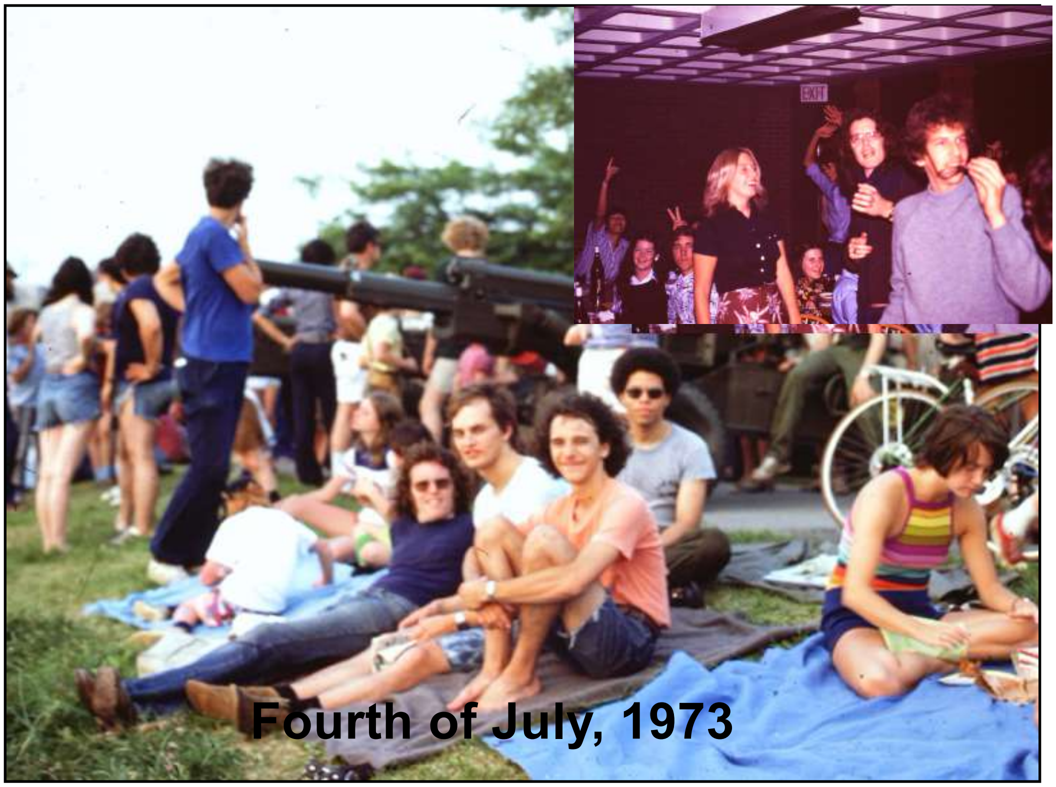
Announcement:

“In anticipation of activating an alumni network in Nebraska, Mark Johnston '76 and the MIT Alumni Association invite the Nebraska MIT community and friends to join a "Welcome Meeting" on Wednesday, November 18 at 7pm central time.”

“All participants will be asked to introduce themselves. Dr. Mark Johnston of Omaha will then give a short presentation on how his MIT experience uniquely prepared him to become one of the pioneers in refractive laser eye surgery. After which, all participants will be asked to join in a Q&A session, a general discussion, and to make suggestions for future meetings.”



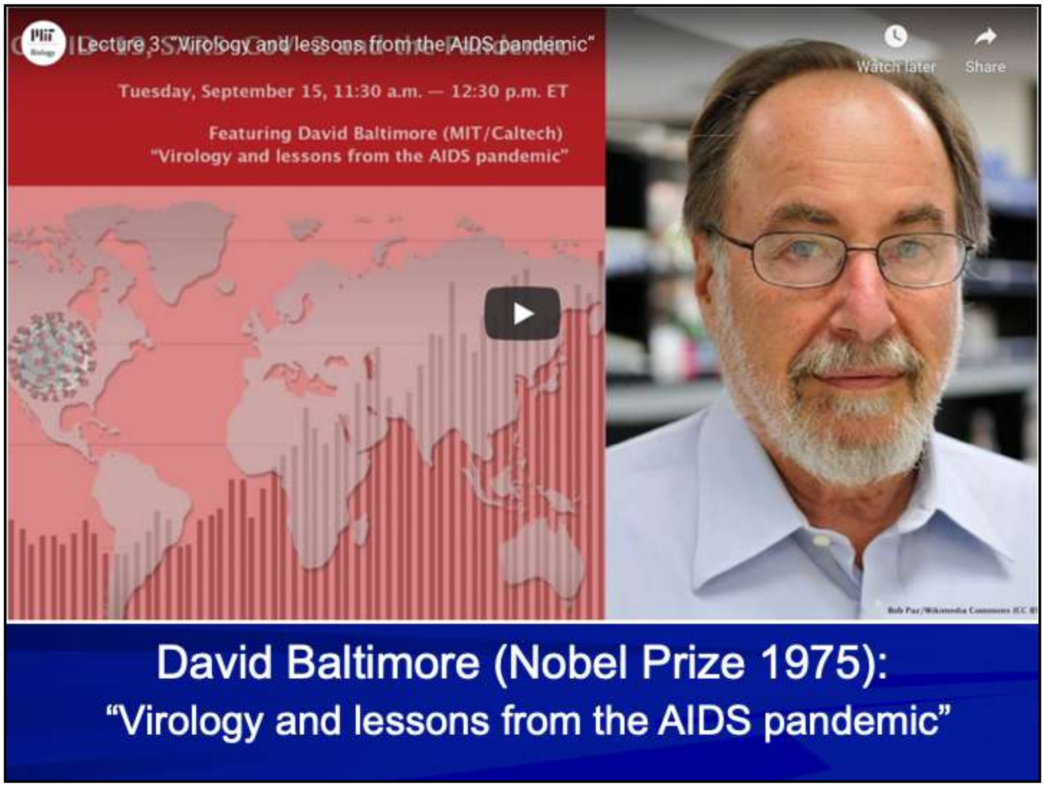
Fourth of July, 1973

I will introduce myself.

I grew up in a small town “Down East”. My father was a physician but his hobby, and our work, was a farm. While our school did not offer Trig or Calculus, I did learn how to get my hands dirty.

At MIT I lived at E-Entry MacGregor and was lucky to have a close group of friends.

MIT teaches that hard work, perseverance and problems solving.
While the motto is "Mind and Hand", as a surgeon, I say "HAND and Mind".



I studied Molecular Biology at MIT.

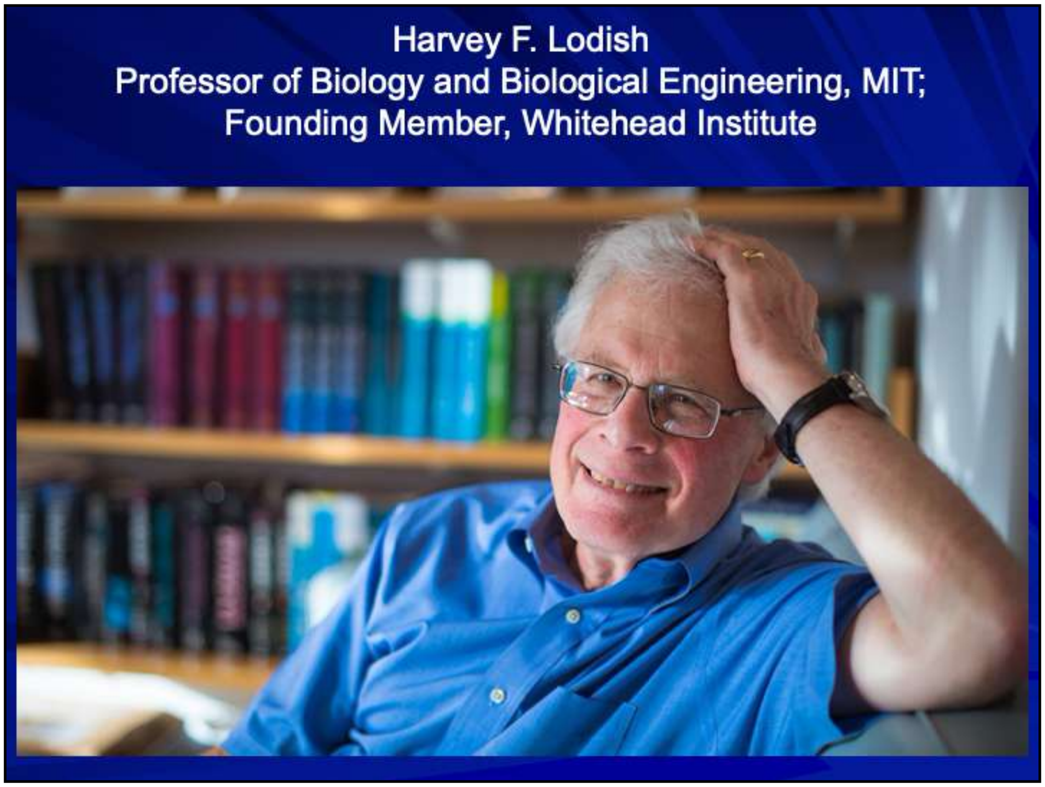
I still remember the day that David Baltimore won his Nobel Prize. At least 20 cases of good champagne showed up in the main lobby of the Biology Building.

More importantly, since that time, the MIT Biology Department, has become the largest Biology Research University in the world.

While I did not have David Baltimore as a professor, this fall I listened to his talk for the special MIT course on Covid-19.

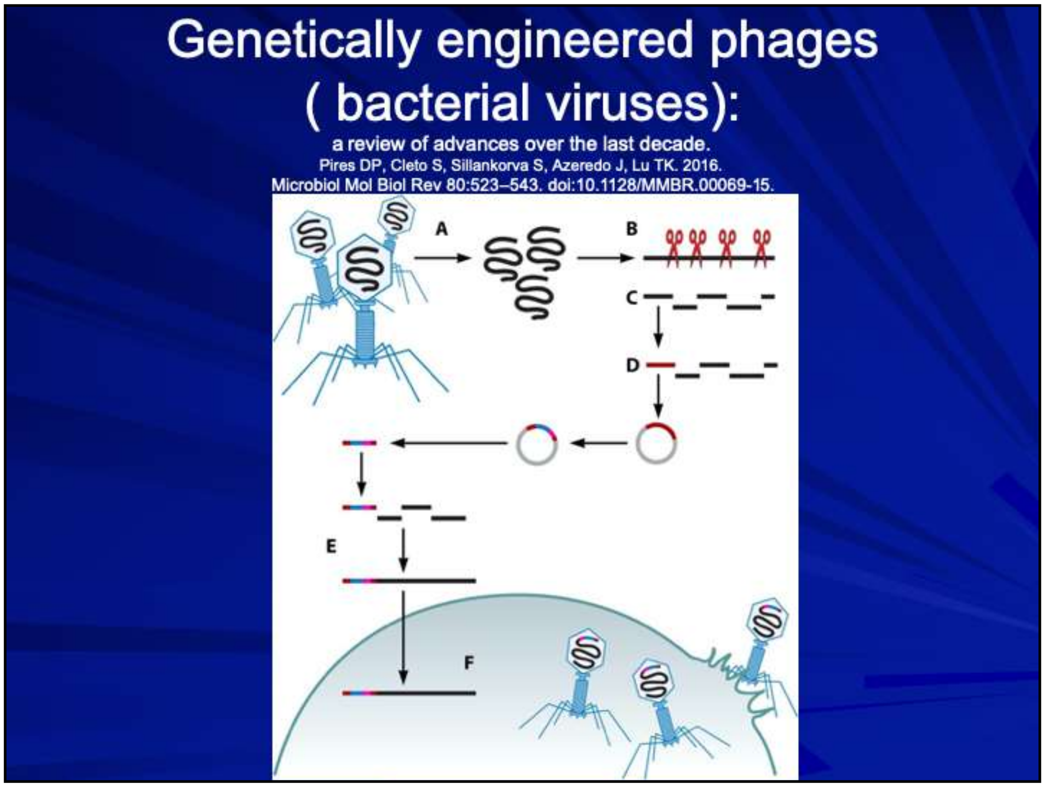
His main theme was the diversity of viruses and how each has it's own set of tricks. Being very "simple" compared to whole cells, viruses have been instrumental in understanding the molecular basis of biology.

