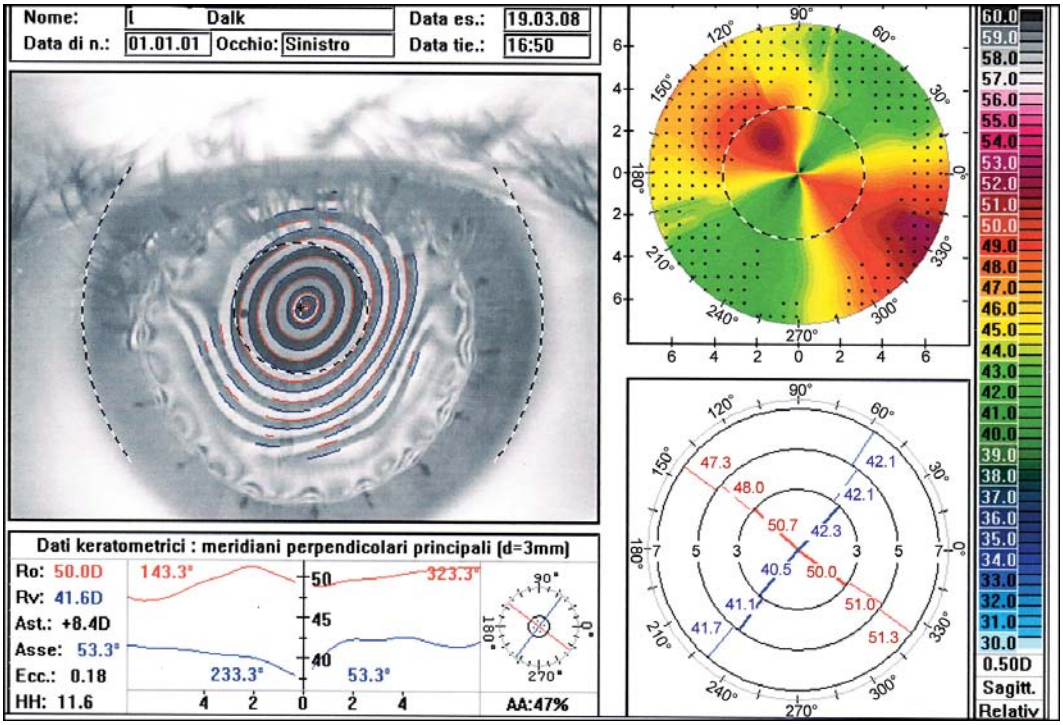


FIGURE 12-32: Tight interrupted sutures at 3 and 4 o'clock cause 8.4 D astigmatism on axial topography, showing high curvature over the corresponding sutures.

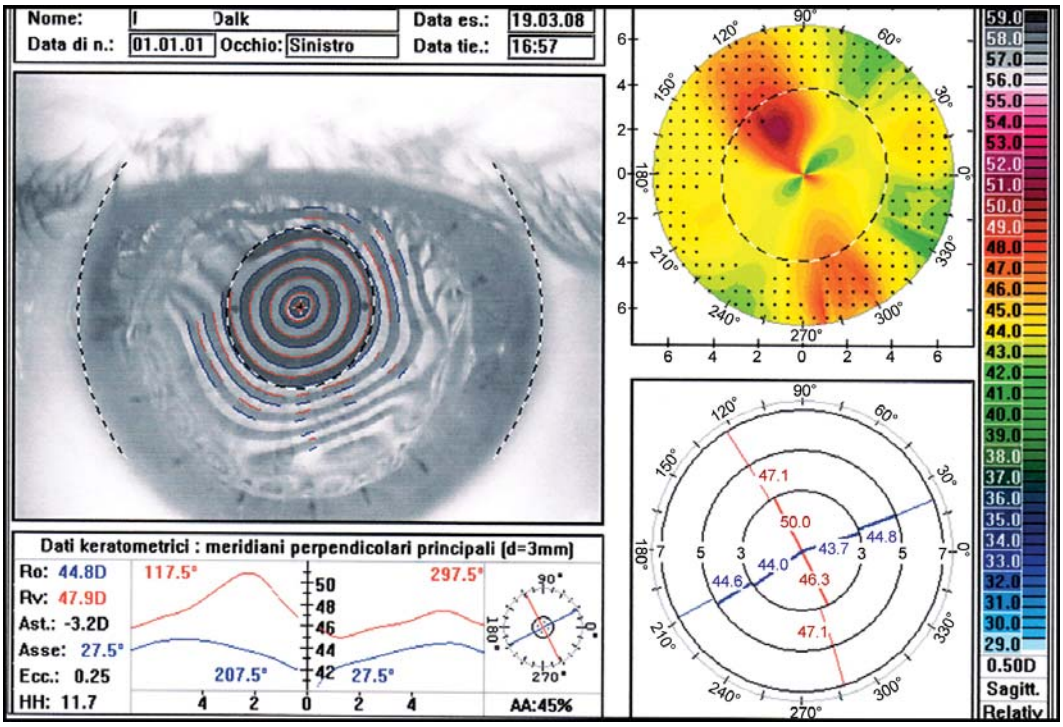


FIGURE 12-33: After removal of the sutures at 3 and 4 o'clock, astigmatism has rotated and reduced to 3.2 D (case of Figure 12-32).

c. *All sutures must go out at 12 months.* To remove all sutures earlier than 12 months can misalign the wound margins, and to wait after 12 months will only make the nylon fragile and difficult to remove. We should not hope that nylon will stay there forever with no complications; it will often break up and the ends will emerge from epithelium.

I currently never use continuous sutures. Continuous sutures are impressive on photographs and are easy to put and to remove, but they have 2 important drawbacks. First, if they loosen early, they have to be fully removed and made again. Second, they cannot be gradually removed at the slit-lamp to improve astigmatism, and a very tight suture has to stay there for months **(Figures 12-34 and 12-35)**.

Perforation

The most feared intraoperative complication is perforation of the Descemet's membrane. This event is not disastrous, but completion of DALK can become difficult or impossible, and a cascade of further complications may arise. Some surgeons readily abandon DALK when facing a perforation, while others struggle to avoid conversion to PKP. The latter attitude is highly justified by the good overall prognosis of perforation, although endothelial damage may result from surgical maneuvers used to maintain the AC formed.[16]

Perforation during Trephination

Perforation can occur at different surgical stages. Perforation during trephination is particularly annoying, but can still be managed. It is revealed by aqueous regression during trephination, which should immediately be stopped and suction released. The first step is to suture the part of trephination

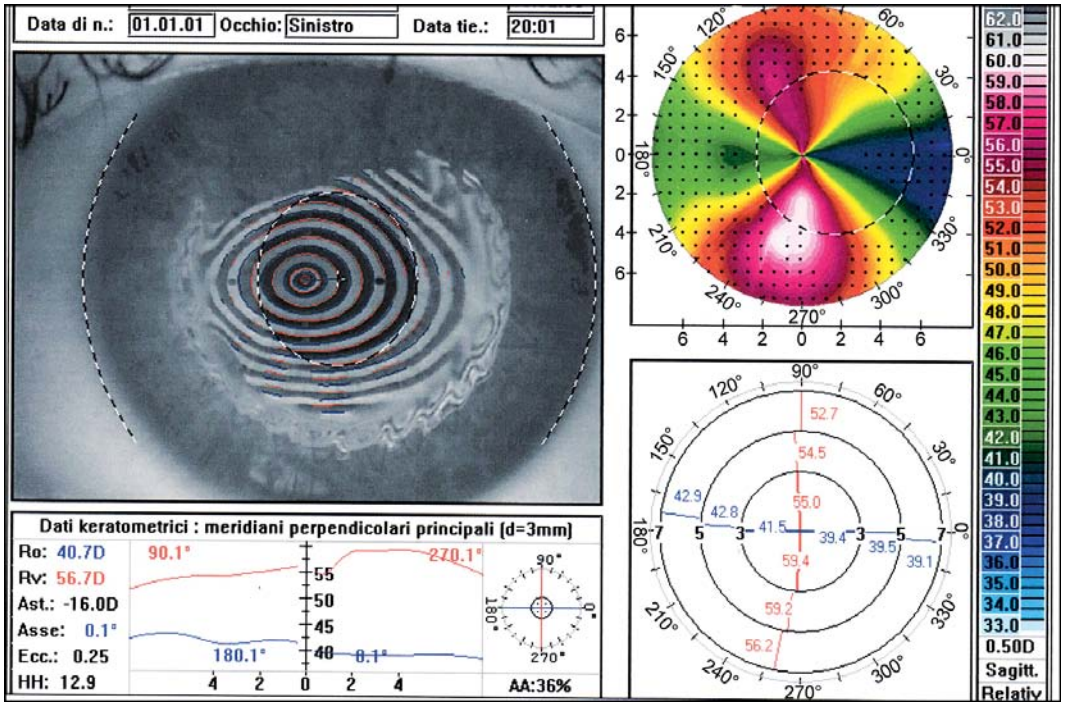


FIGURE 12-34: Tight continuous suture, causing very high astigmatism on axial topography.

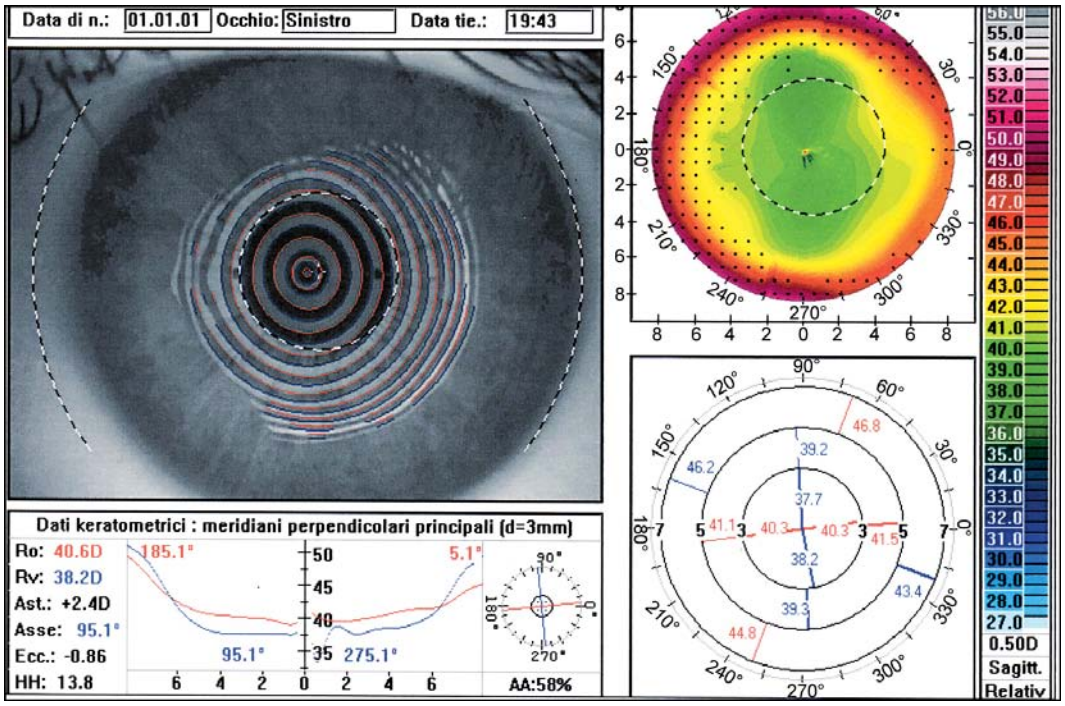


FIGURE 12-35: After removal of the suture, the cornea has returned to an acceptable astigmatism (case of Figure 12-34).

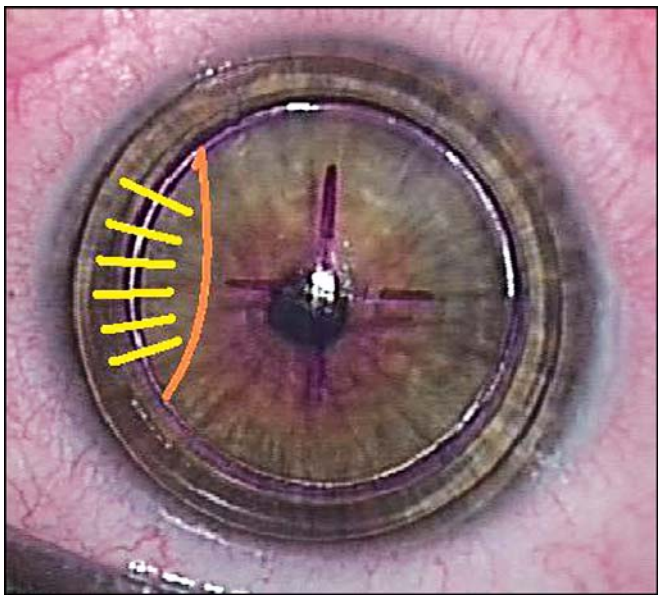


FIGURE 12-36: In case of perforation during trephination, the perforated area should be closed by interrupted sutures, and dissection carried out, leaving a small ellipse of the host button until the last phases.

leaking aqueous with several 10-0 interrupted nylon sutures, not excessively tight **(Figure 12-36)**. A paracentesis is made with a 15° blade and AC is reformed by air. The intrastromal injection of air is still possible, but it should be carried out from the site opposite to that of perforation, very delicately, stopping as soon as air directs toward the perforated area. The others steps are normally performed, but from time to time reformation of the AC may be needed. The anterior dissection and the deep dissection are stopped at 3 mm from the perforation, to leave the suture undisturbed in a small stromal ellipse. The corneal button excision is completed by corneal scissors.

The donor button is prepared as usual, laid on the recipient bed with an edge overlying the ellipse, and fixated with 10-0 nylon sutures in the other quadrants. Finally, the sutures in the remaining ellipse are removed, and the donor button is sutured in the perforated area with deep bites on both margins. Additional sutures may be required to keep the AC formed; in the meanwhile some suture may become loose and must be redone. At the end, the AC is reformed with BSS and a couple of minutes is waited to check whether anterior chamber is maintained. If in doubt, the AC is reformed by air, but the bubble should not completely fill it, and all measures should be taken to prevent an air-induced intraocular pressure (IOP) rise (see below).

Perforation during Air Injection

This complication is exceedingly rare, and is due to excessive or abrupt pressure on the syringe plunger in the attempt to create a big bubble, or to a very deep insertion of the needle. It is never seen with standard near-Descemetic DALK.

Perforation during Stromal Dissection

This complication usually occurs after the removal of the anterior stroma and during deep dissection maneuvers. It is a common occurrence during the learning curve, but it becomes rarer and rarer when the surgeon learns to avoid excessively deep dissections. Continuation of DALK essentially depends on the extent of perforation and on the amount of dissection already performed. If dissection is deemed sufficient and the perforation is small, the AC is reformed by air and the donor button is

sutured. If the dissection is not advanced but the perforation is small, repeat air injection are needed to keep the AC formed while completing dissection, if the subsequent maneuvers do not enlarge the rent. On no account leave the AC completely filled with air, to prevent an air-induced IOP rise (see below).

When perforation is too large to keep the AC formed by any means, DALK should be abandoned and a PKP performed. Hopefully, you have an appropriate donor cornea (corneas exclusively for DALK generally have an endothelial cell density of 2000 – 2400 cell/mm^2). The first thing to do is to punch the donor button (obviously leaving the endothelium in place!). Then the remaining recipient stromal bed is excised, penetrating it with the 15° blade in the trephination groove, filling the AC with viscoelastic, and then completing the circular cut with scissors. Attention should be paid not to leave a transparent Descemet's membrane in place, although this occurrence is more commonly seen with the big bubble technique. The donor button is laid upon the iris, over a layer of viscoelastic, and is sutured by the preferred technique. Also in PKP interrupted sutures retain their advantage, although knot burying is slightly harder, and suture tension less uniform.

DOUBLE ANTERIOR CHAMBER

This term refers to the presence of an aqueous layer between the recipient Descemet's membrane and the donor stroma, resulting from an intraoperative perforation in the former. The complication is generally observed the day after surgery, and its evolution can vary from spontaneous absorption[17] to a permanent condition, causing diffuse stromal edema **(Figure 12-37)**. It is reasonable to wait for a few days in the hope of spontaneous improvement, but usually intervention is needed, in the form of the injection in AC of air or a mixture of air and gas (with 10% of C3F8, or 18% of SF6) to tampon the Descemet's tear, and in a supine position, until the aqueous is absorbed. Atropine should be used to avoid pupillary block. The gas should stay in the AC for at least 8 days, and should not fill more than 75% of AC volume.[18] This procedure may suffice or need repetition; in some cases, the double AC is never absorbed (especially with inferior breaks) and PKP is ultimately needed **(Figure 12-38)**.

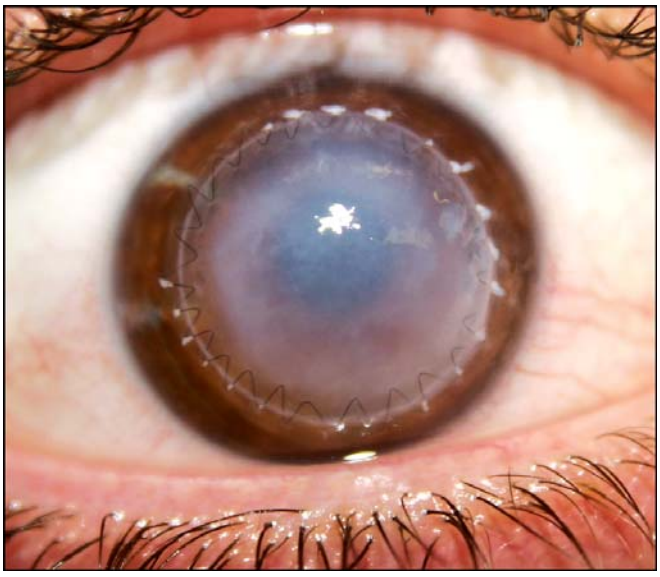


FIGURE 12-37: Donor button edema caused by a double anterior chamber, 2 weeks after DALK. The discolored iris at 9 and 10 o'clock has been provoked by cannulas inserted in the attempt to reform the anterior chamber.

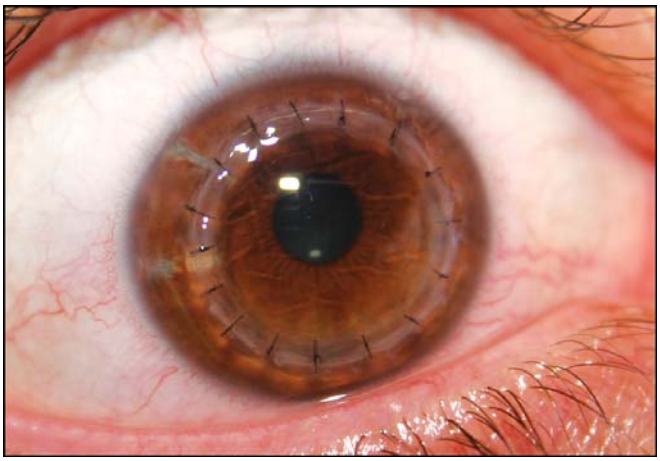


FIGURE 12-38: Penetrating keratoplasty to solve double anterior chamber was performed 1 month after DALK (case of Figure 12-37).

AIR-INDUCED ACUTE INTRAOCULAR PRESSURE RISE

Intraoperative Descemet's membrane perforation forces the surgeon to leave an air bubble in the AC. If large, this bubble may induce an acute IOP rise, similar to that described in the Urrets-Zavalia syndrome after PKP.[16, 19] The mechanism, though sometimes referred as pupillary block, is partly due to peripheral adhesion of iris to the AC angle, caused by the bubble surface tension. The symptoms are those of acute angle closure, with eye and forehead pain, and nausea. The eye is red, and the iris is centrally deformed by the posterior surface of the bubble, and is peripherally attached to the cornea.

The treatment is immediate evacuation at the slit-lamp of the air bubble by an insulin syringe without plunger, after topical anesthesia. This maneuver can be difficult because of the patient's general conditions and because of the iris peripheral position. Care should be taken to retract the needle as soon as a small amount of air is evacuated. Nd:YAG laser iridotomy is less risky but often impossible because of the iris adhesion to the peripheral cornea. If untreated or treated late, high IOP usually resolves in 12-24 hours, when the air bubble is partially absorbed. Long-term sequelae are the classical anterior subcapsular opacities and atrophic, permanently dilated pupil **(Figures 12-39 and 12-40)**. Cataract surgery and iris reconstruction by 2 or more 10-0 prolene sutures can however restore good visual function **(Figure 12-41)**.

From the points above, it is clear that air-induced acute IOP rise must be avoided by all means. This complication is successfully prevented, in case of perforation, by: a) moderate use of air in CA (avoid if AC can be maintained with BSS); b) atropine; c) hourly check of pupil dilation.

UNNOTICED BIG BUBBLE

This rare complication occurs when a big air bubble, inadvertently created between stroma and Descemet's membrane during stromal air injection, is not recognized at surgery. Deep dissection is then carried out, without reaching the air bubble depth. One of the clues is an increased tension on the recipient stromal bed, which can make final suturing difficult, as sutures must be excessively tightened to hold the donor button in place. In addition, a big air bubble is often surrounded by a whiter round edge. If in doubt, create a paracentesis and inject in the AC a few small air bubbles, which will stay in the center if no big bubble exists (and the posterior corneal profile is concave), or in the peripheral AC if a big bubble exists (and the posterior corneal profile is convex).[20]

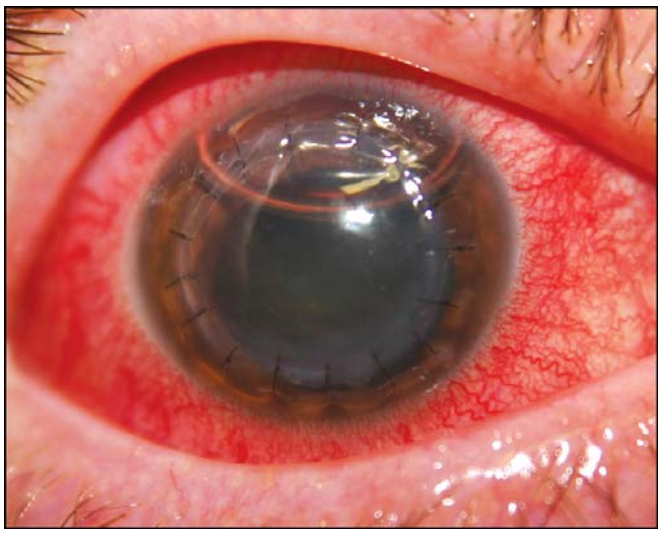


FIGURE 12-39: Twelve hours after an air-induced IOP spike, ciliary hyperemia and fixed dilated pupil.

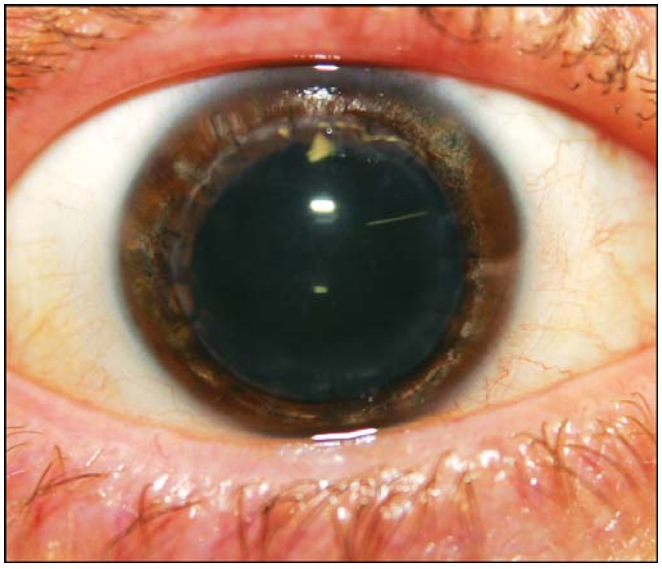


FIGURE 12-40: Two weeks later, iris dilation and atrophy is evident, as well as anterior 'spilled milk' subcapsular opacities (case of Figure 12-39).

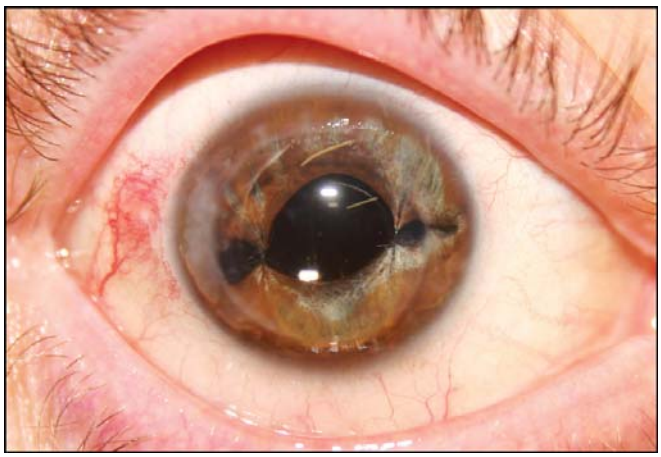


FIGURE 12-41: One year later, after phacoemulsification and iridoplasty by three 10-0 prolene sutures, best-corrected visual acuity is 0.9, with no glare (case of Figure 12-39).

If a big bubble exists, careful and slow excision must follow, until air exits. Both the air bubble and the AC have a high pressure, so the danger is that, when the bubble is pierced, the Descemet's membrane is suddenly pushed towards the blade and punctured. When the bubble is not excised, acute IOP rise can follow, just as when excess air is left in the AC. At the slit-lamp, the presence of a big intrastromal air bubble is unmistakable; the peripheral iris is adherent to the cornea. Eye and forehead pain and nausea are present. After topical anesthesia, evacuation at the slit-lamp of the air bubble by an insulin syringe without plunger should be immediately done, by passing the needle between 2 sutures and under the donor button, perforating the recipient stromal layer over the bubble. The risk is sudden decompression and perforation of Descemet's membrane, with subsequent double anterior chamber, therefore the needle should be inserted quite peripherally and quickly retracted.

REJECTION

Rarely, stromal rejection can occur after DALK.[21] These rejections are usually benign, and respond well to topical steroids if promptly treated. Cases of stromal opacification or melting are however reported.[22] In such cases, the donor button is excised and replaced with a new button, and immunosuppression by topical steroids and oral cyclosporine is recommended for 6 to 12 months.

The prevention of rejection is based upon follow-up, removal of loose sutures, avoidance of pregnancy and vaccines in the first year, patient education to report immediately by phone redness, discomfort, decreased vision.

FOREIGN BODIES

The enclosure of gauze filaments and other foreign bodies in the interface should be prevented by avoiding cleaning instruments by gauze and by only using Merocel sponges for cleaning the operative field. Despite all attentions, the presence of postoperative interface foreign bodies is rather common, but should not raise any concern, because they are usually well tolerated and do not induce inflammatory reactions **(Figure 12-42)**.

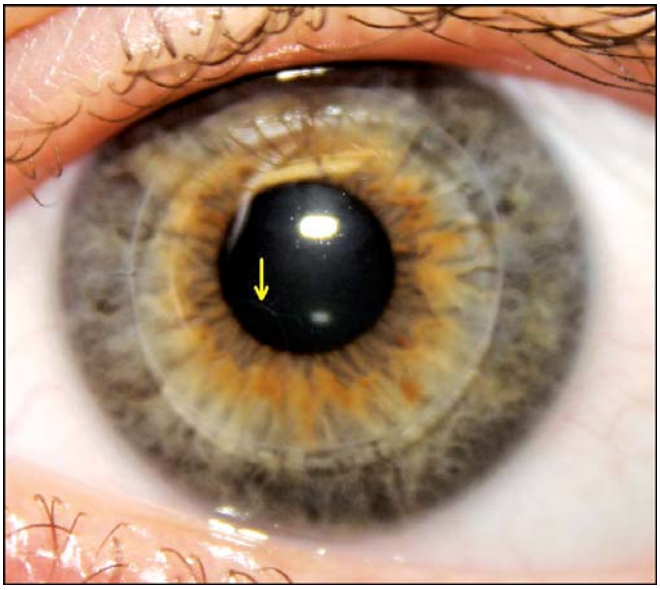


FIGURE 12-42: Well tolerated small gauze thread in the interface, 16 months after DALK.

Refractive Surgery after DALK

When all sutures are removed, our commitment with DALK is not finished yet. A significant refractive error is often present, and spectacles or contact lenses are not always tolerated because of high astigmatism or anisometropia or contact lens intolerance. The post-DALK cornea is usually thick and healthy enough to allow secondary refractive procedures.

High mixed astigmatism can be addressed by astigmatic keratotomy (AK). This technique is simple and relatively safe, but not very predictable in DALK, and sometimes result in a slightly irregular pattern **(Figures 12-43 and 12-44)**. I had some cases of unexpected overcorrection despite a prudent attitude. Therefore, a gradual approach is advised, aiming to reduce the astigmatism by half and leaving space for enhancements by the same technique. Obviously, these limitations must be fully explained to the patient. Astigmatic keratotomy is performed by a guarded diamond blade within the donor button, at an optical zone of 6 mm. The blade is set approximately at full thickness minus 30 micron. Several passes are done to cut the tissue 'bridges' that remain after a single pass. The procedure is done on a dry cornea to immediately recognize any aqueous leakage. The tendency to overcorrection in DALK can be explained by the weaker donor-host adhesion, compared with PKP, in which undercorrection after AK is common and due to the fibrous ring.

