How to improve existing technology

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I would like to thank the panel for the honor of this invitation to attempt to predict the future.
How to improve existing technology:

INTRODUCE ANATOMY

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Simply put, I believe that the single most important thing that we could do to improve refractive surgery would be to introduce anatomy and anatomical diagnosis into the mix.
I acknowledge a financial interest in the Artemis technology - VHF digital ultrasound scanning developed by my colleagues and I at Cornell and licensed to Ultralink LLC. For anyone who has gone from one child to two and then to three, you will understand that having a conflict of interest is not the point, it is how you handle it!
Our work in developing a refractive surgery biometry tool started in 1991 at the bioacoustic research facility at Cornell University. Ron Silverman, now professor of computer science and ultrasound bioengineering is seen here scanning me on our developmental arc-scan device.
The Artemis digital signal processing technology improves measurement precision by a factor of about 5, compared to simple analog processing (measuring directly from the B_scan). The axial measurement precision is of approximately 1–μm within cornea. Because the Artemis scans in multiple meridians, three dimensional mapping of each individual layer within the cornea is possible.
Corneal Pachymetric Topography

Thanks to multimeridional scanning, 3D mapping of corneal thickness is possible. This display has been proposed by us in a 2000 publication in the JRS as a standard display for observing layer by layer how the cornea is altered before and after LASIK. The epithelium, stroma, corneal thickness, stromal change, residual stromal thickness and original flap thickness are all displayed.

Legend from the publication:
"C12" display of the cornea of a patient pre- and six months post-LASIK OS. All 12 maps are pachymetric representations of particular corneal layers depicted on a color scale in microns. The pre-operative epithelial (1), stromal (2) and full corneal (3) thickness maps appear in the first column. To the right of each of these maps (column two) is the post-LASIK pachymetric maps of epithelium (4), stroma (5) and full cornea (6) on identical color scales for direct comparison to pre-op. The third column depicts calculated maps only. The calculated epithelial change map ((7), 3rd column, 1st row) is derived in point-by-point subtraction of the pre-operative from the post-operative epithelial pachymetric map. Thus the epithelial change map shows on a color scale the number of microns increase due to surgery. Note that the pattern of epithelial thickness change is such that it is greatest centrally, with a decrease in a symmetrical centrifugal fashion thus producing an increase in outer curvature of the post-operative cornea. Note that the area of epithelial thickening is confined to the ablation zone or the zone of surgical corneal flattening. The calculated stromal change map ((8), 3rd column, 2nd row) is derived in point-by-point subtraction of the post-operative from the pre-operative stromal
Summary

1. Does topography and wavefront data provide DIAGNOSIS in repair cases?

2. Are topography, wavefront, registration/alignment/tracking, keratome, laser technologies all we need to improve?

I will deal with two main topics: postoperative repair eyes and preoperative virgin eyes.
Let’s start with irregular corneas.
Irregular Cornea
Tissue Effects

Law of epithelial compensation:
“Irregular astigmatism, irregular epithelium”

I coined this phrase about 10 years ago when we realised that the epithelium ALWAYS changes over an irregular stromal curvature. I call this the Law of Epithelial Compensation: “Irregular astigmatism, irregular epithelium”
What is the diagnosis? Most people say: “Decentration”. In fact, this was nothing like a decentration. It was a short nasal flap in a left eye that still received a -8.00 myopic correction.
Irregular Astigmatism, Irregular Epithelium!

- Epithelium *always compensates* for stromal surface irregularities
- Epithelium *masks* true topographic and/or wavefront error to be corrected

Here we see how a short nasal flap in which the surgeon continued to do the ablation has left the cornea with a nasal “bump”. The epithelial thickness profile shows that just inside the bump the epithelium is a lot thicker than over the bump. Topography guided repair based on the Orbscan anterior best fit sphere image (right) would dictate the removal of tissue temporally (remove the yellow-red bump) - which would clearly be the wrong thing to do. What is needed here is a knowledge of the actual stromal surface contour - not the epithelial surface shape. Based on this, these cases can be repaired accurately.