This year is a testament to the importance of the understand the molecular basis of all life and disease.



Harvey Lodish's early academic interest was also the molecular biology of viruses. When I was at MIT his course covered everything there was to know about Lambda Phage, a small bacterial virus,(except why). The course had no textbook, only a six inch pile of photocopied journal articles on the subject. These were hard reading because they were so specialized.

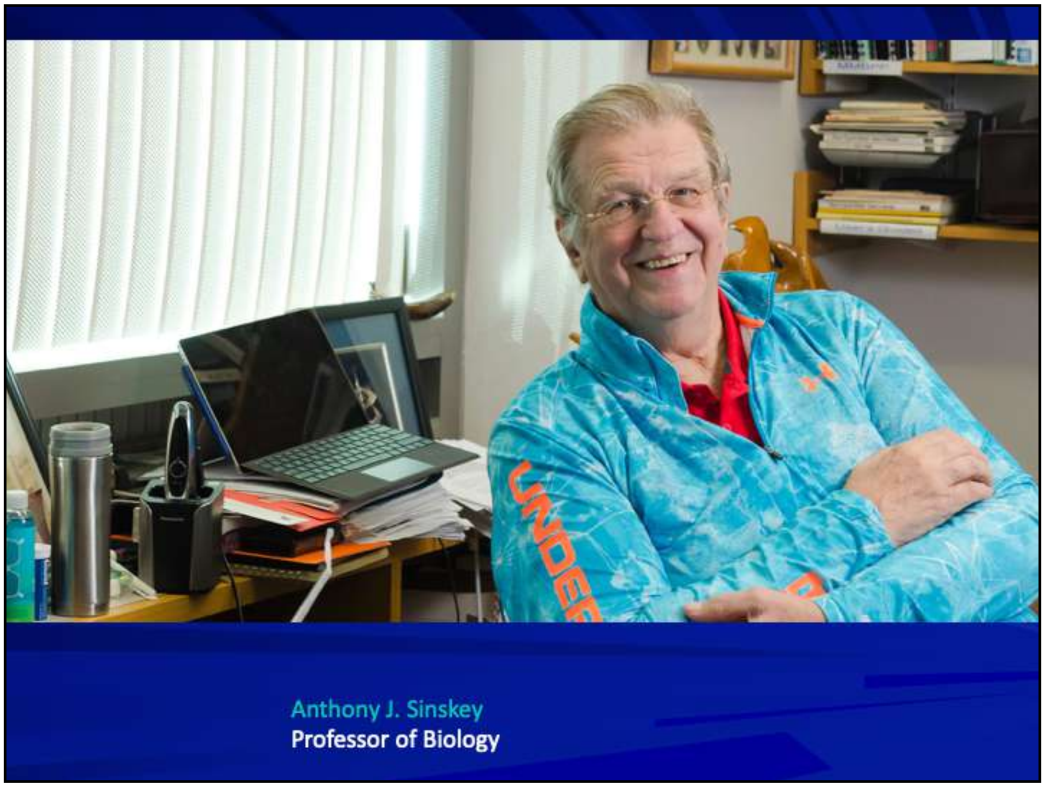
Professor Lodish's enthusiasm about how things work was infectious. In later years, as molecular biology developed into a fuller understanding of how cells worked, he "wrote" the classic textbook on Molecular Cell Biology.



While this picture is from a recent publication, it also looks like the blackboard in Professor Lodish's course.

We see this type of drawing every day now, not on the blackboard of an obscure course at MIT, but at the top of a lead story in the news.

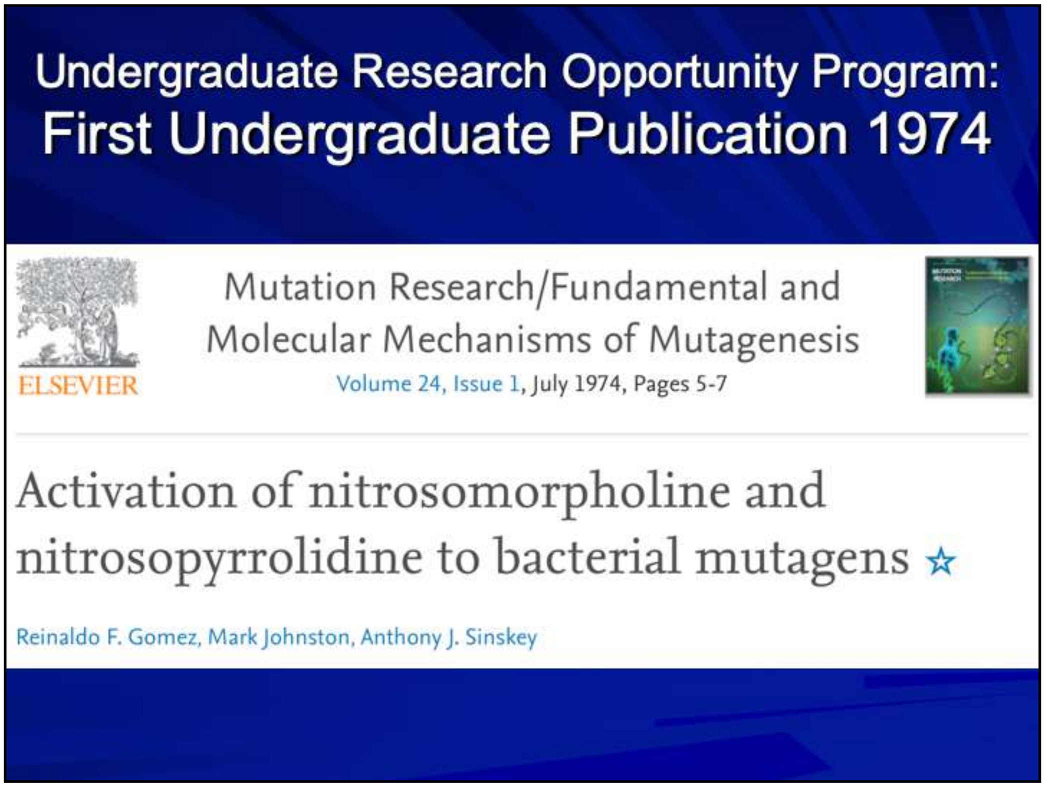
What I learned from Dr. Lodish was never to be intimidated by the details.



While professors Baltimore and Lodish were on the theoretical side of biology- Dr Tony Sinskey was tied into industry before the word Biotech existed.

I worked in Dr. Sinskey's lab throughout my MIT career.

A seminar course I took from Dr. Sinskey studied the Federal Government's "Five Year Plan" to cure cancer. While we knew that the goals were unrealistic, his approach to the material taught me how important it is to learn the language of the bureaucracy.



My first week at MIT I needed to find a part time job and somehow heard about UROP- the Undergraduate Research Project. The program was still in it's infancy and was run by a single brave soul from a small office on the main corridor. I talked to the director and she set up an appointment with Dr Sinskey, who then quickly introduced me to his post-doc, Ray Gomez.

I was given lab bench and a project to start. Being used to having dirty hands on the farm, I found the work easy and finished the project. The UROP director then insisted that Dr Sinskey put my name on the paper.

"Not bad" for a first year undergraduate and great for the Resume.

I will not try to explain the study, but the point was that it was important to the food industry which needed to fully understand the mechanism of activation of compounds into dangerous mutagens.

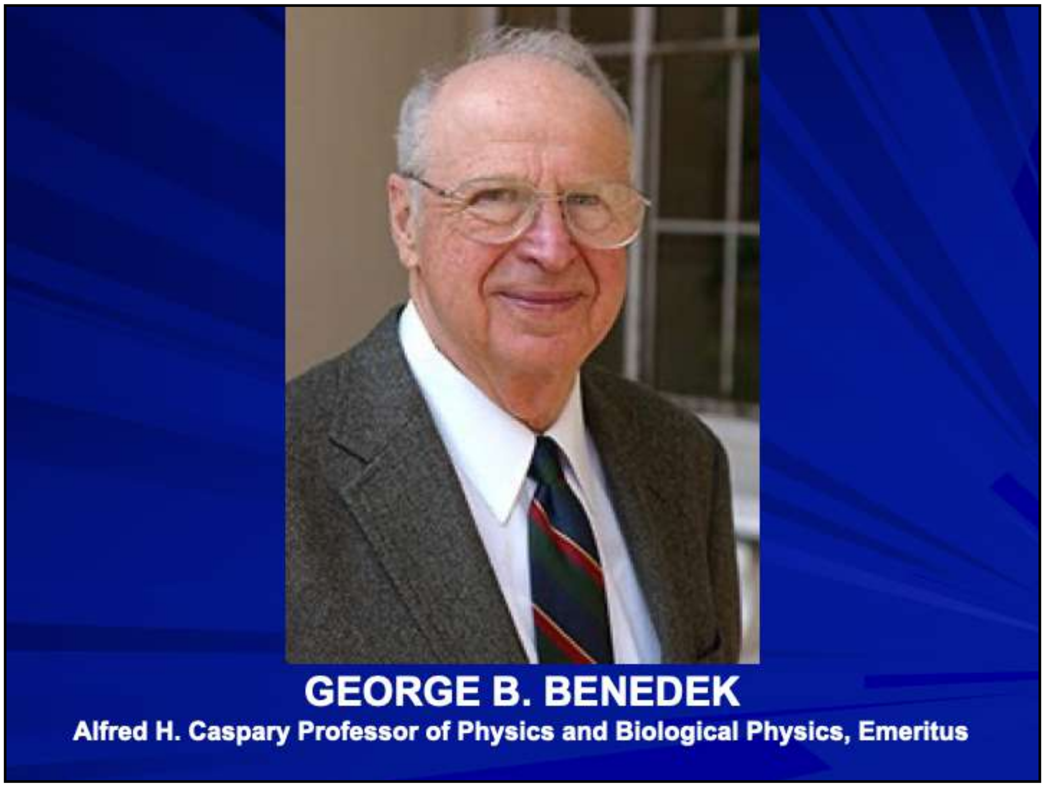
While I found lab work easy, I decided that I would continue my career in the family business-Surgery.

I had little interest in the politics of academia and enjoyed the surgery part of being a surgeon. While I was in solo practice for most of my career, much of what I was doing was at the leading edge of the new specialty of Refractive Surgery.

I have always been lucky to have great mentors. They taught me that one should notice and organize anything new or different that one saw in the course of one's work. I would collect these results and findings into papers and posters that I would present at professional meetings. A number of these papers were chosen as highlights of these conferences. Over time, I incorporated this work into courses that I taught at these conferences.

I am now retired, but I have posted some of the more interesting of these papers on my website.

https://markjohnstonvision.com



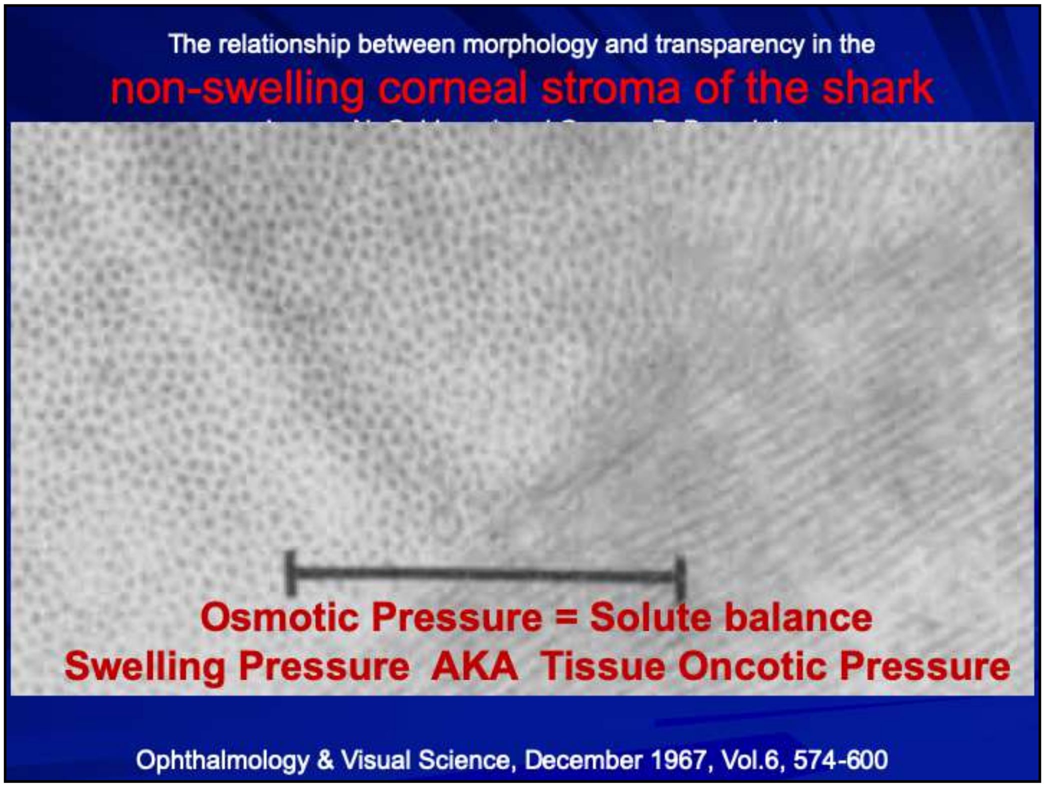
George Benedek is the Professor that had the greatest influence on my later career as a Refractive Surgeon.