Myopic astigmatism and myopia can be treated by LASIK or surface ablation, with the same correction limitations that these techniques have in normal cornea. Astigmatism after DALK is not always regular, and corneal biomechanics differ from that of a normal cornea; therefore, predictability of both spherical and astigmatic components is acceptable but lower than in normal corneas. In addition, surface ablation after DALK stimulates haze formation, and should be only performed with the intraoperative application of mitomycin-C at the concentration of 0.2 mg/ml (0.02%) for 60 seconds. With photorefractive keratectomy (PRK) and mitomycin-C I had satisfactory results, with

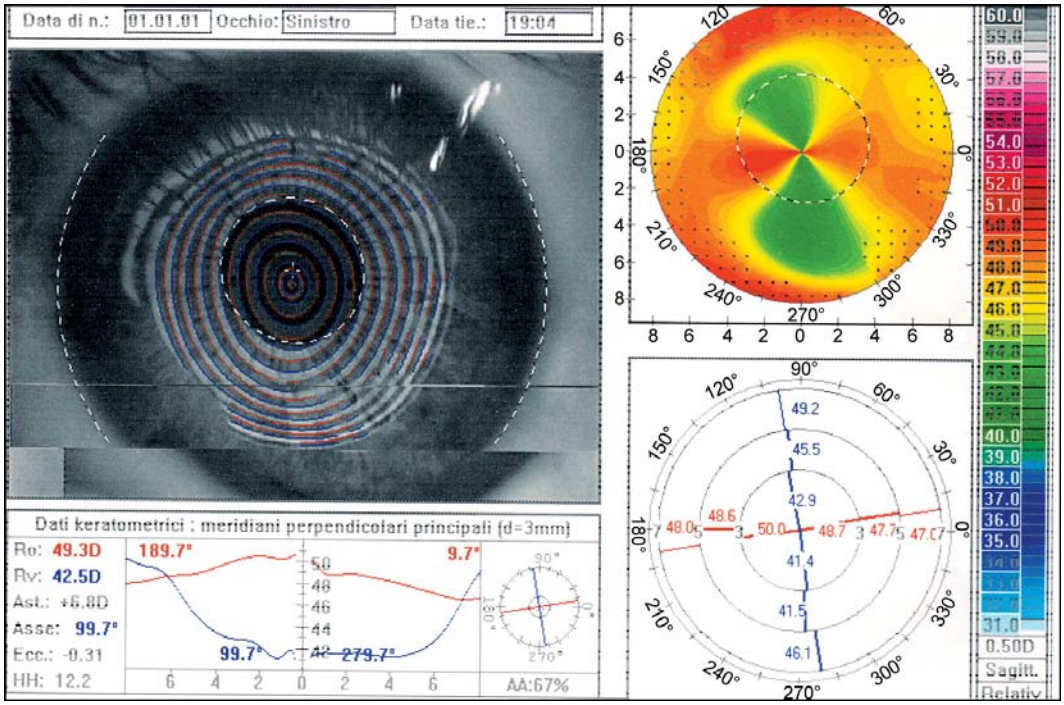


FIGURE 12-43: High regular astigmatism 2 years after DALK.

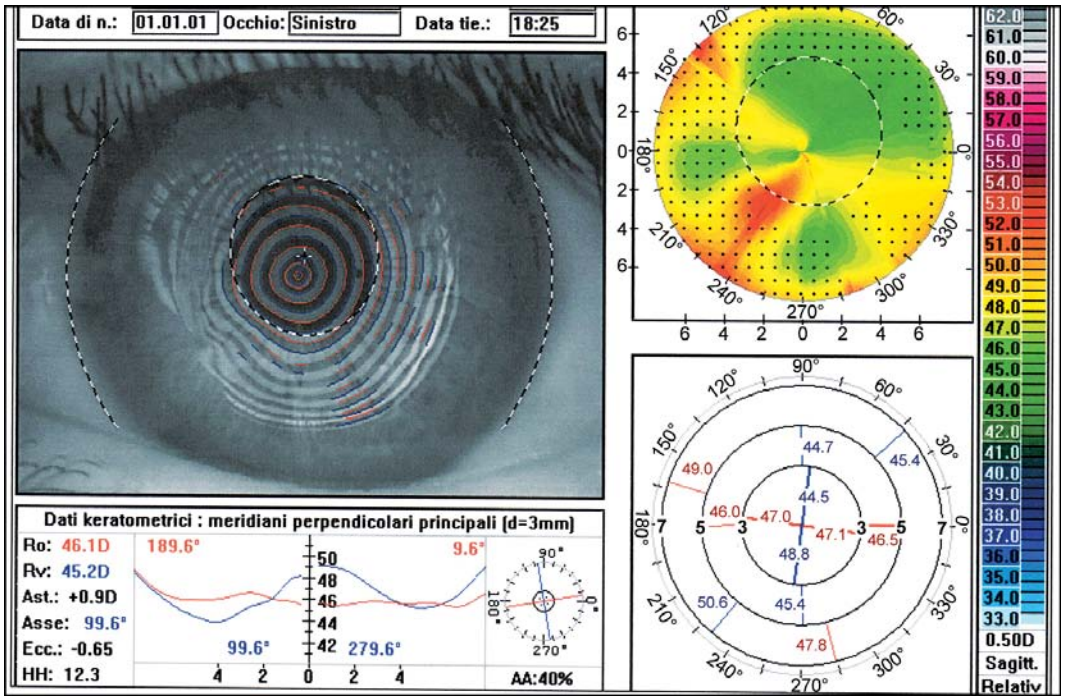


FIGURE 12-44: After astigmatic keratotomy at a 6 mm optical zone, astigmatism has decreased to 0.9 diopters but has a slightly irregular pattern (case of Figure 12-43).

no loss of best corrected visual acuity, trace haze in only 1/5 of eyes, and a final mean defocus equivalent of 1.08 D.[23] Epithelialization is only slightly slower than in normal PRK, and endothelium is not affected. Subtle haze can present at the margins of ablation, or can show paracentrally when post-PRK steroids are withdrawn **(Figure 12-45)**; this is why topical fluorometholone or loteprednol should be continued for at least 5 months and then tapered.

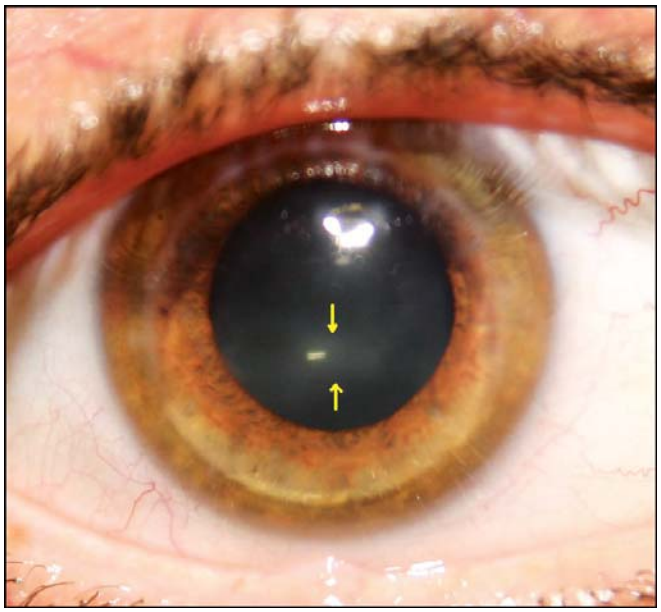


FIGURE 12-45: Moderate semi-peripheral haze after a -7 D PRK with mitomycin-C on DALK.

Larger spherical errors require intraocular techniques, which will be explained in detail in other chapters of this book. Refractive lens exchange is advised in presbyopic age or when a lens opacity is present or developing. Phakic IOL implantation is instead the preferred technique in younger eyes, provided that a good endothelial cell density is present.

Personal Series

I have moved to near-Descemetic in May 2006, after noticing the difficulty of a consistent big bubble formation. Since then, I applied the near-Descemetic technique (as described above) to all cases of KC undergoing DALK. The following series is a consecutive, single-surgeon retrospective analysis of all cases with a minimum follow-up of 1 year, and all refractive data were collected without sutures.

DALK was completed in 37 eyes of 37 patients with KC (mean age 32.6 years, SD 8.4, range 17 to 49). Males were 18. In 1 case a microperforation occurred, but PKP was not needed. In 3 early cases, a big bubble formed, but dissection was only continued to evacuate air, but no attempt was done to bare Descemet's membrane.

In 1 case, a peripheral abscess in the donor button developed in correspondence of a loose suture, 6 months postoperatively, when the patient was abroad and could access to medical assistance only after a week of pain and redness. Topical treatment with gatifloxacin was carried out, but the suture was not removed. The patient returned to our institute, the suture removed, and the abscess healed with no visual consequences.

Inferior unexplained melting of the donor button was noticed in another case, 2 weeks postoperatively. Sutures in the damaged area were instantly removed, and visual acuity remained acceptable (0.7 unaided), but topography showed an inferior steepening. Central pachymetry was 610 micron. At surgery, the donor cornea had appeared less rigid than usual donor corneas, but otherwise normal and transparent.

No cases of rejection occurred.

Despite the near-Descemetic dissection, visual acuity was comparable to my previous cases of DALK by the Big Bubble technique with Descemet's membrane baring. Mean best-spectacle corrected visual acuity (BSCVA) was 0.77 (SD 0.13; range 0.5 to 1). Mean refractive astigmatism was 3.88 D (SD 2.06; range 2 to 8). Mean spherical equivalent was -3.27 D (SD 2.28; range 0 to -9).

Mean BSCVA in the 25-eye Big Bubble series was 0.78 (SD 0.15) (not statistically significant difference with t-test):

Conclusion

The development of DALK and its diffusion have enormously improved the perspectives of patients with advanced KC. Nowadays there is only justification for PKP in KC in very thin or scarred corneas. Surgical difficulty of most proposed DALK technique is essentially derived from the attempt to bare Descemet's membrane at all costs, which is a risky and unnecessary goal. Near-Descemetic DALK yields comparable visual results and is accessible to all corneal surgeons, with a short learning curve and minimal equipment. Since most postoperative complications arise from sutures (and visual acuity can be improved by early removal of tight sutures), follow-up is based upon their timely management, minimal but prolonged topical therapy, patient information, and, eventually, possible management of the final refractive error.

References

1. Borderie VM, Werthel AL, Touzeau O, Allouch C, Boutboul S, Laroche L. Comparison of techniques used for removing the recipient stroma in anterior lamellar keratoplasty. Arch Ophthalmol 2008;126:31-7.
2. Marchini G, Mastropasqua L, Pedrotti E, Nubile M, Ciancaglini M, Sbabo A. Deep lamellar keratoplasty by intracorneal dissection: a prospective clinical and confocal microscopic study. Ophthalmology 2006;113:1289-1300.
3. Ardjomand N, Hau S, McAlister JC, et al. Quality of vision and graft thickness in deep anterior lamellar and penetrating keratoplasty. Am J Ophthalmol 2007;143:228-35.
4. Archila EA. Deep lamellar keratoplasty dissection of host tissue with intrastromal air injection. Cornea 1984/85;3:217-8.
5. Sugita J, Kondo J. Deep lamellar keratoplasty with complete removal of pathological stroma for vision improvement. Br J Ophthalmol 1997;81:184-8.
6. Melles GRJ, Lander F, Rietveld FJR, Remeijer L, Beekhuis WH, Binder PS. A new surgical technique for deep stromal, anterior lamellar keratoplasty. Br J Ophthalmol 1999;83:327-33.
7. Duong MH, Thimel S, Hoang Xuan T. Kératoplastie lamellaire avec aero-visco dissection. J Fr Ophthalmol 2001;24:930-6.
8. Anwar M, Teichmann KD. Big-bubble technique to bare Descemet's membrane in anterior lamellar keratoplasty. J Cataract Refract Surg 2002;28:398-403.
9. Anwar M, Teichmann KD. Deep lamellar keratoplasty. Surgical techniques for anterior lamellar keratoplasty with and without baring of Descemet's membrane. Cornea 2002;21:374-83.
10. Anwar M, Teichmann KD. Planned near-Descemet's dissection in deep lamellar keratoplasty, using air or fluid. In John T (Ed). Surgical Techniques in Anterior and Posterior Lamellar Corneal Surgery. New Delhi: Jaypee, 2006; 125-39.
11. Leccisotti A, Fields VS. Angle-supported phakic intraocular lenses in eyes with keratoconus and myopia. J Cataract Refract Surg 2003;29:1530-6.
12. Leccisotti A. Refractive lens exchange in keratoconus. J Cataract Refract Surg 2006;32:742-6.
13. Wollensak G, Spoerl E, Seiler T. Riboflavin/ultraviolet-A-induced collagen crosslinking for the treatment of keratoconus. Am J Ophthalmol 2003;135:620-7.
14. Colin J, Malet FJ. Intacs for the correction of keratoconus: two-year follow-up. J Cataract Refract Surg 2007;33: 69-74.
15. Jurkunas U, Azar DT. Potential complications of ocular surgery in patients with coexistent keratoconus and Fuchs' endothelial dystrophy. Ophthalmology 2006;113:2187-97.
16. Leccisotti A. Descemet's membrane perforation during deep anterior lamellar keratoplasty: Prognosis. J Cataract Refract Surg 2007;33:825-9.
17. Pakrou N, Fung S, Selva D, Chedade M, Leibovitch I. Deep lamellar keratoplasty in the treatment of keratoconus. Ophthalmologica 2006;220:164-9.
18. Teichmann KD, Anwar M. Intrastromal air, Big-Bubble technique. In John T (Ed) Surgical Techniques in Anterior and Posterior Lamellar Corneal Surgery. New Dehli: Jaypee, 2006;102-16.
19. Maurino V, Allan BD, Stevens JD, Tuft SJ. Fixed dilated pupil (Urrets-Zavalia syndrome) after air/gas injection after deep lamellar keratoplasty for keratoconus. Am J Ophthalmol 2002;133:266-8.
20. Parthasarathy A, Por YM, Tan DT. Use of a "small-bubble technique" to increase the success of Anwar's "big-bubble technique" for deep lamellar keratoplasty with complete baring of Descemet's membrane. Br J Ophthalmol 2007;91:1369-73.
21. Fontana L, Parente G, Tassinari G. Clinical outcomes after deep anterior lamellar keratoplasty using the Big-bubble technique in patients with keratoconus. Am J Ophthalmol 2007;143:117-24.
22. Wylegala E, Tarnawska D, Dobrowolski D. Deep lamellar keratoplasty for various corneal lesions. Eur J Ophthalmol 2004;14:467-72.
23. Leccisotti A. Photorefractive keratectomy with mitomycin C after deep anterior lamellar keratoplasty for keratoconus. Cornea 2008;27:417-20.

13

Penetrating Keratoplasty

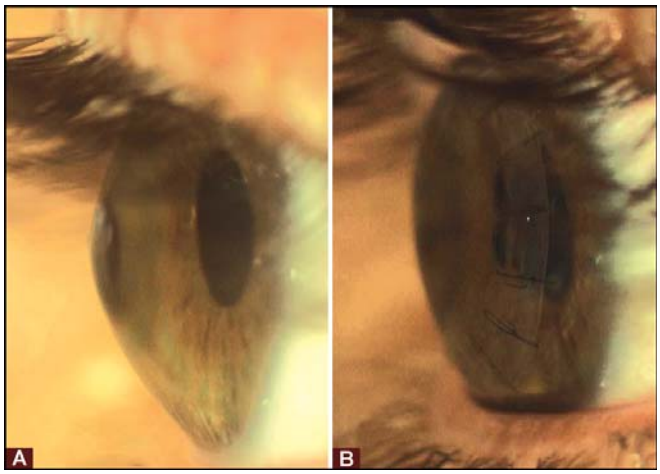
Pierre Fournié
François Malecaze

Introduction

Keratoconus is one of the main indications of penetrating keratoplasty (PK). Rabinowitz[1] reports that around 10 to 20% of patients with keratoconus will require a corneal graft in their lifetime. Keratoconus represents 11 to 31% of operating indications of PK in large series of at least 2000 procedures.[2-6]

Indications

Keratoconus is a surgical indication of PK both optical for restoring visual acuity, but also tectonic for restoring the corneal integrity in terms of thickness and shape **(Figures 13-1A and B)**.



FIGURES 13-1A AND B: Penetrating keratoplasty in keratoconus has the aim of restoring the shape and thickness of the cornea to improve optical quality. (A) Image of a central preoperative cone. (B) The same patient after penetrating keratoplasty.

The factors associated with an increased risk of PK in patients with keratoconus include poor visual acuity,[7-12] contact lens intolerance,[10, 12-14] the presence of corneal opacities,[7, 9, 12] raised keratometry values,[7-12, 15] and young age.[11, 12] The graft is usually carried out in young adults, but it is not unusual to operate on patients aged 50 or over whose keratoconus has been stable for a long time.

In practice, there are two different scenarios depending on whether the patient has central corneal opacities (not including the classical Fleischer's ring and Vogt's striae).

1. In the absence of central corneal opacities, when there is progression of the keratoconus, the indication for PK is to provide optical correction that may not be obtainable with glasses or contact lenses. If lenses no longer provide adequate visual acuity or adapting to them or wearing them becomes impossible, then surgical treatment is required. The implantation of intracorneal rings is a surgical option. They must not be offered too late as a minimum thickness at the site of implantation of 450 mm is necessary, and a central keratometry higher than 55 diopters renders the results more uncertain.[16] If there is a contraindication to the implantation of the intracorneal rings or if there are no satisfactory results after implantation of the rings, then keratoplasty is indicated. As a rule, these patients have stage 4 of the Krumeich classification **(Table 13-1)**.[17]
2. Central corneal opacity involving the visual axis is an indication for PK. It is necessary to distinguish between deep scars and the superficial scar that involve the anterior stroma of the apex of the cone. Superficial scars often have a reticular appearance and represent ruptures of the Bowman's membrane filled with scar tissue **(Figure 13-2)**. Deep scars may be seen at the apex of the cone

TABLE 13-I: Keratoconus classification based on Krumeich and co-authors.[17] For each stage, it is sufficient to have just one of the listed criteria be met

Stage	Characteristics
1	Eccentric corneal steepening Induced myopia and/or astigmatism < 5 D Corneal radii ≤48 D Vogt's striae, no scars Corneal thickness ≥500 µm
2	Induced myopia and/or astigmatism >5 D <8 D Corneal radii ≤53 D No central scars Corneal thickness ≥400 µm
3	Induced myopia and/or astigmatism >8 D <10 D Corneal radii >53 D No central scars Corneal thickness 200 to 400 µm
4	Refraction not measurable Corneal radii >55 D Central scars, perforation Corneal thickness <200 µm

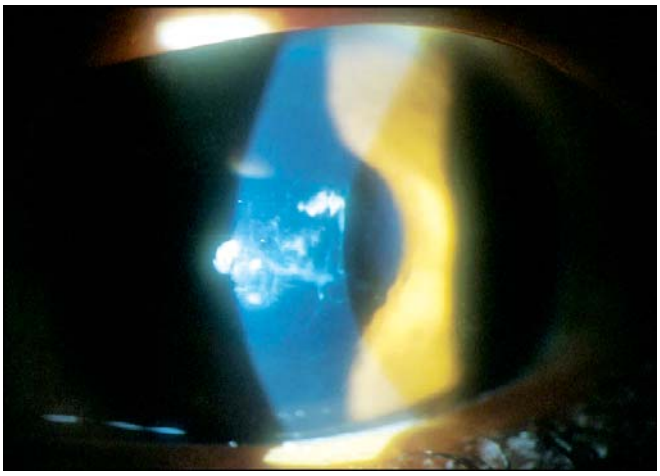


FIGURE 13-2: Reticular, subepithelial, and anterior stromal scars develop within the cone, and they result from breaks in the Bowman's layer.

and result from the rupture of the Descemet's membrane **(Figure 13-3)**. An acute keratoconus or a corneal hydrops is the expression of an acute rupture of Descemet's membrane. The irruption of aqueous humor inside the cornea causes sudden epithelial and stromal edema and the appearance of a deep diffuse opacity **(Figure 13-4)**. After a few weeks, the endothelial cells near the rupture of Descemet's membrane enlarge and reconstitute a new membrane, and the edema is reduced. If the residual scar affects the central visual axis, then the visual acuity is reduced. If it is not axial, the stromal scar may cause a flattening of the cornea such that visual acuity may be increased and using contact lenses becomes possible.

In these two typical scenarios, PK is the last resort when the other means of correction have been exhausted.

Besides the "morphological profile" of keratoconus, the "functional profile" of the patient must also be taken into account. Based on functional profiles, young patients are more often in need of care than older ones. The requirements and professional perspectives for treatment vary greatly

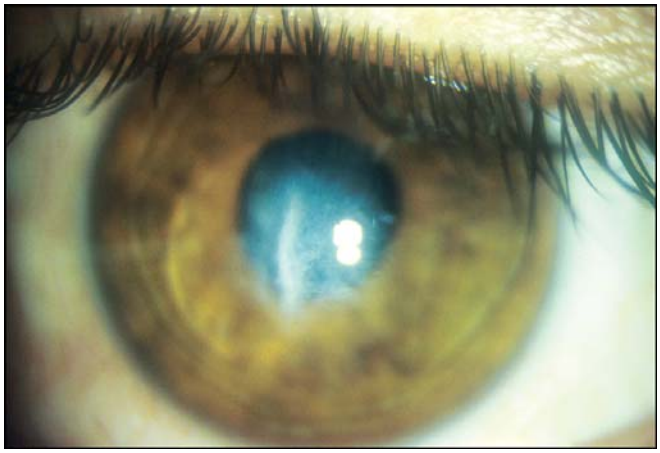
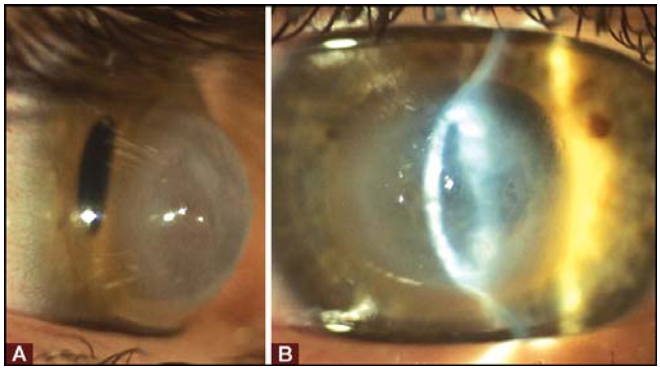


FIGURE 13-3: Deep opacities resulting from ruptures in Descemet's membrane can be seen at the apex of the cone.

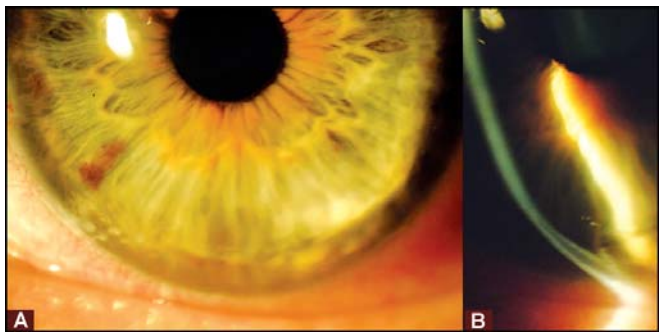


FIGURES 13-4A AND B: Ruptures in Descemet's membrane permit the stromal imbibation of the aqueous humor, and this results in the marked corneal edema seen in photograph (A). Intrastromal fluid-filled clefts can sometimes occur, as seen in slit view (B). Penetrating keratoplasty is usually necessary if edema persists for over 3 months or if scarring is extensive or in the central cornea.

depending on the patient. Unilateral or highly asymmetrical conditions are sometime well tolerated, and the surgical approach of the involved eye is not systematic if the patient does not demand such an approach. Finally, the level of visual acuity does not always correlate with the handicap experienced by the patient. The quality of vision in patients with keratoconus is sometimes difficult to assess (e.g., night driving, distorted vision, restricted sporting activities might factor in their assessment of quality of vision), but it must always be taken into account in considering the indication for the operation.

The development of the new techniques of deep anterior lamellar keratoplasty (DALK) leads us to reconsider the choice of grafting techniques in keratoconus. Although PK has long been considered as the standard treatment for keratoconus, the use of PK for this indication has become less frequent in some surgical teams that prefer DALK. PK is nevertheless a well-codified operation, and it is safe and fully reproducible in keratoconus. It remains, for many surgeons, the "gold standard" for this indication. For surgeons who have begun using DALK, PK is still indicated in keratoconus as a first line of treatment in cases with deep scars involving Descemet's membrane, when the corneal thinness makes lamellar dissection difficult, or as a second line treatment after a DALK procedure when there is intraoperative perforation of Descemet's membrane.

Some particular cases should be mentioned. In patients with a high risk of ocular trauma (e.g. mentally handicapped patients who risk self-inflicted trauma) as well as in patients in whom postoperative follow-up is complicated by difficulties in access to treatment or lack of follow-up, corneal grafts are contraindicated. In an emergency, such as in cases of perforation or cases at high risk of perforation, a graft could be indicated, preferably a lamellar graft.



FIGURES 13-5A AND B: (A) Pellucid marginal degeneration. (B) The slit-lamp photograph demonstrates a band of thinning that is 1 to 2 mm in width in the inferior cornea. The size and location of the trephination site are selected to avoid cutting through areas of corneal thinning, if possible.

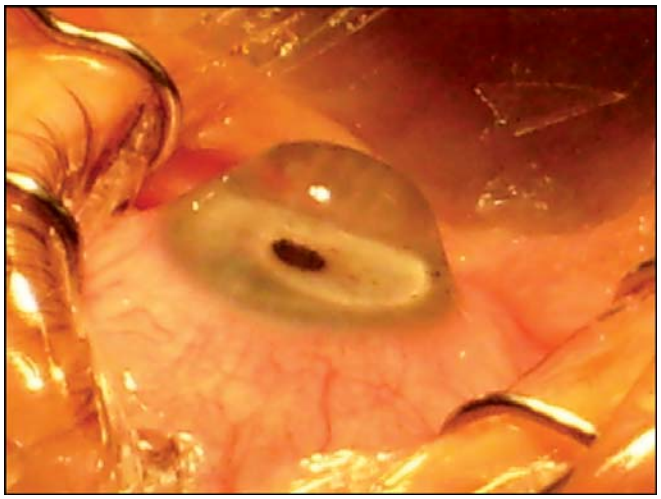


FIGURE 13-6: Intraoperative view of a keratoglobus. Ectasia involves the entire cornea.

Finally, in addition to keratoconus, pellucid marginal degeneration **(Figure 13-5)** may benefit from large off-centered diameter PK. Keratoglobus **(Figure 13-6)** may also benefit from large diameter PK. In this case, PK should be used as a last resort, due to the major risk of immunologic rejection of the graft.

Technique (Step-by-Step)

PREPARATION

Preoperative Miosis

Preoperative application of topical myotics such as pilocarpine is important. Miosis forms a protective shield for the crystalline lens.

Anesthesia

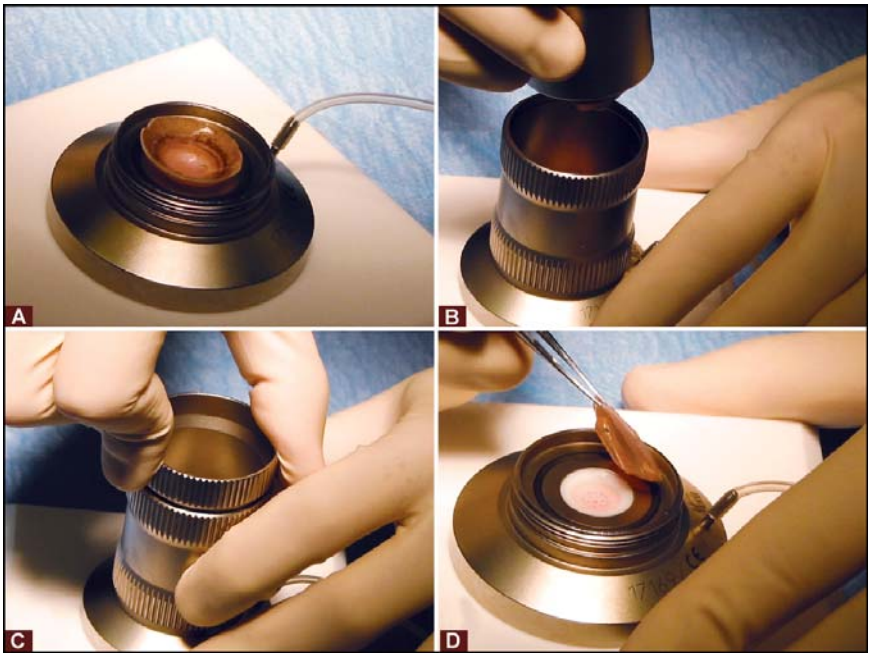
The operation can be carried out under local or general anesthesia. If a peribulbar block is used, it is essential to obtain extraocular muscle akinesia to eliminate intraoperative pressure elevations associated with muscle contraction. Lowering of intraocular pressure, using ocular compression with a Honan balloon or a similar device, prior to surgery may help decrease the posterior pressure during the open-sky phase of the surgery and the risk of vitreous loss and choroidal hemorrhage. In these patients, it is important not to have any open positive vitreous pressure. The best possible control of blood pressure, tachycardia, and anxiety should be achieved. General anesthesia may be especially useful in young and emotional patients.

SURGICAL STEPS

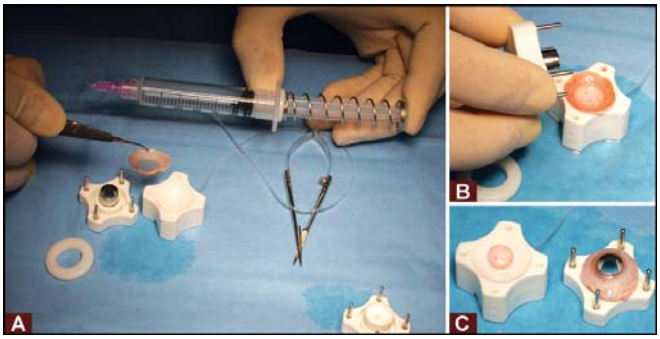
Trephination of Donor Cornea

Trephination of the graft can be done via the endothelial or epithelial side. Trephination of the recipient cornea by the epithelial side creates an anterior opening larger than the trephination of the graft via the endothelial side. To obtain a graft of the same diameter as that of the trephination of the recipient cornea, it is necessary to oversize the graft by 0.25 mm in a trephination via the endothelial side. In contrast, trephination by the epithelial side will on the other hand be carried out with the same diameter. To avoid postoperative myopia with incapacitating anisometropia, the technique of using a graft with a diameter that is smaller than the diameter of the host trephination has been recommended. However, it is not often used in practice due to surgical difficulties and possible wound healing complications from the limiting ring.[18, 19] A graft that is smaller than the recipient cornea can also result in a flat cornea, and such a flat cornea may not be amenable to contact lens fitting.

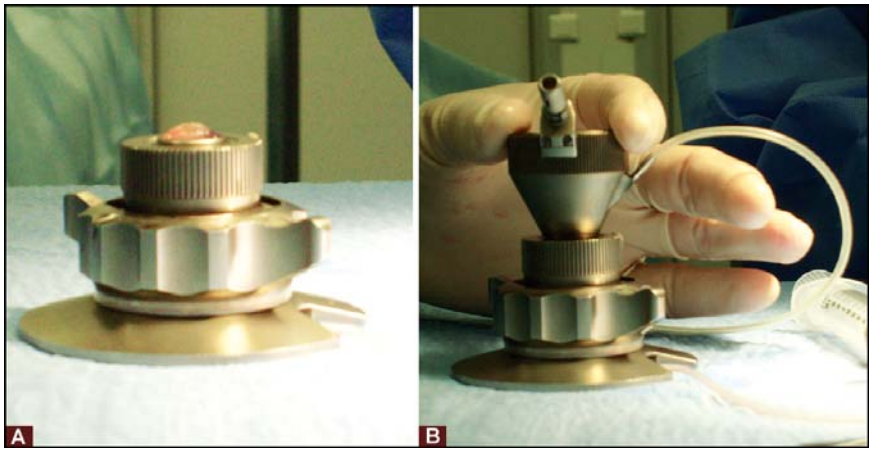
Various trephines have been developed for cutting the donor cornea. In case of trephination by the posterior side, the graft is centered on a cutting block. It is maintained during trephination by a suction system. Trephination is carried out with the help of a guillotine system. Corneal distortion is reduced by a suction chamber device **(Figures 13-7 and 13-8)**. Immobilizing the donor cornea allows the surgeon to cut a perfectly round button from the center of the cornea every time. The suction holds the cornea in place as it is cut and ensures that the corneal button remains in the well and not in the blade after the cut has been made. In case of trephination by the anterior side, the graft is



FIGURES 13-7A TO D: Trephination of the graft by the endothelial side using the Hanna trephine with a single use blade. The graft is centered on the cutting block. It is kept immobile during trephination by a system of suction (A). The well is connected via holes by a silicone tube to a 5 ml air syringe. The guillotine system of the Hanna trephine enables a circumferential cut of the graft by punching (B, C). At the end of trephination, the corneoscleral ring is carefully removed from the punched cut corneal button (D).



