Complications after LASIK or PRK: achieving excellent outcomes in therapeutic corneal refractive surgery

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Introduction
The options for repair of complications after LASIK or PRK have improved over the years and there are now a number of different options to consider, with the three most commonly used treatment modalities being wavefront guided ablation, topography guided ablation and trans-epithelial PTK. However, the most important aspect of treating complications is to first make a confident diagnosis of the problem since some treatment options could actually be detrimental if used in the wrong patients.

This course will cover the treatment options for three main categories of the most common complications: high spherical aberration (small optical zone), decentration, and irregularly irregular astigmatism.

(All layered pachymetric maps of epithelium, stroma and cornea shown in this course were obtained using the Artemis VHF digital ultrasound arc-scanner. The appendix describes the Artemis in detail.)

High spherical aberration (small optical zone)
In the early years of excimer laser treatments, a small optical zone was used for treatments as there was concern about the stability of the cornea if too much tissue was removed. It was quickly realized that this resulted in significant night vision disturbances and was a major problem. Studies then demonstrated that using a larger optical zone decreased the impact of night vision disturbances. It was then found that aspheric ablation further improved vision at night. Despite these advances, patients can still end up with high spherical aberration depending on 1) treating high myopia, 2) the laser platform (and ablation profile) being used, 3) high degree of natural preop spherical aberration. These cases combined with the legacy of small optical zones from early patients means that many of the repair cases are to reduce spherical aberration.

Wavefront guided ablation
In these cases the first option that most surgeons go to is to use a wavefront guided custom ablation. Most laser platforms now have a wavefront guided option and there have been a number of publications on the results in patients with significant aberrations. In all the studies, a subjective improvement is reported, however, the spherical aberration is only partially reduced; the average reduction of spherical aberration across all the studies is only 32%. This is an interesting result and one that suggests that we do no need to “flatten the wavefront” to improve the visual quality. This suggests that there is a tolerable level of aberrations below which the brain can filter out the aberrations. In our study using the MEL 80 wavefront guided system, a 27% reduction in spherical aberration was enough to subjectively improve vision and restore contrast sensitivity to normal levels. In this study, with comparison to a post-LASIK control group with no visual quality symptoms, we found the tolerable level of spherical aberration to be about 0.45 µm (OSA notation).

Topography guided ablation
Topography guided custom ablation is another treatment option for small optical zone. Topography guided algorithms are designed to calculate the ablation profile that would result in a smooth aspheric surface with a large optical zone. The side effect of increasing the topographic optical zone will be a reduction in spherical aberration, so the end result is the same as for a wavefront guided treatment, but the path is different.

Topography guided systems are only available on a few laser systems and there are none currently available for use in the US due to FDA restrictions. In our experience, topography guided ablations are more effective in reducing aberrations, particularly spherical aberration, than wavefront guided ablations. In our study using the MEL 80 topography guided system, the spherical aberration was reduced by 41% on average.

As an example, this patient was complaining of debilitating night vision disturbances twelve years after PRK to correct –6.00 D on a Summit Apex Plus laser. Atlas topography showed a small optical zone of about 4.5 mm leading to significant higher order aberrations, particularly spherical aberration. Six months after TOSCA II
treatment the optical zone had been increased to 7 mm. OSA spherical aberration was reduced 47% from 1.18 µm to 0.63 µm and OSA coma was reduced 84% from 0.62 µm to 0.10 µm. The higher-order RMS was reduced 51% from 1.26 µm to 0.62 µm. The figure below shows the achieved change in topography where the increase in the optical zone can be clearly seen.

Trans-epithelial PTK
If you do not have access to either wavefront or topography guided custom ablation, high spherical aberration can also be treated using a trans-epithelial PTK (TE-PTK). TE-PTK works based on the fact that the epithelium remodelling itself to compensate for stromal irregularity by thinning over the peaks and thickening over the troughs (more later). In cases with high spherical aberration after myopic ablation, the epithelium is thinned around the edge of the optical zone and thicker in the centre, where it has thickened to compensate for the ablated tissue. The figure below shows epithelial and stromal thickness changes (measured by Artemis – see Appendix) in an example of a patient after -9.00 D myopic ablation; the top row demonstrates the change in epithelial thickness profile.

