Wavefront Congress, San Francisco, 2003

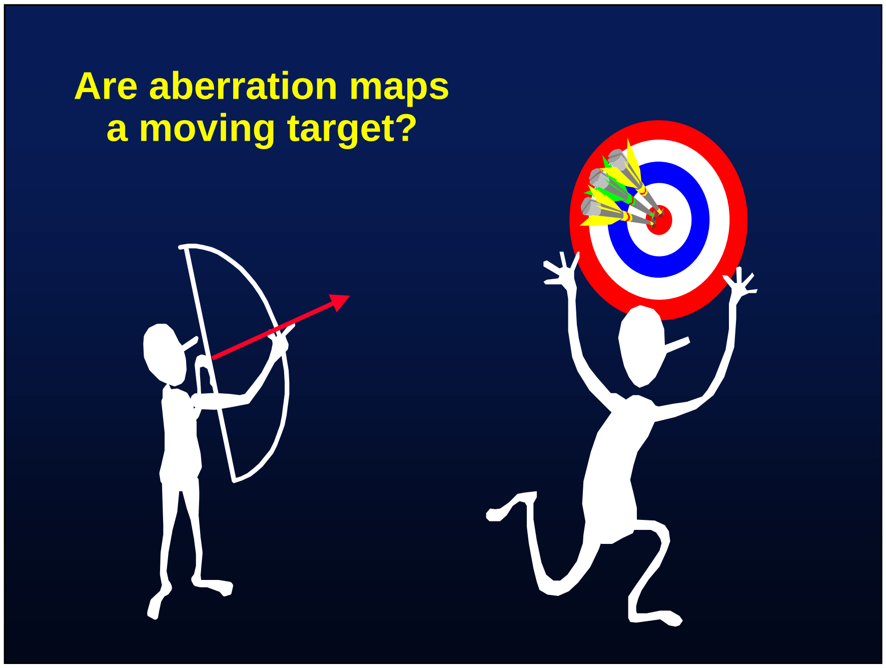
Variation in ocular aberrations over seconds, minutes, hours, days, months, and years

Larry N. Thibos
School of Optometry, Indiana University,
Bloomington, IN 47405
thibos@indiana.edu

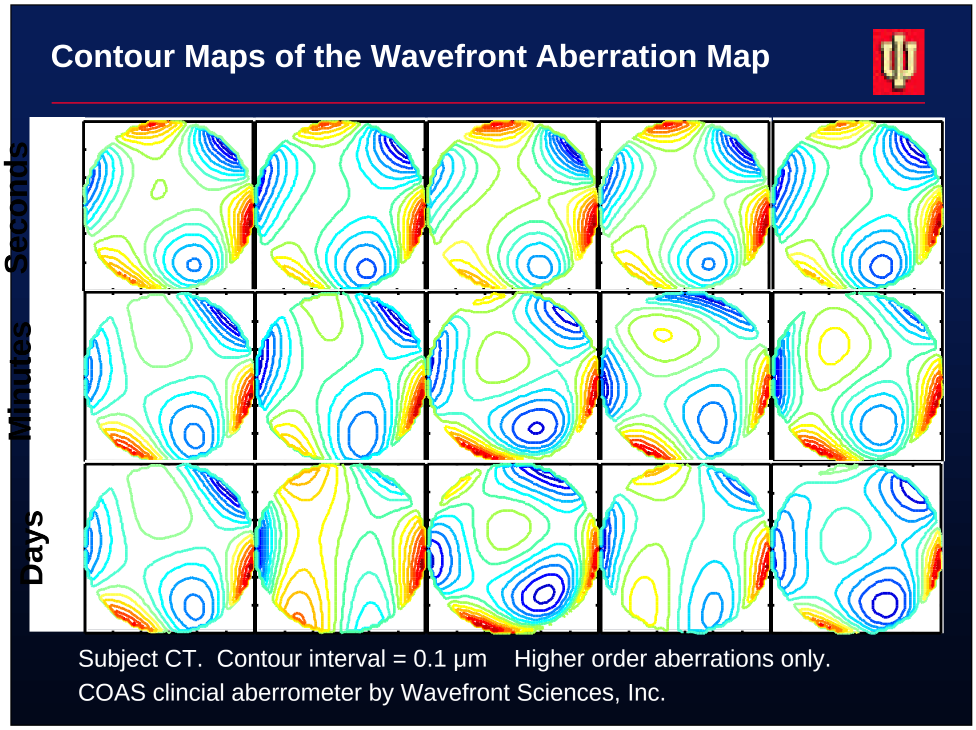
Good morning, ladies and gentlemen.