Dr. Benedek taught freshman year “Physics for Biologists” for many years and collected his lecture notes and problem sets into the bound volume we used in his class.

The course used the same mathematics and approaches as more traditional introductory physics courses and applied them to biological problems. At that time such an approach was novel and intellectually fascinating.

As a student, I could not understand where Professor Benedek found his materials. Now, after a lifetime of work and study, I realize how many different interests one has over the years..

A classic example, which years later was of great interest to me, was a problem on our first exam. Essentially it described how osmotic pressure is measured using a semi-permeable membrane and the induced height of a column of fluid. We had never studied anything close to this problem in class but by applying Newtonian mathematics one could answer the exam question quickly and easily.



“Refractive Surgery” is “Corneal Surgery”. The cornea must stay clear and this depends on it having a regular structure and maintaining strict control of tissue hydration by preventing tissue swelling.

This swelling or oncotic pressure is a function of macromolecules unfolding in the presence of water and salts.

In the late 1990’s,I was trying to understand what I was seeing in surgery and clinic. I dug into the literature on this subject and found multiple applications of the science of corneal swelling to my work.

While preparing this talk, I come upon this seminal paper on this subject by Professor Benedek from **1967.**

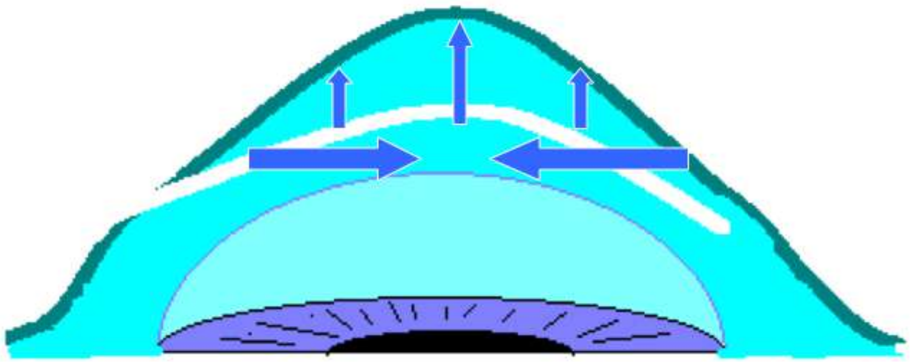
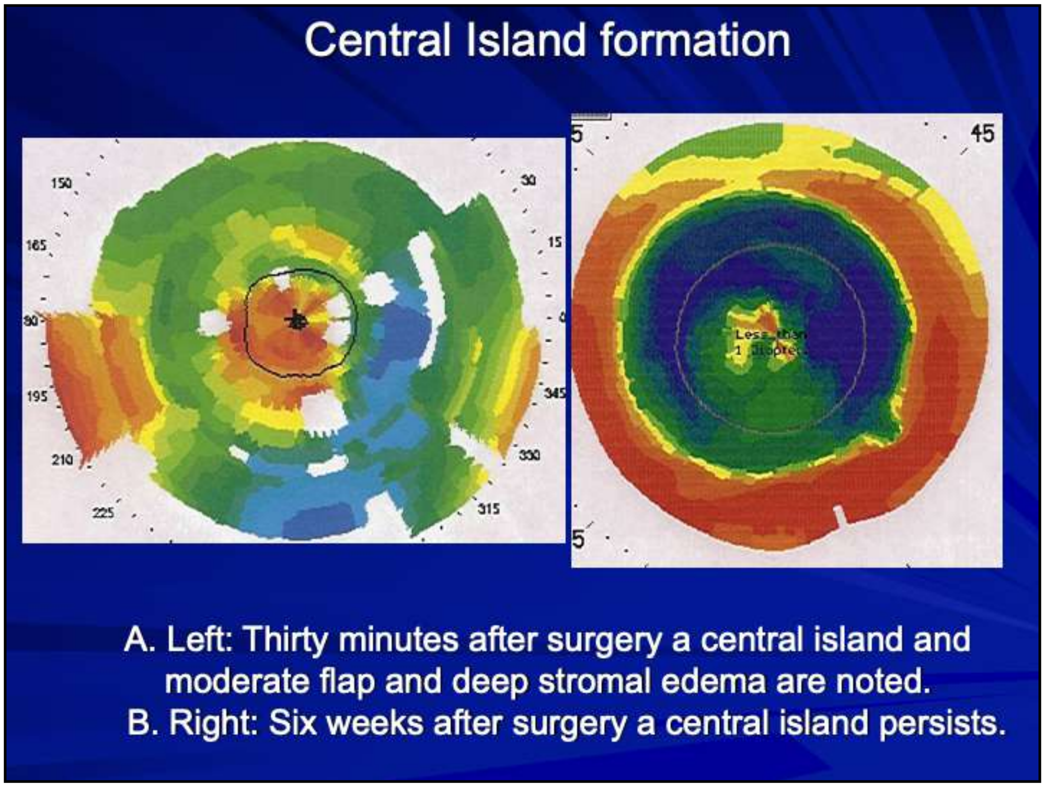


Figure 4
The corneal swelling pressure draws fluid and debris into the Lasik interface.
The swelling pressure is greatest centrally and draws fluid and debris into the central cornea (thereby creating central islands).

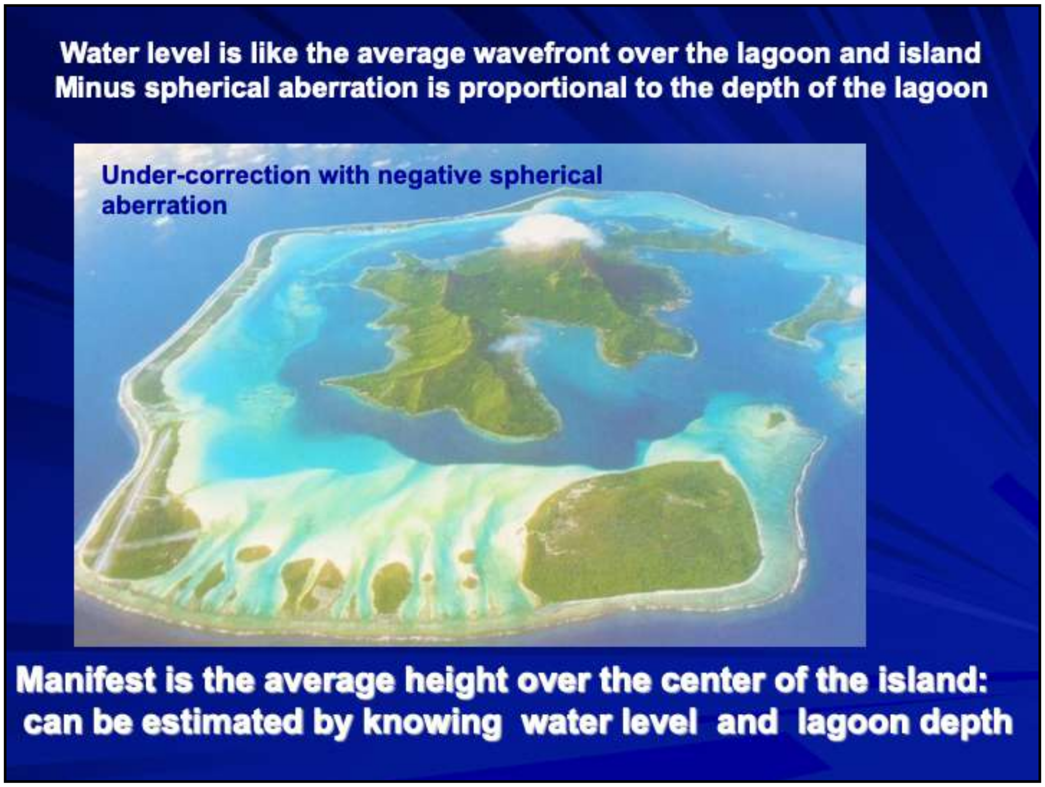
The posterior and centrally cornea has a looser structure and in the presence of excess fluid can adsorb more water.

This creates a gradient in the swelling pressure which can pull both fluid and debris towards the center.



Because of the looser structure of the central cornea, after surgery fluid is drawn towards the center of the cornea.

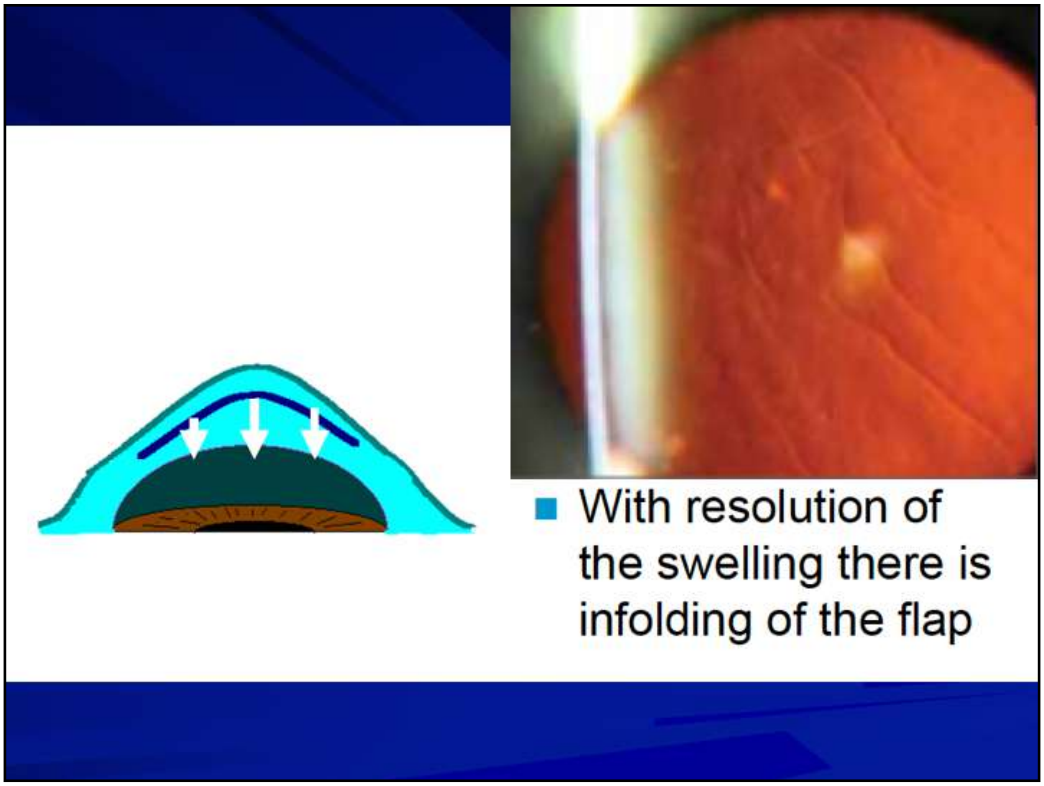
The cells lining the back of the cornea actively pumps fluid out of the cornea so that most of the excess fluid adsorbed during surgery is removed within several days of surgery. The residual apparent swelling, on the right, is not fluid but rather a residual “central island” of tissue. This is related to in-folding of excess corneal tissue and secondary to relative under-treatment of the central cornea by the laser.