In fact, Reinstein’s rule means that ANY cornea with irregular astigmatism on the surface by definition will have maxed out it’s epithelial compensation. Therefore the epithelium will be asymmetric. Therefore surface topography guided treatments would be inaccurate.
So I asked Gerhard Youssefi, PhD of Bausch and Lomb/Technolas in 1999 to calculate a topography guided ablation profile that would take into account the epithelial thickness profile that we had measured in this patient.
This graph shows the epithelial correction function and what effect it would have on modifying the topography based ablation profile.
Here you see the actual epithelial thickness profile in 3D, with the B-scan Artemis cross section through the visual axis below.
Ultrasound Guided Ablation (2000):

Here are the postoperative horizontal scans demonstrating that the ‘bump’ nasally had been significantly reduced, and on the right, the total optical power maps (Orbscan) before (B) and after (A) this ultrasound guided ablation.
Irregular Topography

True diagnosis

Let’s look at another example or two, where the DIAGNOSIS is needed, and the topography fails to give this.
Here is what looks like another ‘decentration’. The year 2000 Zywave map also shows coma consistent with the topography. Was this a decentration?
In fact not! Look at this cross-sectional B-scan of the cornea (shown superimposed over the topography) demonstrating that the patient’s problem was a flap malposition and NOT a decentration - this patient would be wrongly served if a topography or wavefront guided treatment had been done. Simple flap repositioning solved the problem reliably and without removing more tissue.
In this eye, a small undercorrection resulted after LASIK. Enhancement over a predicted 281 residual would have left her with 254 microns in the bed. However, Artemis demonstrated a residual minimum of 218 microns! Whether this was due to inaccurate pre-op pachymetry or a thicker flap than expected or both, …had she undergone enhancement, she would have ended up with considerably less than 200 microns under the flap… By the way, note how the epithelial thickness profile (top left map) demonstrates the pattern of central thickening.
Gross Overcorrection

Preop 58 y.o. F
-10.00 D, 4.5-mm scotopic pupil

Treatment, 2000
• B&L 217C 5.5-mm zone
• Moria CB “110” - FAST - assume 160–µm
• Residual Stromal Thickness = 250–µm

Postop
• +4.50 D

Here is another interesting case of mine from 2000. A grossly overcorrected and unhappy patient after a routine and uncomplicated LASIK. The reflex reaction here would have been to perform a flap-lift hyperopic correction.
Here is her topography before surgery
Gross Overcorrection: Topography

Postop

And after surgery. As you see, a pretty ordinary surgery with no obvious reason for the massive overcorrection.
If we look at the B-scan cross-sectional ultrasound scan, we see that the flap was indeed thin in the centre, but it was actually very thick in the periphery.
Therefore the DIAGNOSIS in this case was of a “dual mechanism” central flattening - she had -10 removed from the center of the cornea, but she had a deep peripheral cut due to deep engagement of the microkeratome on the cornea and hence an RK-like, mechanical peripheral keratectomy which also produced central flattening. The two mechanisms together producing double flattening. Clearly lifting the flap and removing MORE peripheral tissue in this case would have been a very bad move!
So let’s move from complicated corneas to virgin normal eyes. Here is LASIK data from a study that I presented at the ASCRS 4 years ago on over 20,000 eyes.
Nomogram adjustments aside, look at the large scatter in the results - why are we getting all this scatter? I submit that it is epithelial and biomechanical changes.
I will start by presenting results from a study that we first presented in 2000 at ARVO in which...
Deformation of the Cornea - Distinction

- Mechanical deformation
  - Stable (?) elastic “bulge”
- Ectasia
  - Progressive plastic deformity

In our model, a cornea starts with an epithelium (in blue) and a stroma (orange).
Deformation of the Cornea - Distinction

- Mechanical deformation
  - Stable (?) elastic “bulge”
- Ectasia
  - Progressive plastic deformity

A volume of tissue is removed from the center of the cornea under a flap, producing a lamellar keratectomy within the corneal structure.
Deformation of the Cornea - Distinction

- Mechanical deformation
  - Stable (?) elastic “bulge”
- Ectasia
  - Progressive plastic deformity

In this hypothetical model, the cornea bows forward or increases in curvature, and the epithelium thickens.
Method

- 52 eyes
- Routine LASIK
  - Myopia: -1.00 to -10.25 [mean (SD) -4.44 (2.32)]
    - Hansatome/Moria LSK One
    - Nidek EC5000/Technolas 217
- Pre- and post-operative ≥ 3 months
  - Orbscan, (Orbtek/Bausch&Lomb Inc.)
  - VHF 3D Digital Ultrasound scanning - Artemis™

The study included 52 eyes that underwent routine LASIK, all eyes with a predicted residual stromal thickness of more than 250-microns while treating myopia from -1 to -10. Before and at least 3 months after surgery, Orbscan and Artemis VHF digital ultrasound scanning of the cornea was carried out, which provided the epithelial thickness, flap thickness and residual stromal thickness with 1-micron precision in 3D.
Method - Three Surface Corneal Model

- Anterior surface radius of curvature
  - Orbscan
- Back surface radius
  - Orbscan
- Bowman’s surface radius
  - Calculated from anterior surface radius and
  - epithelial thickness profile