FIGURES 13-8A TO C: Trephination of the graft via the endothelial side using the single-use Heesburg-Barron trephine (A). A suction system keeps the graft immobile on the trephine cutting block (A, B). The well has a central positioning hole, as well as four additional holes, and a circular groove connected to a 5 ml syringe with a spring loaded plunger. Trephination is done with the help of a guided guillotine system (C). The cutting block has 4 holes into which the steel guidepost of the blade fit to ensure that the blade is perpendicular without any slipping.



FIGURES 13-9A AND B: Trephination of the graft via the epithelial side using the Hanna trephine. The graft is mounted on the artificial anterior chamber maintainer (A) then cut with the Hanna trephine (B).

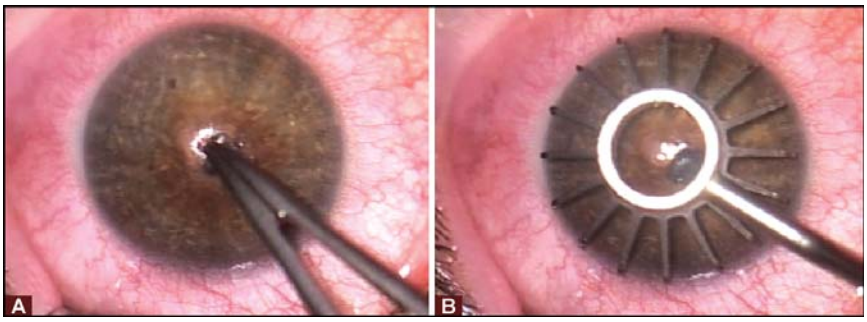
centered on the artificial anterior chamber maintainer (epithelial side up) **(Figure 13-9)** and cut with the same device as that used for trephination of the recipient cornea.

Donor tissue should be kept submerged in the storage medium while the surgeon is preparing the host corneal bed.

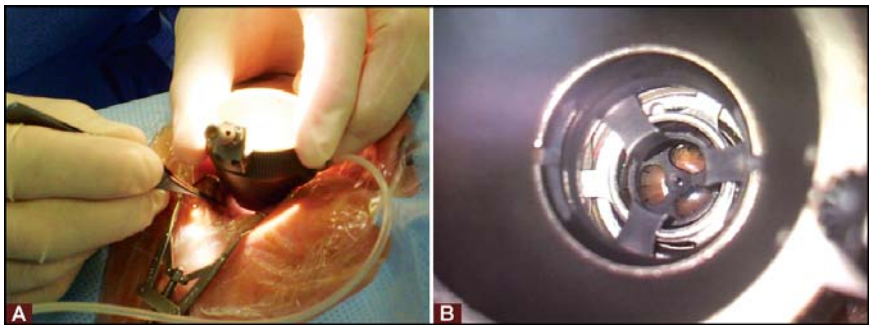
Trephination of Host Cornea

Trephination of the host cornea starts with location of the center of the trephination which represents a compromise between the anatomical center of the cornea and the center of the pupil **(Figure 13-10A)**. In a cornea with peripheral thinning, a large, slightly decentered graft which encompasses the area of thinning and clears the pupil may be preferred. The meridians may be marked with gentian violet to ensure the best placement of sutures **(Figure 13-10B)**. The corneal cut must be wide enough to remove all of the keratoconic tissue to avoid the persistence of a severe postoperative astigmatism or a recurrence of the keratoconus. A lower peripheral cone is the most common form of keratoconus. A slightly decentered graft is well tolerated, although major decentration may be complicated by a giant postoperative astigmatism as well as by potential graft rejection. In case of marked protrusion of the cone, trephination is facilitated after flattening the apex with cauterization.

Trephination is done under the operative microscope using a hand-held disposable trephine held perpendicular to the cornea or with a suction device that enables the trephine to be kept stabilized. The hand-held trephine is progressively rotated, allowing the sharp edge to penetrate the cornea



FIGURES 13-10A AND B: (A) Location of the center of the trephination, using the center of the pupil, where possible, or a compromise position between the pupillary axis and the center of the cornea. (B) 16 arms radial keratotomy markers may be used to assist in donor-host suture symmetry and alignment.

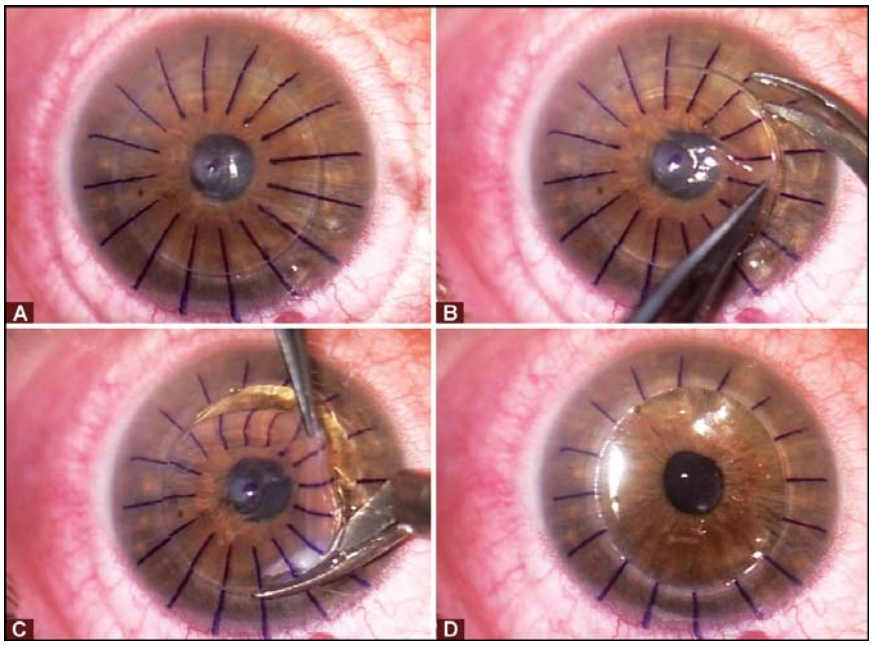


FIGURES 13-11A AND B: (A) Trephination of the recipient cornea with the Hanna trephine. The trephine features a 360° limbal suction ring connected by a silicone tube to a 10 ml air syringe that secures the trephine to the eye. (B) Trephination is examined under the operating microscope as the blade is lowered. A manually operated gear mechanism provides smooth uniform cutting. When aqueous humor appears in the barrel, the plunger of the syringe is pushed in all the way to release the suction, and the trephine is removed from the eye. The trephine produces a symmetric and nearly vertical incision.

until the anterior chamber is entered. With suction trephines, a precisely calibrated rotating mechanism allows the surgeon to advance the blade with each rotation. The two main suction devices are the Hanna trephine **(Figure 13-11)** and the Heesburg-Barron trephine. After a viscoelastic substance is placed in the anterior chamber to protect the intraocular contents, trephination is completed using a blade or beveled corneal scissors **(Figure 13-12)**. To minimize astigmatism, it is of utmost importance that the cut is made perpendicular to the corneal plane.

Femtosecond Laser Trephination

A femtosecond laser can be used for cutting corneal grafts and recipient corneas. Its use in this domain is recent and undergoing evaluation. The femtosecond laser enables non-vertical cuts to be carried out in various ways. This enables grafts to be cut in a hat shape, in a mushroom shape, or with Z borders, and it allows for cuts in the recipient cornea of exactly the same shapes **(Figure 13-13)**. These new shapes would improve the healing surface and increase the congruence between the graft and the recipient cornea. The consequences, in terms of early ablation of the sutures, reduction of postoperative astigmatism, faster visual recovery and endothelial innocuousness around the cut, are under evaluation.



FIGURES 13-12A TO D: After filling the anterior chamber with a ophthalmic viscoelastic device (A), trephination is completed with Katzin scissors (B, C). Upward force is applied to the scissors to avoid damaging the iris or inducing a cataract. The cutting edge must be fully perpendicular to the corneal surface (D).

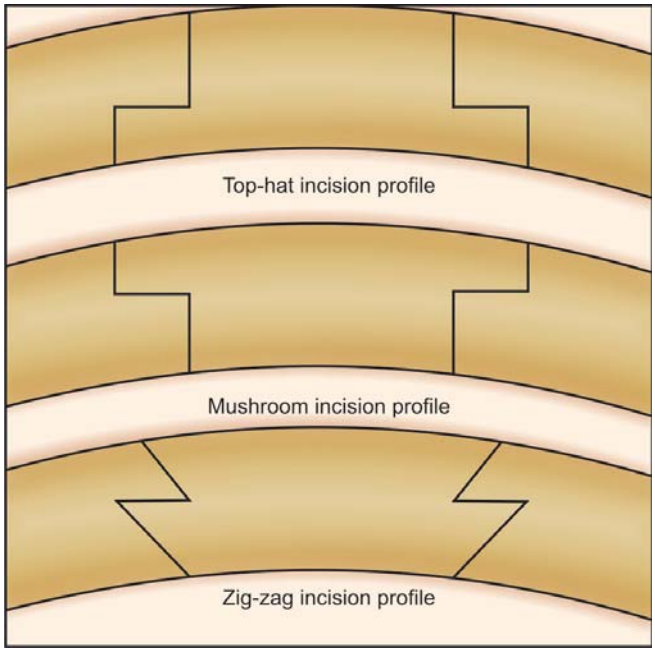
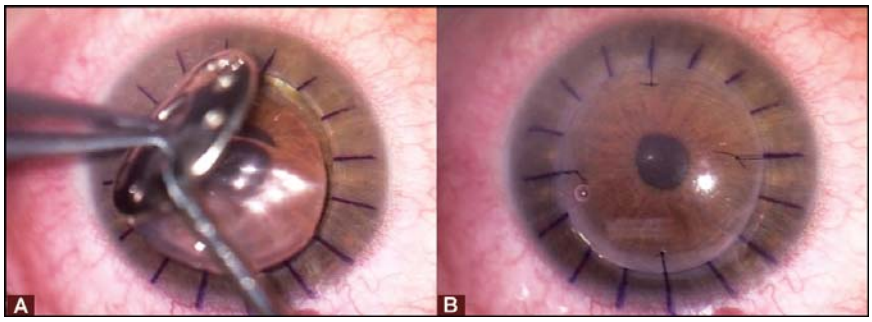


FIGURE 13-13: Examples of corneal cuts with a femtosecond laser. A mushroom cut shape enables endothelial saving, which may be preferred in the case of keratoconus.

Placement of Four Interrupted Radial 10-0 Nylon Cardinal Sutures

The graft, whose endothelium is protected by a viscoelastic material, is delicately placed in the host corneal bed with the help of a graft holder **(Figure 13-14A)**. The first step of the suture consists of



FIGURES 13-14A AND B: (A) Placement of the graft in the host corneal bed with the help of a graft holder ensures that the endothelium is preserved. (B) The 4 separate cardinal sutures delimit 4 quadrants of identical size.

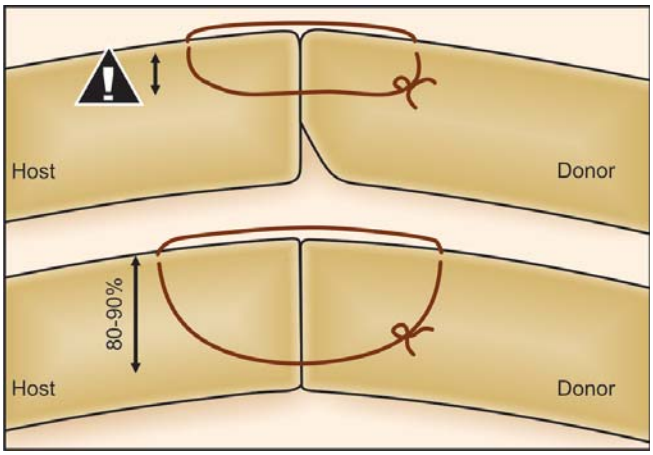
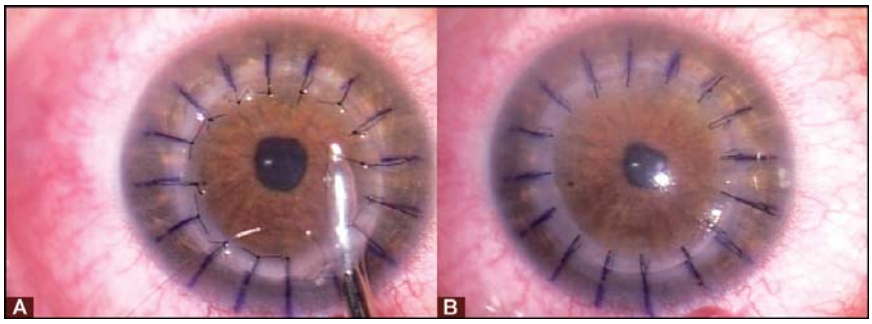


FIGURE 13-15: The interrupted sutures must be deep (80-90%). If they are too superficial, the edges of the incision will not be brought into apposition with a posterior wound gape. Deep suture bites allow for appropriate wound apposition.

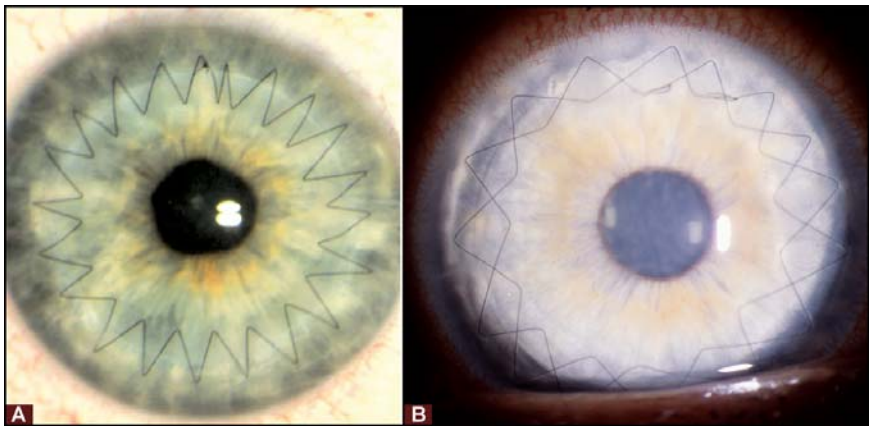
placing 4 cardinal sutures with a 10-0 nylon suture on a spatulated side-cutting needle **(Figure 13-14B)**. The location of the cardinal sutures is essential for the prevention of postoperative astigmatism. They must be deep (80-90%) and fully perpendicular to the incision **(Figure 13-15)**. They must delimit four quadrants of identical size **(Figure 13-14B)**. The tension lines between the anterior insertions of the 4 cardinal sutures form a diamond pattern. Any aberrant cardinal sutures should be replaced.

Complete Suturing

Additional sutures are placed to ensure adequate tissue apposition. A variety of suturing techniques exist: single interrupted sutures **(Figure 13-16)**, single running suture **(Figures 13-17A and 13-18)**, combination of interrupted and running sutures, and double running sutures **(Figures 13-17B and 13-18)**. Different suture methods are used depending on the surgeon's preference. None of these methods have proved superior in astigmatism.[20, 21] The interrupted sutures and running sutures must bring into apposition the Bowman's layers of the graft and of the host cornea **(Figures 13-15 and 13-19)**. The edema of the graft, which will reduce progressively after the operation, results in a major difference of the thickness between the graft and the host cornea. This makes apposition of Descemet's membranes impossible in the intraoperative stage. The knots are buried in the stroma of



FIGURES 13-16A AND B: (A) At the end of the operation, the viscoelastic material is exchanged for a balanced salt solution before tying the last suture. (B) Shown is a set of 16-interrupted sutures after the suture knots are buried.



FIGURES 13-17A AND B: Shown is a single continuous running suture (A) and a double continuous running suture (B).

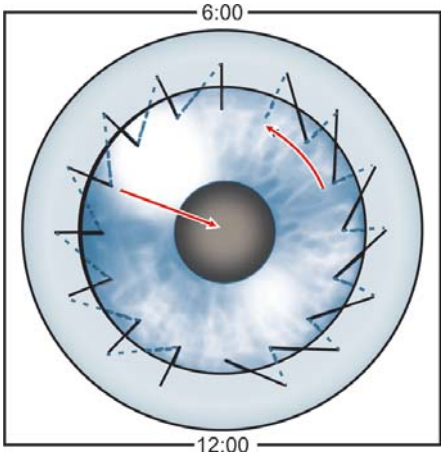


FIGURE 13-18: Schematic suture technique for a single continuous running suture. Some surgeons believe that an anti-torque running suture is helpful in reducing astigmatism, whereas others have not observed any significant effects with such a suture.

Antitorque pattern of single running suture. On the left, the overlying radial sutures (full line) would result in a minimal suture torque and a reduced risk of induced astigmatism. Intrastromal suture bites (dotted line) are antitorque.

Torque pattern of single running suture. On the right, the intrastromal suture is radial (dotted line), and the overlying torquing suture bites (full line) could rotate the graft in the arrow direction and induce astigmatism.

the graft rather than in the recipient side to minimize vascularization. The total number of interrupted sutures and passages of the running suture is usually between 16 and 24.

Readjustment of Sutures to Minimize Astigmatism

When a running suture is carried out, it is necessary to harmoniously distribute its tension before burying the knot. The tension of the sutures may be checked at the end of the operation after replacing the viscoelastic material in the anterior chamber with balanced salt solution **(Figure 13-16)**.

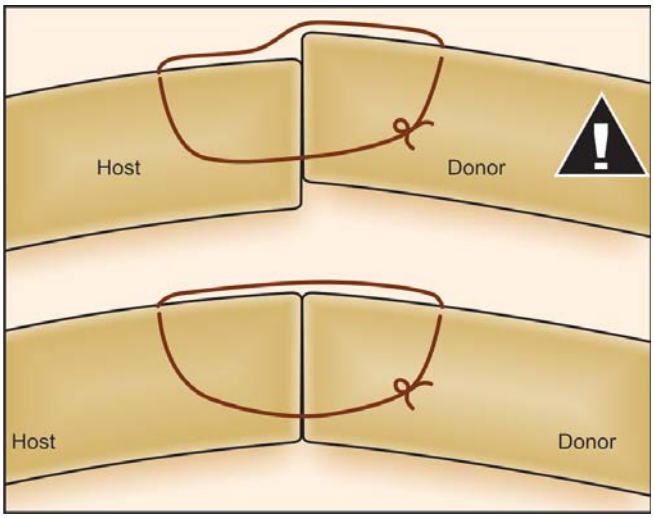
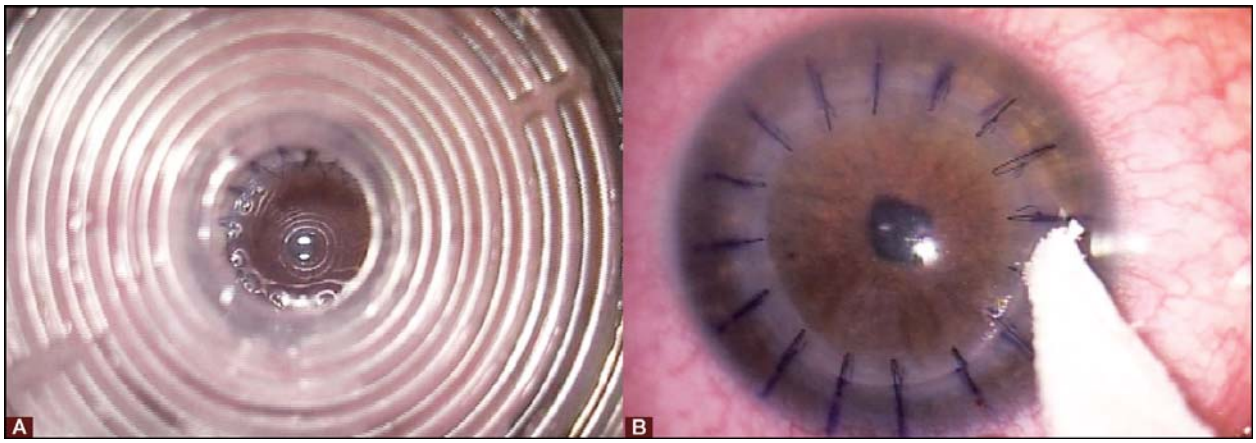


FIGURE 13-19: Alignment of the graft and host epithelial surfaces during suturing is critical. Differences between suture depths in the graft versus the host may cause sectorial overrides of the graft over the host, resulting in a giant postoperative astigmatism.



FIGURES 13-20A AND B: (A) At the end of the operation, the reflex of the circular rings of the keratoscope enables the observation of the suture tensions. The reflex must find circular mires that show homogenous tensions of the sutures. (B) The wound is tested for water tightness. This is done after drying the surface with a cellulose sponge pressing at the limbus and by observing the wound for leakage of aqueous humor.

A disposable keratoscope may be used to this effect **(Figure 13-20A)**. A suture adjustment may be done until regular circular mires are obtained. Interrupted sutures that are too tight along the shorter diameter of the oval may be replaced by sutures that have optimal tension to help achieve a circular shape of the mires. The tension of the running suture can be modified by rotation.

Administering Medications

At the end of the operation, the wound is tested to ensure it is watertight **(Figure 13-20B)**, and topical antibiotic and corticosteroids eyedrops are applied.

POSTOPERATIVE MANAGEMENT

Postoperative treatment usually consists of corticosteroids eyedrops associated with antibiotic eyedrops. The corticosteroids used are Dexamethasone, Fluorometholone, Rimexolone and Hydrocortisone. The treatment can be commenced with 3 to 4 daily instillations and finished with an instillation every two days, and the corticosteroids eyedrops are usually stopped after a period of 12 to 24 months. Topical corticosteroids can be stopped when all of the sutures are removed or even earlier if they aren't going to be removed.

Postoperative management of the sutures enables guided healing and reduces post-graft astigmatism. The choice of sutures to be removed or the areas of a running suture to be loosened can be guided by a corneal topography. Selective ablation of interrupted sutures and adjustment of the tension of a running suture **(Figure 13-21)** give similar results in terms of reduction of postoperative astigmatism.[20, 21] Because of the risk of sutures breaking during the adjustment procedure, suture adjustment should not be attempted unless facilities are available to make the repair. The choice to leave in place the sutures long term or to remove all of the sutures is sometimes difficult. Usually, it is desirable to leave most of the sutures in place for at least 12 to 18 months. An earlier ablation of all of the sutures may lead to a gap in the wound and even to a wound dehiscence. Suture removal, even years out from a PK, should not be viewed as risk free. Prior to and following suture removal or manipulation, all patients should be given corticosteroids prophylaxis to avoid possible corneal allograft rejection.

Successful follow-up of grafted patients is a major factor in the prognosis of the graft. Postoperative complications are often reversible and correctible as long as they are diagnosed and treated early.

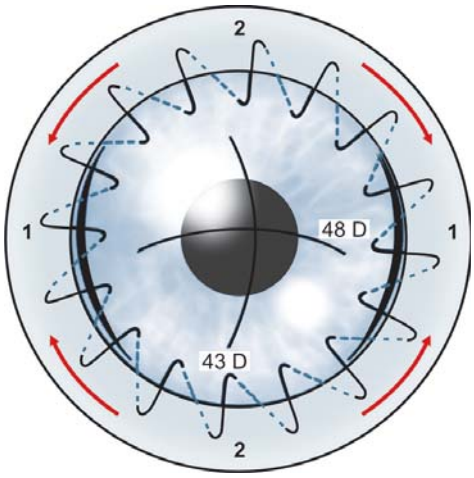


FIGURE 13-21: Rotation of a continuous running suture to correct against the rule astigmatism of 5 diopters. Rotation of the sutures is done from the flat (2) to the steep meridian (1) simultaneously flattening the steep meridian and steepening the flat meridian.

Results

The survival rate of the graft in the medium term follow-up (2 to 5 years) is around 95% in keratoconus.[22-28] Sharif and Casey,[23] using data from a case series of 100 eyes with an average follow-up of 6.1 years, reported a 93% survival rate. Lim, *et al*[26] using data from 93 eyes followed for an average 46.5 months, reported a failure rate of only 1.02%. With a longer follow-up of 13.8 years (range from 0.5 to 30.4 years) of 112 eyes, Pramanik, *et al*[28] reported a 93.7% survival rate. The two essential causes of graft failure after PK for keratoconus are allogenic graft rejection and non-immune secondary endothelial decompensation of the graft. The survival rate of a PK after keratoconus is

one of the highest. Thompson, *et al*[27] reported on a series of 3992 PK with an average follow-up of 43 ± 34 months. The survival rate of the grafts after keratoconus (n=449 eyes) was 98%. By comparison, the survival rate of the grafts after pseudophakic bullous keratopathy (n=315) was 88%, 81% after aphakic bullous keratopathy (n=105), 96% after Fuchs dystrophy (n=908), 88% for herpetic keratitis (n=77), and 68% after a second graft (n=352).

The visual results are good in the majority of cases, with best corrected visual acuity (BCVA) greater than or equal to 0.5 (20/40) in 70 to 91% of patients.[26, 29-35] Olson et al[29] reported that 87% of eyes had a BCVA of 0.8 (20/25). Visual rehabilitation is often slow. The majority of patients require optical correction after PK. In the study by Olson, *et al* the three main causes of postoperative corrected visual acuity limited to less than 0.8 were cataract, graft rejection and superficial punctate keratitis (found in 20% of cases at 6 months). Lim, *et al*[26] reported that visual acuity greater than 0.5 (20/40) was observed 87% of cases at the end of the follow-up (0.63 on average). After PK, 67% of eyes were corrected by glasses, 28% by contact lenses and 7% did not wear any corrective devices.

Patients are often shortsighted following PK for keratoconus. Brierly, *et al*[30] reported a corrected visual acuity greater than 0.5 in 84% of cases at 18 months (0.76 on average). The uncorrected visual acuity was 0.28 at 18 months. The average spherical equivalent at one year was -4.13 ± 4.41 diopters (D) with an average cylinder of 2.52 ± 2.45 D.

PK improves contrast sensitivity and the stereoscopic visual acuity of keratoconus.[36, 37]

Complications and Their Management

INTRAOPERATIVE COMPLICATIONS

The major intraoperative complication of PK is expulsive choroidal hemorrhage during the open-sky phase of keratoplasty. Its incidence varies from 0.47% to 3.3%.[38, 39] Sometimes it presents as a postoperative choroidal detachment or choroidal hemorrhage. With open-sky expulsive hemorrhages, an immediate posterior sclerotomy via a stab incision through the conjunctiva and sclera must be performed. Because number 9-0 or 10-0 nylon may not be sufficient to secure the wound, number 8-0 nylon or even 6-0 or 7-0 silk sutures should be used.

Other, less severe, traumatic complications may appear, such as injury to the lens and iris particularly during trephination in thinned corneas. Iris-lens damage should be repaired. Iris damage or iridodialysis are repaired with a 10-0 polypropylene suture. If the anterior lens capsule has been opened, an extracapsular cataract extraction should be performed with placement of a posterior chamber intraocular lens.

POSTOPERATIVE COMPLICATIONS

Corneal Allograft Rejection

Corneal allograft rejection is the main cause of graft failure after PKs for keratoconus. A higher risk of rejection is associated with a young recipient age, corneal neovascularization of the recipient **(Figure 13-22)**, a large-diameter corneal graft, and prior graft failure, particularly due to rejection. The rejection rate of corneal grafts varies from 20 to 35% in the literature.[29, 35, 40,41] Olson, *et al*[29] reported a corneal allograft rejection in 31% of cases, and in 36 of such cases, 7 had recurrences of rejection. The majority of graft rejections were observed between 1 and 2 years after surgery. The types of rejections were as follows: 12 out of 36 were epithelial rejections, 15 out of 36 were endothelial rejections **(Figure 13-23)** and 9 out of 36 were mixed rejections. In contrast, the graft failure rate

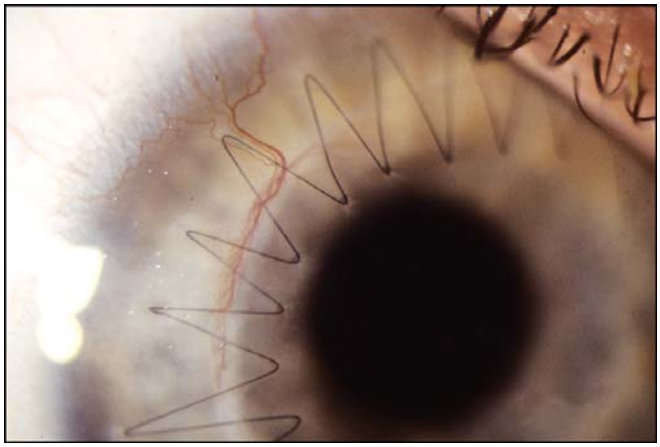


FIGURE 13-22: Corneal vascularization may be favored by an interrupted or continuous suture. Vascularized suture increases the risk of graft rejection.

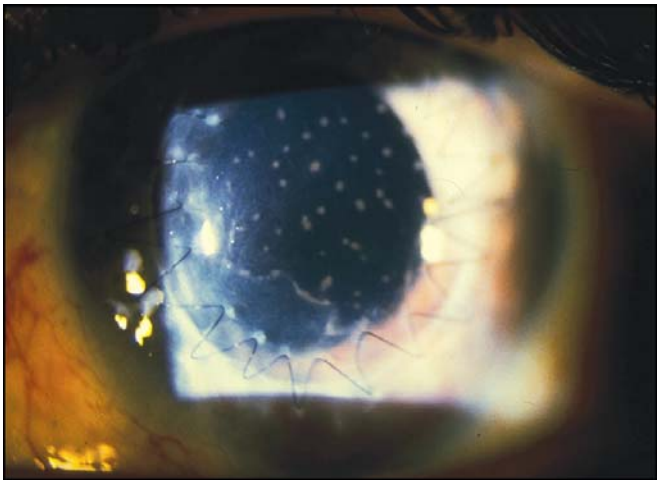


FIGURE 13-23: Allogenic endothelial corneal graft rejection with a Khodadoust rejection line and diffuse keratic precipitates.

after PK is not as important because of the early diagnosis and "aggressive" management of the corneal allograft rejection episodes. Paglen, *et al*[35] reported a survival rate of the graft in keratoconus at 11 years of 90%.