One of the most interesting findings from Artemis layered pachymetry analysis after LASIK is that the stroma actually becomes thicker in the periphery where there was no ablation. This biomechanical change seems to be true cause for the majority of spherical aberation induction (probably about 85%) rather than the more commonly discussed reasons of laser fluence projection and reflection errors in the periphery due to the curvature of the cornea.

A TE-PTK treatment can take advantage of the epithelial thickness changes to isolate stromal ablation in a peripheral annulus, which is effectively a spherical aberration ablation.

Decentration
Decentration is the other most common complication related to laser ablation. The major reason for this is the current misconception among many laser companies and surgeons of centering ablations on the entrance pupil centre instead of the visual axis. In eyes with a large angle kappa, centering the ablation on the entrance pupil centre will result in the creation of a new vertex, whereas the natural vertex is maintained if the ablation is centered on the corneal vertex. In our retrospective study of hyperopic eyes with large angle kappa, the objective and subjective outcomes showed no difference to hyperopic eyes without an angle kappa. Other studies have also found similar results when centering ablations on the corneal vertex.
Wavefront guided ablations have been used to successfully correct decentrations,\textsuperscript{5,16} however, the angle kappa must always be considered before using a wavefront guided treatment in a decentration case. Wavefront is currently calculated centered on the entrance pupil centre, as decided by the OSA committee, since wavefront data can only be obtained within the pupil. Therefore, in an eye with a large angle kappa, the wavefront will not represent the patient’s vision since the patient is not looking through the centre of the pupil (where the wavefront is centered). This means that using a wavefront custom ablation in eyes with a large angle kappa could result in worsening the visual symptoms.

For this reason, a topography guided ablation is a much more reliable and effective treatment option for decentration. For example, a patient presented complaining of debilitating night vision disturbances after radial keratotomy for -6.50 D. Atlas topography showed a superior decentration. This was because the RK incisions had been centered on the entrance pupil centre, but this patient had a large superior angle kappa, as seen on the Atlas eye image. The manifest refraction was +1.50 -1.50 x 111. The figure below shows both a wavefront guided ablation profile and a topography guided ablation profile. The wavefront guided profile is symmetrical since the profile has been based on wavefront data centered about the entrance pupil center, whereas the topography guided profile is asymmetric since it is derived from topography data centered on the corneal vertex. It seems quite clear which profile is going to help to correct the decentration.

A topography guided treatment was performed for this patient. Ten months postop, the topography shows that the decentration had been corrected and the optical zone had been increased. The topography difference map also shows that there was an area of inferior flattening caused by the inferiorly asymmetric ablation profile. The OSA spherical aberration was reduced 46% from 0.88 µm to 0.48 µm and OSA coma was reduced 30% from 0.24 µm to 0.17 µm. The higher order RMS was reduced 42% from 0.92 µm to 0.53 µm.

Below is another example of a decentration taken from our study using the MEL 80 topography guided system.\textsuperscript{11} This patient was complaining of halos and starbursts in the infero-temporal direction in the right eye after LASIK for -8.00 D with the LADARVision followed by a LASIK enhancement for +0.75 -1.25 x 5. Atlas topography showed a supero-temporal decentration. Six months after TOSCA II treatment, the topography shows that the decentration had been corrected. The OSA spherical aberration was reduced 61% from 0.60 µm to 0.23 µm and OSA coma was reduced 43% from 0.52 µm to 0.30 µm. The higher order RMS was reduced 47% from 0.91 µm to 0.48 µm.

However, before a decentration is blindly treated by topography guided ablation, it is important to have first made a confident diagnosis and in particular to have considered the effect of epithelial thickness changes. The next section describes how common diagnostic technologies like topography and wavefront can be misleading and may result in the wrong treatment being performed.