My goal today is to describe the results of recent experiments designed to assess the degree of temporal variability in aberration maps of human eyes.

This study is a collaborative effort supported by the NEI and Indiana University.



The fundamental issue I will be addressing is temporal variability. Simply put, are aberration maps a moving target? If they are, then it would seem important for treatment strategies to take this variability into account by using statistical analysis to determine which aberrations are large enough and stable enough to warrant treatment.

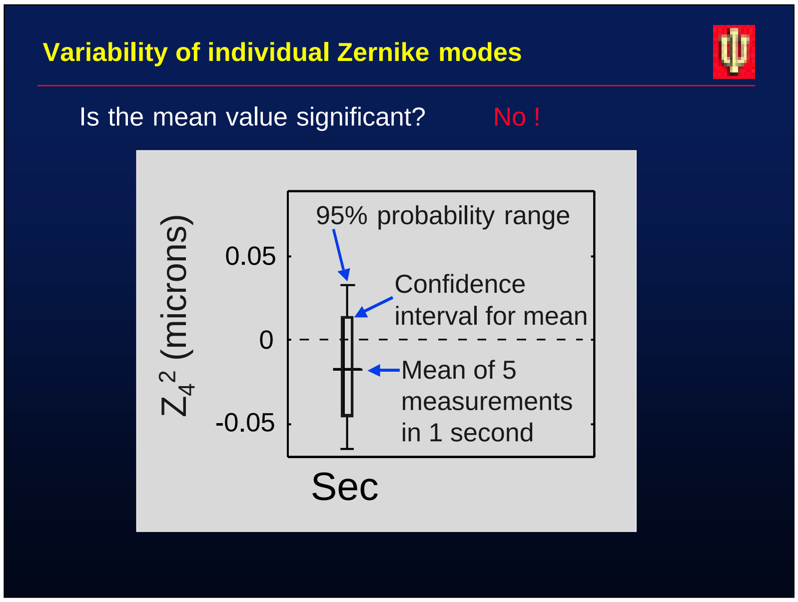


To begin the discussion, consider these aberration maps measured repeatedly for the same eye over 3 different time scales.

The top row shows 5 maps collected in less than one second while the subject was in a freeze position in which he did not move or blink or even breathe. Notice that the pattern is virtually identical in all 5 frames.

The middle row shows 5 aberration maps collected at intervals of a few minutes. Between measurements the patient was allowed to blink and move about, with the instrument being re-aligned before capturing each map. The maps are still pretty similar, but some slight differences are noticeable.

In the bottom row, single images were captured at the same time of day, Monday through Friday. Now we see quite large differences in the map showing up, although the basic pattern is similar from day-to-day.