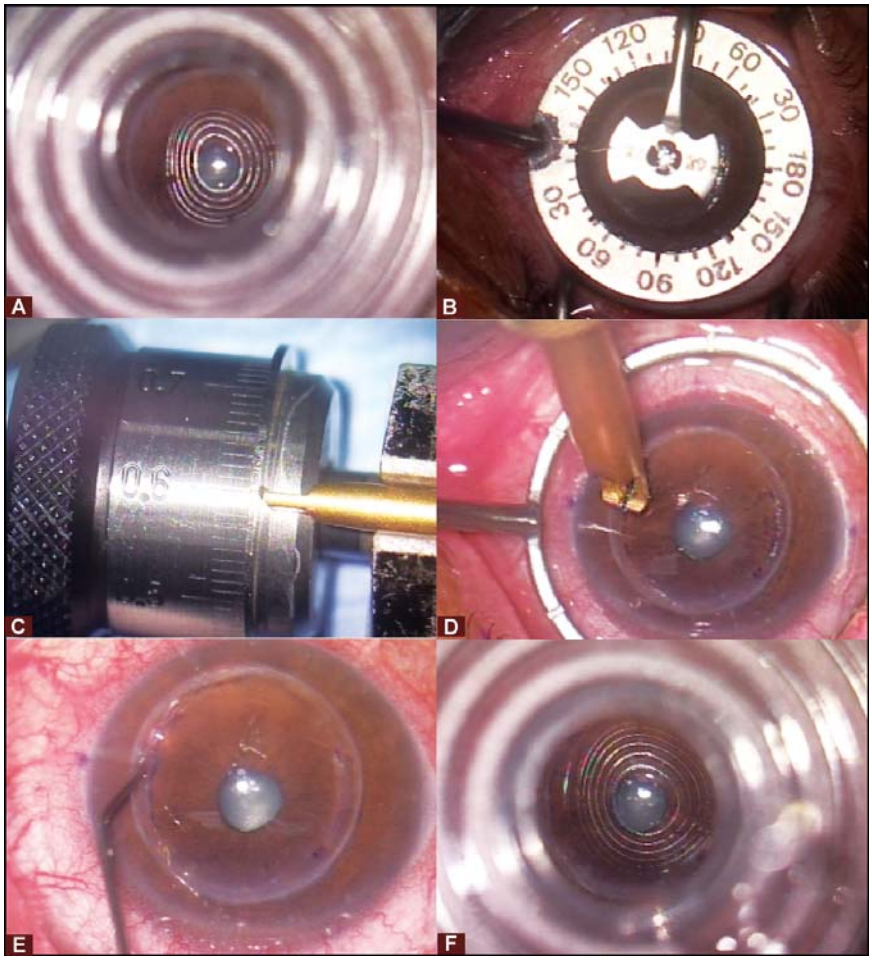
Curative treatment of the rejection must be started as early as possible to minimize endothelial cell loss induced by the rejection reaction and to consequently increase the chances of recovering the transparency of the graft after treatment. This implies that the patient needs to be fully informed of the functional signs and of the need to seek medical advice immediately. The treatment of choice is corticosteroids by topical, periocular, or systemic administrations. In case of acute corneal allograft rejection reactions, frequent topical applications of corticosteroids with good intraocular penetration may be completed with subconjunctival injections. The addition of systemic corticosteroids (intravenous methylprednisolone pulse therapy, 3 to 5 mg/kg IV push per day for 3 days) is indicated in serious cases, such as early rejection, severe inflammation, endothelial involvement, lack of response to topical corticosteroids, and the recipient having a high risk of rejection.

Topically administered 2% Cyclosporin can be used in recipients with a high risk of rejection. Cyclosporin must be used in the early stages of the immune cell response to be effective, and this makes cyclosporin a prophylactic and a non-curative treatment of the rejection.

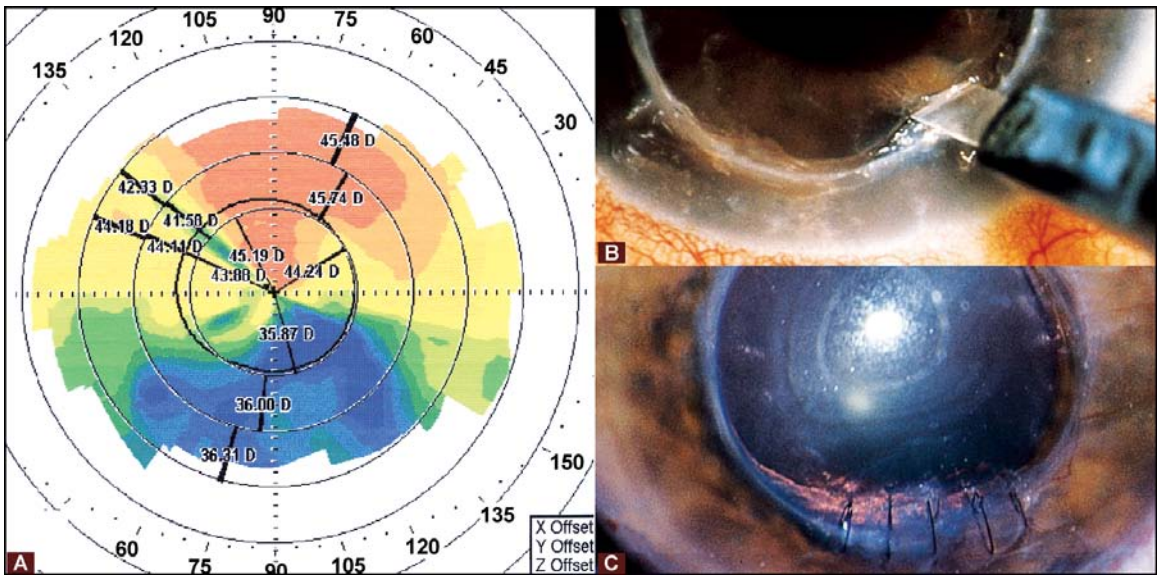
Corneal Graft Astigmatism

Astigmatism is the main source of limitation in visual acuity after PK in patients with a clear graft. Several factors contribute to astigmatism after PK: trephination of the graft and of the recipient cornea, astigmatism of the recipient cornea and of the graft, a gap between the recipient cornea and the graft **(Figure 13-19)**, tension of the sutures, the quality of the wound healing and the experience of the surgeon. Olson et al[29] reported an improved astigmatism with postoperative follow-up: 6.14 ± 4.12 D before surgery, 4.04 ± 2.45 D at 1 month, 2.86 ± 2.14 D at 1 year and 2.76 ± 1.99 D at 2 years (after surgical management of the astigmatism in some cases). If the suture-related astigmatism can be partially corrected by postoperative management of the sutures **(Figure 13-21)**, the other causes of astigmatism can only be corrected surgically. In practice, the most difficult problem is that of giant astigmatism (> 5 D) in a patient who has had all of the sutures removed. When this type of astigmatism limits the corrected visual acuity and correction with glasses or contact lenses cannot be tolerated, surgery for the astigmatism must be considered. This must only be done after some time (after around 6 months minimum) from the ablation of the last suture and in a patient whose astigmatism is stable on at least two examinations with an interval of several months.

The techniques most used are relaxing incisions including arcuate, transverse, and trapezoidal keratotomies made with a diamond knife **(Figure 13-24)**. The complications of astigmatic keratotomies are perforation, infection and rejection. Prophylactic anti-rejection therapy, using topical



FIGURES 13-24A TO F: Astigmatic keratotomy. A) The reflex of the keratoscope mires shows an inverse astigmatism. The steepest meridian is on the horizontal axis (along the shorter diameter of the oval). (B) Location of the 180° meridian on which the incisions are to be made. (C) Micrometer diamond blade is set according to the preoperative pachymetry 1 mm or so inside the periphery of the graft. (D) The incisions must be deep (80 to 90% of the corneal thickness), perpendicular to the graft surface, and located either inside the graft-host junction or in the wound itself. (E) The incisions are washed with BSS. (F) Intraoperative astigmatism reassessment enables a flattening of the horizontal meridian to be observed. The reflex mires of the keratoscope are more circular. The persistence of an inverse astigmatism can require other incisions concentric to the first one during the same session or remotely after having assessed the full effect of the initial incisions.



FIGURES 13-25A TO C: Wedge excision. (A) Corneal graft astigmatism is very asymmetrical in this case. An arcuate wedge of graft tissue is excised from the donor margin in the flat axis (B) causing steepening of the flat axis. (C) The wound is resutured. Excision of a 1 mm wedge of tissue can correct 8 dioptres of astigmatism.

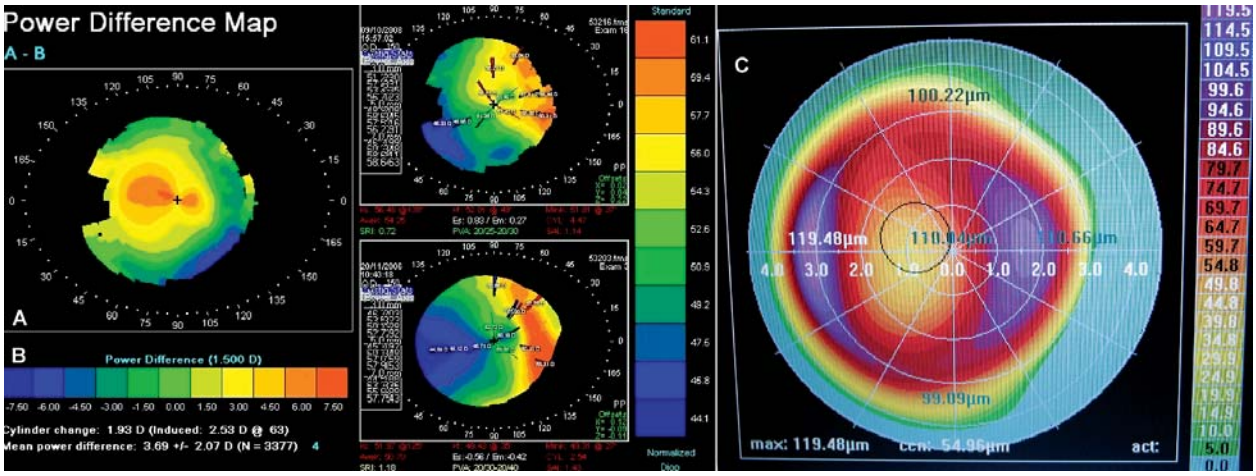


FIGURE 13-26: Topography-guided laser *in situ* keratomileusis (Topolink) for the correction of a corneal graft irregular astigmatism. The preoperative topographic map (B) shows marked asymmetry of the astigmatism. The topolink computer calculates a customized ablation profile (C). The postoperative map (A) shows significantly improved astigmatism symmetry within the 3 mm central zone. The differential map (A-B) shows the asymmetric ablation pattern, customized to this individual eye. Visual acuity improved from 0.3 with –9 –5x25 to 0.6 with –7 –2x30.

corticosteroids, is mandatory for at least a month following relaxing incisions. Other techniques (such as compression sutures alone or in association with relaxing incisions and wedge resection) are less frequently used. Wedge resections **(Figure 13-25)** are aimed at major astigmatisms, often asymmetrical, with often unpredictable results.

The success of LASIK in reducing postkeratoplasty astigmatism has dramatically altered the postoperative management of keratoplasty patients. Topography-guided laser *in situ* keratomileusis (Topolink) **(Figure 13-26)** gives encouraging results in post-graft irregular astigmatisms.

Finally, the use of phakic toric intraocular lenses may be a helpful alternative in treating postkeratoplasty astigmatism and ametropia.

Side Effects of Topical Corticosteroids

Glaucoma and cataract may occur.

Intraocular pressure elevation is the second leading cause of graft failure after PK. In patients with keratoconus, it is then often secondary to corticosteroids. Sustained elevation of intraocular pressure not only damages the optic nerve head, but it also has a deleterious effect on the corneal endothelium. Correction of elevated intraocular pressure refers to a reduction in corticosteroids eyedrops (e.g. replacement of Dexamethasone with Fluorometholone), the use of topical or systemic antiglaucoma medications, and even traditional filtering surgery on rare occasions (when either the optic nerve or the graft is threatened by persistent elevation of intraocular pressure).

Cataract can be extracted through a separate incision after the wound is totally healed. The endothelium must be protected by a good viscoelastic because of the risk of endothelial decompensation. Cataract extraction in a young subject results in a constant loss of accommodation.

Other Complications

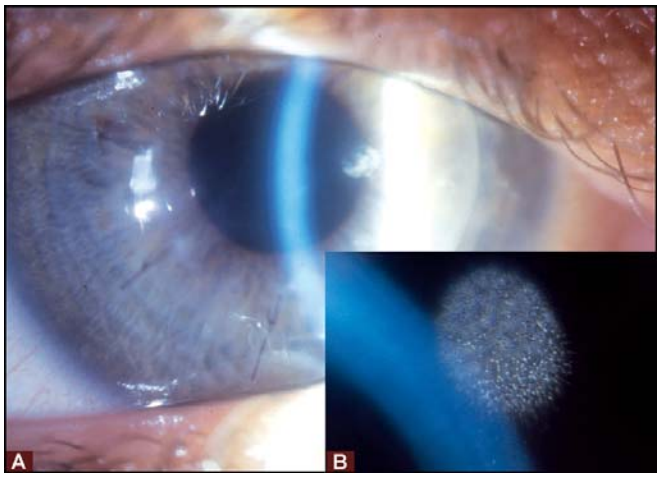
Shallow anterior chamber and wound leak: Lack of water tightness of the wound in the early postoperative period can be due to a full thickness suture or an insufficient number of sutures. Additional sutures may be applied in the operating room under topical anesthesia.

Epithelial defects: Epithelial defects are the source of visual loss, infection, rejection, stromal melting, perforations, and even graft failure. Survival of a corneal graft is critically dependent on an intact epithelial barrier. The quality of the postoperative epithelial wound healing necessitates frequent use of lubricants, preferably preservative-free, to promote epithelial growth, as well as the use of a bandage soft contact lens with high oxygen permeability in certain occasions.

Urrets-Zavalia syndrome: The first description of Urrets-Zavalia syndrome or fixed dilated pupil was made by Urrets-Zavalia after a corneal graft for keratoconus.[42] However, this syndrome is not specific to PK in keratoconus, and it was reported following lamellar grafts and in other indications. The mechanism is poorly understood, but it may involve iris ischemia. The role of mydriatics has been brought up as well as that of early and transitory acute postoperative raised intraocular pressure. Although rare, this complication prompts the use of mydriatics to be limited unless it is absolutely necessary. A careful ablation of viscoelastic at the end of the operation seems just as suitable, in our clinical experience.

Infections after PK: Postoperative endophthalmitis is a rare but sight-threatening complication of PK. Its incidence is around 0.5%.[43] Often, the infectious agents come from the conjunctival and palpebral flora of the patient. The clinical signs, diagnosis and treatment of postoperative endophthalmitis after PK are the same as those for endophthalmitis after cataract surgery.

Bacterial and fungal keratitis are complications that usually involve the graft or the wound. The incidence of microbial keratitis ranges from 1 to 12% in patients operated for PK. Microbial keratitis may be more frequent with topical steroids, persistent epithelial defect and suture related problems. It presents in the form of a stromal abscess with a high risk of graft melting. A particular form is an infectious crystalline keratopathy which takes the appearance of crystalline branching opacities **(Figure 13-27)**. The most common organism causing crystalline keratopathy is *Streptococcus viridans*. The identification of the etiology must be done with corneal scrapings for smear and culture in appropriate media, as fungal species have also been implicated. Treatment for bacterial and fungal keratitis is based on intensive regimen of broad-spectrum, fortified antibiotic eyedrops often with systemic



FIGURES 13-27A AND B: (A) *Streptococcus viridans* infectious crystalline keratopathy. (B) Note the crystalline opacities in the anterior and mid stroma.

drugs. A therapeutic graft is sometimes necessary. Fungal keratitis may necessitate interruption of the corticosteroids in the acute phase. The corticosteroids can be substituted with topical 2% Cyclosporin, which, in addition to its anti-rejection action, possesses an anti-fungal action.[44]

Recurrence of herpes simplex keratitis in a graft is not uncommon. Herpes simplex keratitis may also be observed in a patient who has never had herpes simplex keratitis. It has the distinctive feature of inciting graft rejection. Therefore, the treatment must include topical antiviral agents (administered topically and generally), and corticosteroids in the case of stromal keratitis.

In all cases, the prognosis of the initial graft is affected by these postoperative infections that confer an increased risk of graft failure.

Traumas on the grafted eye: Traumas on the grafted eye may have disastrous consequences and may even lead to the loss of the eye. Even after a long period of time from the trauma, a risk of wound dehiscence may persist.

Non-immunologic endothelial decompensation of the graft: The endothelial decompensation of the graft is another cause of graft failure of PK with progressive endothelial cell loss. Ing, *et al*[45] reported the outcomes of a series of 394 eyes with PK, 119 of which were followed for 10 years. Endothelial cell loss, from all causes, was 4.2% per year over a period of 5 to 10 years after the graft. This was 7 times greater than the average normal loss estimated at 0.6% per year. Out of 48 eyes grafted for keratoconus (40.3%) and followed up after 10 years, the endothelial cell loss was 73 ± 9% in 10 years compared with preoperative values. It was 23 ± 30% between 5 and 10 years after the graft. This progressive endothelial cell loss is the cause of the emptying of the peripheral endothelial reservoir that greatly reduces the chances of survival of the graft and any subsequent grafts. Thus, this must be taken into account in the decision to operate in young subjects.

Vitreoretinal complications: Retinal complications (retinal detachment, macular edema), due to open eye surgery, are rare but may occur.

Recurrence of keratoconus: Lastly, a recurrence of keratoconus may be encountered. The mechanism of progressive myopia observed after a graft for keratoconus is not understood. Ruhswurm, *et al*[46] observed an average myopia of –0.86 D after ablation of the sutures and a myopia of –2.35 D 3 years after the operation. This progressive myopia could be due to a recurrence of keratoconus at the level of the grafted cornea. Published cases of recurrences of keratoconus have increased in number.

Pramanik, *et al*[28] reported on 112 eyes of 84 patients operated with PK for keratoconus with an average follow-up of 13.8 years (range from 0.5 to 30.4 years). A recurrence of keratoconus was confirmed in 6 cases (5.4%) after an average period of 17.9 years (range of 11 to 27 years). The probability of having a recurrence of keratoconus after PK over 25 years was estimated at 11.7%.

It has not yet been clearly established whether a keratoconus recurs or a mild keratoconus from the donor that has gone unnoticed becomes manifest. However, the average time of 17 years until the onset of a recurrence of keratoconus is quite comparable with the time to natural development of keratoconus in a teenager.

Discussion/Conclusions

Will the number of indications of corneal graft for keratoconus be reduced? Would the advances in contact lenses, suppressive (corneal collagen cross-linking with Riboflavin: CXL) and additive (intracorneal rings) treatments be able to avoid or delay a corneal graft?

CXL is aimed at progressive keratoconus.[47] Its purpose is to "rigidify" a cornea which is biomechanically unstable. This effect that was observed *in vitro*[48, 49] is more difficult to quantify *in vivo*. However, the first clinical results are encouraging,[50-52] and the efficacy will continue to be assessed over a longer period.

Of course, contact lenses, which are essentially rigid, remain the basic treatment for eyes with keratoconus. Unfortunately, lenses are not tolerated in some patients who are often those with allergies and whose corneas remain transparent. In these cases, the implantation of intracorneal rings is a worthwhile alternative treatment to a corneal graft.[53, 54] A longer period of time is also necessary to assess what will become of these corneas. A combination of these two treatments (CXL/rings) or even of these three treatments (CXL/lenses/rings) may also be used.

When the progression of keratoconus leads to central corneal scarring or major thinning, a corneal graft is required. In this case, will the proportion of PK be reduced in favor of lamellar grafts?

The growing number of publications of lamellar graft techniques already marks this trend. Several studies comparing the results of PK and lamellar grafts in keratoconus have shown identical visual results.[55-57] The operating technique in lamellar grafts is more difficult than that of PK but they offer notable advantages in terms of conservation of the endothelium, graft rejection, faster corneal wound healing, and a shorter duration of the use of corticosteroids.

In certain cases, when the endothelium is involved, PK remains the only surgical alternative. If not, the choice between PK and lamellar grafts depends essentially on the preference and experience of the surgeon.

Long considered as the reference surgical treatment for keratoconus, today, PK is part of a therapeutic arsenal that has been considerably enriched in the past few years. PK in keratoconus requires a perfect surgical technique. The benefits of the femtosecond laser in the surgical technique remains to be demonstrated, and the technique may still benefit from future improvements. The visual results of PK in keratoconus are good in the majority of cases. This surgery, carried out most often in young patients, may lead to complications which should be early detected, in order to detect them early and provide appropriate solutions. Thus, the surgical indication of PK in a patient with keratoconus must always take into account this benefits/risks ratio. Although PK may be increasingly replaced with lamellar grafts, nevertheless, PK is an established surgical technique in keratoconus that has been greatly studied for its efficacy.

References

1. Rabinowitz YS. Keratoconus. Surv Ophthalmol 1998;42:297-319.
2. The Australian Corneal Graft Registry. 1990 to 1992 report. Aust N Z J Ophthalmol 1993;21:1-48.
3. Legeais JM, Parc C, d'Hermies F, Pouliquen Y, Renard G. Nineteen years of penetrating keratoplasty in the Hotel-Dieu Hospital in Paris. Cornea 2001;20:603-6.
4. Lois N, Kowal VO, Cohen EJ, Rapuano CJ, Gault JA, Raber IM, Laibson PR. Indications for penetrating keratoplasty and associated procedures, 1989-1995. Cornea 1997;16:623-9.
5. Maeno A, Naor J, Lee HM, Hunter WS, Rootman DS. Three decades of corneal transplantation: indications and patient characteristics. Cornea 2000;19:7-11.
6. Dobbins KR, Price FWJ, Whitson WE. Trends in the indications for penetrating keratoplasty in the midwestern United States. Cornea 2000;19:813-6.
7. Crews MJ, Driebe WT Jr, Stern GA. The clinical management of keratoconus: A 6 year retrospective study. CLAO J 1994;20:194-7.
8. Lass JH, Lembach RG, Park SB, Hom DL, Fritz ME, Svilar GM, Nuamah IF, Reinhart WJ, Stocker EG, Keates RH, et al. Clinical management of keratoconus. A multicenter analysis. Ophthalmology 1990;97:433-45.
9. Sray WA, Cohen EJ, Rapuano CJ, Laibson PR. Factors associated with the need for penetrating keratoplasty in keratoconus. Cornea 2002;21:784-6.
10. Dana MR, Putz JL, Viana MA, Sugar J, McMahon TT. Contact lens failure in keratoconus management. Ophthalmology 1992;99:1187-92.
11. Reeves SW, Stinnett S, Adelman RA, Afshari NA. Risk factors for progression to penetrating keratoplasty in patients with keratoconus. Am J Ophthalmol 2005;140:607-11.
12. Gordon MO, Steger-May K, Szczotka-Flynn L, Riley C, Joslin CE, Weissman BA, Fink BA, Edrington TB, Olafsson HE, Zadnik K. CLEK Study Group. Baseline factors predictive of incident penetrating keratoplasty in keratoconus. Am J Ophthalmol 2006;142:923-30.
13. Smiddy WE, Hamburg TR, Kracher GP, Stark WJ. Keratoconus. Contact lens or keratoplasty? Ophthalmology 1988;95:487-92.
14. Belin MW, Fowler WG, Chambers WA. Keratoconus. Evaluation of recent trends in the surgical and nonsurgical correction of keratoconus. Ophthalmology 1988;95:335-9..
15. Tuft SJ, Moodaley LC, Gregory WM, Davison CR, Buckley RJ. Prognostic factors for the progression of keratoconus. Ophthalmology 1994;101:439-47.
16. Colin J. European clinical evaluation: use of Intacs for the treatment of keratoconus. J Cataract Refract Surg 2006;32:747-55.
17. Krumeich JH, Daniel J, Knulle A. Live-epikeratophakia for keratoconus. J Cataract Refract Surg 1998;24:456-63.
18. Wilson EE, Bourne WM. Effect of recipient-donor trephine size disparity on refractive error in keratoconus. Ophthalmology 1989;96:299-305.
19. Girald LJ, Esnaola N, Rao R, Barnett L, Rand WJ. Use of grafts smaller than the opening for keratoconic myopia and astigmatism. J Cataract Refract Surg 1992;18:380-4.
20. Karabatsas CH, Cook SD, Figueiredo FC, Diamond JP, Easty DL. Combined interrupted and continuous versus single continuous adjustable suturing in penetrating keratoplasty: a prospective, randomized study of induced astigmatism during the first postoperative year. Ophthalmology 1998;105:1991-8.
21. Spadea L, Cifariello F, Bianco G, Balestrazzi E. Long-term results of penetrating keratoplasty using a single or double running suture technique. Graefes Arch Clin Exp Ophthalmol 2002;240:415-9.
22. Ehlers N, Olsen T. Long term results of corneal grafting in keratoconus. Acta Ophthalmol 1983;61:918-26.
23. Sharif KW, Casey TA. Penetrating keratoplasty for keratoconus: complications and long-term success. Br J Ophthalmol 1991;75:142-6.
24. Price FW Jr, Whitson WE, John S, Gonzales JS. Risk factors for corneal graft failure. J Refract Surg 1996;12:134-47.
25. Dandona L, Naduvilath TJ, Janarthanan M, Ragu K, Rao GN. Survival analysis and visual outcome in a large series of corneal transplants in India. Br J Ophthalmol 1997;81:726-31.
26. Lim L, Pesudovs K, Coster DJ. Penetrating keratoplasty for keratoconus: visual outcome and success. Ophthalmology 2000;107:1125-31.
27. Thompson RW, Price MO, Bowers PJ, Price FW. Long-term graft survival after penetrating keratoplasty. Ophthalmology 2003;110:1396-402.
28. Pramanik S, Musch DC, Sutphin JE, Farjo AA. Extended long-term outcomes of penetrating keratoplasty for keratoconus. Ophthalmology 2006;113:1633-8.
29. Olson RJ, Pingree M, Ridges R, Lundergan M, Alldredge C, Clinch TE. Penetrating keratoplasty for keratoconus: a long-term review of results and complications. J Cataract Ref Surg 2000;26:987-91.

30. Brierly SC, Isquierdo L, Mannis MJ. Penetrating keratoplasty for keratoconus. Cornea 2000;19:329-32.
31. Silbiger JS, Cohen EJ, Laibson PR. The rate of visual recovery after penetrating keratoplasty for keratoconus. CLAO J 1996;22:266-9.
32. Italon C, Pieh S, Hansemayer G, Kahraman G, Kaminski S, Skorpik C, Dejaco-Ruhswurm I. Changes of axial length and keratometry after keratoplasty for keratoconus using the guided trephine system. Am J Ophthalmol 2002;134:696-700.
33. Tuft S, Gregory W. Long-term refraction and keratometry after penetrating keratoplasty for keratoconus. Cornea 1995;14:614-7.
34. Tuft S, Fritzke FW, Buckley RJ. Myopia following penetrating keratoplasty for keratoconus. Br J Ophthalmol 1992;76:642-5.
35. Paglen PG, Fine M, Abbott RL, Webster RG. The prognosis for keratoplasty in keratoconus. Ophthalmology 1982;89:651-4.
36. Brahma A, Ennis F, Harper R, Ridgway A, Tullo A. Visual function after penetrating keratoplasty for keratoconus: a prospective longitudinal evaluation. Br J Ophthalmol 2000;84:60-6.
37. Pesudovs K, Schoneveld P, Seto RJ, Coster DJ. Contrast and glare testing in keratoconus and after penetrating keratoplasty. Br J Ophthalmol 2004;88:653-7.
38. Purcell JJ Jr. Expulsive hemorrhage. In Brightbill F(Ed): Corneal Surgery, Theory Technique and Tissue (2nd edn). St. Louis, Mosby, 1993;221-4.
39. Taylor DM, Stern AL, McDonald P. The triple procedure: 1 to 10 year follow-up. Trans Am Ophthalmol Soc 1986;84:221-49.
40. Kirkness CM, Ficker LA, Steele ADMcG, Rice NSC. The success of penetrating keratoplasty for keratoconus. Eye 1990;4:673-88.
41. Chandler JW, Kaufmann HE. Graft rejections after keratoplasty for keratoconus. Am J Ophthalmol 1973;77:543-7.
42. Urrets-Zavalia A. A fixed, dilated pupil iris atrophy and secondary glaucoma. A distinct clinical entity following penetrating keratoplasty in keratoconus. Am J Ophthalmol 1963;56:257-65.
43. Eifrig CW, Flynn HW Jr, Scott IU, Newton J. Acute-onset postoperative endophthalmitis: review of incidence and visual outcomes (1995-2001). Ophthalmic Surg Lasers. 2002;33:378-8.
44. Bell NP, Karp CL, Alfonso EC, Schiffman J, Miller D. Effects of methylprednisolone and cyclosporine A on fungal growth in vitro. Cornea 1999;18:306-13.
45. Ing JI, Ing HH, Nelson LR, Hodge DO, Bourne WM. Ten-year postoperative results of penetrating keratoplasty. Ophthalmology 1998;105:1855-65.
46. Ruhswurm I, Scholz U, Pfleger T, Zehetmayer M, Hanselmayer G, Skorpik C. Three-year clinical outcome after penetrating keratoplasty for keratoconus with the guided trephine system. Am J Ophthalmol 1999;127:666-73.
47. Spoerl E, Huhle M, Seiler T. Induction of cross-links in corneal tissue. Exp Eye Res 1998;66:97-103.
48. Wollensak G, Spoerl E, Seiler T. Stress-strain measurements of human and porcine corneas after riboflavin-ultraviolet-A-induced cross-linking. J Cataract Refract Surg 2003;29:1780-5.
49. Spoerl E, Wollensak G, Seiler T. Increased resistance of crosslinked cornea against enzymatic digestion. Curr Eye Res 2004;29:35-40.
50. Wollensak G, Spoerl E, Seiler T. Riboflavin/Ultraviolet-A-induced collagen crosslinking for the treatment of keratoconus. Am J Ophthalmol 2003;135:620-7.
51. Caporossi A, Baiocchi S, Mazzotta C, Traversi C, Caporossi T. Parasurgical therapy for keratoconus by riboflavin-ultraviolet type A rays induced cross-linking of corneal collagen: preliminary refractive results in an Italian study. J Cataract Refract Surg 2006;32:837-45.
52. Raiskup-Wolf F, Hoyer A, Spoerl E, Pillunat LE. Collagen crosslinking with riboflavin and ultraviolet-A light in keratoconus: long-term results. J Cataract Refract Surg 2008;34:796-801.
53. Colin J, Cochener B, Savary G, Malet F. Correcting keratoconus with intracorneal rings. J Cataract Refract Surg 2000;26:1117-22.
54. Colin J, Cochener B, Savary G, Malet F, Holmes-Higgin D. Intacs inserts for treating keratoconus: one year results. Ophthalmology 2001;108:1409-14.
55. Shimazaki J, Shimmura S, Ishioka M, Tsubota K. Randomized clinical trial of deep lamellar keratoplasty vs. penetrating keratoplasty. Am J Ophthalmol 2002;134:159-65.
56. Watson SL, Ramsay A, Dart JKG, Bunce K, Craig E. Comparison of deep lamellar keratoplasty and penetrating keratoplasty in patients with keratoconus. Ophthalmology 2004;111:1676-82.
57. Borderie VM, Werthel AL, Touzeau O, Allouch C, Boutboul S, Laroche L. Comparison of techniques used for removing the recipient stroma in anterior lamellar keratoplasty. Arch Ophthalmol 2008; 126:31-7.