The apparent “central island” on the elevation map after surgery is partly instrument artifact.

When the “wavefront” optical properties of the surface are analyzed, a slight central elevation has less induced spherical aberration.

(The deeper depression seen on the elevation maps with earlier lasers is optically less desirable because of higher amounts of induced “spherical aberration”.)



After lifting the flap, the laser removes central corneal tissue. This creates redundant flap tissue which must then fold in, resulting in some “bunching of the central flap tissue and very mild folds.

When analyzed with wavefront optics, these mild microfolds have no significant optical effects.

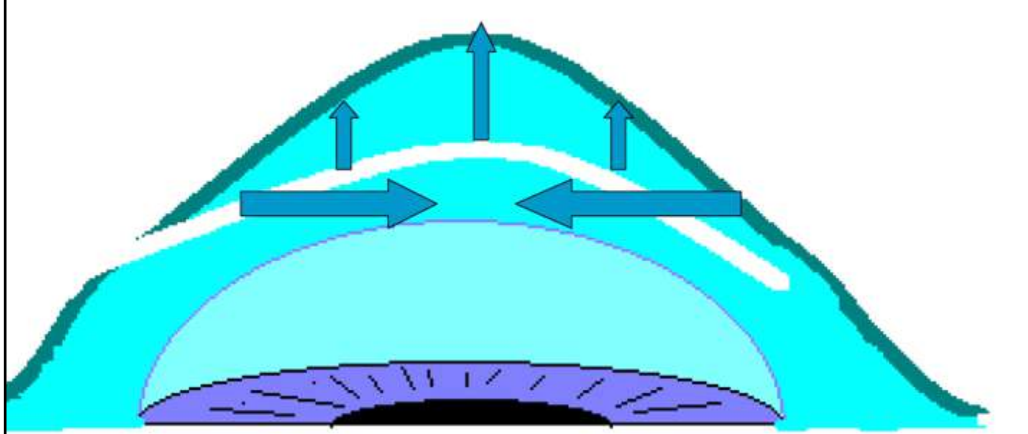


Figure 4
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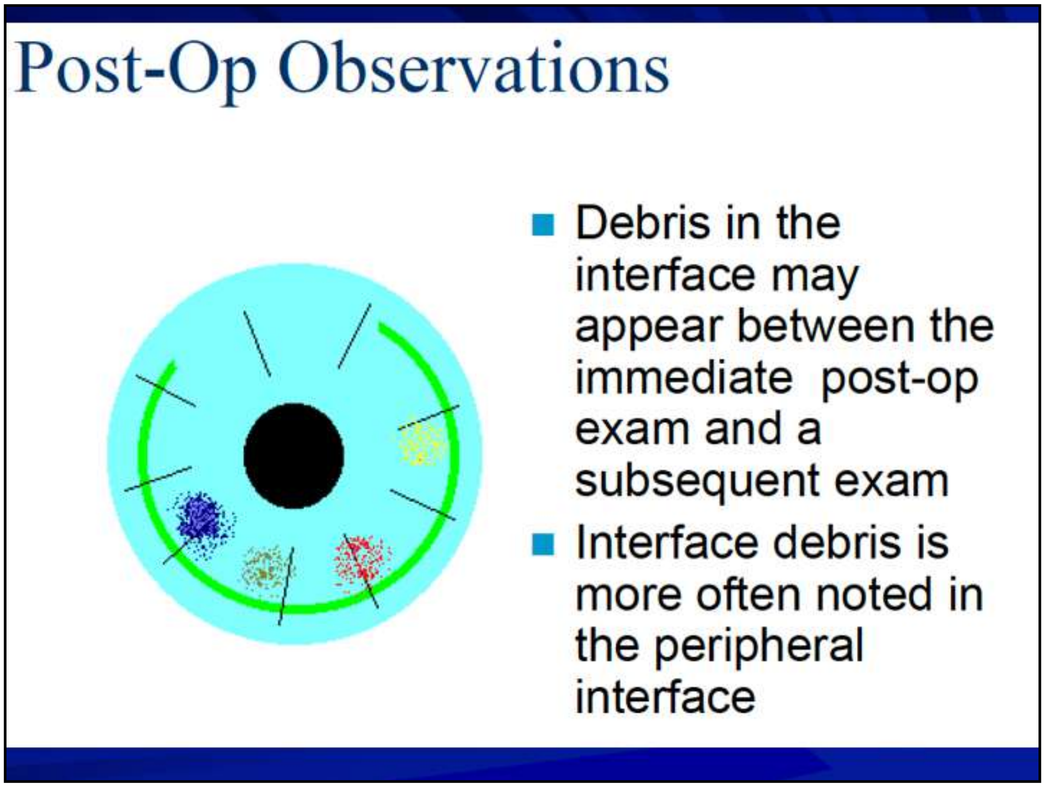
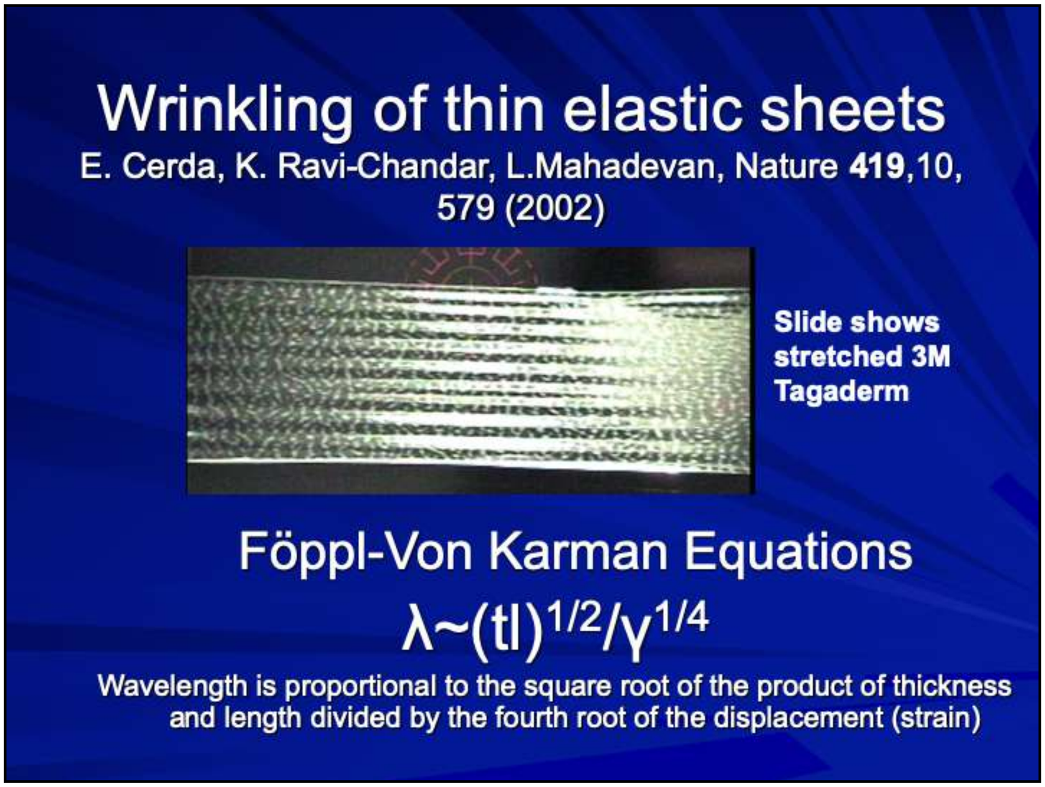


During surgery the flap is lifted to perform the laser ablation. (The LASIK flap has a hinge for stability.)

The edges of the flap seals within hours of the surgery, but in the interim, the negative swelling pressure of the corneal tissue “sucks” debris into the peripheral corneal bed. This debris includes blue pigment from the marker, lipid from the oil glands in the lids, red cells from small vessels and white cells from inflammation of the eye surface. These are usually of minimal clinical importance as they are easily adsorbed by the tissues.

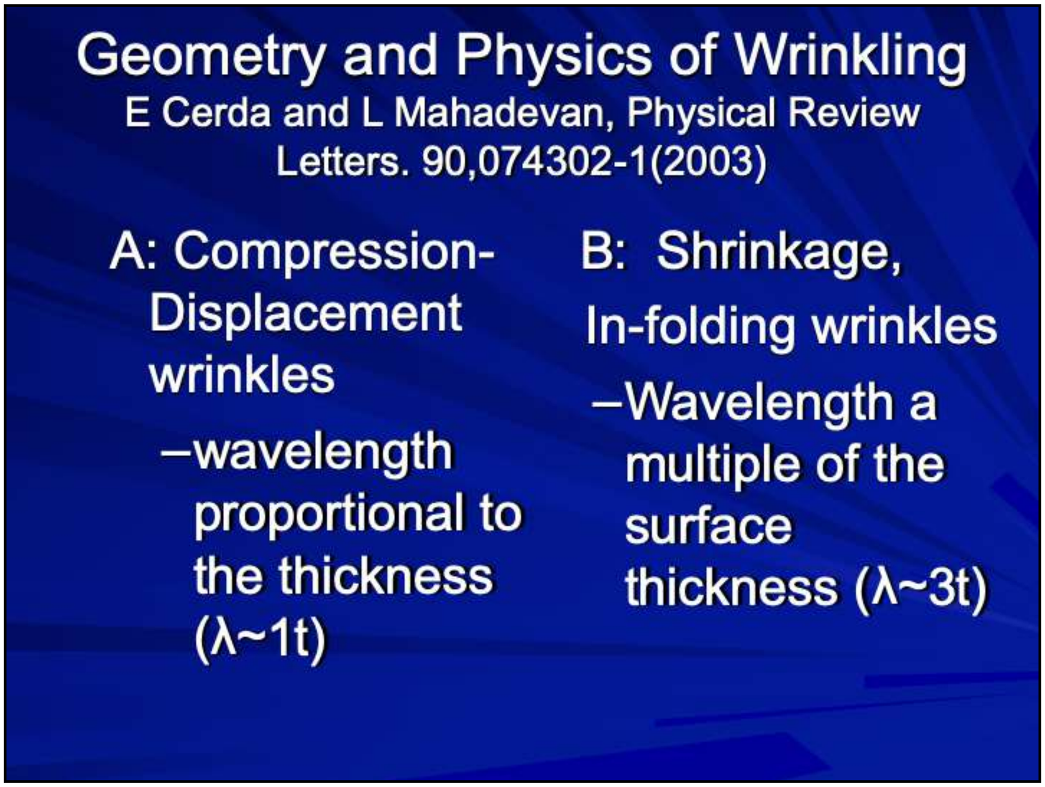
Understanding this mechanism of helps to minimize the presence of this debris.



Mild folding of the cornea has minimal optical importance. Larger folds are more important and specific measures are needed to avoid or remove these folds.

Exploring the literature, one can explore the physics of folding. Displacement, such as stretching this piece of thin plastic, creates a regular pattern of folds with a regular distance between these folds- the wavelength.