It is also important to realize that topography guided ablation (and wavefront guided) will never be a complete solution because it does not account for the epithelial thickness changes.
Irregularly irregular astigmatism

Topography can provide a misleading diagnosis
Despite all the advances in corneal topography and ocular wavefront measurement, it is not always possible to diagnose the cause of subjective visual complaints by these means alone. This is due to the fact that internal corneal refractive interfaces (such as the epithelial-stromal interface) are not being measured independently.

In 1994, we coined Reinstein’s Law of Epithelial Compensation for irregular astigmatism: “Irregular astigmatism results in irregular epithelium”. The epithelium has been shown to remodel itself to compensate for stromal surface irregularities; the epithelium overlying bumps in the stromal surface becomes progressively thinner and the epithelium overlying troughs in the stromal surface becomes progressively thicker. The epithelium often compensates fully for stromal surface irregularities. According to Reinstein’s Law of Epithelial Compensation, if a patient presents with stable irregular astigmatism, by definition the epithelium has reached its maximum compensatory function.

Here, we show a couple of examples where the epithelium has masked the true topographic and/or wavefront error to be corrected.

The first example shows a short nasal flap which has resulted in a nasal “bump” on topography after ablation. The epithelial thickness profile shows that just inside the bump the epithelium is a lot thicker than over the bump. A large amount of epithelial compensation takes place in cases like this, in which there are large steps in the shape of the stromal surface, which is why neither topography-guided nor wavefront-guided ablations will be sufficient to correct such complications. In this case, the epithelium has compensated as much as it can for the stromal surface asymmetry, but irregularity exists. Thus, the patient presents with asymmetric astigmatism topographically. If one were to base the corrective ablation profile on the topography or ocular wavefront, there would clearly be ineffective correction of the stromal surface shape. If such a procedure were performed, the epithelium may or may not compensate fully for the remaining stromal surface asymmetry. If it does, the topography would become regular but the patient may still have symptoms, due to the significant refractive index difference between epithelium and stroma. What is needed here is knowledge of the actual stromal surface contour - not the epithelial surface shape. Based on this, these cases can be repaired accurately.

Decentration is a diagnosis made postoperatively by inspection of topography. Decentration denotes off-center ablation, but we have found that a decentration by topography is not always due to off-center ablation. A patient presented to us complaining of monocular diplopia after LASIK. The initial refraction was -6.50 D. On post-operative examination, his UCVA was 20/70 and manifest refraction was +3.00 -3.75 x 96 yielding a BSCVA of 20/40. Slit-lamp examination showed a clear cornea, with an unremarkable flap possessing a few very faint, faded, shallow appearing, vertical microfolds. Orbscan anterior best fit sphere mapping provided a differential diagnosis of decentration of the ablation zone or ectasia. Zywave® (Bausch & Lomb, St. Louis) aberrometry of the same eye demonstrated coma-like higher-order aberrations. Horizontal 3D VHF digital ultrasound B-scan cross-section of the cornea revealed anatomical features that provided further diagnostic information; the B-scan demonstrated a flatter (F) nasal side of the cornea, with a raised (R) surface temporally. Beneath the raised area the epithelial thickness was seen to be reduced, due to invagination by the underlying Bowman’s layer (B). Bowman’s layer was highly irregular, showing three major ultrasonic discontinuities (*) representing either cracks or microfolds in the flap surface. The epithelial thickness profile was seen to vary continuously, filling-in and smoothing-out the surface of Bowman’s layer. A diagnosis was made of flap malposition and possible asymmetric biomechanical shift. This
case clearly illustrates the importance of anatomical diagnosis, in contrast to a topographical description, in planning the management of the complications of LASIK. By topography alone, this case may well have been diagnosed as a decentration and a topography guided treatment may have been performed.

**Topography sometimes does not provide a diagnosis**

The previous examples demonstrated that topography can sometimes provide a misleading diagnosis. Below are two examples where the true diagnosis was not possible using conventional diagnostic tools (topography, Wavefront, Scheimpflug scanning).

**Case example #1:** Diagnosis of optical scatter caused by an irregular stromal surface not detected by topography

This patient presented with severe visual symptoms following multiple corneal refractive procedures including automated lamellar keratoplasty (ALK), arcuate keratotomy, LASIK, LASIK enhancement by re-cutting of another flap, followed by a further LASIK enhancement by flap-lift.