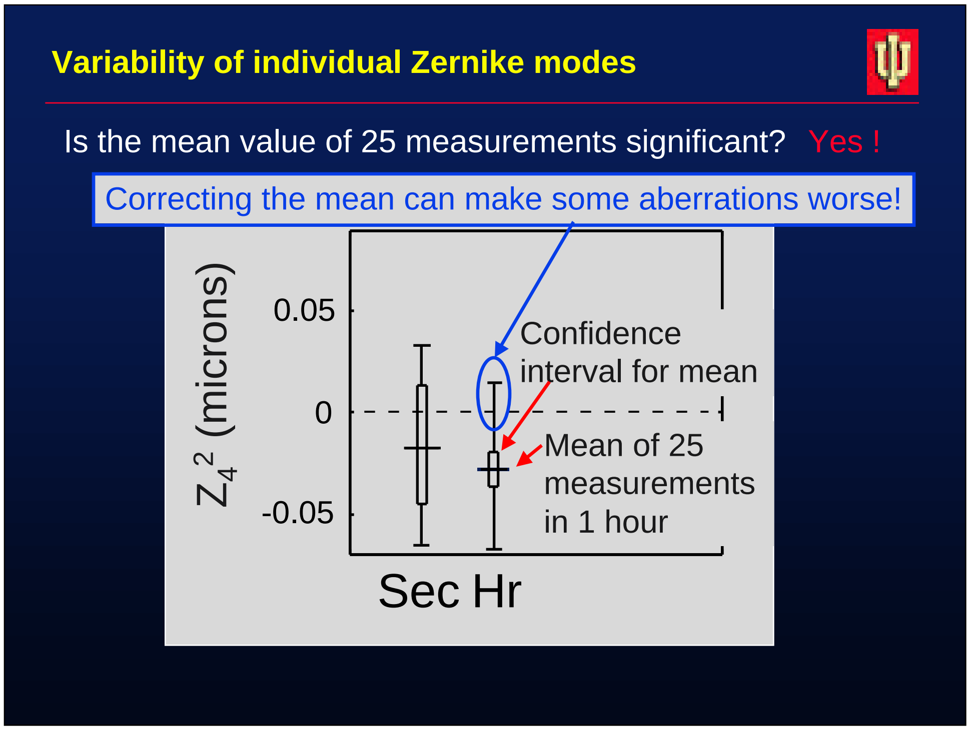


If Zernike analysis of aberrations is used to program refractive surgery, then it makes sense to treat only those aberrations for which the Zernike coefficients are not zero. Given multiple measurements of individual aberration coefficients, we can use statistics to determine whether the mean of the repeated trials is significantly different from zero.

For example, in our first experiment, we measured the aberration map 5 times within 1 second to get 5 estimates of one of the 4th order aberrations called secondary astigmatism. In this graph we plot the mean of those 5 measurements as a short horizontal line. To answer the question "Is the mean value significant?" we need to compute the confidence interval for the mean.

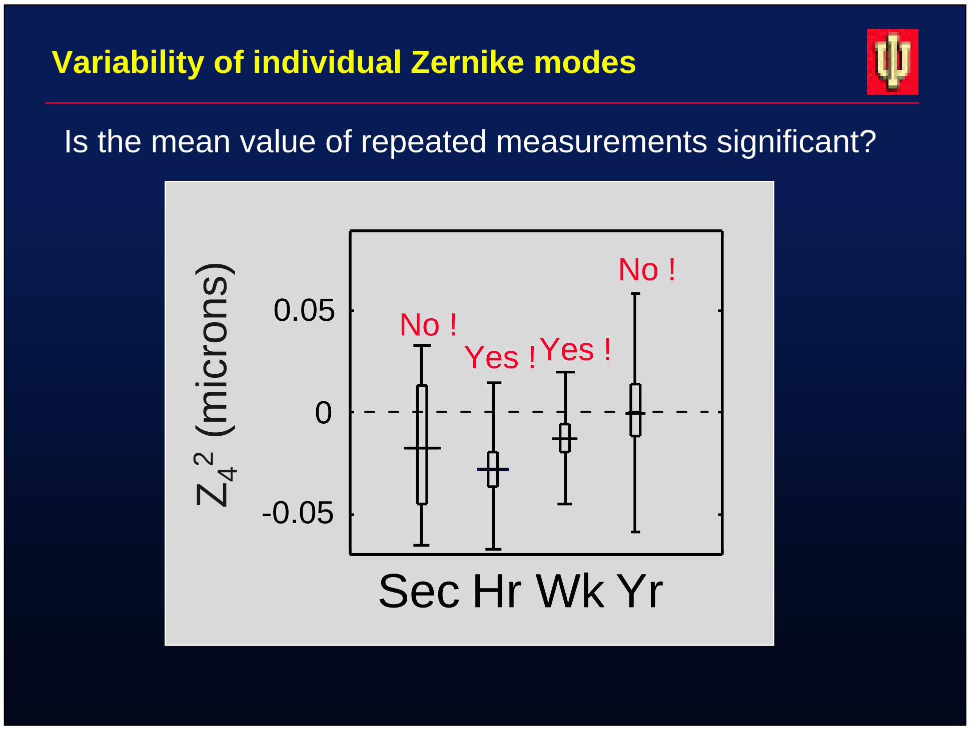
The resulting confidence interval is shown here by a rectangular box. The height of the box indicates the range of uncertainty for the true mean value. Since the confidence interval includes zero,the answer to the question is NO, the mean is not significantly different from zero and therefore we should NOT try to correct this particular aberration in a treatment plan.

Another piece of information that can be plotted on this graph is the 95% probability range, shown by the whiskers extending beyond the box. We interpret these whiskers to mean there is a 95% proababilty that any additional measurements on this eye would have fallen somewhere inside this range.



In fact, we did collect more data on this eye. In our second experiment we measured the aberration map 5 times in less than 1 second, and then repeated this burst of measurements 5 times during a single hour for a total of 25 measurements. Because we have 5 times more data, the mean value is known with greater precision. So now when we ask the question, "is the mean value significant?",] … this time the answer is YES because the confidence interval for the mean shown by the box is much smaller and the zero line no longer goes through the box. So based on this additional data we should now include this aberration in a treatment plan.