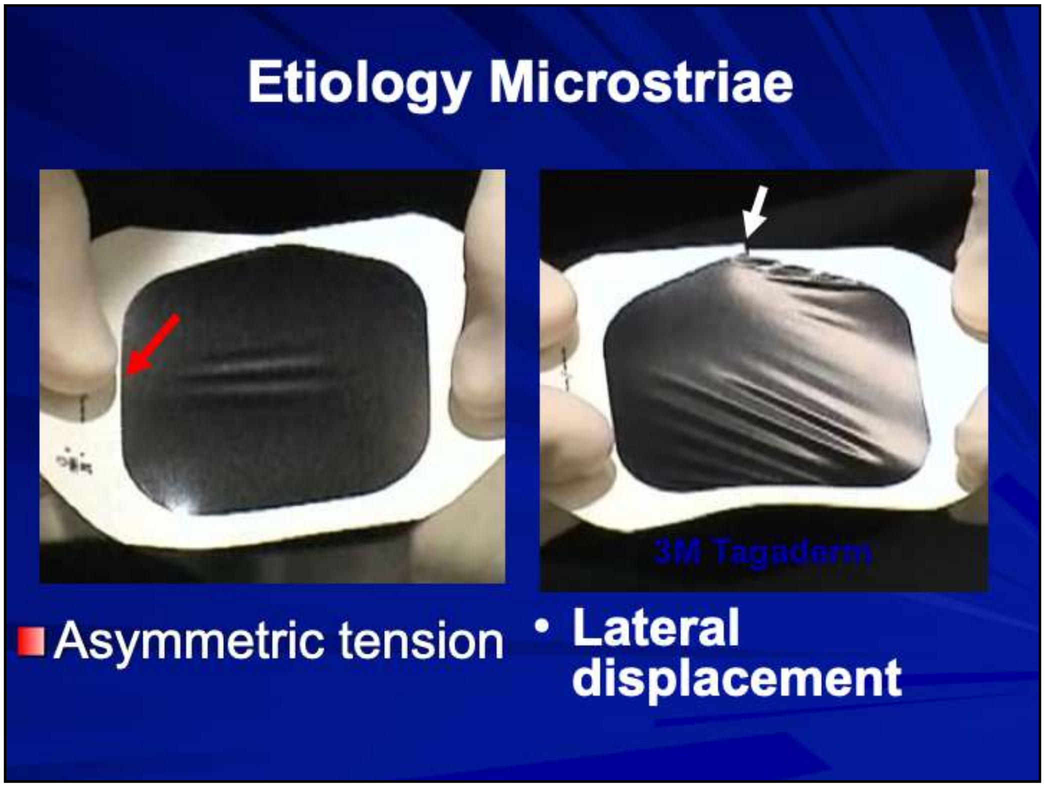
(This type of folding was interesting to Von Karman, the original German "Rocket Scientist" who founded the Jet Propulsion Lab. The German scientist Foppl wrote a book on Maxwell's Equations that Einstein read as he was formulating his ideas on relativity.)



Folding can be from displacement of tissue or shrinkage over the underlying tissue.

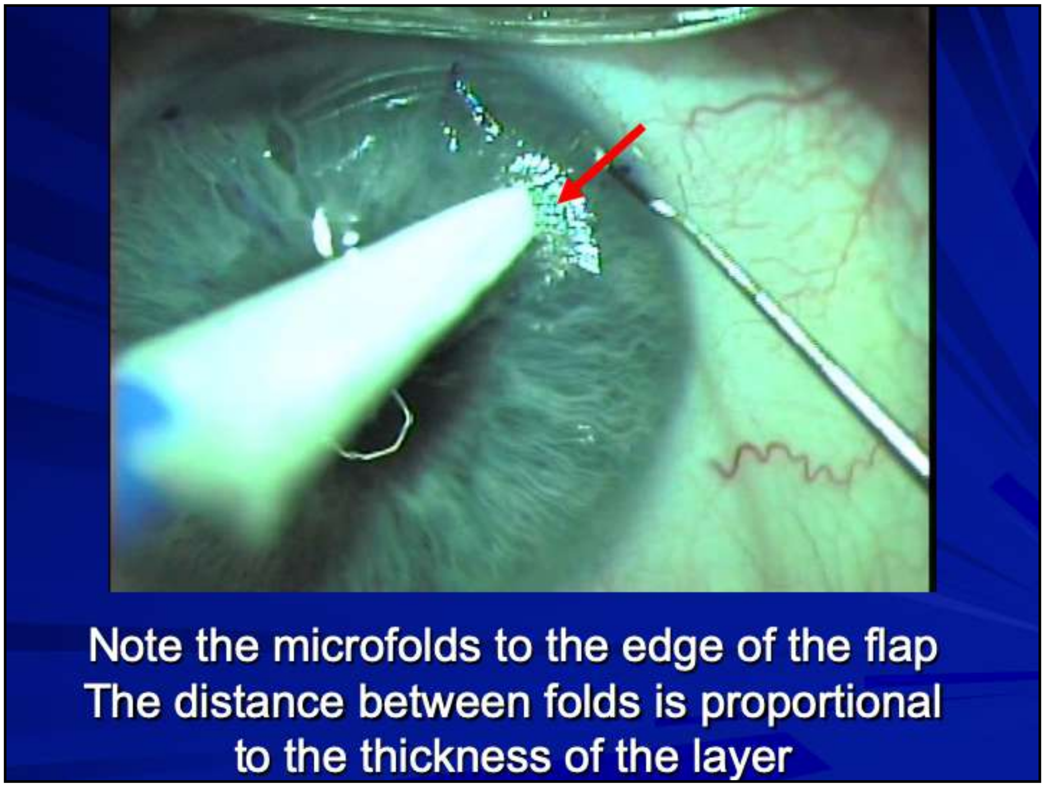
The mathematics are different and the physics correlates with clinical findings.

Again, understanding a phenomenon can be very helpful in developing methods to avoid or treat these folds.



Observe the paper on the edges of this small plastic surgical drape.

There is a difference between asymmetric tension versus lateral displacement at the edge.



Understanding folding can also be used during surgery to assist in observation of the tissues.

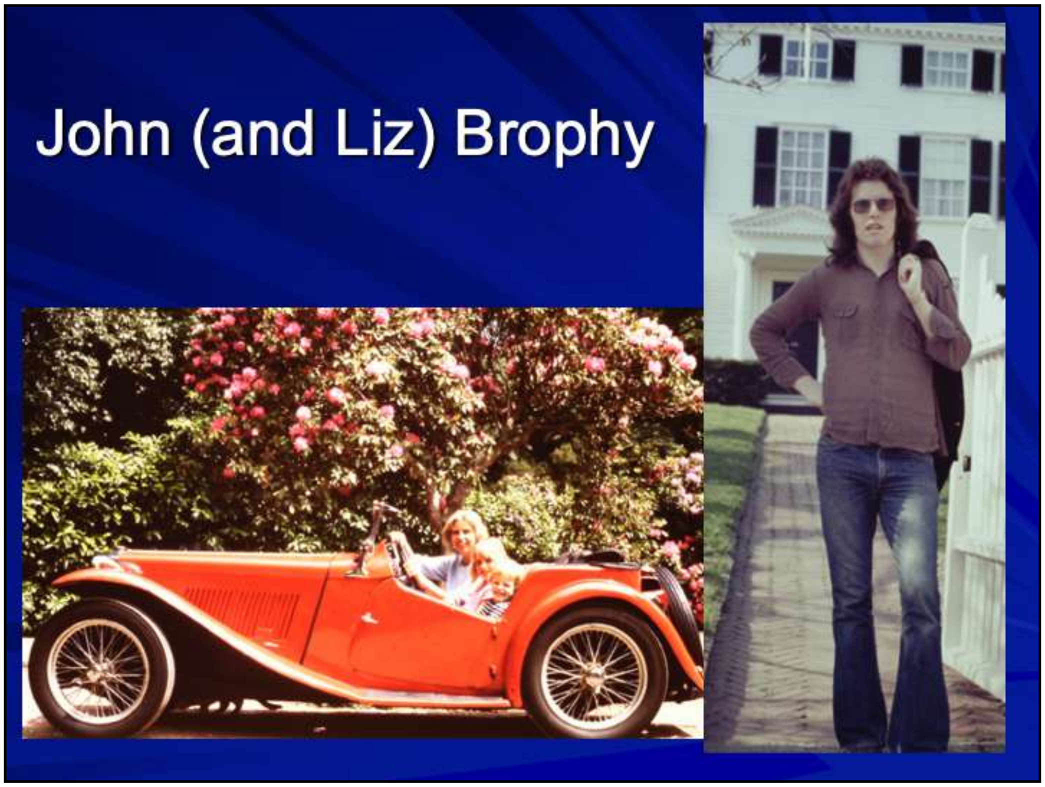
This is a photograph of the initial step in lifting the edge of a flap months after surgery (to make a small adjustment of the correction with laser ablation).

By pushing down on the flap there are folds which, as predicted, are about as far apart as the thickness of the flap.

The edge of the flap can be seen as a transition from the small folds in the flap to the area of peripheral cornea with no folds (no flap).

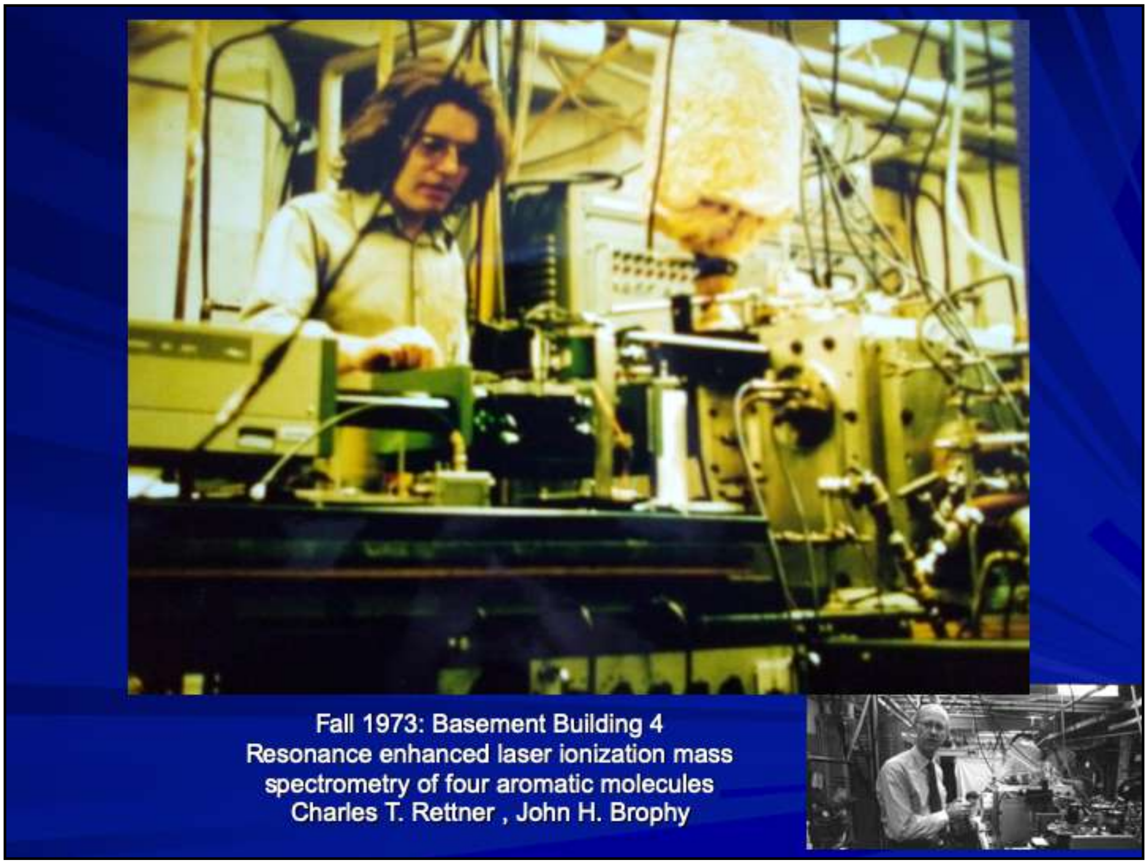
Knowing where the edge of the flap is facilitates gently lifting this edge to proceed with the surgery.

(An other example, not shown, is noting the distant between folds to estimate the amount of cataract tissue left for removal.)



When I lived in E-Entry, MacGregor House our entry tutor was an English post-doc fellow in Physical Chemistry. He and his wife Liz provided some (mostly) adult supervision of a rowdy bunch of all male undergraduates.

John's real passion, besides Liz, is a fleet of Classic English Cars. He still has this MG and likes to use it to "get around town". He prefers his classic Lotus for the motorway.