Topography was irregularly irregular with a BSCVA of 20/25. Artemis VHF digital ultrasound analysis of the anatomical irregularities of the epithelium and stroma revealed a central area of thin epithelium surrounded by concentric rings of thick and thin epithelium. This was an example of the known phenomena of the epithelium remodeling itself to try to regularize the front surface of the cornea; it had become thicker to fill in troughs in the stromal surface and thinner over peaks in the stromal surface. It was found that each ring of thickened epithelium coincided with rings of flattening on topography, indicating that the epithelium had not been able to completely compensate for the stromal irregularities.
In this case, topography did not provide information on the etiology of the surface irregularities and wavefront analysis was not able to describe the micro-optical irregularities most probably responsible for optical scattering within the cornea. Therefore, VHF digital ultrasound assisted trans-epithelial photo-therapeutic keratectomy (PTK) together with a wavefront guided treatment was used to reduce the stromal surface irregularities and the higher order aberrations respectively. The treatment successfully regularized the stromal surface, confirmed by the regularization of the epithelial thickness profile. The higher order aberrations were dramatically reduced, the contrast sensitivity was improved from below normal to high normal and the BSCVA was improved to 20/20.

Case example #2: Resolution of irregular astigmatism caused by mis-rotation of an irregular LASIK free cap

We present a patient in whom a symmetrically round free cap occurred during LASIK, and flap repositioning was performed without laser ablation. A loss of 3 lines of BSCVA, monocular diplopia and topographic irregular astigmatism confirmed that the free cap orientation was incorrect. Two subsequent free cap rotations based on refraction and topography failed to realign the free cap into its original position. Artemis VHF digital ultrasound analysis found the thickness profiles of the stromal component of the free cap and the residual stromal bed to be irregular and mismatched. The rotation required for anatomical realignment was determined by digitally generating a “lock and key” superimposition of the free cap and stromal bed thickness profiles. Following Artemis guided free cap rotation, the eye regained preoperative BSCVA and symmetrical corneal topography with a +0.50 D change in spherical equivalent. Postoperative Artemis scan showed that the irregularities in the stromal component of the free cap and the residual stromal bed were successfully realigned.

This case also demonstrates that a topography guided ablation is not always the default option for any irregular astigmatism, as has been described.11 Epithelial thickness changes are not taken into account by topography guided algorithms, which can lead to a large error and hence a remaining irregularity postop. In this case, the epithelium had changed dramatically with a central step from 42 to 82 µm. After the cap rotation, the epithelium remodeled overnight to a regular thickness profile. Evaluation of the layers of the cornea allowed the correct rotation to be found without the need for tissue removal by an unpredictable topography guided ablation.

Refractive effect of the epithelium in TE-PTK

Trans-epithelial PTK is an excellent treatment option in irregularly irregular astigmatism. However, the refractive effect of the epithelium should be considered to evaluate the predicted outcome and impact that this will have on future treatments.
The refractive effect of the epithelium is demonstrated very well by the following case.

On presentation to London Vision Clinic in February 2009, the patient’s refraction was +6.50 -8.00 x 110 achieving CDVA of 20/50, 17 years after radial keratotomy including trapezoidal incisions inferiorly and superiorly (for presbyopia). Atlas front corneal surface topography was irregularly irregular showing an asymmetric bow-tie pattern decentred superiorly. The Artemis epithelial thickness profile was very irregular in thickness with up to 35 µm variation within the central 4 mm corneal diameter. The epithelial thickness map demonstrated two small zones of thin epithelium (40 µm), approximately 1 mm in diameter each, at a 2 mm radius inferiorly and superiorly from the corneal vertex; these regions of thin epithelium were coincident with the trapezoidal incisions. The epithelium was thicker (up to 75 µm) along the horizontal meridian centrally, extending nasally, and at the 3 mm radius infero-nasally. In this case, the epithelial thickness profile was masking a significant proportion of the stromal irregularity from front corneal surface topography, meaning that this proportion of the stromal irregularity would not be taken into account by a topography guided ablation algorithm. Therefore, the optimal treatment plan was to perform an Artemis assisted trans-epithelial PTK procedure to target the component of the stromal irregularity compensated for by the epithelium.