14

Refractive Surgery after Penetrating Keratoplasty

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Introduction

Refractive anisometropia and high postoperative astigmatism are common problems after penetrating keratoplasty (PKP) and can jeopardize patient's visual rehabilitation and return to binocular function.[1] First studies on astigmatism after PKP reported mean corneal astigmatism of 4-5 D,[2,3] and estimated that 10% of penetrating grafts resulted in at least 5-6 D of keratometric astigmatism.[4-7] In keratoconic eyes this percentage could be as high as 27%.[8] Topographic studies on post-PKP astigmatism have shown that regular astigmatism is found in 24% of patients, while irregular astigmatism is found in 72% of patients. Moreover, the incidence of irregular astigmatism increases over time after surgery.[9] Advances in microsurgical techniques and better knowledge of the factors that influence the refractive outcome of PKP have reduced the incidence of high postoperative astigmatism.[1,10-12] However, astigmatism after PKP is still a problem in some cases.[13,14]

Several factors determine postoperative astigmatism **(Table 14-1)**. Some may be controlled by the surgeon and others not, and include variations in corneal hydration, changes in forces that develop at the graft-host interface,[15] refractive characteristics of the donor,[16-20] graft-host interactions,[21-26] and the effect of sutures **(Figure 14-1A)**.[22,27-30] Most studies have evaluated those factors that may be modified by the surgeon such as the type of suture, intraoperative or postoperative management of the suture, and trephine-punch size and technique.[21-30]

Femtosecond (IntraLase® Corp, AMO, CA; VisuMax, Carl Zeiss Meditec AG, Jena, Germany; or Femtec, 20/10 Perfect Vision AG, Heidelberg, Germany) laser has been used to perform the cut of both the host and the donor button in a variety of shapes (e.g. mushroom, mushroom inverted, zig-zag, top-hat, etc…),[31-36] and shows good promise in surgical management of corneal diseases. The multiplanar fit and increased area of wound healing between the donor and recipient cornea may allow early suture removal and visual rehabilitation.[31,32,34] However, the effect of femtosecond laser-assisted keratoplasty on postoperative astigmatism in the long-term needs to be established.

PKP has shown good long-term outcomes when performed in keratoconic eyes.[37-39] Due to concerns on the risk of endothelial rejection of the corneal graft and long-term progressive endothelial cell loss associated with PKP procedures, deep anterior lamellar keratoplasty (DALK) has been proposed as an alternative for the treatment of keratoconus and any other corneal condition with a healthy endothelium. Apart from the obvious advantages of maintaining the native endothelium (rejection and endothelial cells' survival), with DALK the strength of the wound when facing ocular trauma is greater, and, theoretically, visual rehabilitation may be faster and the amount of residual ametropia lower.[36,40-42] In our experience, although DALK seems a safer approach from a mechanical and

TABLE 14-1: Factors determining residual astigmatism after penetrating keratoplasty

Not controlled by surgeon	May be controlled by surgeon
Corneal hydration	Donor's refractive characteristics[16-20]
Epitelial/stromal wound healing[15]	Graft-host interactions:[21-26] - Apposition[21] - Thickness - Trephine-punch size/shape[22,24] - Eccentricity corneal graft[23,25]
Remodeling[15]	Sutures:[22,27-30] - Type (interrupted, running,…) - Intra/postoperative management

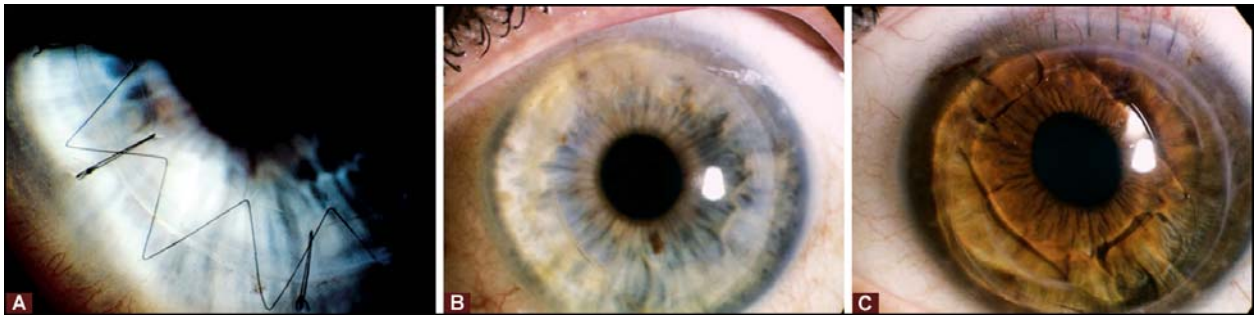


FIGURE 14-1: (A) Combination of running and interrupted sutures in penetrating keratoplasty. (B) Arquate keratotomies (AK) to correct residual astigmatism after penetrating keratoplasty. Two AK of 60° of arc are performed on the steeper meridian, and are centered over the pupil. (C) Implantation of the iris-claw toric phakic IOL (Artisan/Verisyse) to correct residual astigmatism after penetrating keratoplasty and AK.

endothelial point of view, PKP provides better optical quality, and similar refractive results (Guell JL, *et al*. Personal report for the American Academy of Ophthalmology 2004). Because improved surgical approaches for DALK have been developed, optical and visual results are improving.[43,44]

Spectacle correction is tolerated in those cases presenting small to moderate ametropia with less than 3 D of anisometropia or astigmatism less than 4 D.[45,46] Around 25-60% of PKP for keratoconus (KC) do not achieve their best-corrected visual acuity (BCVA) only with spectacles, and may be aided with contact lenses (CL), specially rigid gas-permeable CL if significant irregular astigmatism is present.[47-49] Contact lens fitting has been reported to be successful in 80-90% of these cases. However, 27% of chronic CL users become intolerant, and a considerable amount of patients do not want to wear CL. In such cases, surgical intervention may be required to achieve optimal visual rehabilitation.[50-53]

Different surgical options have been proposed for visual and refractive rehabilitation after PKP: incisional corneal refractive surgery [relaxing incisions, astigmatic keratotomy (AK),[54-56] or wedge resections],[57,58] ablational corneal refractive procedures [laser-assisted *in situ* keratomileusis (LASIK) and photorefractive keratectomy (PRK)], additive corneal refractive surgery (intrastromal corneal ring segments (ICRS),[59] implantation of spherical or toric phakic or pseudophakic IOLs,[60,61] and when severe irregularity and/or decentration is present, PKP may be repeated **(Figures 14-1B and C)**. This chapter deals with surgical tips, results, and complications of both LASIK and implantation of toric phakic IOLs as the most common procedures in our practice for visual rehabilitation after PKP in keratoconic eyes.

Corneal Refractive Surgery and Penetrating Keratoplasty

Both LASIK[62-65] and PRK[66,67] have been used to correct refractive errors after PKP. LASIK has been used more commonly to correct myopia and myopic astigmatism, as it usually presents several advantages over PRK, including rapid visual rehabilitation, decreased stromal scarring, less irregular astigmatism, and minimal regression. Moreover, LASIK is theoretically able to treat a wider range of ametropia.[63, 68]

On the other hand, PRK has been associated with loss of BCVA related to significant residual stromal haze,[68-73] which has been related to the magnitude of the ablations required and has been coupled with the regression of the obtained refractive effect.[68] Despite the recent advances in surface

ablation techniques which might change our standard in the near future, LASIK is currently the technique of choice to correct low and moderate post-PKP refractive errors.

In those cases with high levels of astigmatism, AK may be performed first to reduce astigmatism to a level at which a more predictable refractive surgery such as LASIK or implantation of a phakic IOL can be used to correct residual ametropia.[54,65,74-77]

INDICATIONS

Excimer refractive surgery should be considered to correct refractive errors after PKP when anisometropia is not successfully corrected with spectacles, and in cases of CL intolerance. The primary goal of LASIK after PKP is to reduce the degree of ametropia, which allows spectacle correction and return to binocularity. The inclusion criteria for LASIK after PKP are the same as for LASIK in non-PKP patients. However, some additional cautions must be taken into account **(Table 14-2)**.[78-80]

TABLE 14-2: Indications and contraindications for laser-assisted in-situ keratomileusis for residual ametropia after penetrating keratoplasty

Indications	Contraindications
• Refractive stability at least 6 months after extraction of sutures • Minimal maintenance or no topical corticosteroids • CCT > 500 µm[79] • Residual stromal bed > 250 µm • Sim K 38 – 55 D[80]	• Graft rejection, recurrence of herpetic ocular disease, or inflammatory condition • Marked peripheral corneal vascularization • Significant corneal anesthesia • Thin host tissue • Wound ectasia • Significant graft override/Wound malapposition:[78,80] - misalignment graft-host junction > 10% - internal gaping > 20%

Although refractive stability after PKP is not easily determined, it has been generally accepted to perform corneal refractive surgery at least 6 months after extraction of all sutures, which means, at least about 18 months after PKP. Apart from the time elapsed after PKP, the stability of refraction and corneal topography suggest a low level of active wound remodeling. The amount of whitening and scarring, as well as its thickness profile, of the wound should also be verified to avoid wound dehiscence or problems when cutting the flap.[81]

Dry eye or corneal hypo/anesthesia are more common in post-PKP patients, especially the elderly ones, and increase the risk of ocular surface problems after PKP. Therefore, management of ocular surface problems is mandatory before LASIK. Endothelial cell count should also be performed. The effect of LASIK on endothelial cell counts on PKP eyes remains unclear. Although some studies report an endothelial cell loss of 8.6%-10.56%,[62,82] other series have found no significant alterations.[63,83]

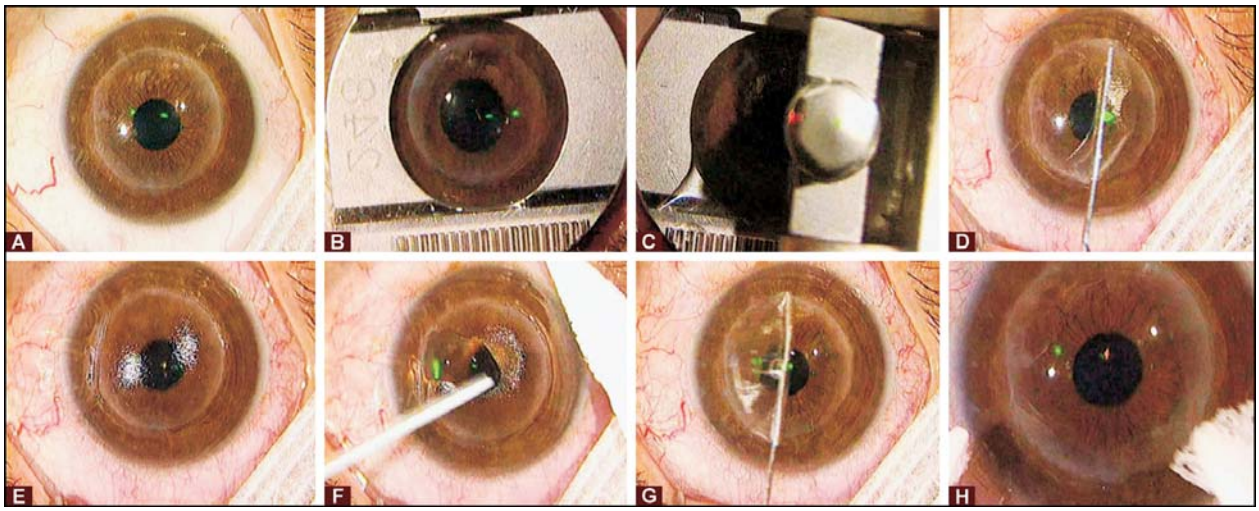
STEP-BY-STEP SURGICAL TECHNIQUE

LASIK technique in PKP eyes is essentially the same as our standard LASIK procedure. Diazepam (5 to 10 mg) is administered orally about 30 minutes before surgery. Topical anesthesia (proparacaine hydrochloride 1%) is instilled 1 drop every two minutes starting 6 minutes before surgery. In cases

of LASIK for moderate-high astigmatism, the horizontal meridian is marked at the limbus while the patient is sitting at the slit-lamp in order to verify the correct alignment once under the surgical microscope.

Betadine solution 10% is applied to the closed eyelid and the lashes of the operative eye are isolated with a sterile plastic drape as in any other standard anterior segment surgical procedure. Various types of microkeratomes and machines may be used. Currently, we use the Amadeus microkeratome (Ziemer Ophthalmic Systems AG, Switzerland) to cut the flap and we perform the ablations with the MEL 80 excimer laser (Carl Zeiss Meditech, Jena, Germany). Once the personalized parameters have been set at the console unit, the microkeratome suction ring is centered over the pupil, and the guides and corneal surface are moisturized before cutting the flap. The microkeratome's head should be individually adapted depending on preoperative K-readings and corneal graft diameter. A head of 8.5-mm diameter and 140-µm thickness is generally used for graft sizes up to 8.5 mm. For longer grafts, the 9-mm diameter head is used. To achieve better wound apposition of the flap, it is recommended to avoid initiation of the flap edge at the graft-host junction, even though this is difficult to achieve, especially with larger grafts.[62] The flap is then folded to the nasal side of the eye using our modified iridodialysis spatula.

The stromal bed is dried and the laser beam is focused on the center of the pupil, the proper axis centration is checked, the eye-tracker system is activated, and the ablation is performed. After the ablation, the stromal bed is washed with filtered balanced saline solution (BSS, Alcon) and the flap is repositioned and its border carefully dried with microesponges. To confirm adequate adhesion, the peripheral cornea is indented with a microsponge to check for the presence of striae. As adherence of the flap takes longer in post-keratoplasty patients due to poorer endothelial function, a prolonged waiting period of 5 minutes is recommended.[62,84] Finally, the lid speculum is gently removed, and a drop of tobramycin and dexamethasone are instilled. Steroidal drops will be used for several weeks under a slow taper regimen **(Figure 14-2)**. When performing LASIK in PKP eyes, some additional



FIGURES 14-2A TO H: Step-by-step surgical technique for LASIK after penetrating keratoplasty. (A) The lashes of the operative eye are isolated with a sterile plastic drape. (B) After setting excimer laser's parameters, the microkeratome (Amadeus, Ziemer Ophthalmic Systems AG, Switzerland) suction ring is centered over the pupil. (C) The guides and corneal surface are moisturized, and the flap is cut. (D) The flap is then folded to the nasal side of the eye using an iridodialysis spatula. (E) The stromal bed is dried and the laser beam is focused on the center of the pupil, the eye-tracker system is activated, and the ablation is performed. (F) The stromal bed is washed with filtered balanced saline solution (BSS, Alcon). (G) The flap is repositioned. (H) The border of the flap is carefully dried with microsponges.

difficulties may be encountered. It is of utmost importance to check the correct apposition and scarring of the graft-host interface. As there is a long-term instability of PKP wounds, partial wound dehiscence may occur while cutting the flap. If this is the case, LASIK may be performed uneventfully and, in some cases, the wound may require suture.

High keratometry readings are relatively common in PKP patients. Therefore, flap complications typical of steep corneas such as thin flaps or buttonholes may occur. Moreover, it has also been postulated an increased risk of recurrence of keratoconus in the graft after excimer laser ablations.

Topography-guided ablations constitute adequate options to correct or reduce irregular astigmatism. However, the efficacy of guided ablations compared to the standard approach is still controversial.[85-87] In those cases with high levels of astigmatism, AK may be performed first to reduce astigmatism to a level at which LASIK can be used to correct residual ametropia, while less tissue is ablated.[54,65,88,89] It is generally recommended to perform LASIK at least 6 months after incisional surgery.[62]

Simply performing a hinged lamellar keratotomy induces a biomechanical response of the cornea that results in changes of its shape.[90,91] Also, cutting a 160-µm corneal flap in eyes after PKP results in significant changes of both spherical equivalent refraction and astigmatism that may result in inaccurate refractive corrections if pre-flap refraction is applied.[92,93] For this reason, several authors advocate to perform LASIK after PKP as a 2-stage procedure. Excimer ablation by relifting the flap is performed once the corneal shape is stabilized (1 to 3 months after keratotomy).[93-99] Nevertheless, as we have previously mentioned with topo-guided or wavefront-guided ablations, a superior efficacy of the 2-step approach is still controversial.

Toric Phakic Intraocular Lenses and PKP

INDICATIONS

Inclusion and exclusion criteria for implantation of phakic IOLs are summarized in **Table 14-3**. The toric Artisan-Verisyse is our phakic IOL of choice for the correction of residual moderate-high myopic or hyperopic astigmatism after PKP. The toric Artisan/Verisyse pIOL is a one piece, 5-mm optic, PMMA lens which is available in powers ranging from +12 D to -23.5 D in 0.5-D increments,

TABLE 14-3: Generally recommended inclusion and exclusion criteria for phakic IOL implantation

Inclusion criteria	Exclusion criteria
• Age > 21 years • Stability of refraction at least 1 year • Ametropia not correctable with excimer laser surgery • Unsatisfactory vision with/intolerance of contact lenses or spectacles • Irido-corneal angle ≥ 30° • cECC > 2300 cells/mm²*: (> 2500 cells/mm² if >21 years old, > 2000 if >40 years old) • No anomaly of the iris or pupil function • Scotopic pupil size < 5-6 mm • Toric PIOL if astigmatism > 2 D	• Background of active disease in the anterior segment • Recurrent or chronic uveitis • Any form of clinically significant cataract • Previous corneal or intraocular surgery (to be evaluated) • IOP > 21mmHg or glaucoma • Preexisting macular degeneration or macular pathology • Abnormal retinal condition • Systemic diseases (e.g. autoimmune disorder, connective tissue disease, atopia, diabetes mellitus)

* Lower cECC are accepted in selected cases

with additional cylinder from 1.0 D to 7.0 D, also in 0.5-D increments. There are two available models for correcting, with a similar surgical technique and incision positioning, any astigmatic axis: a toric Artisan phakic IOL with a cylinder axis at 0 degrees (model A) and a toric Artisan phakic IOL with a cylinder axis at 90 degrees (model B) with respect to the position of the haptics. When the axis of the cylinder is between 0 and 45 degrees or 135 and 180 degrees, model A is recommended; when the axis of the cylinder is between 45 and 135 degrees, model B is recommended.

The foldable model of the iris-claw lens is the Artiflex (Ophtec, Groningen, The Netherlands).[100,101] It is a Hydrophobic Polysiloxane foldable design with a 6.0-mm optic and powers ranging from –2 D to –14.5 D in 0.5 D steps. Currently, we participate in an ongoing multicenter European clinical trial on the toric model of the Artiflex lens, which can be implanted through a 3.1-mm incision.[102]

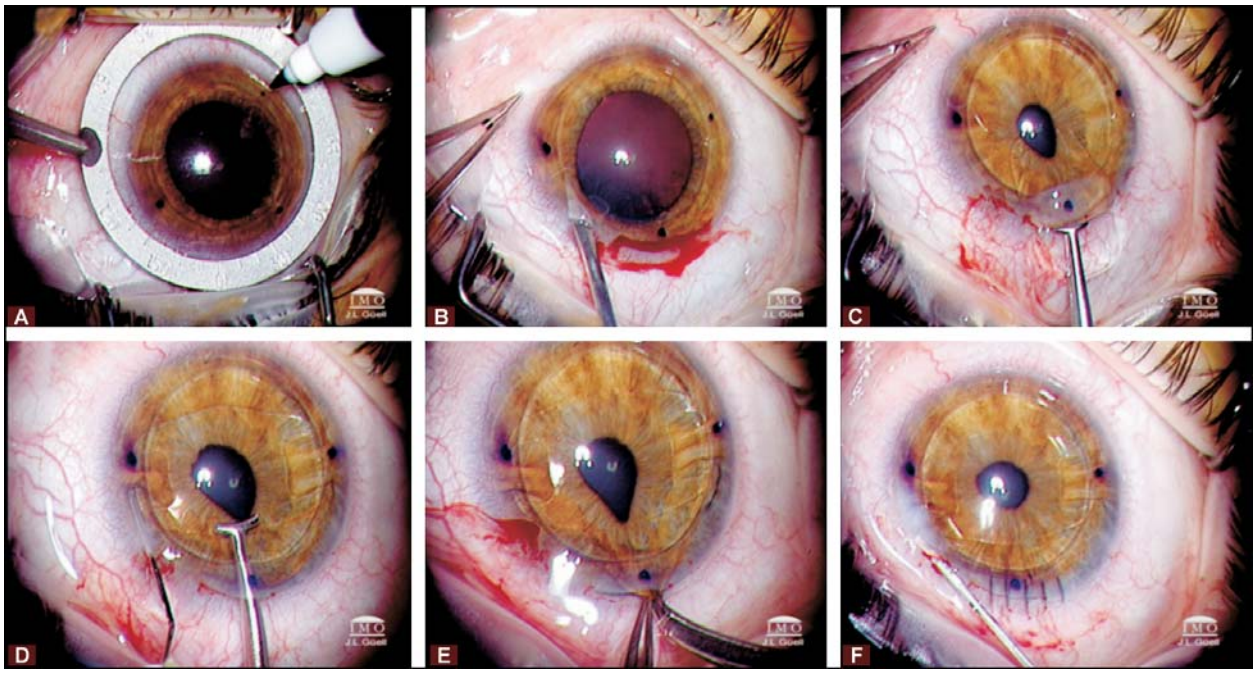
Lens power is calculated using Van der Heijde's formula,[103] which includes patient's refraction, keratometry and adjusted ultrasound or anterior segment optical coherence tomography (OCT) central anterior chamber depth (ACD). For a proper placement of the TPIOL, the surgeon receives an illustration of the correct TPIOL position.

STEP-BY-STEP SURGICAL TECHNIQUE

Depending on the surgeon's familiarity with the technique, general, retrobulbar, peribulbar or topical anesthesia may be used. For the Verisyse® PIOL implantation procedure retrobulbar or peribulbar anesthesia is generally recommended. Toric Verisyse implantation requires careful preoperative marcation of the axis of implantation. Marcation of the axis should be performed preoperatively at the slit-lamp, or in the Argon laser, to avoid implantation errors due to cyclotorsion and/or position changes induced by the retro or peribulbar anesthesia injection, and the positioning of the patient under the surgical microscope.

According to our recommended technique, a two-plane, 5.2-mm posterior corneal incision is centered 90° apart the axis of enclavation, and two vertical paracenteses are directed towards the enclavation area. Alternatively, a scleral incision may be used. Wound construction is important to minimize induced astigmatism or wound leaks. Most surgeons center the incision at the steep meridian when using model A toric phakic Artisan.

The pupil should be constricted so as to protect the crystalline lens from the contact with the PIOL or surgical instruments during the surgery. This can be achieved either instilling 1% pilocarpine preoperatively or injecting acetylcholine (Myochol, Ciba Vision) in the anterior chamber at the beginning of the procedure, or both. We do not usually use pilocarpine before the surgery. Taking advantage of the capability to locate this type of implant over the center of the pupil, it should be marked on the cornea ("entrance pupil") preoperatively if using 1% pilocarpine, or at the beginning of the surgery if using intracameral acetylcholine, so as to enable a proper, final centration of the PIOL. Once the anterior chamber is filled with a cohesive viscoelastic material, the lens is introduced and rotated up to the axis of enclavation. The PIOL is fixed with an enclavation needle that pushes the iris into both claws. The needle is introduced through one of the paracentesis and holds the fold of iris while the lens is slightly depressed with the implantation forceps so that the claws will automatically grasp the iris. Then, hands are switched and the same maneuver is performed through the other paracentesis. Both the fixation of the iris claws and the proper centration of the PIOL over the pupil should be checked before the next step, which is one of the main advantages of this PIOL style. It is not unusual to have a mild ovalization of the pupil because of the effect of the miotic. If the lens is not well centered or oriented, the lens enclavation can be released by pushing in the central portion of the claw with the enclavation needle.



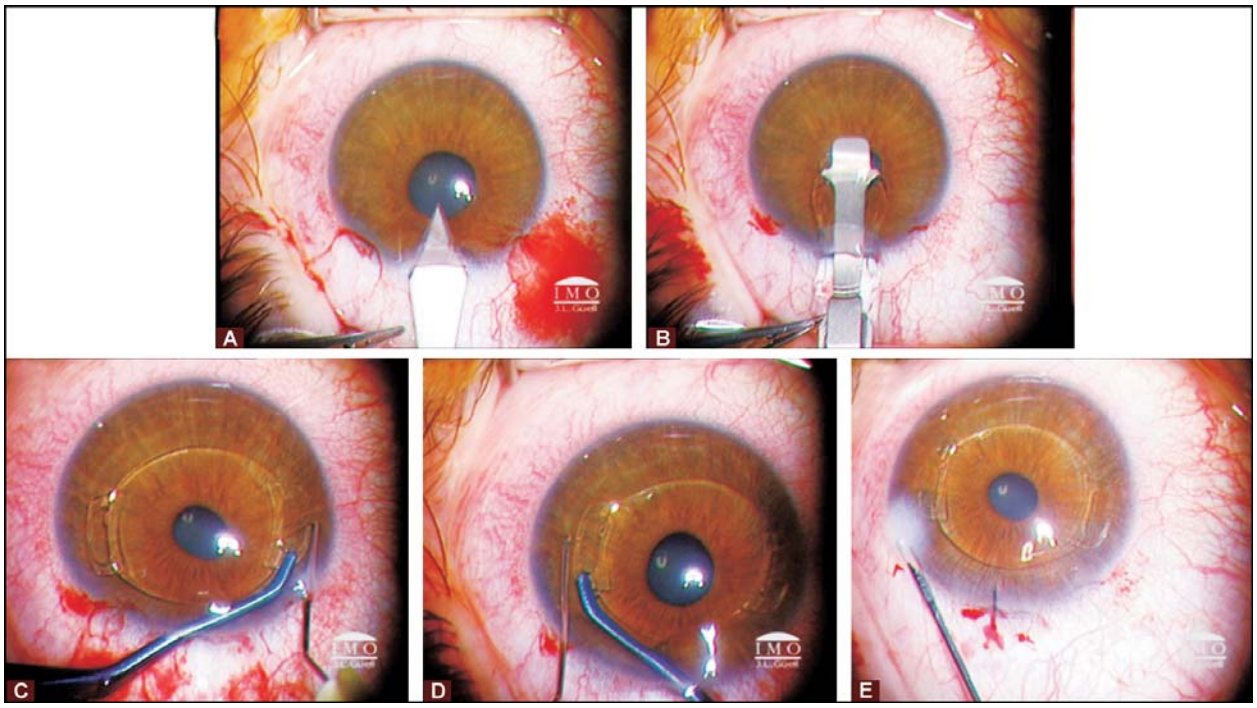
FIGURES 14-3A TO F: Step-by-step surgical technique for the implantation of iris-claw toric phakic IOL for the correction of astigmatism after PKP. (A) Preoperative marcation of the axis of implantation. (B) Two vertical paracentesis directed towards the site of enclavation are performed. (C) Pupil constriction is achieved by injecting acetylcholine (Myochol, Ciba Vision) in the anterior chamber. The anterior chamber is filled with a cohesive viscoelastic material, the lens is introduced by means of a special forceps and rotated up to the axis of enclavation. (D) Enclavation process. The enclavation needle is introduced through one of the paracentesis and holds the fold of iris and the claws automatically grasp the iris. (E) A peripheral iridectomy using scissors is performed to prevent pupil block. (F) The wound is then sutured with five interrupted 10-0 nylon stitches.

A peripheral iridectomy should be performed to prevent postoperative pupil block. Alternatively, Nd:YAG laser can be used to create two small iridotomies 90° apart preoperatively. The wound is then sutured with five interrupted 10-0 nylon stitches. At the end of the procedure, the proper tension of the sutures is checked with a standard qualitative Maloney keratoscope **(Figure 14-3)**. Beginning at week 4, and over a period of 3 months, sutures are selectively removed, depending on the patient's refractive and topographic astigmatism.

Implantation of the foldable model requires a 3.1-mm incision, which corresponds to the width of the PMMA haptics. The Artiflex lens is inserted using a specially designed spatula, and the process of enclavation is the same as for the PMMA lens. The only difference is that the lens is grasped with the implantation forceps by the base of the haptic instead of by the edge of the optic. The posterior corneal 3.1-mm incision is usually water-tight, but we prefer to suture it with a 10/0 nylon suture. Suture is removed by three weeks after surgery **(Figure 14-4)**.

Refractive Surgery after Penetrating Keratoplasty for Keratoconus: Our Experience

From 1998 to 2006, Dr. J.L. Guell performed 663 keratoplasties at our institution, Instituto de Microcirugia Ocular, Barcelona, Spain. Overall, primary or secondary corneal ectasia accounted for 28% of cases (190/663): 23% (155/663) keratoconus, 4% (29/663) ectasia secondary to corneal refractive



FIGURES 14-4A TO F: Implantation of the Artiflex/Veriflex phakic IOL (A) A 3.1-mm incision is required. (B) The Artiflex lens is inserted using a specially designed spatula. (C) The enclavation needle is introduced through one of the paracentesis and holds the fold of iris while the lens is grasped with the implantation forceps by the base of the haptic. (D) Hands are switched and the same maneuver is repeated to enclavate the other claw. (E) The incision is sutured with a 10/0 nylon suture.