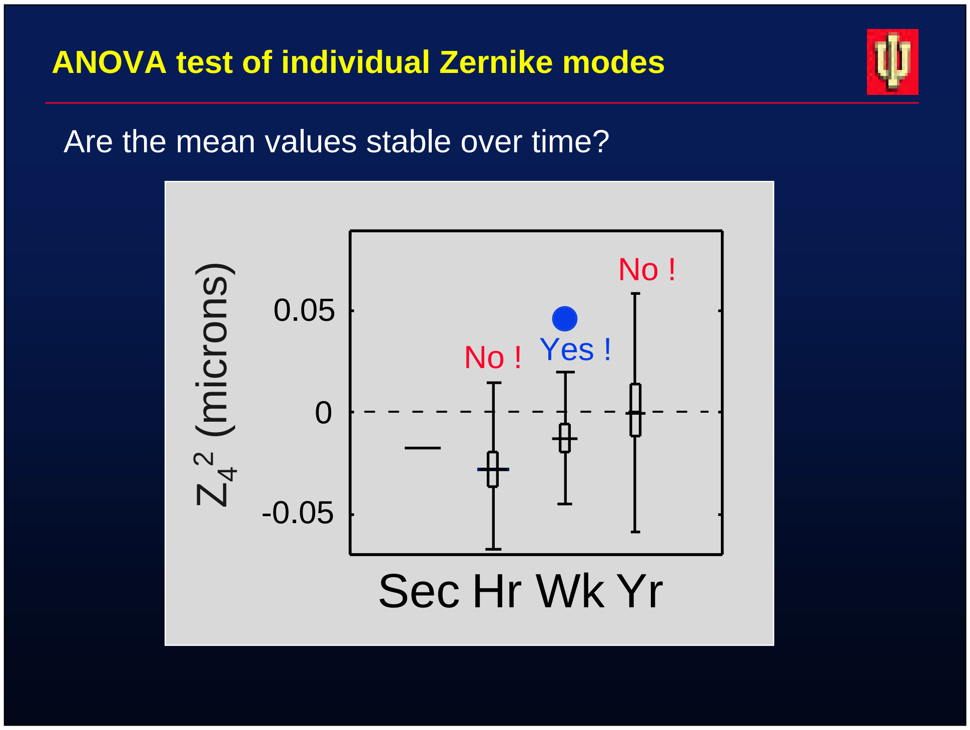
Notice however that the 95% probability range still extends well beyond zero. This is important because it indicates that on some occasions the eye had very small amounts of this particular aberration. However, if we were to treat this eye by correcting for the mean value of aberration, these small values of aberration would now become large. In other words, correcting the mean can sometimes have the unexpected consequence of making the eye worse than it was to begin with.



Not only did we collect data on the time scale of seconds and hours, we also collected data on the time scale of weeks.

Over this longer time span the mean value has become closer to zero, but the confidence interval box doesn't quite cross the zero line so the answer to the question is "YES", the mean value is still significant.

However, when we made further measurements over several months, the mean got even closer to zero] and now the zero line passes through the confidence interval. Thus, on the time scale of one year, the answer is "NO", this aberration coefficient is NOT significant.