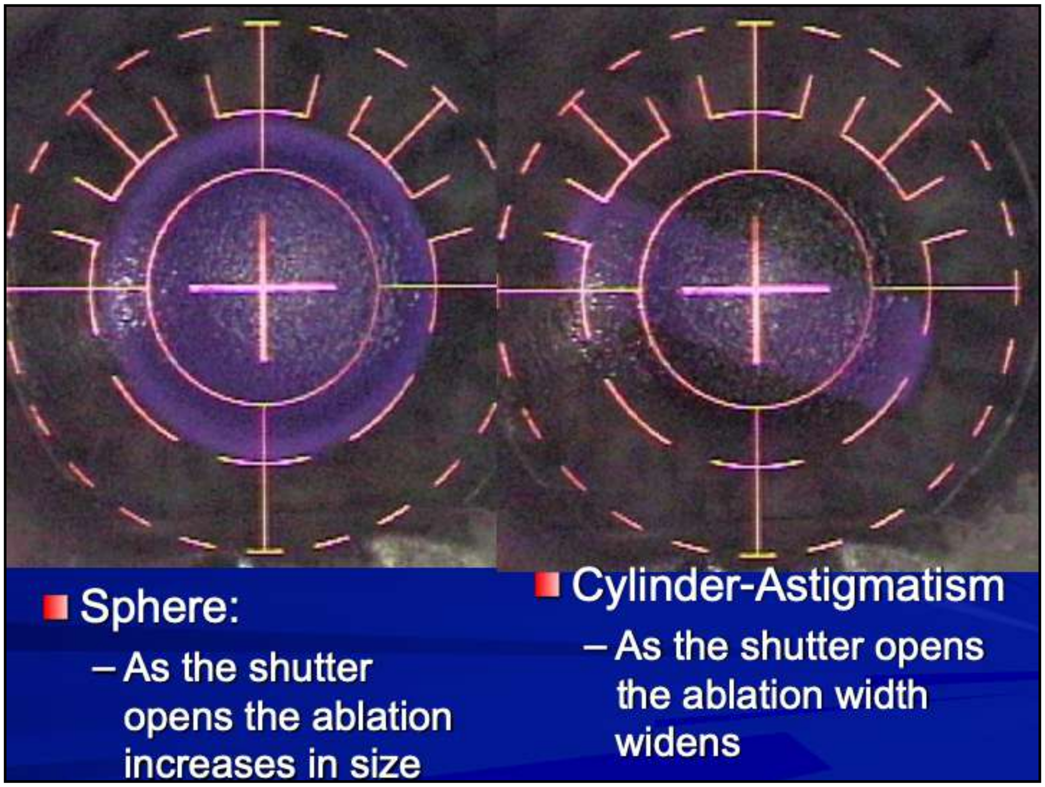
John invited us to visit him in his lab in the basement of ”Building 4”.

He had built a dye laser and was studying an ultra-violet wavelength that interacted with the carbon-nitrogen bond in an analine ring.

In LASIK, this wavelength is adsorbed into the carbon-nitrogen bond between amino acids, thereby splitting the protein chains into its component amino acids, without producing any significant heat or tissue damage.

The evening after my visit to his lab, we were discussing the properties of the laser and he told me that I “ would be using this laser to do surgery” .

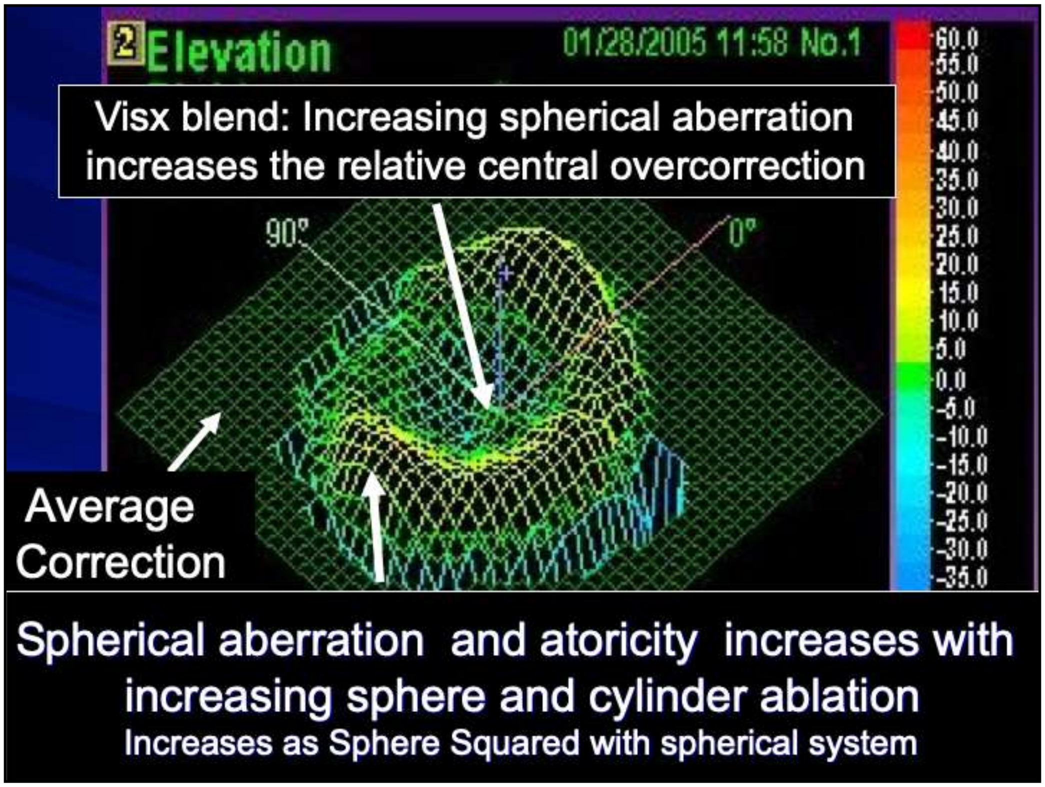
Seems his crystal ball was working or I do as I am told.



The excimer laser is not in the visible range, but after it is adsorbed, it emits (florescence) a blue light.

Each pulse of the laser ablates about one tenth of a micron of tissue and the average refractive surgery ablation is about 50 microns.

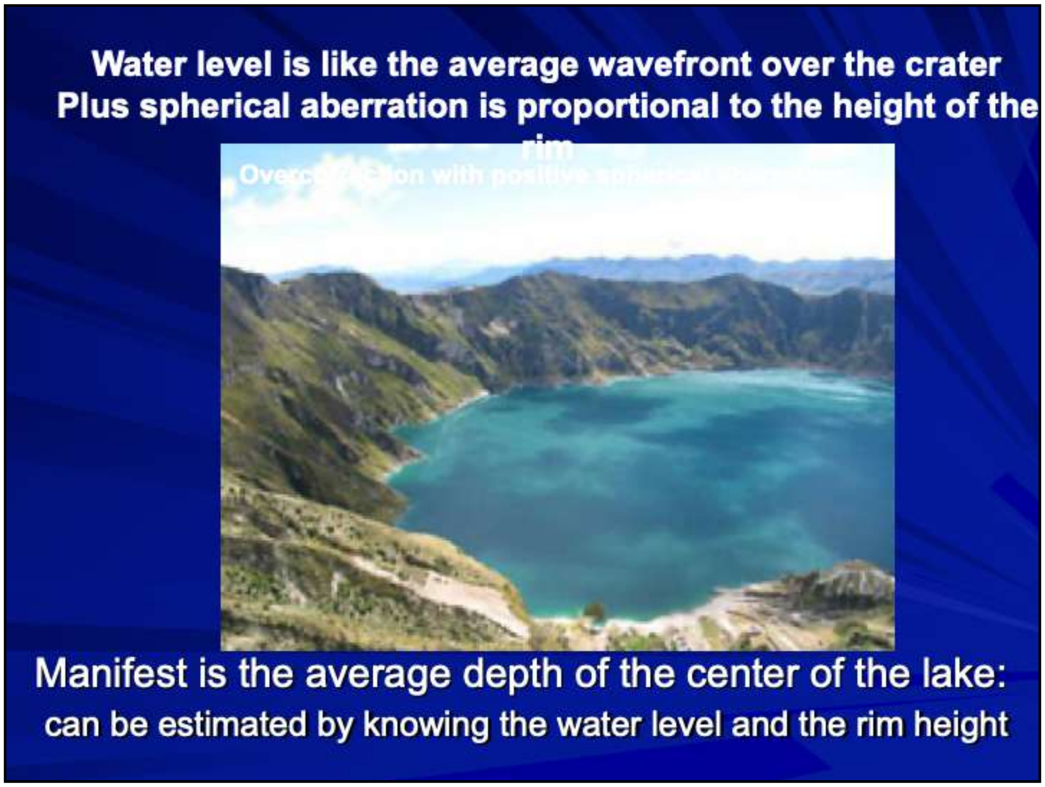
In the first generation of lasers, by opening a round shutter, a spherical correction is produced. By opening a slit, a cylindrical or astigmatic correction is made.



The first generation of laser were calibrated by making a spherical correction in plastic.

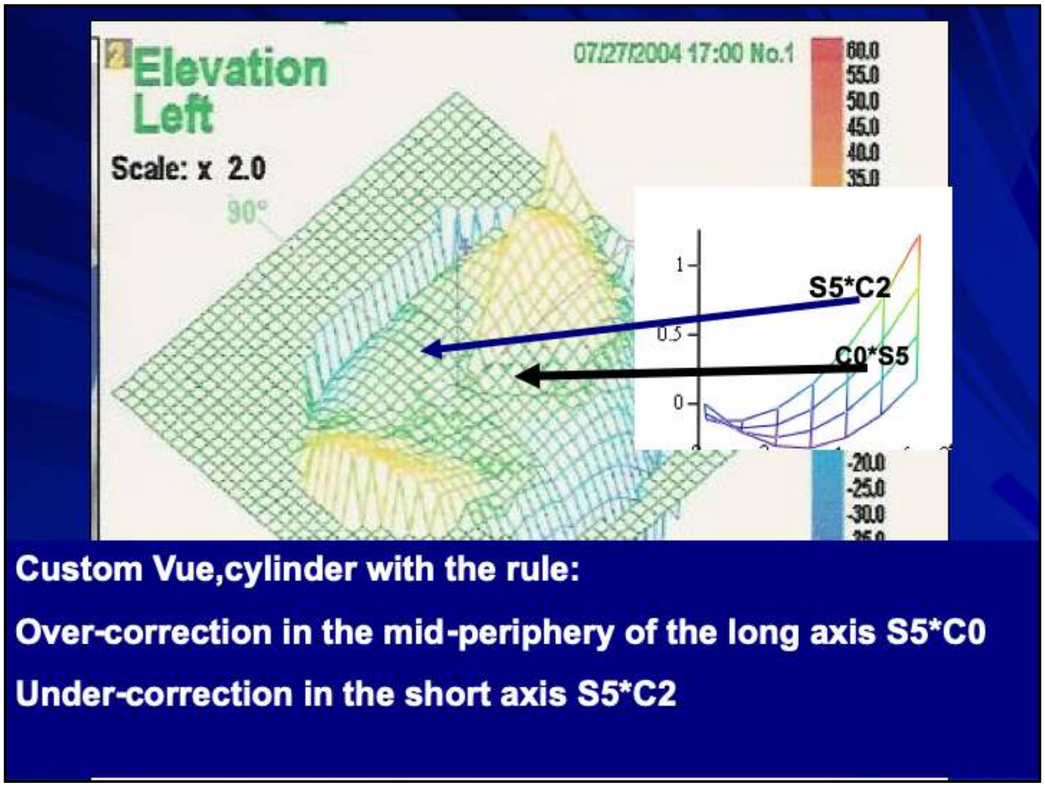
When this ablation is applied to human tissue there is a relative over-ablation of the central tissue and an under-correction of the peripheral tissue.

This slide shows an elevation map of the cornea after surgery.



This overcorrection of the central cornea is partly mitigated by the “filling in” of tissue onto the central cornea. This effect is not very predictable but the result is a very smooth central ablation with good optical properties.