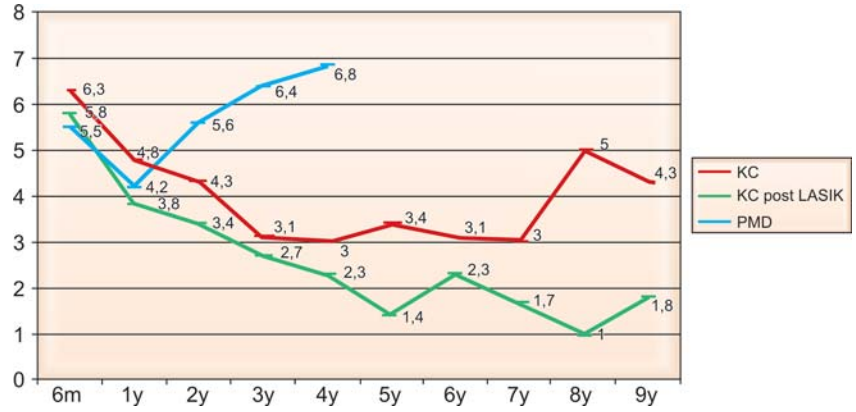


FIGURE 14-5: Evolution of postoperative astigmatism after penetrating keratoplasty for corneal ectasia: ectasia secondary to corneal refractive surgery (CRS), keratoconus (KC), and pellucid marginal degeneration (PMD). Postoperative astigmatism is highest in PMD, followed by KC, and lowest in CRS.

procedures, and 1% (6/663) pellucid marginal degeneration (PMD). As it has been previously described, significant astigmatism is one of the main causes that impair visual rehabilitation after PKP. Interestingly, PKP performed in patients with PMD have higher postkeratoplasty astigmatism than patients with keratoconus or secondary ectasia (6.8 ± 4.6 vs 2.98 ± 1.63 and 2.25 ± 2.38, respectively) **(Figure 14-5)**. This phenomenon may be due to the greater peripheral thinning that exists in PMD and KC, and not in CRS.

TABLE 14-4: Additional refractive procedures to correct residual ametropia after penetrating keratoplasty			
	KC n=155	CRS n=29	PMD n=6
RP required	108/155 (69.6%)	25/29 (86.2%)	4/6 (66.6%)
LASIK	18/108 (16.66%)	3/25 (12%)	0
AK	38/108 (35.18%)	6/25 (24.1%)	1/4 (25%)
TPIOL	9/108 (8.33%)	7/25 (28%)	0
CATARACT	30/108 (27.77%)	7/25 (28%)	3/4 (75%)
PKP	7/108 (6.48%)	0	0
OTHER	6/108 (5.5%)	2/25 (8%)	0

KC = keratoconus; CRS = corneal refractive surgery; PMD = pellucid marginal degeneration; n = number of patients; RP = refractive procedures; LASIK = laser-assisted in situ keratomileusis; AK =arquate keratotomies; TPIOL = toric phakic intraocular lens; PKP =penetrating keratoplasty

Due to postoperative astigmatism and ametropia, and both patient's and surgeon's increasing demands, a significant amount of patients require additional procedures to achieve visual rehabilitation and restore binocular vision. In our series refractive procedures were required by 69.6% of patients undergoing PKP for keratoconus, 86.2% of patients undergoing PKP for secondary ectasia, and 66.6% of patients undergoing PKP for PMD. **Table 14-4** summarizes surgical procedures performed and their prevalence for each group of patients.

Twenty-one percent of patients required more than one procedure to achieve optimal correction. Corneal graft rejection episodes were only observed in 7 KC eyes (4.5%), while no case of rejection occurred among secondary ectasia and PMD patients.

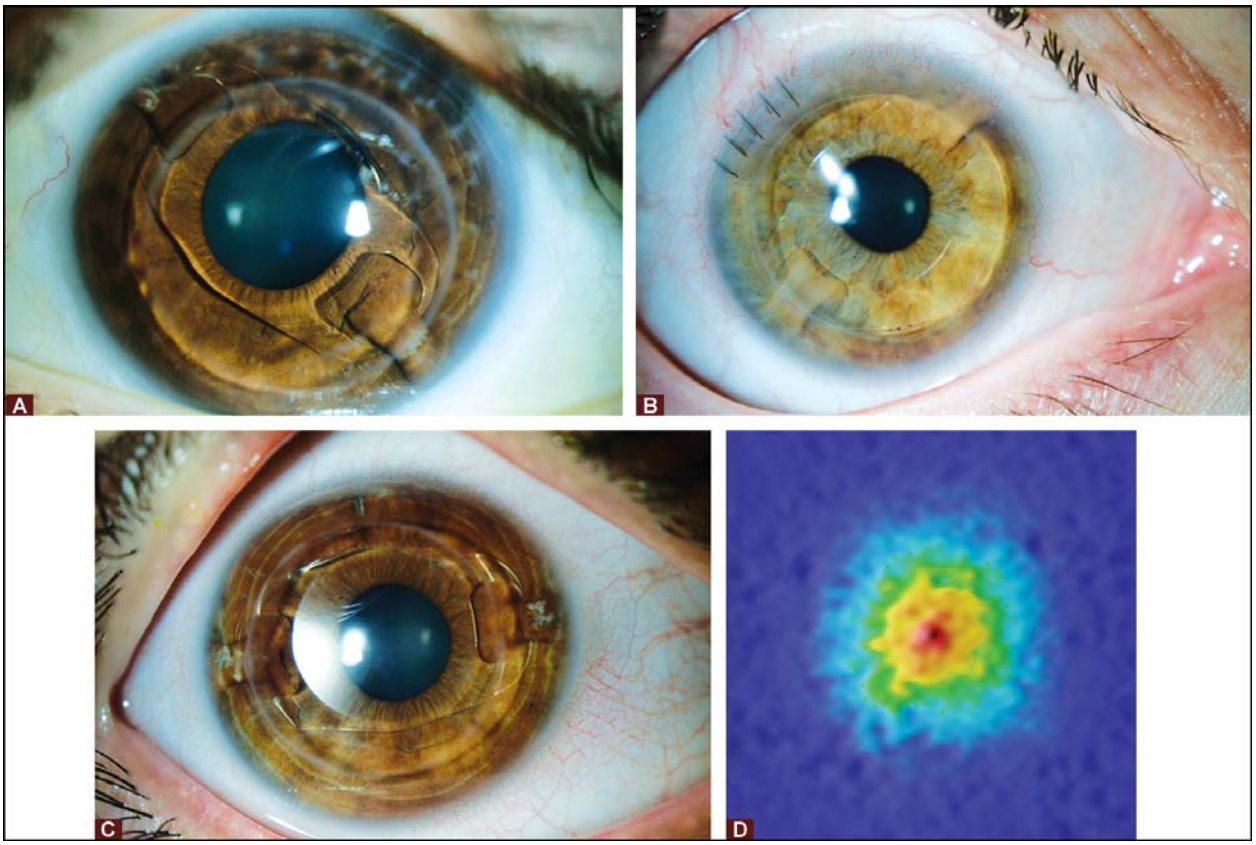
Both corneal refractive surgery and toric phakic IOL implantation significantly reduced the amount of post-PKP astigmatism (from 3.58 ± 1.59 preoperatively to 2.83 ± 1.89 and 0.88 ± 0.53, respectively). However, in our hands, toric phakic IOL implantation showed better predictability and stability. As far as safety is concerned, none of the eyes lost any line of BSCVA, and the vast majority of them (>90%) gained one or more lines of BSCVA.

VERISYSE TORIC PHAKIC IOL TO CORRECT RESIDUAL ASTIGMATISM AFTER PKP

We report follow-up data of implantation of Verysise™ TPIOLs in 19 eyes of 14 patients with residual astigmatism after PKP **(Figure 14-6)**. After suture removal and refractive stabilization, we implanted Verysise™ TPIOLs in 19 eyes of 14 patients with residual astigmatism after PKP for corneal ectasia (11 eyes primary keratoconus, 8 eyes secondary ectasia due to previous refractive surgery).

Mean (± standard deviation) spherical equivalent (SE) and cylinder before TPIOL surgery were –4.15±0.16 D and –4.54±1.55 D, respectively. After 4 years, they were -0.34±0.95 D and –1.32±0.90 D, respectively **(Figure 14-7)**. **Table 14-5** summarizes refractive, visual and endothelial cell count preoperative data and after 4 years of follow-up. Sixteen eyes (84.2%) were within 1 D of intended spherical correction, and 10 eyes (52.63%) were within 1 D of intended cylinder correction.

Preoperative BSCVA was 0.55±0.16. Four years postoperatively, BSCVA was 0.66±0.18, and UCVA was 0.54±0.21. BSCVA and UCVA improved over the follow-up period **(Figure 14-8)**. Efficacy and safety indexes were 0.98 and 1.18, respectively.



FIGURES 14-6A TO D: Clinical photographs. (A) Iris-claw toric phakic intraocular lens (TPIOL) four years after implantation to correct residual astigmatism after penetrating keratoplasty (PKP) for keratoconus (KC). UCVA is 20/50 and BSCVA is 20/40 with 140° -2 +1.25. (B) PKP in a patient with corneal ectasia secondary to CRS. Preoperative BSCVA was 20/40 with 5° -4.5 -8. Six months after TPIOL implantation UCVA was 20/30, and BSCVA was 20/25 with 30° -1.25. (C) PKP in a patient with KC. Preoperative BSCVA was 20/40 with 5° -4.5 -8. Four years after TPIOL implantation UCVA was 20/40, and BSCVA was 20/25 with 70° -2 +0.25. (D) Optical quality of patient C. Point-spread function image obtained with the Optical Quality Analysis System (OQAS, Visiometrics SL) shows good optical quality after TPIOL implantation.

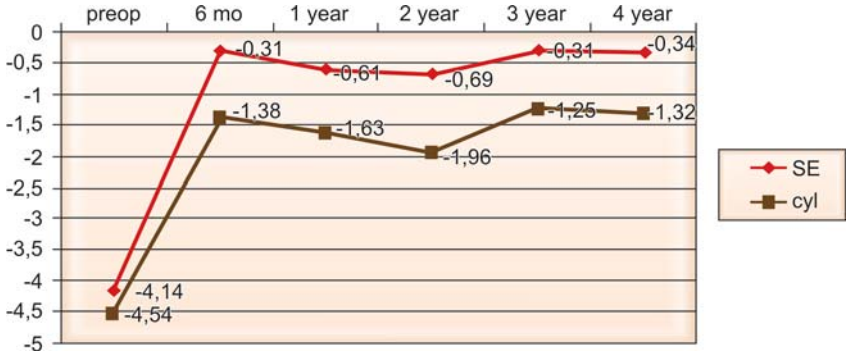


FIGURE 14-7: Stability of spherical equivalent and cylinder after toric phakic intraocular lens (TPIOL) implantation throughout the 4-year follow-up period.

Our 4-year follow-up data fits with that of Tahzib and cols, showing better reduction of the refractive cylinder than most reported LASIK series. Reported enhancement rates after LASIK in PKP eyes ranges from 9.1% to 53% of cases.[65,87,104-106] None of our TPIOL patients required any CRS

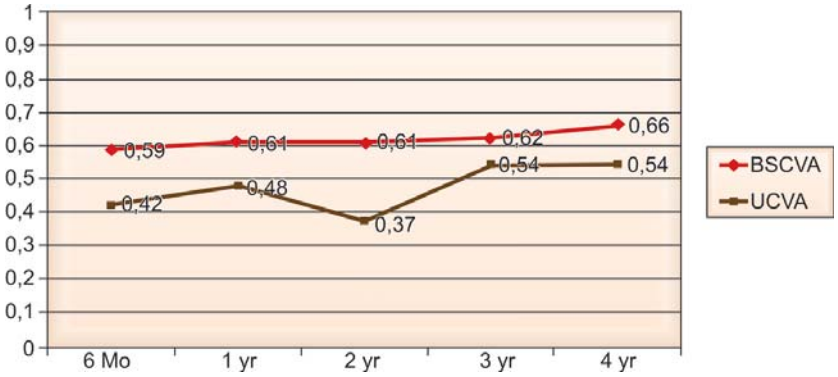


FIGURE 14-8: Best-spectacle corrected (BSCVA) and uncorrected visual acuity (UCVA) slightly improved throughout the 4-year follow-up period.

TABLE 14-5: Baseline data and four years after implantation of toric Verisyse phakic intraocular lens to correct residual ametropia after penetrating keratoplasty

	PREOPERATIVELY	4 YEARS
SE	-4.15±0.16 D (-21 to +7 D)	-0.34±0.95 D (-1.5 to +1.4 D)
CYL	-4.54±1.55 D (-9 to -2D)	-1.32±0.90 D (-2.5 to 0 D)
UCVA	< 20/400	20/30 (20/100 - 20/27)
BSCVA	20/40 (20/50 - 20/25)	20/30 (20/40 - 20/27)
ECC cells/mm²	1947 ± 645 (3128 to 823)	1598 ± 243 (2530 to 973)

SE = spherical equivalent; CYL = cylinder; UCVA = uncorrected visual acuity; BSCVA = best-spectacle corrected visual acuity; ECC = endothelial cell count; D = diopters

enhancement. Moreover, the stability of the postoperative refractive cylinder after Verisyse TPIOL implantation up to 4 years was excellent. In contrast, progressive changes have been reported in refraction and topography in 35.7% of cases after LASIK after a mean follow-up time of 26.9 months.[79] Moreover, high enhancement rates after LASIK may be explained by the effect of the flap cut alone that may induce a significant change in refractive astigmatism.[90-93] To reduce the incidence of enhancements, a 2-step approach has been proposed,[93-99] but it is unclear whether it bears a higher risk for complications like epithelial ingrowth, wound-healing problems, and flap dislocation.

None of our patients lost any line of BSCVA, which contrasts with the 2-line loss in 8.3% of cases after Artisan implantation,[60] or the 2-line loss in 4.3%[62] to 16%[64] (Hardten) of eyes after LASIK for postkeratoplasty astigmatism. In postPKP eyes, optical quality may also be better after PIOL implantation than after LASIK, as it has been reported in non-PKP eyes.[107,108]

Endothelial cell loss rate was 18% at 4 years **(Figure 14-9)**, which is higher than the rate reported for non-PKP eyes (4.8% at 3 years,[109] 1.7% at 2 years,[110] and 5.11% at 5 years[111]). A previous study from Tahzib, *et al* reported a mean endothelial cell loss of 30.4% ± 32.0% at 36 months. They also noticed that there was a significant continuing progressive endothelial cell loss at each time point as compared with preoperative cell density levels and at 6 months as compared with 12, 24, and 36 months.[60] This may be due to the increased vulnerability of the corneal graft endothelium, which usually has low cell densities and may cause a higher rate of endothelial cell loss.[60,112] After routine keratoplasty, the annual rate of endothelial cell loss from 3 to 5 years after keratoplasty is 7.8% per

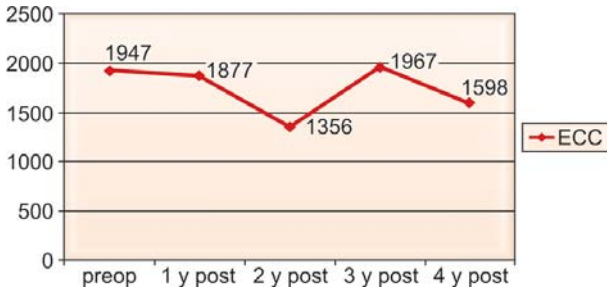


FIGURE 14-9: Endothelial cell count showed 18% decrease at 4 years.

year,[112] and from 5 to 10 years is 4.2% per year,[112-114] which is higher than the 'physiological' endothelial cell loss of 0.6% per year with age.[115] Although LASIK seems safer for the endothelium than the implantation of TPIOL, it may be complicated by flap complications, including diffuse lamellar keratitis,[105] buttonhole flaps,[79,83] wound dehiscence,[116] and epithelial ingrowth.[79] Also, LASIK has limitations due to corneal graft thickness and the amount of ametropia and astigmatism suitable for correction.[67,79,80,83,92,106,117-119]

In conclusion, additional refractive surgery is frequently required for visual rehabilitation after PKP. Several surgical options have been used to correct significant ametropia. In our experience, Verisyse™ TPIOL implantation has been a predictable, effective, and safe refractive procedure for the correction of high spherical and astigmatic errors after PKP. However, longer follow-up is mandatory to clarify the effect of this surgery on the corneal endothelium of the graft, as well as compared to chronic use of contact lenses.

References

1. Brooks SF, Johnson D, Fischer N. Anisometropia and binocularity. Ophthalmology 1996;103(7):1139-43.
2. Troutman RC, Meltzer M. Astigmatism and myopia in keratoconus. Trans Am Ophthalmol Soc 1972;70:265-77.
3. Richard JM, Paton D, Gasset AR. A comparison of penetrating keratoplasty and lamellar keratoplasty in the surgical management of keratoconus. Am J Ophthalmol 1978;86(6):807-11.
4. Jensen AD, Maumenee AE. Refractive errors following keratoplasty. Trans Am Ophthalmol Soc. 1974;72:123-31.
5. Troutman RC. Microsurgical control of corneal astigmatism after cataract and keratoplasty. Trans Am Acad Ophthalmol Otorrynol 1973;77:563-72.
6. Troutman RC, Swinger C. Relaxing incision for control of postoperative astigmatism following keratoplasty. Ophthalmic Surg 1980;11:117-20.
7. Swinger CA. Postoperative astigmatism. Surv Ophthalmol 1987;31:219-48.
8. Troutman RC, Gaster RN. Surgical advances and results of keratoconus. Am J Ophthalmol 1980;30:131-6.
9. Karabatsas .CH, Cook SD, Sparrow JM. Proposed classification for topographic patterns seen after penetrating keratoplasty. Br J Ophthalmol 1999;83(4):403-9.
10. Busin M, Mönks T, al-Nawaiseh I. Different suturing techniques variously affect the regularity of postkeratoplasty astigmatism. Ophthalmology 1998;105:1200-5.
11. Perlman EM. An analysis and interpretation of refractive errors after penetrating keratoplasty. Ophthalmology 1981;88:39-45.
12. Perl T, Charlton KH, Binder PS. Disparate diameter grafting. Astigmatism, intraocular pressure, and visual acuity. Ophthalmology 1981;88:774-81.
13. Riddle HK Jr, Parker DA, Price FW Jr. Management of postkeratoplasty astigmatism. Curr Opin Ophthalmol 1998;9:15-28.
14. Hammoudi DS, Segev F, Abdolell M, Rootman DS. Outcome of penetrating keratoplasty performed by cornea fellows compared with that of an experienced staff surgeon. Cornea 2005;24:410-6.
15. O'Brart DPS, Corbett MC, Rosen ES. The topography of corneal disease. Eur J Implant Ref Surg 2005;7:173-83.

16. Liu Y, Seitz B, Langenbucher A, et al. Impact of preoperative corneal curvature on the outcome of penetrating keratoplasty in keratoconus. Cornea 2003;22:409-12.
17. Ousley PJ, Terry MA. Use of a portable topography machine for screening donor tissue for prior refractive surgery. Cornea 2002;21:745-50.
18. Lin RC, Li Y, Tang M, et al. Screening for previous refractive surgery in eye bank corneas by using optical coherence tomography. Cornea 2007;26:594-9.
19. Hick S, Laliberte JF, Meunier J, et al. Topographic screening of donor eyes for previous refractive surgery. J Cataract Refract Surg 2006;32:309-17.
20. Krivoy D, McCormick S, Zaidman GW. Postkeratoplasty keratoconus in a nonkeratoconus patient. Am J Ophthalmol 2001;131:653-4.
21. Kaiserman I, Bahar I, Rootman DS. Corneal wound malapposition after penetrating keratoplasty: an optical coherence tomography study. Br J Ophthalmol 2008;92(8):1103-7.
22. Seitz B, Langenbucher A, Küchle M, Naumann GO. Impact of graft diameter on corneal power and the regularity of postkeratoplasty astigmatism before and after suture removal. Ophthalmology 2003;110:2162-7.
23. Kerenyi A, Süveges I. Corneal topographic results after eccentric, biconvex penetrating keratoplasty. J Cataract Refract Surg 2003;29:752-6.
24. Jaycock PD, Jones MN, Males J, et al. Outcomes of same-sizing versus oversizing donor trephines in keratoconic patients undergoing first penetrating keratoplasty. Ophthalmology. 2008;115(2):268-75.
25. Chern KC, Meisler DM, Wilson SE, et al. Small-diameter, round, eccentric penetrating keratoplasties and corneal topographic correlation. Ophthalmology 1997;104:643-7.
26. Troutman RC. Astigmatic considerations in corneal graft. Ophthalmic Surg. 1979;10(5):21-6.
27. Van Rij G, Waring GO. Changes in corneal curvature induced by sutures and incisions. Am J Ophthalmol 1984;98:773-83.
28. Javadi MA, Naderi M, Zare M, et al. Comparison of the effect of three suturing techniques on postkeratoplasty astigmatism in keratoconus. Cornea 2006;25(9):1029-33.
29. Serdarevic ON, Renard GJ, Pouliquen Y. Randomized clinical trial of penetrating keratoplasty. Before and after suture removal comparison of intraoperative and postoperative suture adjustment. Ophthalmology 1995;102(10):1497-503.
30. Mader TH, Yuan R, Lynn MJ, Stulting RD, Wilson LA, Waring GO 3rd. Changes in keratometric astigmatism after suture removal more than one year after penetrating keratoplasty. Ophthalmology. 1993;100(1):119-26; discussion-127.
31. Cheng YY, Tahzib NG, van Rij G, et al. Femtosecond laser-assisted inverted mushroom keratoplasty. Cornea 2008;27:679-85.
32. Price FW, Price MO. Femtosecond laser shaped penetrating keratoplasty: one-year results utilizing a top-hat configuration. Am J Ophthalmol 2008;145:210-4.
33. Por YM, Cheng JY, Parthasarathy A, et al. Outcomes of femtosecond laser-assisted penetrating keratoplasty. Am J Ophthalmol 2008;145:772-4.
34. Buratto L, Böhm E. The use of the femtosecond laser in penetrating keratoplasty. Am J Ophthalmol 2007;143: 737-42.
35. Farid M, Kim M, Steinert RF. Results of penetrating keratoplasty performed with a femtosecond laser zigzag incision initial report. Ophthalmology 2007;114:2208-12.
36. Bahar I, Kaiserman I, Srinivasan S, Ya-Ping J, Slomovic AR, Rootman DS. Comparison of Three Different Techniques of Corneal Transplantation for Keratoconus. Am J Ophthalmol 2008;22:e-pub ahead of print.
37. Pramanik S, Musch DC, Sutphin JE, Fario AA. Extended long-term outcomes of penetrating keratoplasty for keratoconus. Ophthalmology. 2006;113(9):1633-8.
38. Gracia Garcia GP, Martinez JB. Outcomes of penetrating keratoplasty in mentally retarded patients with keratoconus. Cornea 2008;27(9):980-7.
39. Beckingsale P, Mavrikakis I, Al-Yousuf N, et al. Penetrating keratoplasty: outcomes from a corneal unit compared to national data. Br J Ophthalmol 2006;90(6):728-31.
40. Watson SL, Ramsay A, Dart JK. Comparison of deep lamellar keratoplasty and penetrating keratoplasty in patients with keratoconus. Ophthalmology 2004;111:1676-82.
41. Vabres B, Bosnjakowski M, Bekri L, et al. Deep lamellar keratoplasty versus penetrating keratoplasty for keratoconus. J Fr Ophthalmol 2006;29:361-71.
42. Shimazaki J, Shimmura S, Ishioka M, Tsubota K. Randomized clinical trial of deep lamellar keratoplasty vs penetrating keratoplasty. Am J Ophthalmol 2002;134:159-65.
43. Borderie VM, Werthel AL, Touzeau O, et al. Comparison of techniques used for removing the recipient stroma in anterior lamellar keratoplasty. Arch Ophthalmol 2008;126:31-7.
44. Anwar M, Teichmann KD. Big-bubble technique to bare Descemet's membrane in anterior lamellar keratoplasty. J Cataract Refract Surg 2002;28:398-403.

45. Wietharn BE, Driebe WT Jr. Fitting contact lenses for visual rehabilitation after penetrating keratoplasty. Eye Contact Lens 2004;30(1):31-3.
46. Vajpayee RB, Sharma N, Sinha R, et al. Laser in-situ keratomileusis after penetrating keratoplasty. Surv Ophthalmol 2003;48:503-14.
47. Riddle HK, Parker DA, Price FW. Management of postkeratoplasty astigmatism. Curr Opin Ophthalmol 1998;9: 15-28.
48. Chastang PJ, Borderie VM, Carvajal-Gonzalez S, et al. Prediction of spectacle-corrected visual acuity using videokeratography. J Refract Surg 1999;15:572-9.
49. Speaker MG, Cohen EJ, Edelhauser HF, et al. Effect of gas-permeable contact lenses on the endothelium of corneal transplants. Arch Ophthalmol 1991;109:1703-6.
50. Lim N, Vogt U. Characteristics and functional outcomes of 130 patients with keratoconus attending specialist contact lens clinic. Eye 2002;16:54-9.
51. Geerards AJ, Vreugdebhil W, Khazen A. Incidence of rigid gas-permeable contact lens wear after keratoplasty for keratoconus. Eye Contact Lens 2006;32:207-10.
52. Espana EM, Tseng SC. Analysis of contact lens intolerance by exploring neuroanatomic integration of ocular surface defense. Cont Lens Anterior Eye 2003;26:131-7.
53. Glasson MJ, Stapleton F, Keay L, et al. Differences in clinical parameters and tear film of tolerant and intolerant contact lens wearers. Invest Ophthalmol Vis Sci 2003;44:5116-24.
54. Poole TR, Ficker LA. Astigmatic keratotomy for post-keratoplasty astigmatism. J Cataract Refract Surg 2006;32:1175-9.
55. Harissi-Dagher M, Azar DT. Femtosecond laser astigmatic keratotomy for postkeratoplasty astigmatism. Can J Ophthalmol 2008;43:367-9.
56. Hoffart L, Touzeau O, Borderie V, Laroche L. Mechanized astigmatic arcuate keratotomy with the Hanna arcitome for astigmatism after keratoplasty. J Cataract Refract Surg 2007;33:862-8.
57. Lugo M, Donnenfeld ED, Arentsen JJ. Corneal wedge resection for high astigmatism following penetrating keratoplasty. Ophthalmic Surg 1987;18:650-3.
58. Belmont SC, Lazzaro DR, Muller JW, Troutman RC. Combined wedge resection and relaxing incisions for astigmatism after penetrating keratoplasty. J Refract Surg 1995;11:472-6.
59. Krumeich JH, Daniel J. Perforating keratoplasty with an intracorneal ring. Cornea 1999;18:277-81.
60. Tahzib NG, Cheng YY, Nuijts RM. Three-year follow-up analysis of Artisan toric lens implantation for the correction of postkeratoplasty ametropia in phakic and pseudophakic eyes. Ophthalmology 2006;113:976-84.
61. Nuijts RM, Abhilakh Missier KA, Nabar VA, Japing WJ. Artisan toric lens implantation for correction of postkeratoplasty astigmatism. Ophthalmology 2004;111:1086-94.
62. Donnenfield ED, Kornstein HS, Amin A, et al. Laser in situ keratomileusis for correction of myopia and astigmatism after penetrating keratoplasty. Ophthalmology 1999;106:1966-74, discussion 1974-5.
63. Arenas E, Maglione A. Laser in situ keratomileusis for astigmatism and myopia after penetrating keratoplasty. J Refract Surg 1997;13:27-32.
64. Hardten DR, Chittcharus A, Lindsrom RL. Long-term analysis of LASIK for the correction of refractive errors after penetrating keratoplasty. Trans Am Ophthalmol Soc 2002;100:143-50.
65. Guell JL, Gris O, Muller A, Corcostegui B. LASIK for the correction of residual refractive errors from previous surgical procedures. Ophthalmic Surg Lasers 1999;30:341-9.
66. La Tegola MG, Alessio G, Sborgia C. Topographic customized photorefractive keratectomy for regular and irregular astigmatism after penetrating keratoplasty using the LIGI CIPTA/LaserSight platform. J Refract Surg 2007;23: 681-93.
67. Yoshida K, Tazawa Y, Demong TT. Refractive results of post penetrating keratoplasty photorefractive keratectomy. Ophthalmic Surg Lasers 1999;30:354-9.
68. Lazzaro DR, Haight DH, Belmont SC, et al. Excimer laser keratectomy for astigmatism occurring after penetrating keratoplasty. Ophthalmolgy 1996;103:458-64.
69. Chan WK, Hunt KE, Glasgow BJ, Mondino BJ. Corneal scarring after photorefractive keratectomy in a penetrating keratoplasty. Am J Ophthalmol 1996;121:570-1.
70. Leccisotti A. Photorefractive keratectomy with mitomycin C after deep anterior lamellar keratoplasty for keratoconus. Cornea 2008;27:417-20.
71. Fraenkel G, Sutton G, Rogers C, Lawless M. Paradoxical response to photorefractive treatment for postkeratoplasty astigmatism. J Cataract Refract Surg 1998;24:861-5.
72. Georgaras SP, Neos G, Margetis SP, Tzenaki M. Correction of myopic anisometropia with photorefractive keratectomy in 15 eyes. Refract Corneal Surg 1993;9:S29-34.
73. Nordan LT, Binder PS, Kassar BS, et al. Photorefractive keratectomy to treat myopia and astigmatism after radial keratotomy and penetrating keratoplasty. J Cataract Refract Surg 1995;21:268-73.