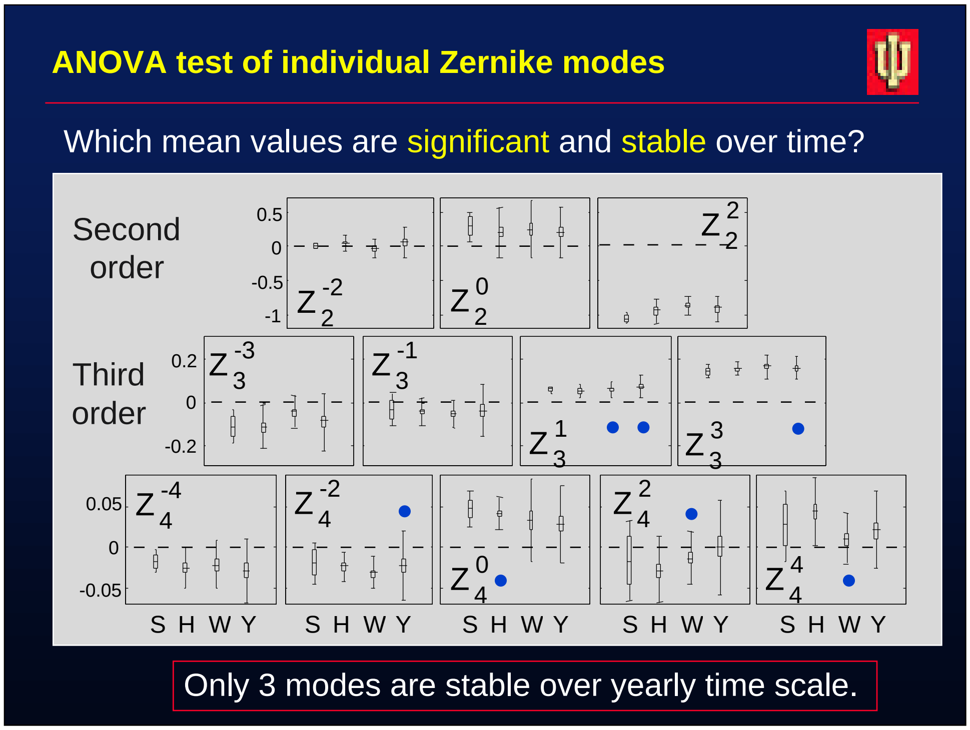


In addition to being statistically significant, a rational treatment plan would also require that the aberration be stable over time, otherwise we are chasing a moving target.

To answer the question “Are the mean values obtained on any given time scale stable?” we used the statistical technique of Analysis of Variance. For example, the data collected over 1 hour on this eye indicated that there was more variability over the duration of 1 hour than there was over one second and consequently the answer is “NO”, the means are NOT stable.

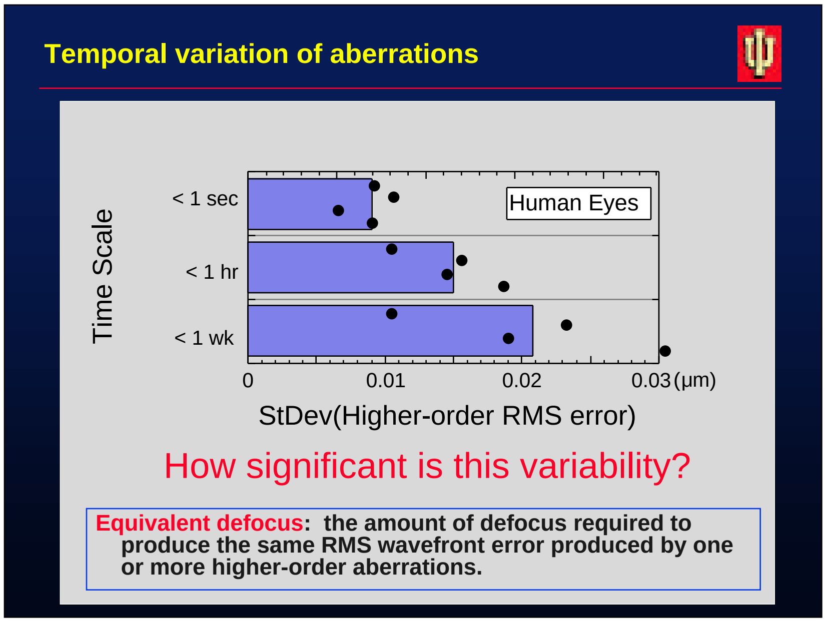
On the other hand, the data were reasonably stable over a period of 1 week, but then again the data appeared unstable over the longer time course of 1 year.

In summary then, it would appear that this particular aberration in this particular eye was indeed a moving target.



This detailed statistical analysis needs to be repeated for every Zernike coefficient that is a candidate for inclusion in a treatment plan for eliminating the eye's optical aberrations.

In this graph we use a blue spot to identify all those conditions for which the aberration coefficient was statistically significant AND stable over time. The striking result for this patient is that although most of the modes were significantly different from zero, only 3 of the 12 modes shown here satisfied the dual criteria of significance and stability over a time frame of 1 year.