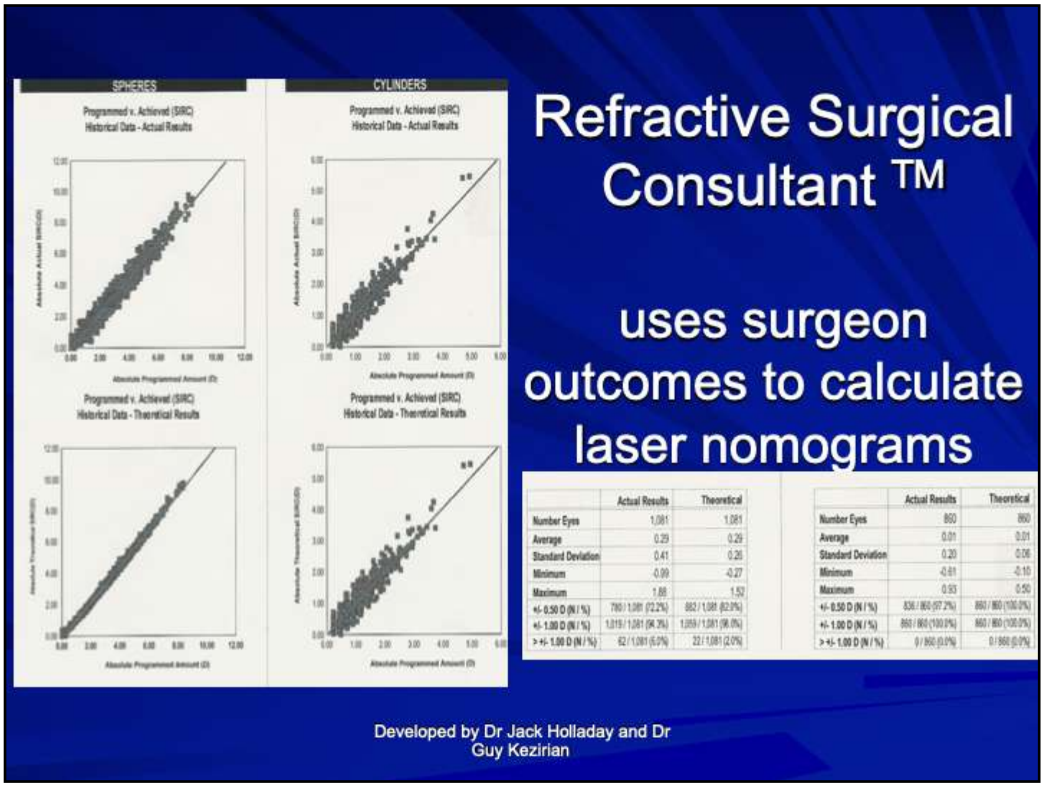
Since the eye mostly uses the central light rays, the peripheral excess tissue had minimal overall optical effects.



With time the laser manufacturers were able to create flying spots lasers with small ablations spots delivered at higher speeds.

This refinement allows some fine tuning of the ablation profiles.

Shown here there is less over-correction of the center but still some under-correction of the peripheral cylinder axis.



	Actual Results	Theoretical
Number Eyes	1,081	1,081
Average	0.29	0.29
Standard Deviation	0.41	0.26
Minimum	-0.99	-0.27
Maximum	1.88	1.52
+/- 0.50 D (N / %)	780 / 1,081 (72.2%)	882 / 1,081 (82.0%)
+/- 1.00 D (N / %)	1,019 / 1,081 (94.3%)	1,059 / 1,081 (98.0%)
> +/- 1.00 D (N / %)	62 / 1,081 (6.0%)	22 / 1,081 (2.0%)

	Actual Results	Theoretical
Number Eyes	860	860
Average	0.01	0.01
Standard Deviation	0.20	0.06
Minimum	-0.61	-0.10
Maximum	0.93	0.50
+/- 0.50 D (N / %)	836 / 860 (97.2%)	860 / 860 (100.0%)
+/- 1.00 D (N / %)	860 / 860 (100.0%)	860 / 860 (100.0%)
> +/- 1.00 D (N / %)	0 / 860 (0.0%)	0 / 860 (0.0%)

When we first started doing laser we developed our own database and used our results to adjust our treatment profiles, thereby improving our results.

(Later we used commercial database product for the same purpose.)

Refractive Surgical Consultant ™ Results

Laser	Sphere (s) nomogram	Cyl (c) nomogram	# Eyes s/c	R^2 s SE	R^2 c SE
Visx Blend	$1.21s +0.04s^2$ $+0.04sc$	$0.06s+0.01s^2$ $+1.18c +0.03c^2$ $+0.05sc$	216 199	0.97 0.45	0.97 0.30
Visx Custom	$1.49 s + 0.07s^2$ $+0.08sc$	$1.07c + 0.07c^2$	128 128	0.97 0.45	0.97 0.28
B&L Zyoptix	$1.09s + 0.02s^2$ $+0.31c +0.11c^2$ $+0.07sc$	$0.05s +0.01s^2$ $+0.96c -0.03c^2$ $+0.05sc$	439 439	0.95 0.31	0.96 0.18
Visx Fourier	$1.02 s + 0.29c$ $+0.07c^2+0.06sc$	$0.09s+0.02s^2$ $+0.80c -0.07c$	371 369	0.97 0.39	0.97 0.23

This is a summary slide showing the theoretical adjustment for three different lasers that we used.

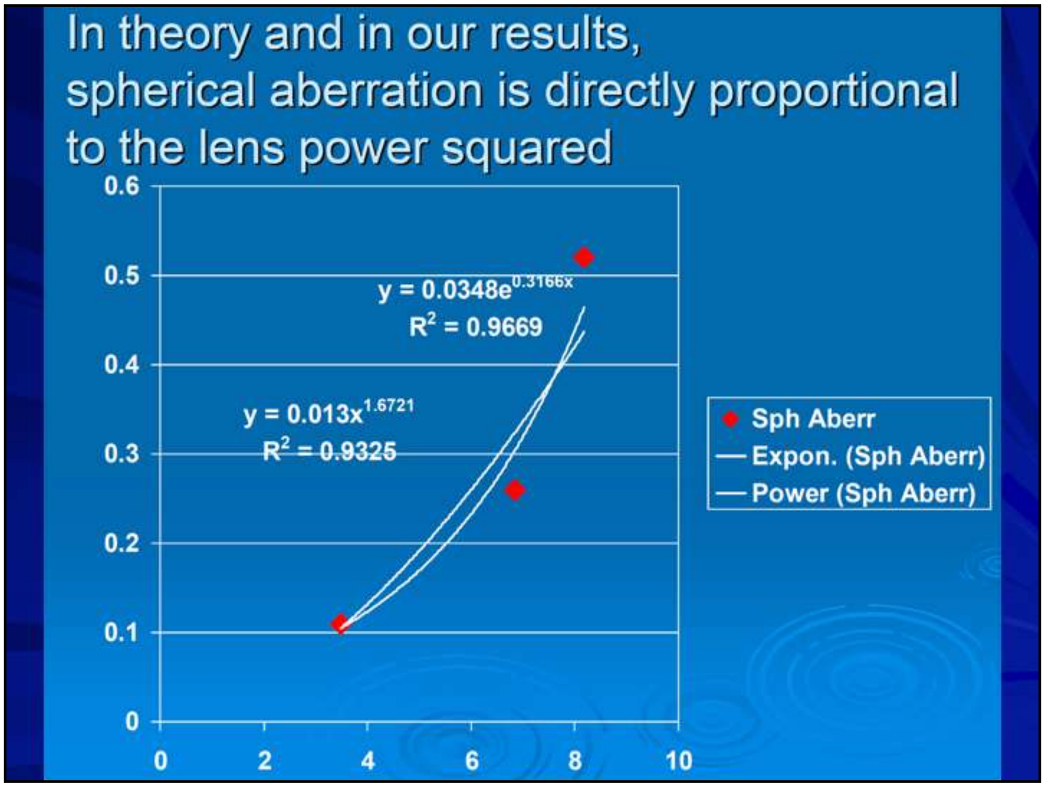
Not only did we need to adjust the sphere and cylinder treatment but it was also necessary to adjust the product of the combined sphere and cylinder.

This complex “Coupling’ of the results shows how complex it was to refine the treatments used.

Many of our results we presented as papers at conferences.

The manufacturers are obliged to report any reported studies to the FDA, as most FDA approvals were provisional on long term follow-up parameters.

Clinicians reporting results thereby put pressure on the manufactures to improve their laser performance and profiles.



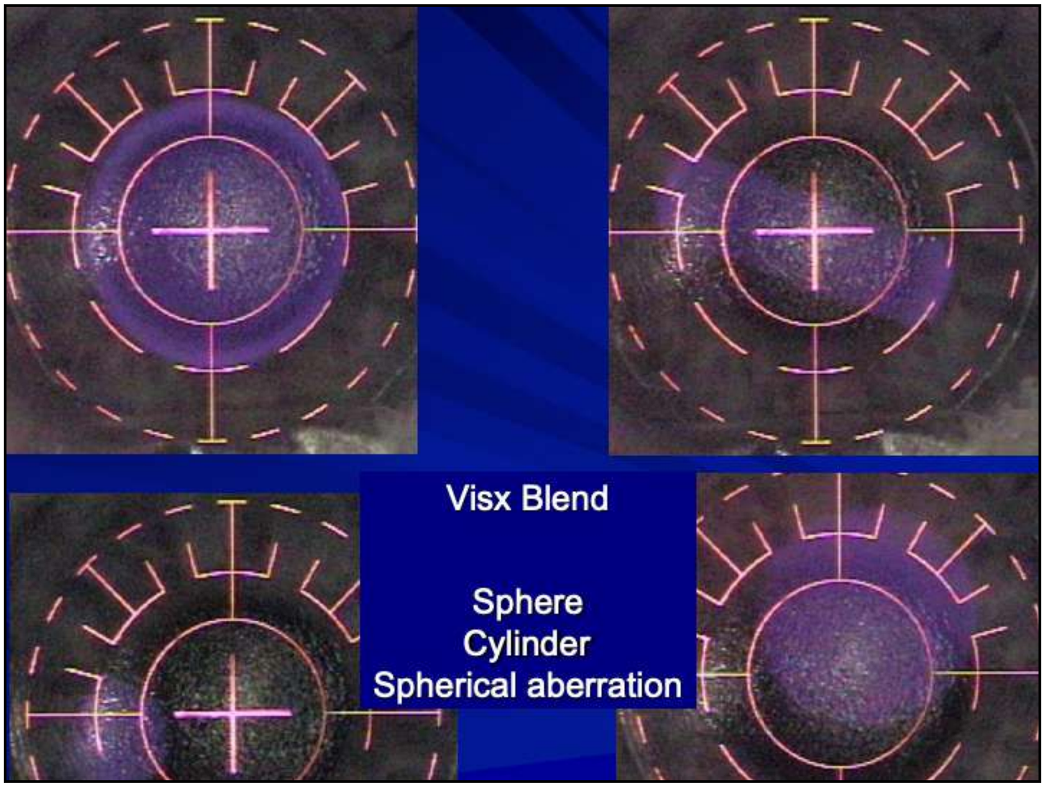
The ideal visual profile is not a straight sphere but should adjust for spherical aberration.

This spherical aberration is proportional to the square of the spherical correction.

Looking at our results, the amount of sphere-squared in our regression formula of treatment versus was proportional to the amount of measured post-op optical spherical aberration.