74. Afshari NA, Schirra F, Rapoza PA, et al. Laser in situ keratomileusis outcomes following radial keratotomy, astigmatic keratotomy, photorefractive keratectomy, and penetrating keratoplasty. J Cataract Refract Surg 2005;31:2093-2100.
75. Guell Jl, Vazquez M. Correction of high astigmatism with astigmatic keratotomy combined with laser in situ keratomileusis. J Cataract Refract Surg 2000;26:960-6.
76. Bochmann F, Schipper I. Correction of post-keratoplasty astigmatism with keratotomies in the host cornea. J Cataract Refract Surg 2006;32(6):923-8.
77. Harissi-Dagher M, Azar DT. Femtosecond laser astigmatic keratotomy for postkeratoplasty astigmatism. Can J Ophthalmol 2008;43(3):367-9.
78. Serdarevic ON, Renard GJ, Pouliquen Y. Randomized clinical trial comparing astigmatism and visual rehabilitation after penetrating keratoplasty with and without intraoperative suture adjustment. Ophthalmology 1994;101: 990-9.
79. Kwitko S, Marinho DR, Rymer S, Ramos Filho S. Laser in situ keratomileusis for ametropia after penetrating keratoplasty. J Cataract Refract Surg 2001;27:374-9.
80. Koay PY, McGhee CN, Weed KH, Craig JP. Laser in situ keratomileusis after penetrating keratoplasty. J Refract Surg 2000;16:140-7.
81. Lam DS, Leung A, Wu JT, et al. How long should one wait to perform LASIK after PKP? J Cataract Refract Surg 1998;24:6-7.
82. Nassaralla BR, Nassaralla JJ, Horst J. Laser in situ keratomileusis after penetrating keratoplasty. J Refract Surg 2000;16:431-7.
83. Forseto AS, Francesconi CM, Nose RA, Nose W. Laser in situ keratomileusis to correct refractive errors after keratoplasty. J Cataract Refract Surg 1999;25:479-85.
84. Preschel N, Hardten DR, Lindstrom RL. LASIK after penetrating keratoplasty. Int Ophthalmol Clin 2000;40:111-23.
85. Alessio G, Boscia F, La Tegola MG, Shorgia C. Corneal Interactive Programmed Topographic Ablation Customized photorefractive keratectomy for correction of postkeratoplasty astigmatism. Ophthalmology 2001;108:2029-37.
86. Knorz MC, Jendritza B. Topographically-guided laser in situ keratomileusis to treat corneal irregularities. Ophthalmology 2000;107:1138-43.
87. Guell JL, Velasco F. Topographically guided ablations for the correction of irregular astigmatism after corneal surgery. Int Ophthalmol Clin 2003;43:111-28.
88. Afshari NA, Schirra F, Rapoza PA, et al. Laser in situ keratomileusis outcomes following radial keratotomy, astigmatic keratotomy, photorefractive keratectomy, and penetrating keratoplasty. J Cataract Refract Surg 2005; 31:2093-2100.
89. Guell Jl, Vazquez M. Correction of high astigmatism with astigmatic keratotomy combined with laser in situ keratomileusis. J Cataract Refract Surg 2000;26:960-6.
90. Roberts C. The cornea is not a piece of plastic. J Refract Surg 2000;16:407-13.
91. Guell JL, Velasco F, Roberts C, et al. Corneal flap thickness and topography changes induced by flap creation during laser in situ keratomileusis. J Cataract Refract Surg 2005;31:115-9.
92. Busin M, Arffa RC, Zambianchi L, et al. Effect of hinged lamellar keratotomy on postkeratoplasty eyes. Ophthalmology 2001;108:1845-51.
93. Dada T, Vajpayee RB, Gupta V, et al. Microkeratome-induced reduction of astigmatism after penetrating keratoplasty. Am J Ophthalmol 2001;131:507-8.
94. Busin M, Zambianchi L, Garzione F, et al. Two-stage laser in situ keratomileusis to correct refractive errors after penetrating keratoplasty. J Refract Surg 2003;19:301-8.
95. Mularoni A, Laffi GL, Bassein L, Tassinari G. Two-step LASIK with topography-guided ablation to correct astigmatism after penetrating keratoplasty. J Refract Surg 2006;22:67-74.
96. Dada T, Vajpayee RB. Laser in-situ keratomileusis after PKP. J Cataract Refract Surg 2002;28:7-8.
97. Tuunanen TH, Ruusuvaara PJ, Uusitalo RJ, Tervo TM. Photoastigmatic keratectomy for correction of astigmatism in corneal grafts. Cornea 1997;16:48-53.
98. Vajpayee RB, Dada T. LASIK after penetrating keratoplasty. Ophthalmology 2000;107:1801-2.
99. Kohnen T, Bühren J. Corneal first-surface aberration analysis of the biomechanical effects of astigmatic keratotomy and a microkeratome cut after penetrating keratoplasty. J Cataract Refract Surg 2005;31:185-9.
100. Güell JL, Morral M, Gris O, et al. Evaluation of Verisyse and Artiflex phakic intraocular lenses during accommodation using Visante optical coherence tomography. J Cataract Refract Surg 2007;33(8):1398-1404.
101. Guell JL, Velasco F. Phakic intraocular lens implantation. Int Ophthalmol Clin 2002;42(4):119-30.
102. Dick HB, Tehrani M. Short-term follow-up after implantation of a foldable iris-fixated intraocular lens in phakic eyes. Ophthalmology 2005;112:2189-95.
103. Van der Heijde GL. Some optical aspects of implantation of an intraocular lens in a myopia eye. Eur J Implant Refract Surg 1989;1:245-8.

104. Donnenfeld ED, Solomon R, Biser S. Laser in situ keratomileusis after penetrating keratoplasty. Int Ophthalmol Clin 2002;42(4):67-87.
105. Malecha MA, Holland EJ. Correction of myopia and astigmatism after penetrating keratoplasty with laser in situ keratomileusis. Cornea 2002;21:564-9.
106. Rashad KM. Laser in situ keratomileusis for correction of high astigmatism after penetrating keratoplasty. J Refract Surg 2000;16:701-10. 1291-6, discussion 1297.
107. Malecaze FJ, Hulin H, Bierer P, et al. A randomized paired eye comparison of two techniques for treating moderately high myopia: LASIK and artisan phakic lens. Ophthalmology 2002;109:1622-30.
108. El Danasoury MA, El Maghraby A, Gamali TO. Comparison of iris-fixed Artisan lens implantation with excimer laser in situ keratomileusis in correcting myopia between 9.00 and 19.50 diopters: a randomized study. Ophthalmology 2002; 109:955-64.
109. Stulting RD, John ME, Maloney RK. US Verisyse Study Group. Three-Year results of Artisan/Verisyse phakic intraocular lens implantation results of the United States Food and Drug Administration Clinical Trial. Ophthalmology 2008;115(3):464-72.
110. Budo C, Hessloehl JC, Izak M, et al. Multicenter study of the Artisan phakic intraocular lens. J Cataract Refract Surg 2000;26(8):1163-71.
111. Güell JL, Morral M, Gris O, et al. Five-year follow-up of 399 phakic Artisan®-Verisyse® implantation for myopia, hyperopia and/or astigmatism. Ophthalmology 115(6):1002-12.
112. Bourne WM. Corneal endothelium five years after transplantation. Am J Ophthalmol 1994;118:185-96.
113. Bourne WM, Nelson LR, Hodge DO. Continued endothelial cell loss ten years after lens implantation. Ophthalmology 1994;101:1014-22, discussion 1022-3.
114. Patel SV, Hodge DO, Bourne WM. Corneal endothelium and postoperative outcomes 15 years after penetrating keratoplasty. Am J Ophthalmol 2005;139:311-9.
115. Bourne WM, Nelson LR, Hodge DO. Central corneal endothelial cell changes over a ten-year period. Invest Ophthalmol Vis Sci 1997;38(3):779-82.
116. Ranchod TM, McLeod SD. Wound dehiscence in a patient with keratoconus after penetrating keratoplasty and LASIK. Arch Ophthalmol 2004;122:920-1.
117. Nassaralla BR, Nassaralla JJ. Laser in situ keratomileusis after penetrating keratoplasty. J Refract Surg 2000;16: 431-7.
118. Buzard K, Febbraro JL, Fundingsland BR. Laser in situ keratomileusis for the correction of residual ametropia after penetrating keratoplasty. J Cataract Refract Surg 2004;30:1006-13.
119. Barraquer CC, Rodriguez-Barraquer T. Five-year results of laser in-situ keratomileusis (LASIK) after penetrating keratoplasty. Cornea 2004;23:243-8.

15

Toric Intraocular Lenses after Keratoplasty

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Introduction

High astigmatism is one of the most common and difficult problems after grafting, representing one of the major vision-limiting factors after penetrating keratoplasty (PK). Some known causes for post-keratoplasty astigmatism are size thickness and shape differences between donor and host eccentric placement, irregular scarring at host junction and asymmetric forces in the cornea resulting in shape alterations.[1, 2] Despite substantial improvement in visual acuity after PK and a clear graft, significant postoperative astigmatism can remain and limit visual performance and decrease patient satisfaction after successful PK. A thorough study that classified astigmatism patterns after PK found that 24% showed regular astigmatic patterns and 72% showed irregular astigmatic patterns.[3] We know that patients generally do not tolerate more than 3-4 diopters (D) of anisometropia and/or astigmatism.[4]

Currently, there is no standard approach for the management of astigmatism after PK. Treating this type of astigmatism remains a challenge and many techniques can be applied. Various methods have been tried to treat post-keratoplasty astigmatism and include wedge resections, relaxing incisions, customized laser ablation such as photorefractive keratectomy (PRK), laser in situ keratomileusis (LASIK) and laser-assisted subepithelial keratectomy (LASEK). Until now, LASIK appears to be the preferred technique for correction of anisometropia and astigmatism after keratoplasty.[5-13] The reduction of refractive astigmatism after LASIK varies from 48% to 88%. However, enhancements were reported in 9.1%,[14] 15%,[15] 42.9%,[6] 45%[16] and 53%[8] of cases and in one study, LASIK was combined with arcuate incisions in the stromal bed in 54% of eyes **(Table 15-1)**.[17]

Another treatment option is the surgical implantation of a toric phakic intraocular lens (IOL). The advantage of this surgical technique is the fact that the implantation requires no direct manipulation or ablation of the donor cornea. The iris-fixated toric Artisan IOL can provide a wide field for correction of post-keratoplasty astigmatism and ametropia. A study by Nuijts, *et al*[18] demonstrated the safety and efficacy of this procedure, showing a 91.0% reduction of the refractive cylinder, which is higher than LASIK post-PK studies have shown. None of the treated eyes lost best-corrected visual acuity (BSCVA) lines and 50% gained at least 2 lines of BSCVA. They also showed that the postoperative refractive error remained stable up to 12 months after the Artisan lens implantation. They reported an endothelial cell loss of 7.6% at 3 months, 21.7% at 6 months, and 16.6% at the last follow-up (mean of 8.4 months).[18] Moshirfar, *et al* have described 2 successful cases of implantation of the iris-fixated phakic IOL for the correction of myopic refractive error after keratoplasty, demonstrating no significant endothelial cell loss.[19] A more recent study by Moshirfar, *et al* showed 2 cases of Artisan lens implantation post-PK, demonstrating an endothelial cell loss of 25.6% in one case and 42% in the other.[20] The Artisan lens also has shown to be rotationally stable,[21-23] which is of great value when attempting to correct higher degrees of astigmatism, since minimal differences between achieved and intended lens axis alignment can lead to a reduced corrective value of the lens. Approximately one-third of the cylindrical correction is lost if the IOL is rotated 10° off the axis. Axial misplacement of the Artisan toric IOL is probably related to incorrect alignment during the surgical procedure, since the lens is fixed firmly to the midperipheral iris stroma.

Recently, new imaging devices became available, which enable us to visualize the phakic IOL in the anterior chamber. The position of the phakic IOL is important as it provides information about the distance of the IOL to its surrounding structures. To ensure their long-term safety, the distance from the phakic IOL to the corneal endothelium and to the crystalline lens should be carefully monitored. Anterior segment optical coherence tomography (AS-OCT) is a non-contact device, which

TABLE 15-1: Results of comparative studies for correction of post-keratoplasty astigmatism

Reference	No. of Eyes	Technique	Follow-up Months, Mean (range)	Refractive Astigmatism Mean ± SD			Spherical Equivalent or Sphere* Mean ± SD			UCVA ≥ 20/40 (%)	BCVA ≥ 20/40 (%)	BCVA ≥ 2 lines gain (%)	BCVA ≥ 2 lines loss (%)	Additional Procedures or Complications
				Preop	Postop	Reduction (%)	Preop	Postop	Reduction (%)					
Donnenfeld[33]	23	LASIK	7.6 (1-14)	3.64±1.7	1.64±1.14	64.6	-6.88±4.4	-1.42±1.05	79.3	36.0	74.0	26	4.3	9.1% enhancements
Webber[2]	25	LASIK	(1-12)	8.67±3.22	2.92±1.71	66.3	-5.2±2.31	-1.31±1.63	74.8	28.0	83.0	12	0	53.8% arcuate keratotomy 1 perforation
Forseto[22]	22	LASIK	10.1 (6-18)	4.44±2.1	1.75±1.1	60.6	-4.55±3.66	-0.67±1.24	85.3	54.5	90.9	18	9.1	1 flap perforation 1 flap dislocation
Nassarella[21]	8	LASIK	6	3.5±1.22	1.25±0.74	64.3	-4.50±1.52	-0.75±0.75	83.3	37.5	87.5	25.0	0	none
Rashad[20]	19	LASIK	7.0 (6-10.5)	9.21±1.95	1.09±0.33	87.9	-2.14±2.11*	+0.43±0.82	79.9	73.7	100.0	42	0	53% enhancements
Koay[19]	8	LASIK	8.6	6.79±3.3	1.93±1.2	71.6	-6.79±4.17	-0.64±1.92	90.6	12.5	NA	37.5	0	1 buttonhole
Kwitko[18]	14	LASIK	26.9 (12-42)	5.37±2.1	2.82±2.4	47.5	-7.51±3.87	-1.25±2.30	83.3**	28.6	85.7	21	7.1	42.9% enhancements 1 buttonhole 2 epithelial ingrowths
Busin[17]	9	Flap cut	3	5.03±1.35	3.42±1.29	32.0	-5.40±1.69	-4.37±1.72	19.1	0	77.8	33	0	none
Malecha[34]	19	LASIK	5 (1-14)	4.05±1.71	1.22±1.14	69.9	-4.24±2.81	-0.85±0.84	80.0	73.7	89.5	0	5.2	3 DLK 3 enhancements
Barraquer[25]	46	LASIK	60	3.66	1.69	53.8	-7.29	-1.28	82.4	33	98	36.9	6.5	19.6% enhancements 1 wedge resection, 1 arcuate keratotomy
Buzard[24]	26	LASIK	6-12	2.71±2.33	1.06±0.67	60.9	-4.94±2.79	-0.35±0.65	92.9	86	NA	5	0	38.5% enhancements 3 resection 7 flap lifts
Hardten[23]	57 15	LASIK AK	21.4 (3-60)	4.67±2.18	1.94±1.35	58.5	-4.19±3.38	-0.61±1.81	85.4	43	86	28	16	9% enhancements 16% epithelial ingrowth 9% flap dislocation 5% DLK
Current study	36	Toric iris-fixated lens	28.5 (12-51)	7.06±2.01	2.00±1.53	88.8	0.34±4.36*	-0.03±1.23*	107.5*	31.6	80.6	8.3	8.3	1 lens exchange 1 haptic replacement

SD = standard deviation; UCVA = uncorrected visual acuity; BCVA = best-corrected visual acuity; preop = preoperatively; postop = postoperatively; NA = not available; DLK = diffuse lamellar keratitis; AK = arcuate keratotomy; *, sphere; **, myopic sphere

images the anterior chamber using 1310 nm wavelength infrared light. Baikoff, *et al* demonstrated that AS-OCT is rapid, easy to use and capable of producing good-quality images.[24] Furthermore, the software includes a measuring system capable of calculating distances between 2 points. Baikoff, *et al* mention that in normal eyes the minimum distance from the edge of the optic of the phakic IOL to the endothelium, must be 1.5 mm to minimise the risk to corneal decompensation.[25] In the future, this edge-distance will be an important distance to monitor the safety of toric phakic IOLs in post-keratoplasty eyes.

Another surgical option for the correction of post-keratoplasty astigmatism, is the implantation of a toric pseudophakic posterior chamber IOL. A few studies have described post-PK eyes in which standard phaco-emulsification and subsequent implantation of this toric IOL were performed. The serrated Z-design haptic of the lens is intended to prevent risk of lens rotation and subsequent change in the angle of the corrective cylinder. These studies suggest that this toric lens can provide a very good refractive outcome for eyes suffering from high degrees of post-keratoplasty astigmatism without significant effects on graft survival.[26-29]

This book chapter will only discuss the iris-fixated toric Artisan IOL for the correction of post-keratoplasty astigmatism.

Indications

Toric IOLs can be used for the surgical correction of post-keratoplasty astigmatism.

Step-by-Step Technique

THE ARTISAN TORIC IOL

The Artisan toric IOL has a convex-concave toric optic with a spherical anterior surface and a spherocylindrical posterior surface (Ophtec B.V., Groningen, the Netherlands). The material of this single-piece lens consists of polymethyl methacrylate and is manufactured using compression molding technology. This particular type of toric lens is iris claw-fixated, has a 5-mm optical zone and an overall length of 8.5 mm **(Figure 15-1)**. The IOL is available in dioptric powers of –3.0 to –20.5 D, +2.0 to +12.0 D and in cylindrical powers of 2.0 to 7.5 D. The Artisan toric IOL is available in 2 models. The cylinder can either be in line with the haptics or at an angle of 90° with the haptics **(Figures 15-2 and 15-3)**.

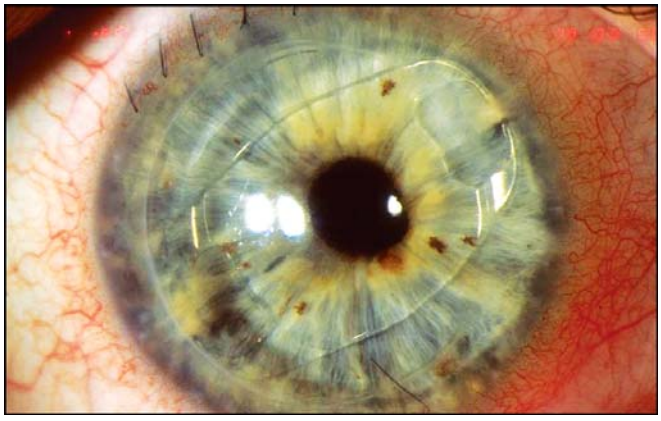

FIGURE 15-1: Artisan toric lens implantation for correction of post-keratoplasty astigmatism (patient no. 2). Preoperatively, best corrected visual acuity (BCVA) was 20/50 with +4.0 –8.0 x 120°. Six months after implantation of an Artisan toric lens with a power of +6.0 –7.0 x 90° and enclavated in the axis 30°, BCVA increased to 20/32 with –1.0 –1.50 x 125° and uncorrected visual acuity (UCVA) to 20/60. Four years after implantation, UCVA is 20/30 with a clear graft.

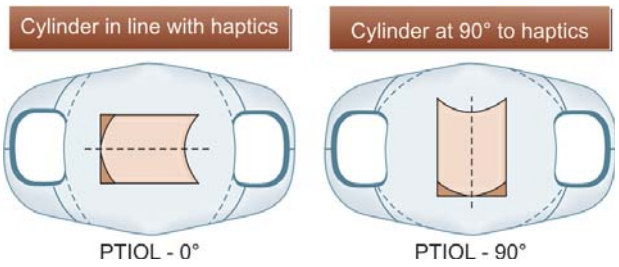

FIGURE 15-2: In the Artisan toric lens, the cylinder can either be in line with the haptics or at an angle of 90° with the haptics.

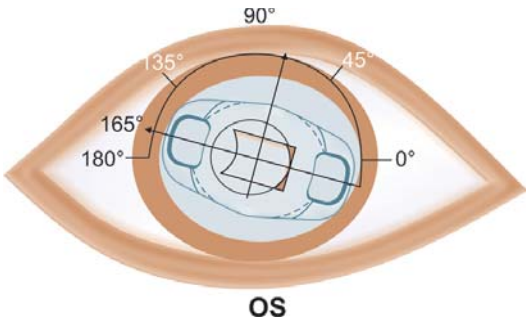

FIGURE 15-3: Example of the Artisan toric lens model where the cylinder is in line with the haptics.

Refractive error, refractive cylinder power, anterior chamber depth, and topographically derived keratometric dioptric values were inserted into the Van der Heijde[30] formula to calculate the dioptric power of the lens for two meridians. The axis of the cylinder identified by the subjective refraction was used to determine the correct axis for the surgical enclavation. The power of the IOL was chosen to obtain emmetropia (n=30) or a postoperative spherical equivalent (SE) of –1.0 D (n=4), -2 (n=1) or +1.0 D (n=1) to match the ametropia in the untreated eyes. For a proper placement of the Artisan toric IOL in the cylindrical axis (or perpendicular to the axis) and to avoid placement errors, the surgeon used an illustration of the correct IOL position, as provided by the manufacturer. In 9 of the 36 treated eyes, the cylinder dioptric power of the toric IOL was less than 75% of the calculated power required for full correction of the cylinder.

PATIENT POPULATION

The thirty-six eyes of 35 patients that were included in our study could not be corrected by spectacle wear due to anisometropia, the magnitude of the refractive cylinder and/or due to contact lens intolerance. Exclusion criteria were the following: a preoperative BSCVA worse than 20/60, an anterior chamber depth less than 3.0 mm, presence of glaucoma and/or retinal pathology, or an endothelial cell count lower than 500 cells/mm^2.

Investigational review board approval was obtained from the Academic Hospital Maastricht.

SURGICAL TECHNIQUE

All procedures were performed under general anesthesia by one surgeon (RN). The surgical technique for Artisan toric IOL implantation is generally the same as that used with standard Artisan refractive

phakic IOLs. Preoperatively, the horizontal and vertical axis of the eye were marked at the limbus; and preoperatively the axis for lens enclavation was marked. A two-plane 5.3 mm primary corneoscleral incision was centered at 12-o'clock. Two stab incisions were performed at 2- and 10 o'clock and directed towards the iris enclavation sites. In order to prepare the iris for lens fixation, an intracameral injection of acetylcholine was given. The IOL was then introduced into the anterior chamber by using a Budo forceps (Duckworth and Kent, Ltd, Baldock Herts, England) and an ophthalmic viscoelastic device (Healon GV, Pharmacia, Uppsala, Sweden). After gentle rotation, the IOL was fixated in the midperipheral iris stroma with a disposable enclavation needle in the marked axis site (Ophtec BV, Groningen, Netherlands). A slit iridotomy was performed at 12 o'clock to avoid the occurrence of pupillary block glaucoma. The viscoelastic material was exchanged for BSS Plus (Alcon, Fort Worth, Texas). The wound was sutured with 3 to 5 interrupted 10 - 0 nylon sutures (Alcon, Fort Worth, Texas).

Postoperatively, topical tobramycin 0.3% combined with dexamethasone 0.1% (Tobradex, Alcon, Couvreur, Belgium) and ketorolactrometamol 0.5% (Acular, Westport Co., Mayo, Ireland) were used four times daily for 3 weeks in a tapered schedule and three times daily for 1 week, respectively. In cases with an initial diagnosis of herpes simplex virus keratitis, a treatment with acyclovir 400 mg 3 times daily (GlaxoSmithKline, Zeist, the Netherlands) was applied for 6 months. Selective suture removal was performed depending on the subjective refraction.

PATIENT EXAMINATION

Patients were examined preoperatively and at day 1, week 1, month 1, month 3, month 6, and from then at 6 months intervals. Preoperatively, uncorrected visual acuity (UCVA) and BSCVA with subjective refraction, cycloplegic refraction, slit-lamp microscopy, applanation tonometry, corneal topography (Alcon Eyemap EH-290, Alcon, Fort Worth, TX), dilated fundus examination and pupil size measurement at dim illumination with the Colvard pupillometer (Oasis, Glendora, CA) were performed. On postoperative day 1, uncorrected and best-corrected visual acuity and biomicroscopic examination with registration of intraocular pressure were performed. Thereafter, uncorrected and spectacle-corrected visual acuity with subjective refraction, slit-lamp microscopy, applanation tonometry, and corneal topography were assessed. The simulated keratometry values of the steep and flat meridians were used for calculation of the topographically induced surgical astigmatism. Preoperatively and at 6 months, 1 year, 2 years, and 3 years postoperatively, specular microscopy of the corneal endothelium using a noncontact specular microscope (Konan Noncon Robo, SP 8000, Konan, Hyogo, Japan) was performed.[31,32] Preoperatively and at 6 months postoperatively, the patients were asked to rate the quality of vision of the eye with their present correction on a visual analog scale of 1 to 10 (1 is very poor, 10 is excellent), based on a previously validated questionnaire.[33]

OUTCOME MEASURES AND STATISTICS

Main outcome measures were refractive and visual outcome as reflected by UCVA and efficacy (reduction in refractive and topographic astigmatism, reduction in anisometropia of spherical and defocus equivalent, and number of eyes losing/gaining lines of UCVA), BSCVA and safety (number of eyes losing more than 2 lines of BSCVA). A patient satisfaction questionnaire, specular microscopy (endothelial cell loss) and incidence of complications were assessed. Snellen UCVA or BSCVA was converted to logMar values in order to facilitate statistical analysis. Comparison between preoperative and postoperative data was performed by a paired t-test (SPSS for Windows (SPSS Inc., Chicago, IL)). All averages in the text are mean ± standard deviation (SD).

ANALYSIS OF ASTIGMATISM

Both vector analysis and non-vector analysis of the cylinder was performed. The efficacy of the procedure (i.e., the proportion of astigmatism correction which was achieved) was quantified using the correction index expressed as a percentage of the surgically induced astigmatism (SIA) divided by the target induced astigmatism (TIA) for each individual eye and aggregated.[34] The Holladay method to convert polar values (cylinder and axis) to a Cartesian (X and Y) coordinate system was used to determine the mean ± SD value of the refractive and topographical keratometric astigmatism.[35] The coordinates were plotted in a doubled-angle plot and the centroid was determined.

Results

PATIENT POPULATION

Twenty-seven patients were female and eight were male. The mean age was 63.8 ± 17.0 (range, 23-82 years). The mean time interval between PK and toric lens implantation was 57.1 ± 30.2 months (range, 26 to 142 months) and the interval between suture removal and lens implantation was 30.8 ± 28.2 months (range, 3 to 144 months). Twenty-five eyes were pseudophakic after previous implantation of a posterior chamber IOL and one eye was aphakic. The initial diagnosis requiring corneal transplantation was Fuchs endothelial dystrophy (33.3%), (pseudophakic) bullous keratopathy (13.9%), herpes simplex keratitis (16.7%), keratoconus (13.9%), corneal scarring (11.1%) re-grafting (8.3%) and high astigmatism (2.8%).

The baseline parameters were a mean sphere of 0.34 ± 4.36 D (range, + 9.0 to –10.0 D), a mean SE refraction of –3.19 ± 4.31 D (range, +5.5 to –14.25 D), a mean baseline refractive cylinder power of -7.06 ± 2.01 (range, -3.0 to –11.0 D), a mean defocus equivalent of 6.99 ± 2.59 D (range, 3.25 to 14.25 D) and a mean baseline topographically derived simulated keratometric cylinder of 7.00 ± 2.27 D (range, +3.51 to +11.65 D). There were no significant differences for the baseline parameters between the pseudophakic eye group and the phakic eye group. The mean follow-up was 28.5 ± 12.5 months (range, 12 to 51 months).

VISUAL ACUITY OUTCOME

The mean preoperative logMar UCVA was 1.39 ± 0.44 and increased to 0.55 ± 0.35 at the last follow-up ($p < 0.001$, paired t-test). Postoperatively, 31.6% of eyes had a UCVA better than 20/40, 63.9% of eyes better than 20/80 as compared to 0% preoperatively. In the phakic and pseudophakic eye groups, 27.8% and 35.3% of eyes had a UCVA better than 20/40, respectively ($p = 0.71$, Pearson chi-square). The mean number of gained lines of UCVA in all eyes was 8.50 ± 5.51 (range, -2 to 18 lines). The mean preoperative logMar BSCVA was 0.26 ± 0.17 and postoperatively it was 0.26 ± 0.24 ($p = 0.802$, paired t-test). Postoperatively, 80.6% of eyes had a BSCVA better than 20/40 as compared to 69.4% preoperatively and 25.0% had a BSCVA better than 20/25 **(Figure 15-4)**. In the phakic and pseudophakic eye groups, 77.8% and 82.4% of eyes had a BSCVA better than 20/40, respectively ($p = 0.83$, Pearson chi-square). The mean number of gained lines of BSCVA in all eyes was -0.06 ± 2.14 (range, -6 to 4 lines). There was a loss of BSCVA of greater than 2 lines in 8.3% of eyes and a gain of at least 2 lines in 8.3% of eyes **(Figure 15-5)**. The predictability of intended versus achieved cylinder correction showed 26 of 36 eyes (72.3%) within 2 D and 18 of 36 eyes (50.0%) within 1 D of the intended correction. In the phakic eye group, 66.7% and 50.0% of eyes were within 2 D and 1 D of the intended correction, and in the pseudophakic eye group 76.5% and 52.9% of eyes were within

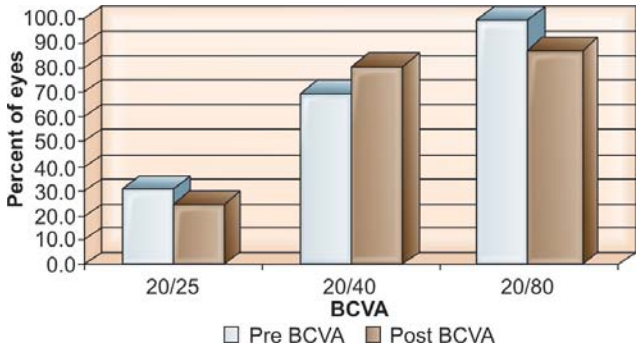

FIGURE 15-4: Percentage of eyes within given range of best-corrected visual acuity (BCVA) preoperatively and at last follow-up after toric lens implantation. The safety-index (mean postoperative BCVA divided by mean preoperative BCVA was 0.98.

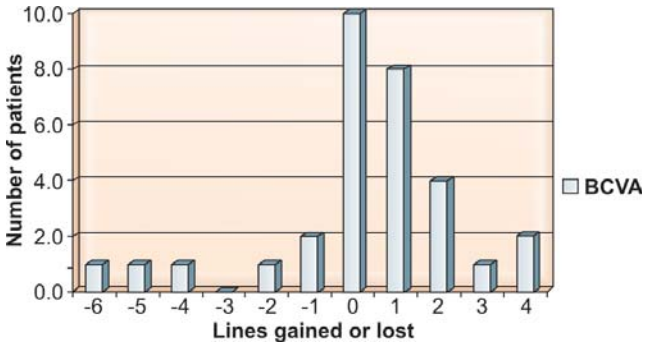

FIGURE 15-5: The number of gained or lost lines of best corrected visual acuity (BCVA) at last follow-up after toric lens implantation.

2 D and 1 D of the intended correction (p = 0.67 and p = 0.59, Pearson chi-square). The predictability of intended versus achieved defocus equivalent showed 22 of 36 eyes (61.1%) within 2 D and 9 of 36 eyes (25.0%) within 1 D of the intended correction.

REFRACTIVE OUTCOME

The mean sphere at the last follow-up was –0.03 ± 1.23 D (range, + 2.50 to –3.75 D), the mean SE refraction was –1.03 ± 1.20 D (range, +1.0 to –5.25 D), and the mean defocus equivalent was +1.65 ± 1.67 D (range, +7.13 to +0.0 D). The refractive cylinder was reduced to –1.73 ± 1.25 D, –1.69 ± 1.15 D, -1.94 ± 1.68 D, -2.02 ± 1.93 D and -2.00 ± 1.53 D at 6 months (n=36), 1 year (n=36), 2 years (n=29), 3 years (n=15) and the final follow-up examination (28.5 ± 12.5 months), respectively ($p < 0.001$ for all time points, paired t-test). There was no significant difference in refractive cylinder between the phakic eye group and the pseudophakic eye group at any of the postoperative time points. Concerning stability, there was no significant change in refractive cylinder values from 6 months postoperatively to 3 years postoperatively (**Figure 15-6**, p = 0.065, paired t-test).