Due to the epithelial masking, the stromal ablation was concentrated superiorly and inferiorly in the vertical meridian which meant that the stromal ablation pattern was similar to a hyperopic astigmatic ablation. Indeed, nine months after the procedure, the astigmatism had been halved so that the manifest refraction +4.50 -4.50 x 101 and the CDVA had improved to 20/20. The postoperative Artemis epithelial thickness profile showed that the epithelium was much more regular in thickness. The epithelial thickness difference map demonstrated that the epithelium had become thicker in the superior and inferior regions where the maximum ablation was performed and had become thinner centrally where the epithelium was thickest before the procedure. The change could also be seen on Atlas front corneal surface topography where the difference map showed a significant astigmatic change. The PTK procedure had succeeded in reducing the stromal irregularity and the presence of a smoother epithelium meant that the impact of epithelial masking on front corneal surface topography was also reduced.

This case demonstrates the influence the epithelium can exert on the manifest refraction; in this case, a refraction change of +2.24 -3.97 x 120 was achieved with a trans-epithelial PTK ablation alone. This example shows that the pattern of irregular epithelium and the associated refractive effect must be taken into account when planning PTK and/or custom ablation (topography guided or wavefront guided).
Conclusion
We have demonstrated a number of cases in which topography was inadequate in providing a true etiology of the problem. In some cases, topography or wavefront analysis alone would have led to an inappropriate treatment plan. The extraordinary power of the epithelium to remodel and partially compensate for stromal surface irregularity is remarkably advantageous in many forms of corneal refractive surgery. The epithelium acts as a low pass filter over the stoma, regularizing high frequency noise. The epithelium is regulated by the blinking motion of the eyelid\textsuperscript{23,24} and is therefore designed to improve regularly irregular astigmatism about the visual axis. Unfortunately, this evolutionary power of the epithelium to remodel itself to a smooth surface poses a problem when trying to diagnose sub-surface causes of irregularities in corneal front surface shape. We believe that epithelial thickness mapping has the potential to greatly improve our diagnostic capabilities, as well as improve treatment planning in the correction of irregular astigmatism.

Topography guided custom ablation seems to offer a more effective treatment option in cases of small optical zone and decentration, however, a confident diagnosis is required before deciding what treatment to perform. In cases of irregularly irregular astigmatism, it is usually beneficial to first perform a trans-epithelial PTK to target the irregularities masked by the epithelium, since a highly irregular epithelium will significantly affect the efficacy of a topography guided ablation. Once the epithelium is more regular, a topography guided ablation can be used to correct the remaining irregularity. An epithelial thickness map is useful to use as a reference during a TE-PTK treatment to monitor the ablation depth so that stromal tissue is conserved (tissue is often at a premium in repair cases) and to predict the refractive effect of the treatment.

In conclusion, the final solution in repair treatments is going to be a custom ablation profile based on stromal surface topography. Currently, both topography guided ablation and TE-PTK can only provide a partial treatment for irregularities meaning that a second (or third) treatment will be required in almost all cases.

Ultrasound imaging has the advantage of detecting physical interfaces within the cornea, as opposed to optical interfaces. This is why VHF ultrasound scanning provides much better LASIK interface detection than optical systems. It can map individually the epithelial thickness profile, the stromal thickness profile and the flap thickness profile. Despite some of the inconvenience of immersion scanning, Ultrasound Biomicroscopy provides a unique tool for diagnosis, treatment planning and postoperative monitoring of corneal (and other intraocular) surgery.
Appendix: Artemis very high-frequency (VHF) digital ultrasound technology

All layered pachymetric maps of epithelium, stroma and cornea shown in this course were obtained using the Artemis VHF digital ultrasound arc-scanner.