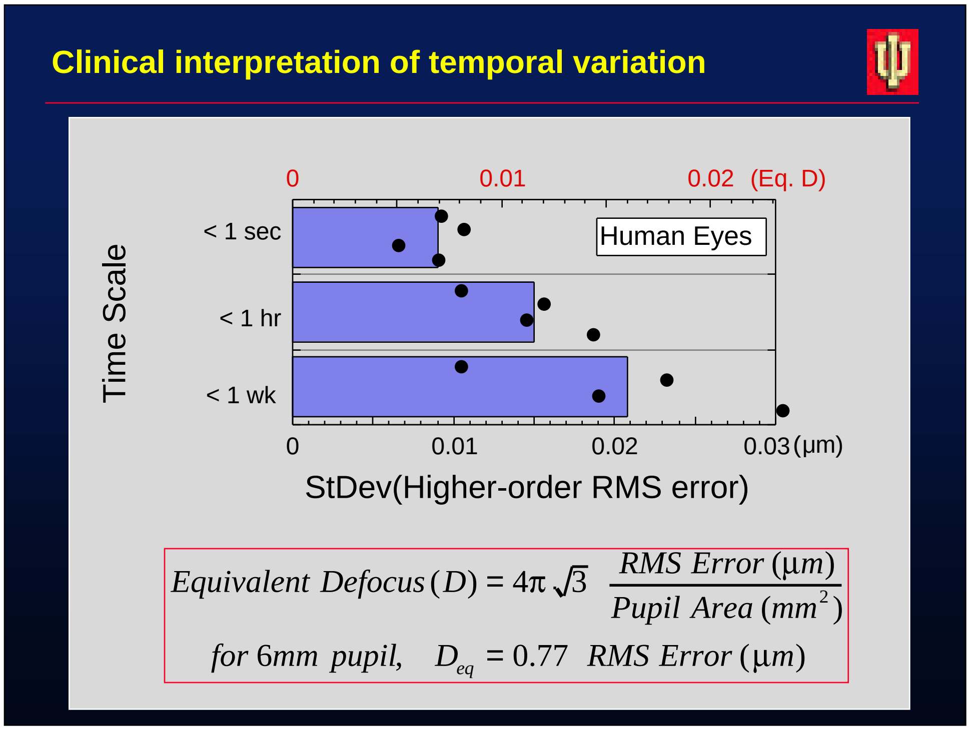


The analysis of individual Zernike aberrations I've just described is too detailed to permit easy comparisons between different individauls. Therefore,in the remainder of my talk I will use the summary metric of RMS wavefront error, which describes how warped the aberration map is without concern for the exact shape of the map. Temporal variation in the RMS error can then be quantified by the standard deviation of repeated measures. We used this approach to compare the amount of variability we observed on different time scales as shown here.

The top bar of this graph shows the standard deviation of 5 measurements of RMS error collected in less than 1 second. Results for individual subjects are shown by the black circles and the mean across subjects is shown by the blue bar.

Variability almost doubles when the data were collected over a period of several minutes, as shown in the middle bar of the graph, and grows even more when collected over 1 week, as shown by the bottom bar of the graph.

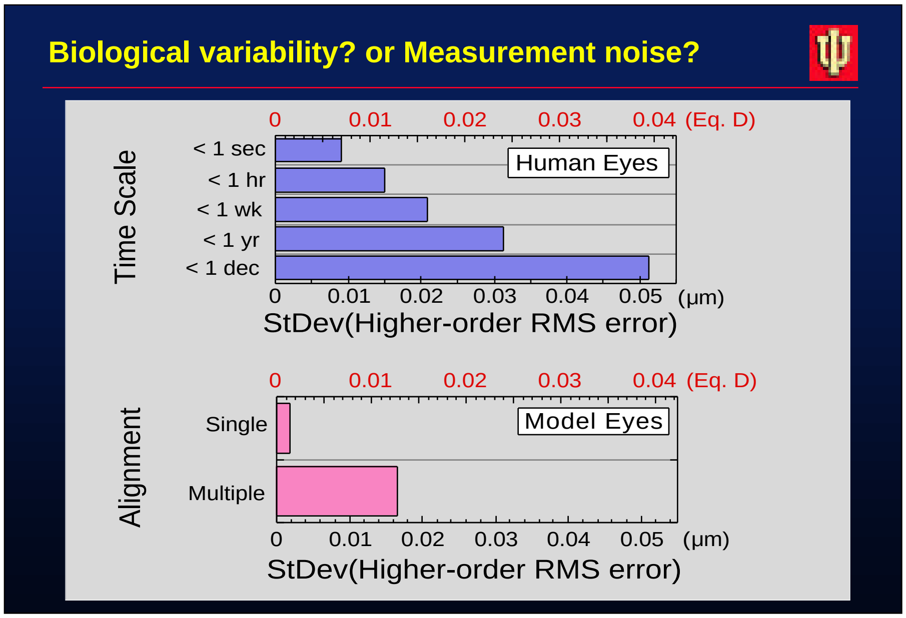
One way to judge clinical significance of these levels of variability is to put the results into familiar units of Diopters. We can do this by using the concept of equivalent defocus, which is defined as the amount of defocus needed to produce the same RMS wavefront error produced by one or more higher-order aberrations. It is important to remember that 1 diopter of a higher-order aberration does not have exactly the same visual effect as 1 diopter of defocus. Indeed, the same could be said of astigmatism. I D of astigmatism does not have exactly the same effect as 1D of defocus, yet the use of a common metric helps us judge their relative importance. In this same way, the concept of equivalent defocus allows us to compare the order of magnitude of different kinds of aberrations and judge their clinical significance.



A simple formula shows that diopters of equivalent defocus depends on the ratio of RMS error to pupil area.