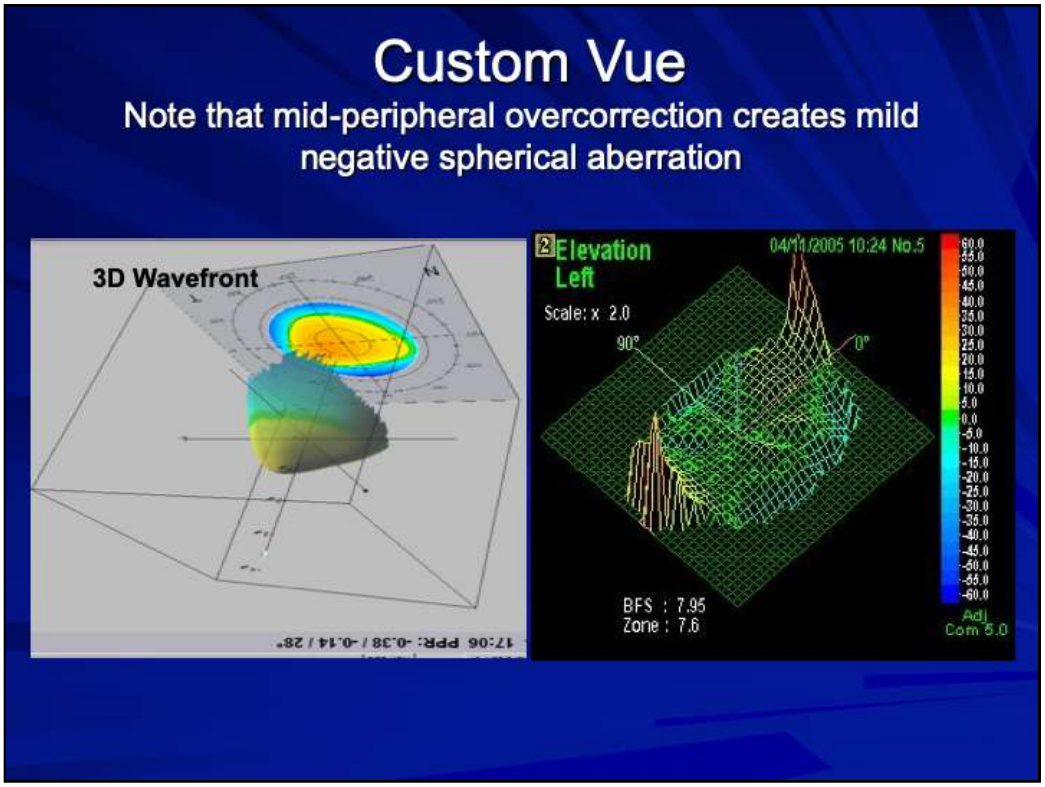
This correlation allowed us to compare laser manufacturers treatment profiles.

Again, by presenting our results, we felt we were encouraging the manufacturers into improving their technologies.



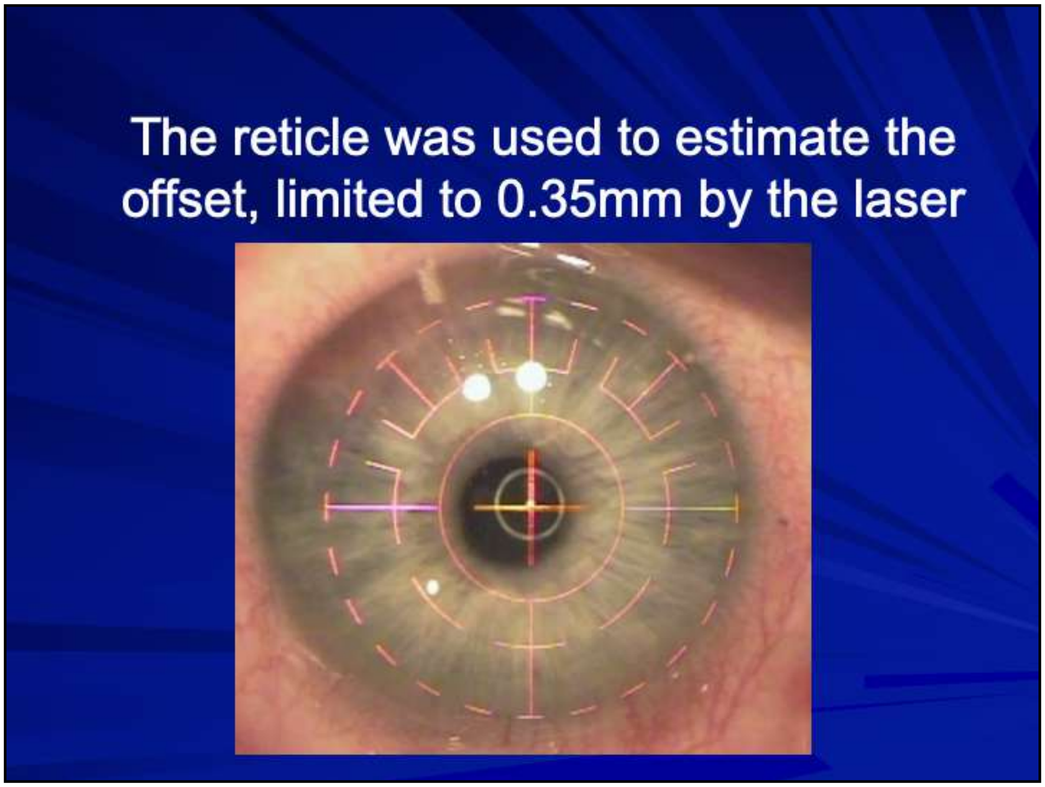
A broad beam laser has a more predictable output and therefore achieves more predictable results. Eventually the leading manufacturer added prism and rotation to their delivery system to improve their ablation profiles.

However, because of the difficulties with a flying spot lasers, it was fully twenty years before flying spot lasers had more predictable results then the more traditional and robust broad- beam platform.



This is the optical wavefront map and the surface elevation map following treatment with a broad-beam laser with prismatic and rotational smoothing.

The ablation profile is improved but we see that optically there is still a slight excess of the central treatment and too little peripheral treatment.



Not only must the laser have the correct profile but it must be applied accurately to the surface.

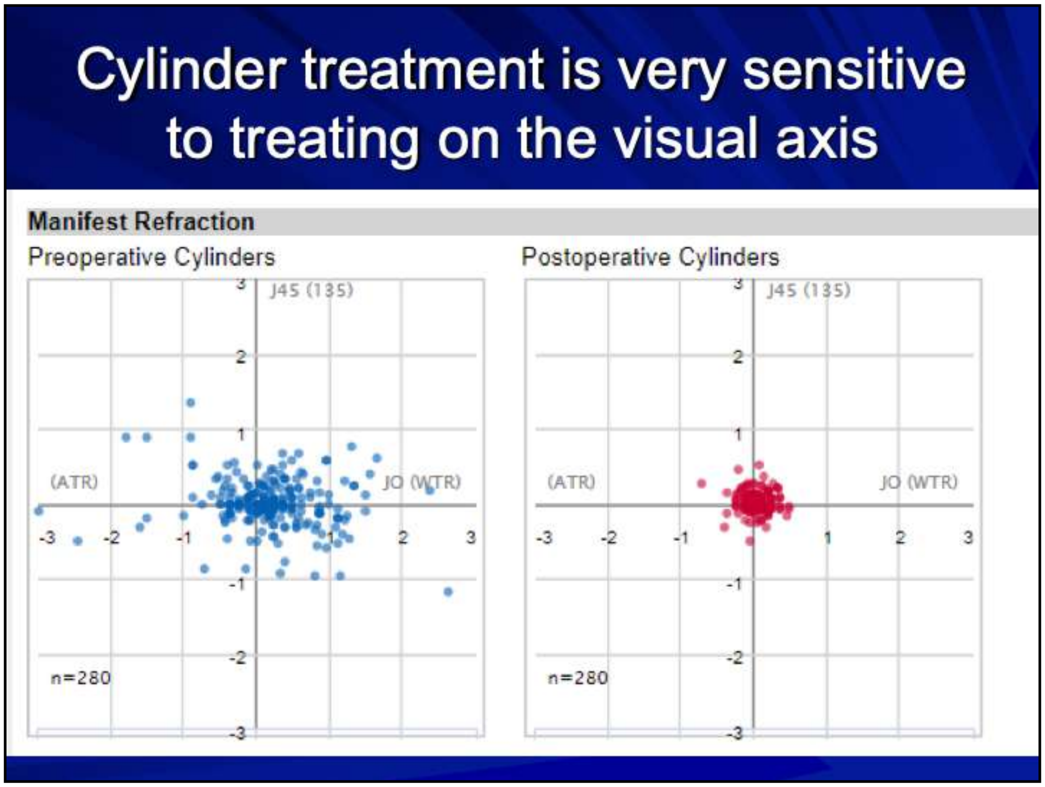
During the surgery the eye always has small movements and occasional total loss of fixation .

Using a broad-beam laser makes small movements less important. All flying spots laser must have very good tracking properties to outperform a broad beam laser.

All early laser had no tracking system or even worse, error prone trackers.

Most trackers use the pupil to follow eye movement. Since most patients “do not look” through he center of the pupil, the proper offset for each patient is critical.

Again, surgeons presenting their results pushed the manufacturers to provide equipment with better performance profiles.



Problem: Is there a simple method to compare how well different lasers treat on the visual axis?

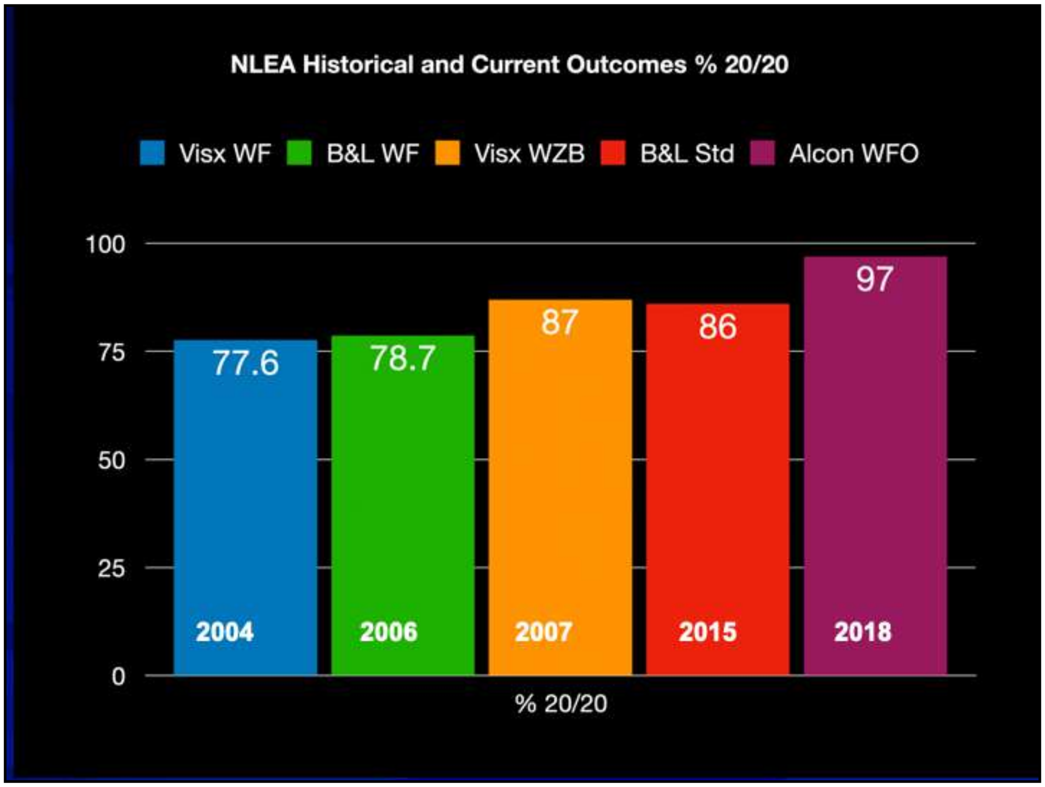
This required some thought.

Given that :

Treating off axis will induce astigmatism (Cylinder), we simply compare the amount of cylinder before and after surgery.

In patients with minimal cylinder correction before surgery, any increase in cylinder may be related to relative decentration of the ablation.

With larger numbers of cases studied there is signal amplification. Earlier laser had a centroid shift of the average result which we do not see here in a modern laser.



I started performing refractive laser surgery in 1995, the year the FDA approved laser in the USA.

Since then I, like my colleagues, have seen a gradual improvement in the results with laser. Most of these are related to improved equipment.

From the graph shown, it can be seen that this improvement was much slower than we would have predicted when we started in 1995.

The results are for 20/20 vision without glasses. Because the average patient has a high correction, the first procedure typically produces a very small correction which is easily enhanced to the desired excellent result.

Over time fewer patients have required such “touch-up” surgery.

In conclusion, decreasing adverse events and improving results has been a long process.

It has required collaboration, hard work and perseverance. There were always new “problems “ to solve.

MIT’s gift is that it teaches that problems can be solved.

I would like to thank all my excellent mentors, professional partners and co-workers for giving me the opportunity to have lived a life that was part of the solution.