Background of Artemis technology

The Artemis very high-frequency (VHF) digital ultrasound arc-scanner was specifically designed as a tool capable of imaging and measuring the whole anterior segment, or the whole cornea in one scan sweep. It was designed to help ophthalmologists in all disciplines, but particularly in refractive, cataract and presbyopic surgery, to improve anatomical diagnosis for surgical planning and post-operative diagnostic monitoring.

Details of the scanning and signal processing technology have been described comprehensively elsewhere.\textsuperscript{12, 23, 25, 26} Briefly, a broad-band 50 MHz VHF ultrasound transducer (bandwidth approximately 10 to 60 MHz) is swept by a reverse arc high-precision mechanism to acquire B-scans as arcs that follow the surface contour of anterior or posterior segment structures of interest. The Artemis possesses a unique scan-arc adjustment mechanism to enable maximum perpendicularity (and signal-to-noise ratio) to be obtained for scanning any of the different curvatures within the globe (cornea, iris plane, retina). Ultrasound data is first digitized and stored. The digitized ultrasound data is then transformed, using Cornell digital signal processing technology, which significantly reduces noise and enhances signal-to-noise ratio. Some of the digital signal processing used originated from military naval research for improving signal-to-noise ratio for underwater sonar systems, and were first applied by Jackson Coleman, MD and colleagues to improve resolution and measurement precision of ocular tumors.\textsuperscript{27} Later, such techniques were refined to greatly improve image resolution to approximately 20 µm, and measurement precision to approximately 1 µm using 50 MHz transducers.\textsuperscript{12, 28} We have also demonstrated that using digital signal processing on 50 MHz ultrasound data doubles resolution and increases measurement precision by a factor of three when compared to conventional analog processing of the same very high-frequency data.\textsuperscript{29}

The world’s first VHF digital ultrasound arc-scanner was constructed in 1996. The first commercial prototype Artemis, the Artemis 1, was built in 1999. Artemis VHF digital ultrasound is carried out using an ultrasonic standoff medium, and so provides the advantages of immersion scanning(e.g. the tear-film is not incorporated into the corneal or epithelial thickness measurement, and there is no physical contact of the transducer with the cornea). The patient sits and positions the chin and forehead into a headrest while placing the eye in a soft rimmed eye-cup. Warm sterile normal saline (33°C) is filled into the darkened scanning chamber. The patient fixates on a narrowly focused aiming beam which is coaxial with the infra-red camera, the corneal vertex and the centre of rotation of the scanning system. The technician adjusts the center of rotation of the system until it is coaxial with the corneal vertex. In this manner, the position of each scan plane is maintained about a single point on the cornea and corneal mapping is therefore centered on the corneal vertex. A speculum is not required as patients find it comfortable to open the eye without blinking in the warm saline bath and voluntary elevation of the upper lid produces exposure of the central 10 mm of cornea in virtually all patients. Performing a 3D scan set with the Artemis 1 takes approximately 2 to 3 minutes per eye.

Three-dimensional layered corneal pachymetric topography

The resolution of the Artemis, when set to scan cornea, is sufficient to distinguish individual corneal layers such as the epithelium, stromal component of the flap, residual stromal bed, and others, all in 3D, thanks to multi-meridional scanning. The Artemis VHF digital ultrasound technology is able to consistently detect internal corneal lamellar interfaces (such as the keratotomy track) because of the permanent “mechanical” interface present, even years after surgery, and despite total optical transparency. Three-dimensional thickness profiles are calculated based on data from four meridional B-scans, comprising of eight hemi-meridians. A linear polar/radial interpolation function is used to interpolate between scan meridians to produce a Cartesian matrix over a 10 mm diameter in 0.1 mm steps. This is our standard scanning protocol as it provides sufficiently high density of information in the central cornea with lower density of information in the periphery where it is less needed. 3D pachymetric maps of each individual corneal layer can be displayed as well as difference maps to highlight changes before and after LASIK for example.

Measurement precision within the cornea in LASIK has been formally tested and published.\textsuperscript{12, 30} Central reproducibility for single-point pachymetry was 0.58 µm for epithelium, 1.68 µm for flap and 1.68 µm for full cornea.\textsuperscript{30}
References