From the Orbscan we derived the radius of the best-fit-sphere of the central 3-mm zone for the front and back surfaces of the cornea. The Artemis provided the epithelial thickness profile, from which the radius of Bowman’s surface was calculated.
Method - Calculating Corneal Power

• Calculated Power of the Cornea
  – Thin lens approximation:
    \[ \frac{n_2 - n_1}{r} \]
  – Total Corneal Power = epithelial + Bowman’s + back

• Corneal Power Change (CPC) = post-pre

Using a thin lens approximation and refractive indices for epithelium, stroma and aqueous, the Total Corneal Power was calculated by adding the power of each of the three interfaces.
…derived from Orbscan and Artemis scanning…we could calculate the power of the cornea by adding the power of each surface before surgery…
Calculated Corneal Power

- Post-LASIK

And then, calculate the cornea power from the surfaces after surgery.
Calculated Corneal Power

- Post-LASIK - no "epithelial" effect
  - Use pre-operative epithelium

And then we could simulate a post-lasik cornea that did NOT display epithelial changes by substituting the preoperative epithelium onto the postoperative stroma. Then calculate the power …
Calculated Corneal Power

- Post-LASIK - no “epithelial” effect
  - Use pre-operative epithelium

Here we digitally substituted the postop epithelium with the preop epithelium from the Artemis data to show what the power would be postop had there been no epithelial changes but leaving the mechanical changes intact.
Calculated Corneal Power

- Post-LASIK - no “bowing”
  - Subtract back surface radius change from all surfaces

We can do the same for mechanics: remove the “bowing” from all three surfaces...
By subtracting the observed curvature change of the back surface (from before to after surgery) from all three surfaces, leaving the epithelial change in place - and calculating the power through this theoretical cornea.
Calculated Corneal Power

- Post-LASIK - no epithelial or “bowing” effects
  - Subtract back surface radius change from all surfaces
  - Use pre-operative epithelium

Finally, we can subtract the bowing and the epithelial changes from the postoperative stroma.
Calculated Corneal Power

- Post-LASIK - no epithelial or “bowing” effects
  - Subtract back surface radius change from all surfaces
  - Use pre-operative epithelium

Subtracting bowing is shown here.
Calculated Corneal Power

- Post-LASIK - no epithelial or “bowing” effects
  - Subtract back surface radius change from all surfaces
  - Use pre-operative epithelium

Subtracting epithelial changes is shown here so the three surfaces now represented what the corneal power would have been had there been no epithelial or biomechanical curvature changes.
From all this data, we set out to find the following outcome measures:

First, we simply looked at the magnitude of the epithelial and biomechanical changes as a percentage of the total refractive changes that had taken place.

Then we investigated correlation between the manifest achieved effect (determined by refraction), and the calculated corneal power change as determined by the manipulations that we just went through (removing either the epithelial, biomechanical or both effects).
Results - Accuracy of Treatment

- Attempted vs. Achieved (by refraction)

This graph simply shows the attempted vs achieved results for the whole group of eyes, showing that it represented a typical set of myopic surgical data.
Validation

- Change in Power of the cornea (CPC) Calculation
  - Correlation of corneal power change by calculation, with refractive change observed

\[ y = -0.9019x + 0.7472 \]
\[ R^2 = 0.671 \]

If we examine the correlation between the change in manifest refraction (along the x axis) and the calculated change in corneal power… this validates the method of corneal power power calculation by showing a relatively high R square correlation. Notice here however, that the calculated corneal power change is somewhat underestimated - with a slope of the correlation at approximately 0.90.
Removing Epithelial Effect

- Correlation of corneal power change by calculation, with refractive change observed
  - $\emptyset$ epithelium
  - $\emptyset$ “bowing”
  - $\emptyset$ epithelium $\emptyset$ "bowing"

… what was interesting, is that if we looked at the correlation between the change in manifest refraction (again along the x axis) and the calculated change in corneal power while subtracting the epithelial changes we see that the slope of the correlation increased to 0.94.
Removing Bowing Effect

- Correlation of corneal power change by calculation, with refractive change observed
  - ∅ epithelium
  - ∅ “bowing”
  - ∅ epithelium ∅ ”bowing”

\[ y = -0.9932x + 1.0672 \]
\[ R^2 = 0.4662 \]

…if we then looked at the correlation between the change in manifest refraction (again along the x axis) and the calculated change in corneal power while subtracting the mechanical changes we see that the slope of the correlation increased to 0.99.
Removing Epithelial + Bowing Effects

- Correlation of corneal power change by calculation, with refractive change observed
  - ∅ epithelium
  - ∅ “bowing”
  - ∅ epithelium ∅ “bowing”

…and finally when both epithelial and biomechanical effects were removed, the slope of the correlation between refraction change and calculated corneal power change became ONE.
Impact of Epithelial and Bowing Effects on Accuracy of LASIK