For a 6mm pupil, a red dioptric scale at the top of this graph can be constructed simply by multipying RMS error by 0.77.

Now we see that the variability of higher-order aberrations in our patients was on the order of 1/100th of a diopter, which is pretty small by clinical standards! Nevertheless, I will argue that this seemingly trivial amount of variability can significantly reduce the benefit expected from correction of higher-order aberrations.



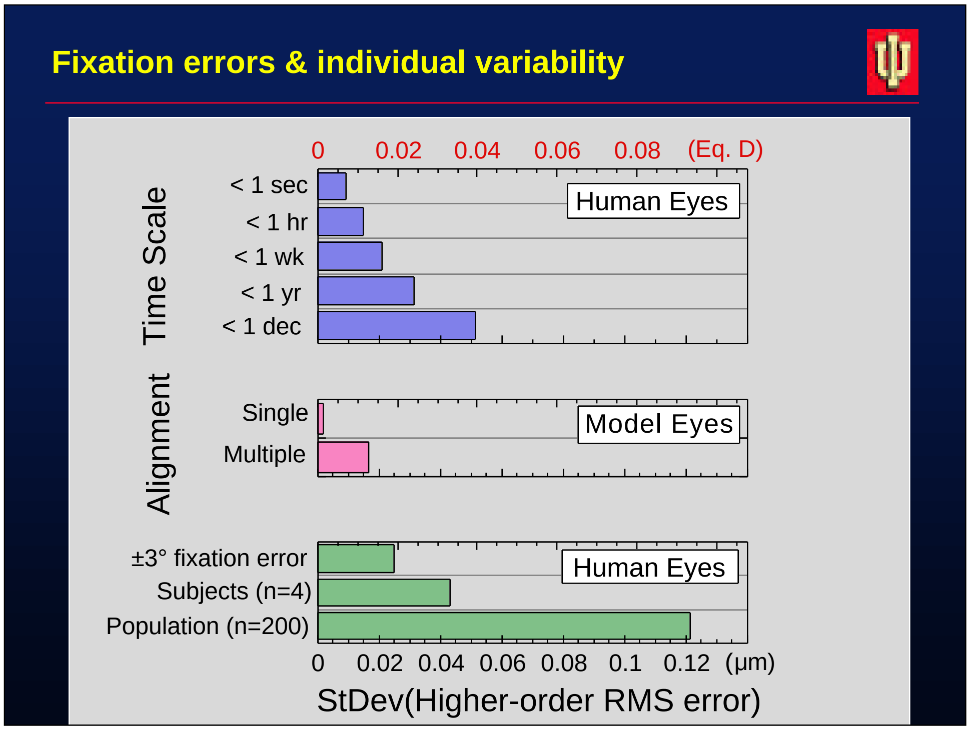
But first, where is this variability coming from? Is it measurement noise, or normal biological fluctuations?

To answer this question, we repeated the experiment on a physical model eye which has a single refracting surface similar to the human cornea. When we collected multiple aberration maps after aligning the instrument just once, the variability was practically zero as shown by the short red bar.

However, when we re-aligned the instrument to the model eye before each measurement, the variability was similar in magnitude to that obtained from human eyes, as shown by the long red bar.

We concluded from this experiment that most of the variability we observed in human eyes on an hourly time scale could be accounted for by measurement noise associated with re-aligning the instrument. On the other hand, the small increase in variability observed on a weekly time scale probably reflects real biological changes.

This blue bar-graph also shows the results from three subjects examined on a monthly basis for half a year, and for 2 subjects examined on a yearly basis for half a decade. The variability continues to increase with these longer time scales, which we believe to be a manifestation of true biological variability.