At the last follow-up, 10 of 36 eyes (27.8%) had a refractive cylinder less than 1 D, 21 of 36 eyes (58.3%) had a refractive cylinder less than 2 D, and 33 of 36 eyes (91.7%) had a cylinder less than 4 D. The mean topographically derived simulated keratometric cylinder did not change significantly

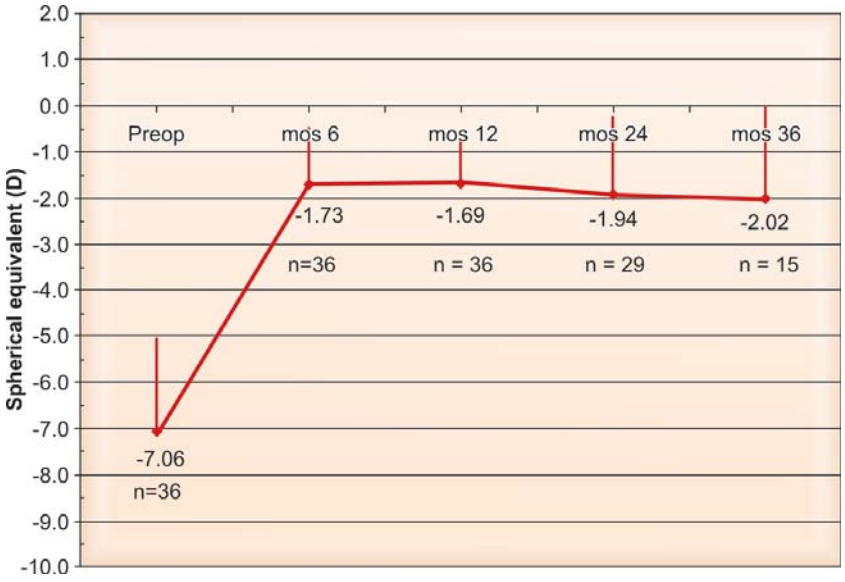

FIGURE 15-6: Mean refractive cylinder preoperatively and at postoperative time intervals. Number of patients at each time point are shown. D = diopters.

from 6.23 ± 2.26 D at 3 months postoperatively to 6.68 ± 3.06 D at 12 months (p = 0.968, paired t-test), and to 6.59 ± 3.57 D (p = 0.894, paired t-test) at the last follow-up. The percent reduction in refractive and topographical astigmatism was 88.8 ± 29.5% and 7.8 ± 49.1%, respectively **(Table 15-1)**. In 9 eyes, the required dioptric power for correction of the refractive astigmatism exceeded the available maximal cylindric power of 7.5 D. There was a reduction of 103.6 ± 33.0% and 77.8 ± 19.3% in sphere and defocus equivalent (for eyes with preoperative defocus values > 3.0 D, n=24), respectively. The correction index (SIA/TIA) was 96.0 ± 24.2% at the last follow-up. The centroid (± SD) in the double angled plot changed from –2.83 D at 141.3° (± 6.43 D) preoperatively to –0.51 D at 91.9° (± 2.15 D) postoperatively **(Figure 15-7)** (p < 0.001, paired t-test). The mean SIA of the topographical cylinder by the placement of the corneoscleral incision centered at 90° was 2.53 ± 1.57 D (range, 0.25 D to 6.25 D) at 6 months postoperatively.

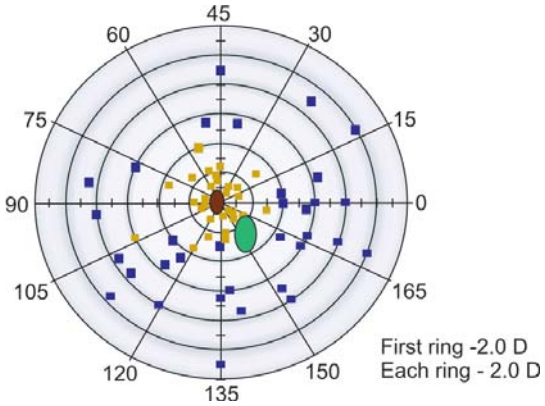

FIGURE 15-7: The centroid ± standard deviation (SD) in the double angled plot changed from –2.83 diopters (D) at 141.3° (± 6.43 D) before Artisan toric lens implantation (blue squares, green centroid) to –0.51 D at 91.9° (± 2.15 D) at the last follow-up after implantation (yellow squares, red centroid).

Subjective patient satisfaction increased from 3.6 preoperatively to 8.0 postoperatively (10 meaning totally satisfied) ($p < 0.001$, paired t test).

The intraocular pressure (IOP) was 14.5 ± 2.9 mmHg preoperatively, 15.2 ± 4.2 mmHg at 1 month postoperatively, 13.5 ± 3.2 mmHg at 6 months postoperatively, and 12.9 ± 2.7 mmHg at the last follow-up (p = ns, paired t test for all time points).

The endothelial cell loss as compared to preoperatively was 13.8 ± 18.7% (n=34), 21.2 ± 21.8% (n=33), 29.6 ± 27.3% (n=26), 30.4 ± 32.0% (n=18), and 34.8 ± 26.3% (n=6) at 6 months (P=0.001), 1 year (P<0.001), 2 years (P<0.001), 3 years (P=0.001), and 4 years postoperatively (P=0.1), respectively. In addition, there was a progressive endothelial loss from 6 months to 12 months (p=0.004), to 24 months (p=0.002) and to 36 months (p=0.017), and from 12 months to 24 months (p=0.016).

COMPLICATIONS

A 77-year-old male (patient no. 6) underwent PK of the right eye in April 1997 for HSV stromal keratitis. Seven months after implantation of an Artisan toric lens with a power of +5.0/–7.0 × 0° BSCVA increased to 20/25 with +0.75/–1.50 × 155°. One month later metastasized lung cancer was diagnosed and a recurrence of HSV keratitis followed by irreversible graft rejection developed. Twenty-five months after Artisan implantation BSCVA was 20/100 with +0.5/–1.50 × 160°. No further surgical treatment followed.

An 81-year-old female (patient no. 12) underwent PK of the left eye in September 1999 for pseudophakic bullous keratopathy. Before Artisan implantation the endothelial cell density was 1384 cells/mm^2. Five months after Artisan implantation (lens power of –1.50/–7.0 × 0°, enclavation axis 162°), the BSCVA was 20/30 with –0.75/–2.25 × 63°. At 12 months after Artisan toric lens implantation the endothelial cell density had decreased to 385 cells/mm^2. Twenty months after implantation, gradual endothelial decompensation occurred and BSCVA decreased to 20/100 after metastasized colon cancer was diagnosed. Twenty-eight months after Artisan implantation, a re-keratoplasty with explantation of the Artisan IOL was performed. One year after re-keratoplasty, the corneal graft was clear and BSCVA was 20/30 with -6.5/0 × 0°.

A 62-year-old female (patient no. 18) underwent a re-PK of her right eye due to graft failure in July 1999 after an initial PK for keratoconus in 1984. In May 2001, phacoemulsification with subsequent IOL implantation was performed, followed by a reversible graft rejection in September 2001. In May 2003, seven months after the Artisan IOL implantation (lens power of +8.0/–7.5 × 0°, enclavation axis 138°), the BSCVA was 20/40 with –0.50/–1.50 × 50°. One month later an irreversible immunological graft failure occurred. In March 2004, a re-PK was performed with explantation of the toric Artisan IOL. At the last follow-up in May 2005, the UCVA was 20/40 with a clear graft.

In 6 patients, signs of adult retinal macular degeneration were noted. In patient no. 13, one haptic of the toric Artisan IOL was repositioned 6 weeks after initial surgery, due to axis misalignment; and in patient no. 17, the Artisan IOL was replaced due to an axis error in the delivered lens (lens power of +7.0/–7.5 × 0°, in stead of +7.0/–7.5 × 90°), which was not noted at the time of surgery. No chronic inflammation of the anterior chamber or retinal detachment was seen in any of the patients.

Discussion

This prospective study of 36 eyes demonstrates the long-term efficacy and stability of the Artisan toric IOL for correction of post-keratoplasty astigmatism. The use of the Artisan toric IOL with a

power range of 7.5 D of cylinder and -20.5 D of myopia to +12.0 D of hyperopia, provides a wide field for correction of post-keratoplasty astigmatism and ametropia. In our series this is reflected by the magnitude of baseline spherical error (range + 9.0 to –10.0 D) and cylindrical error (range -3.0 to –11.0 D), which is much higher than in most post-keratoplasty LASIK series. To our knowledge, the reduction of the refractive cylinder by 88.8 ± 29.5% (without any enhancements) is better than in most reported LASIK series.[5-15]

Improving the percentage of eyes with an UCVA of 20/40 or better from 0% preoperatively to 31.6% at the last follow-up illustrates the efficacy of the Artisan toric IOL procedure in this patient group with highly ametropic eyes. In most LASIK series with lower preoperative ametropia UCVA better than 20/40 varied from 28% to 74%.[6, 8, 10, 14, 15, 17] With respect to safety, there was a loss of BSCVA of greater than 2 lines in 8.3% of eyes and a gain of at least 2 lines in 8.3% of eyes. This is in accordance with two recent randomized studies in routine refractive surgery for the correction of high myopia that showed a greater gain of BSCVA with Artisan phakic IOL implantation as compared to a greater loss of BSCVA with LASIK and a better quality of vision with the Artisan lens in moderate to high myopia.[36, 37] The loss of greater than 2 lines of BSCVA in 8.3% in our series is comparable to series of LASIK for postkeratoplasty astigmatism that show a greater than 2 lines loss of BSCVA in 4.3%,[38] 7.1%,[6] 9.1%[10] and 16%.[11]However, the pattern of complications induced by the two techniques is very different. LASIK surgery may be complicated by flap complications in steep corneas and has limitations due to corneal graft thickness and amount of ametropia and astigmatism suitable for correction.[5-13] LASIK related complications like diffuse lamellar keratitis,[15] buttonhole flaps,[6, 10] wound dehiscence[39] and epithelial ingrowth[6] have been reported. Because the majority of eyes in the reported LASIK series were grafted in young patients for keratoconus with a rapid wound healing, wound dehiscence problems were less likely to occur than in a group of older patients grafted for Fuchs endothelial dystrophy or bullous keratopathy.[40] Since the effect of the flap cut alone may induce a significant reduction of refractive astigmatism in up to 50% in some patients and because of the high enhancement rate a two-stage LASIK procedure has been proposed.[5, 41-43] However, it is unclear whether a two-stage procedure bears a higher risk for complications like epithelial ingrowth, wound healing problems and flap dislocation. In our present Artisan series, irreversible corneal decompensation occurred in two patients after metastasized cancer was diagnosed. Before the diagnosis of malignant disease BSCVA was 20/25 in both patients and no signs of immunological rejection had been noted. We believe that changes in the immune system due to the concomitant development of malignant systemic disease might have initiated the graft failures. In a third patient with a re-keratoplasty for a graft failure after an initial diagnosis of keratoconus an immunological irreversible graft failure occurred. This was the second rejection period after the re-keratoplasty following a previous reversible rejection period 4 months after cataract surgery. We cannot exclude that the last rejection, although 8 months after surgery, may have been related to the Artisan toric lens implantation. Two of the three cases with corneal decompensation underwent successful regrafting with explantation of the toric Artisan intraocular lens. In 6 patients signs of adult retinal macular degeneration that decreased BSCVA were seen as can be expected in this age group. No other complications like chronic inflammation of the anterior chamber or retinal detachment in any of the patients were noted.

The stability of the postoperative refractive cylinder after Artisan toric lens implantation up to 36 months was excellent. After LASIK however, progressive changes were seen in refraction and topography in 35.7% of cases after a mean follow-up time of 26.9 months.[6] A potential limitation of the Artisan toric IOL for the correction of post-keratoplasty astigmatism is SIA by implantation of

the rigid polymethylmethacrylate IOL through a 5.3 mm incision. In a recent series of implantation of the Artisan toric IOL for correction of myopia or hyperopia with astigmatism the SIA was 0.53 D.[44] However, after keratoplasty the biomechanical response of the corneoscleral tissue to the incision may be somewhat unpredictable and a greater variability in SIA may be seen. Indeed, in our series the mean SIA was 2.53 D six months postoperatively and varied from 0.25 D to 6.25 D. Due to this variability we believe that the SIA cannot be incorporated into the power calculation of the lens. Since the goal of correcting post-keratoplasty astigmatism is mainly to reduce the refractive astigmatism and ametropia to enable patients to wear spectacles, we feel that a lesser predictability of astigmatism reduction may be acceptable.

Concerns have been raised especially with respect to the development of complications like endothelial cell loss, chronic inflammation and cystoid macular edema after Artisan toric lens implantation. A study using fluorometry showed inflammation comparable with cataract surgery at 6 months postoperatively[45] whereas a study using a flare-cell meter found chronic inflammation 1 to 2 years after implantation of the older Worst-Fechner intraocular lens.[46] We found no chronic inflammation by slit-lamp examination in the present study and cystoid macular edema with concomitant loss of best corrected visual acuity was not seen in the immediate postoperative phase.

After routine PK, the mean annual rate of endothelial cell loss from 3 to 5 years seems to be 7.8% per year and from 5 to 10 years it seems to be 4.2% per year.[47-50] The corneal endothelium seems to remain relatively stable between 10 and 15 years after PK and it has also been suggested that the rate of endothelial cell loss from 10 to 15 years after surgery may be similar to that of normal corneas.[47] It was hypothesized that late endothelial cell loss may be caused by an aspecific, non-rejection-like inflammation, or perhaps a chronic breakdown of the blood aqueous barrier, but not by an allograft rejection mechanism.

The mean endothelial cell loss in our study group was 13.8 ± 18.7%, 21.2 ± 21.8%, 29.6 ± 27.3%, and 30.4 ± 32.0% at 6, 12, 24 and 36 months. There was a significant continuing progressive endothelial cell loss at each time point as compared to preoperative cell density levels and between 6 months as compared to 12, 24, and 36 months. For an experienced surgeon, the implantation of the Artisan toric lens in post-keratoplasty eyes does not appear to be more traumatic as compared to Artisan lens implantation in phakic eyes for correction of myopia. However, the endothelial cell loss in the present series is much higher than the reported endothelial cell loss in studies of Artisan IOL implantation for correction of high myopia in virgin phakic eyes, which varies from 0.7% to 11.7% over 3 years time.[36, 37, 51-55] Risk factors that may lead to higher levels of endothelial cell loss after PK are low donor endothelial cell count, older donor age, aphakia, pseudophakia, and older recipient age. In addition, the implantation of an Artisan lens in post-keratoplasty eyes could be more traumatic for the corneal endothelium, relating to decreased visualization, as compared to virgin eyes. This could lead to higher endothelial cell loss in the post-keratoplasty group. At the time of toric Artisan lens implantation, 50% of our patients were between 3 to 5 years, 27.7% between 5 to 10 years and 5.6% longer than 10 years after PK. For our 24 months cohort, the cell loss rate was 14.8% per year and for the 36 months cohort it was 10.1% per year. If we correct these values for the expected cell loss induced by the PK, there appears to be an additional cell loss of 6% to 7% per year. Therefore, we cannot exclude that the Artisan IOL in the presence of a corneal graft with low cell densities may cause a higher rate of endothelial cell loss due to the compromised endothelium. Cell counts as low as 370 cells/mm^2 and 515 cells/mm^2 have been measured before decompensation.[56-59] Nevertheless, we feel that an endothelial cell density of at least 500 cells/mm^2 as exclusion criterion is permitted since no other treatment modalities exist but corneal regrafting, and the Artisan lens is perfectly

removable at future regrafting procedures, as has been shown in two patients in our series. It should also be taken into account that accuracy of non-contact specular microscopy for determining endothelial cell density, which is usually around 5%, is not known in grafts with low cell counts and may introduce bias in the interpretation of our results. Risk factors for endothelial decompensation in corneal grafts with low cell densities have not been clearly defined.

Due to the development of new imaging technologies, such as the AS-OCT, we might be able to determine other possible risk factors for endothelial cell loss in the future. One of the mentioned risk factors for corneal decompensation in healthy eyes is a distance from the edge of the phakic IOL to the endothelium of less than 1.5 mm.[25] Therefore, in addition to endothelial cell counts, anterior chamber morphometrics should be analyzed during long-term follow-up to evaluate the safety of phakic IOLs in eyes after PK **(Figure 15-8)**. Several studies analyzed the position of iris-fixated phakic IOLs in healthy eyes.[22, 60] Tehrani, *et al* evaluated 17 myopic eyes implanted with a foldable iris-fixated phakic IOL and reported mean distances from the center and the edge of the IOL to the endothelium of 2.01±0.26 mm and 1.34±0.21 mm, respectively.[61] However, the effect of the distance from the edges of the phakic IOL to the endothelium on endothelial cell loss after toric Artisan IOL implantation in post-keratoplasty eyes is unclear and should be investigated.

Based on the objective medical outcomes, the subjective patient satisfaction that increased from 3.6 preoperatively to 8.0 postoperatively (scale 1-10) and the suitability of all patients for spectacle correction, Artisan toric lens implantation appears to be a valuable option for correction of post-keratoplasty astigmatism and anisometropia. However, more patients with a longer follow-up up to 5 years are needed to identify the risk factors for progressive endothelial cell loss and a randomized study of Artisan toric lens implantation versus LASIK with larger numbers of patients could clarify the advantages and disadvantages of both techniques with respect to efficacy, safety and complications.

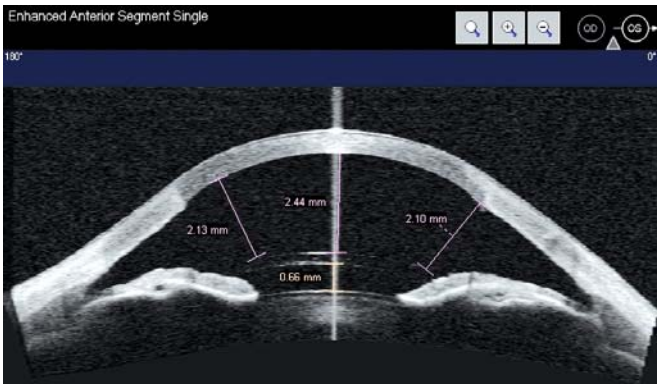

FIGURE 15-8: Anterior segment optical coherence tomography image of post-keratoplasty eye after toric phakic intraocular lens (pIOL) implantation with measured distances from center of pIOL to endothelium (2.44 mm), pIOL to crystalline lens (0.66 mm), and edges of pIOL to endothelium (2.13 mm nasal side; 2.10 mm temporal side).

Conclusion

Artisan toric IOL implantation after PK can result in decreased post-keratoplasty refractive astigmatism and ametropia. This can allow contact lens intolerant patients to wear spectacles and obtain binocular vision after surgery. Decreasing endothelial cell counts can occur and should be monitored carefully with anterior imaging systems.

A potential drawback of implanting an Artisan toric IOL for treatment of post-keratoplasty astigmatism is SIA, related to the required 5.3 mm incision size. The biomechanical response of the corneoscleral tissue to the incision may be somewhat unpredictable after PK, and a greater variability in SIA may be seen. A recent study on implantation of the Artisan toric lens for correction of myopia or hyperopia with astigmatism in virgin non-operated eyes, showed a SIA of 0.53 D.[44] However, in a post-keratoplasty astigmatism treatment group a lesser predictability of astigmatism reduction may be acceptable, since the primary goal of treating of astigmatism after PK is the correction of sufficient myopia and astigmatism in order to enable patients to wear spectacles or contact lenses.

References

1. van Rij G, Cornell FM, Waring GO, 3rd, et al. Postoperative astigmatism after central vs eccentric penetrating keratoplasties. Am J Ophthalmol 1985;99:317-20.
2. Kerenyi A, Suveges I. Corneal topographic results after eccentric, biconvex penetrating keratoplasty. J Cataract Refract Surg 2003;29:752-6.
3. Karabatsas CH, Cook SD, Sparrow JM. Proposed classification for topographic patterns seen after penetrating keratoplasty. Br J Ophthalmol 1999;83:403-9.
4. Brooks SE, Johnson D, Fischer N. Anisometropia and binocularity. Ophthalmology 1996;103:1139-43.
5. Busin M, Arffa RC, Zambianchi L, et al. Effect of hinged lamellar keratotomy on postkeratoplasty eyes. Ophthalmology 2001;108:1845-51; discussion 1851-52.
6. Kwitko S, Marinho DR, Rymer S, Ramos Filho S. Laser in situ keratomileusis after penetrating keratoplasty. J Cataract Refract Surg 2001;27:374-9.
7. Koay PY, McGhee CN, Weed KH, Craig JP. Laser in situ keratomileusis for ametropia after penetrating keratoplasty. J Refract Surg 2000;16:140-7.
8. Rashad KM. Laser in situ keratomileusis for correction of high astigmatism after penetrating keratoplasty. J Refract Surg 2000;16:701-10.
9. Nassaralla BR, Nassaralla JJ. Laser in situ keratomileusis after penetrating keratoplasty. J Refract Surg 2000;16: 431-7.
10. Forseto AS, Francesconi CM, Nose RA, Nose W. Laser in situ keratomileusis to correct refractive errors after keratoplasty. J Cataract Refract Surg 1999;25:479-85.
11. Hardten DR, Chittcharus A, Lindstrom RL. Long term analysis of LASIK for the correction of refractive errors after penetrating keratoplasty. Cornea 2004;23:479-489.
12. Buzard K, Febbraro JL, Fundingsland BR. Laser in situ keratomileusis for the correction of residual ametropia after penetrating keratoplasty. J Cataract Refract Surg 2004;30:1006-13.
13. Barraquer CC, Rodriguez-Barraquer T. Five-year results of laser in-situ keratomileusis (LASIK) after penetrating keratoplasty. Cornea 2004;23:243-8.
14. Donnenfeld ED, Solomon R, Biser S. Laser in situ keratomileusis after penetrating keratoplasty. Int Ophthalmol Clin 2002;42:67-87.
15. Malecha MA, Holland EJ. Correction of myopia and astigmatism after penetrating keratoplasty with laser in situ keratomileusis. Cornea 2002;21:564-9.
16. Guell JL, Gris O, de Muller A, Corcostegui B. LASIK for the correction of residual refractive errors from previous surgical procedures. Ophthalmic Surg Lasers 1999;30:341-9.
17. Webber SK, Lawless MA, Sutton GL, Rogers CM. LASIK for post penetrating keratoplasty astigmatism and myopia. Br J Ophthalmol 1999;83:1013-8.
18. Nuijts RM, Abhilakh Missier KA, Nabar VA, Japing WJ. Artisan toric lens implantation for correction of postkeratoplasty astigmatism. Ophthalmology 2004;111:1086-94.
19. Moshirfar M, Barsam CA, Parker JW. Implantation of an Artisan phakic intraocular lens for the correction of high myopia after penetrating keratoplasty. J Cataract Refract Surg 2004;30:1578-81.
20. Moshirfar M, Feilmeier MR, Kang PC. Implantation of Verisyse phakic intraocular lens to correct myopic refractive error after penetrating keratoplasty in pseudophakic eyes. Cornea 2006;25:107-11.
21. Tehrani M, Dick HB, Schwenn O, et al. Postoperative astigmatism and rotational stability after artisan toric phakic intraocular lens implantation. J Cataract Refract Surg 2003;29:1761-6.
22. Baumeister M, Buhren J, Kohnen T. Position of angle-supported, iris-fixated, and ciliary sulcus-implanted myopic phakic intraocular lenses evaluated by Scheimpflug photography. Am J Ophthalmol 2004;138:723-31.

23. Bartels MC, Saxena R, van den Berg TJ, et al. The influence of incision-induced astigmatism and axial lens position on the correction of myopic astigmatism with the Artisan toric phakic intraocular lens. Ophthalmology 2006;113: 1110-7.
24. Baikoff G, Lutun E, Ferraz C, Wei J. Static and dynamic analysis of the anterior segment with optical coherence tomography. J Cataract Refract Surg 2004;30:1843-50.
25. Baikoff G. Anterior segment OCT and phakic intraocular lenses: a perspective. J Cataract Refract Surg 2006;32: 1827-35.
26. Viestenz A, Kuchle M, Seitz B, Langenbucher A. Toric intraocular lenses for correction of persistent corneal astigmatism after penetrating keratoplasty. Ophthalmologe 2005;102:148-52.
27. McMullan TF, Goldsmith C, Illingworth CD. Toric posterior chamber (in-the-bag) intraocular lens implantation to correct postpenetrating keratoplasty astigmatism. Eye 2007;21:150-2.
28. Kersey JP, O'Donnell A, Illingworth CD. Cataract surgery with toric intraocular lenses can optimize uncorrected postoperative visual acuity in patients with marked corneal astigmatism. Cornea 2007;26:133-5.
29. Buchwald HJ, Lang GK. Cataract surgery with implantation of toric silicone lenses for severe astigmatism after keratoplasty. Klin Monatsbl Augenheilkd 2004;221:489-94.
30. van der Heijde GL, Fechner PU, Worst JG. [Optical consequences of implantation of a negative intraocular lens in myopic patients]. Klin Monatsbl Augenheilkd 1988;193:99-102.
31. Waring GO, 3rd. Standard graphs for reporting refractive surgery. J Refract Surg 2000;16:459-66.
32. Koch DD, Kohnen T, Obstbaum SA, Rosen ES. Format for reporting refractive surgical data. J Cataract Refract Surg 1998;24:285-7.
33. Nijkamp MD, Dolders MG, de Brabander J, et al. Effectiveness of multifocal intraocular lenses to correct presbyopia after cataract surgery: a randomized controlled trial. Ophthalmology 2004;111:1832-9.
34. Alpins N. Astigmatism analysis by the Alpins method. J Cataract Refract Surg 2001;27:31-49.
35. Holladay JT, Cravy TV, Koch DD. Calculating the surgically induced refractive change following ocular surgery. J Cataract Refract Surg 1992;18:429-43.
36. Malecaze FJ, Hulin H, Bierer P, et al. A randomized paired eye comparison of two techniques for treating moderately high myopia: LASIK and artisan phakic lens. Ophthalmology 2002;109:1622-30.
37. El Danasoury MA, El Maghraby A, Gamali TO. Comparison of iris-fixed Artisan lens implantation with excimer laser in situ keratomileusis in correcting myopia between -9.00 and -19.50 diopters: a randomized study. Ophthalmology 2002;109:955-64.
38. Donnenfeld ED, Kornstein HS, Amin A, et al. Laser in situ keratomileusis for correction of myopia and astigmatism after penetrating keratoplasty. Ophthalmology 1999;106:1966-74; discussion 1974-75.
39. Ranchod TM, McLeod SD. Wound dehiscence in a patient with keratoconus after penetrating keratoplasty and LASIK. Arch Ophthalmol 2004;122:920-1.
40. Abou-Jaoude ES, Brooks M, Katz DG, Van Meter WS. Spontaneous wound dehiscence after removal of single continuous penetrating keratoplasty suture. Ophthalmology 2002;109:1291-96; discussion 1297.
41. Busin M, Zambianchi L, Garzione F, et al. Two-stage laser in situ keratomileusis to correct refractive errors after penetrating keratoplasty. J Refract Surg 2003;19:301-8.
42. Alio JL, Javaloy J, Osman AA, et al. Laser in situ keratomileusis to correct post-keratoplasty astigmatism; 1-step versus 2-step procedure. J Cataract Refract Surg 2004;30:2303-10.
43. Dada T, Vajpayee RB, Gupta V, et al. Microkeratome-induced reduction of astigmatism after penetrating keratoplasty. Am J Ophthalmol 2001;131:507-8.
44. Dick HB, Alio J, Bianchetti M, et al. Toric phakic intraocular lens: European multicenter study. Ophthalmology 2003;110:150-62.
45. Perez-Santonja JJ, Bueno JL, Zato MA. Surgical correction of high myopia in phakic eyes with Worst-Fechner myopia intraocular lenses. J Refract Surg 1997;13:268-281; discussion 281-4.
46. Perez-Santonja JJ, Iradier MT, Benitez del Castillo JM, et al. Chronic subclinical inflammation in phakic eyes with intraocular lenses to correct myopia. J Cataract Refract Surg 1996;22:183-7.
47. Patel SV, Hodge DO, Bourne WM. Corneal endothelium and postoperative outcomes 15 years after penetrating keratoplasty. Am J Ophthalmol 2005;139:311-9.
48. Ing JJ, Ing HH, Nelson LR, et al. Ten-year postoperative results of penetrating keratoplasty. Ophthalmology 1998;105:1855-65.
49. Bourne WM, McLaren JW. Clinical responses of the corneal endothelium. Exp Eye Res 2004;78:561-72.
50. Bourne WM, Nelson LR, Hodge DO. Continued endothelial cell loss ten years after lens implantation. Ophthalmology 1994;101:1014-22; discussion 1022-23.
51. Maloney RK, Nguyen LH, John ME. Artisan phakic intraocular lens for myopia: short-term results of a prospective, multicenter study. Ophthalmology 2002;109:1631-41.

52. Menezo JL, Cisneros AL, Rodriguez-Salvador V. Endothelial study of iris-claw phakic lens: four year follow-up. J Cataract Refract Surg 1998;24:1039-49.
53. Menezo JL, Peris-Martinez C, Cisneros AL, Martinez-Costa R. Phakic intraocular lenses to correct high myopia: Adatomed, Staar, and Artisan. J Cataract Refract Surg 2004;30:33-44.
54. Güell JL, Vazquez M, Malecaze F, et al. Artisan toric phakic intraocular lens for the correction of high astigmatism. Am J Ophthalmol 2003;136:442-7.
55. Lifshitz T, Levy J, Aizenman I, et al. Artisan phakic intraocular lens for correcting high myopia. Int Ophthalmol 2004;25:233-8.
56. Hoffer KJ. Corneal decomposition after corneal endothelium cell count. Am J Ophthalmol 1979;87:252-3.
57. Nuyts RM, Boot N, van Best JA, et al. Long term changes in human corneal endothelium following toxic endothelial cell destruction: a specular microscopic and fluorophotometric study. Br J Ophthalmol 1996;80:15-20.
58. Breebaart AC, Nuyts RM, Pels E, et al. Toxic endothelial cell destruction of the cornea after routine extracapsular cataract surgery. Arch Ophthalmol 1990;108:1121-5.
59. Armitage WJ, Dick AD, Bourne WM. Predicting endothelial cell loss and long-term corneal graft survival. Invest Ophthalmol Vis Sci 2003;44:3326-31.
60. Guell JL, Morral M, Gris O, et al. Evaluation of Verisyse and Artiflex phakic intraocular lenses during accommodation using Visante optical coherence tomography. J Cataract Refract Surg 2007;33:1398-1404.
61. Tehrani M, Dick HB. Scheimpflug biometry of the anterior segment after implantation of foldable iris-fixated lenses. J Refract Surg 2006;22:243-6.

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