Validation of Calculated Power Change in Cornea

\[ y = -0.9019x + 0.7472 \]

\[ R^2 = 0.671 \]

Removing Epithelial Change from Treatments

\[ y = -0.9352x + 0.8981 \]

\[ R^2 = 0.6608 \]

Removing Bowing from Treatments

\[ y = -0.9932x + 1.0672 \]

\[ R^2 = 0.4662 \]

Removing Epithelial Changes and Bowing from Treatments

\[ y = -1.0256x + 1.2145 \]

\[ R^2 = 0.4757 \]

...in other words, as we continued to remove epithelial and/or biomechanical factors from the corneal response, the relationship between achieved refractive change and calculated refractive change became closer and closer to ONE and arguing that epithelial and biomechanical factors account for the inaccuracy in LASIK.
To characterise the magnitude of these changes, the first bar represents the average refractive change for the group as a whole, the second represents the average refractive change by corneal power calculation - and these two were statistically the same. However, on paired t-testing, the analysis showed that if biomechanics were removed from the cornea a further 15% of flattening would have occurred. If epithelial changes alone were removed, a further 5% flattening would have been achieved, and combined, epithelial and biomechanical changes accounted for a 20% loss of flattening overall. This in fact coincides with some of the empirical nomogram adjustments that have been made to the initial Munnerlyn based ablation profiles, so it fits with our experience.
Now let’s look at the epithelium in more detail. We have long known that the epithelium has an inherent capacity to “fill-in” the nooks-and-crannies or other surface irregularities of the stromal surface. Here is an example of a section of cornea scanned by VHF digital ultrasound, after healing of a deep crater formed by a contact-lens related corneal ulcer. It
ARVO 1999

Effect of Epithelial Changes on Refractive Outcome in LASIK

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This work was presented in 1999 at ARVO by Dr. Sabong Srivannaboon who was working with me in Vancouver.
Methods

• 3 groups: Low, Moderate, High myopia
• Changes of the epithelial thickness were determined annularly for the:
  – Center
  – Anulus at zone diameters of:
    • 3, 4, 5, 6 and 7 mm

What we did was to scan a group of patients before and at least 3 months after LASIK. The epithelial thickness was measured in the center, and in annulus fashion averaged for the 3, 4, 5, 6 and 7-mm diameter zones.
Here is an example of one of the cases, where the epithelial thickness map is shown before surgery on the left and after surgery on the right. Both thickness maps are in microns on the same color scale for direct comparison. We can see that before surgery the epithelium was between about 50 to 55 microns throughout, whereas three months after LASIK the central epithelium had thickened to about 80–µm. Central thickening amounts to a relative increase in
If we plotted the level of myopia treated on the x axis, against the amount of epithelial thickening in the center, at the 3, 4, 5, 6 and 7-mm zones we found a strong correlation between amount of epithelial thickening and the level of myopia treated. But there were two things that stood out from this graph. The first is that there was more thickening in the central cornea than the peripheral, and the second is that the epithelial thickening response was steep and
We divided the study eyes into three groups: low, moderate and higher myopia, and determined the thickening profile for each group separately.
This graph shows the average amount of epithelial thickening observed at the central, 3, 4, 5, 6 and 7-mm zones for each of the three groups. Of course, if the epithelium were to thicken evenly, by say 3–μm as shown in the horizontal green line. We can see that for the low myopic group, there was considerably more thickening in the center than the periphery - 8 versus 4 microns, and as we increased myopia, the difference between the central and peripheral
So we set up a hypothesis based on these observations. This figure represents a stromal surface, with an overlying epithelium. As we remove tissue from the stroma of the cornea in a lens shape fashion, the epithelium will thicken more in the center than the periphery – producing a myopic shift. If we remove even more tissue from the center, there will be even more central thickening. This continues until at a certain point, the central epithelium “maxes out” on it’s
…to test this biphasic relationship we fit a parabola to the graph of spherical equivalent treated vs. epithelial power shift - and …
..indeed found that there was a strong statistically significant correlation, supporting our hypothesis.
Summary

1. We cannot rely on even the most accurate topography or wavefront measurements to provide the correct **DIAGNOSIS** and hence **MANAGEMENT** in repair cases

2. Ideal wavefront, registration/alignment/tracking, keratome, laser technologies are not all we need to improve to treat ordinary patients.
Wish-list

1. Integration of DIANGOSIS into treatment plans: ANATOMICAL considerations within the cornea

2. Better clarity from manufacturers as to what their “wavefront guided” treatment really is

3. To make repair technology more effective so the overall safety is higher and more people want it

4. To live long and prosper