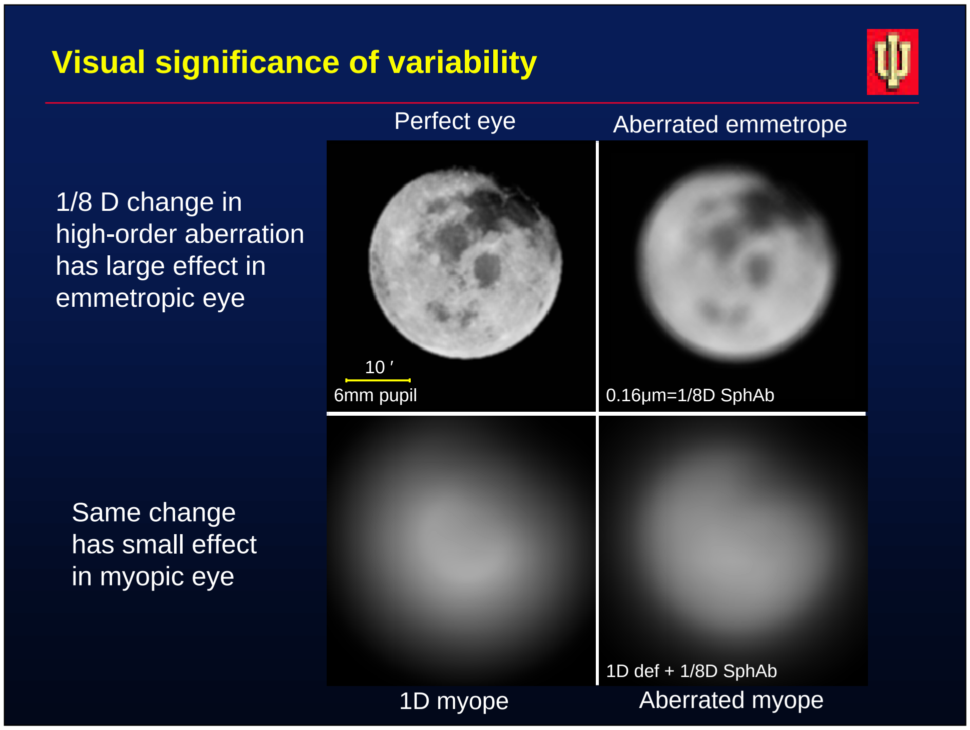


Another way to put these results into perspective is to compare individual variability with that caused by fixational eye movements or the variability between subjects.

When subjects deliberately introduced up to 3 degrees of fixation error, we found the amount of variability in their aberration maps was about the same as the weekly variability we had measured earlier, as shown by the upper green bar.

Variation due to fixation errors and weekly variations were both small compared to the variability between subjects in our study, shown by the middle green bar, and were very much smaller than the variability between the greater population of normal eyes, shown by the lower green bar.

The importance of these results is that although measurements on any given eye are variable, this variability is not large enough to obscure individual differences between different eyes.

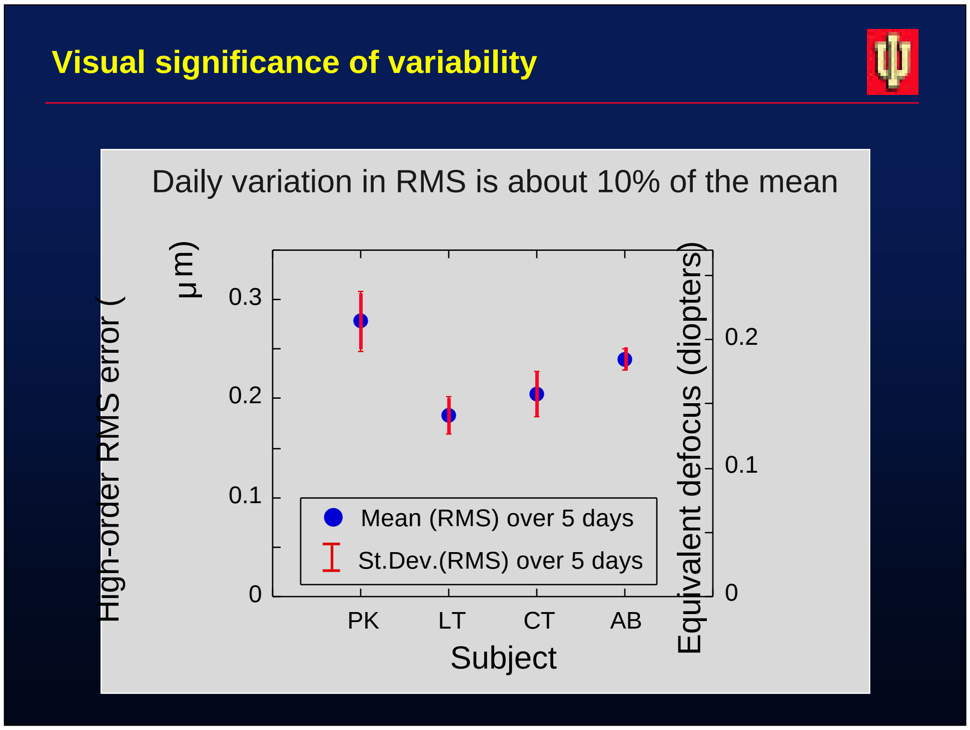


Ultimately, we would like to know the impact of variability of the aberration map on vision, but that depends on the total amount of aberration in the eye, including spherical and cylindrical errors.

We can appreciate this fact by considering the visual effect of optical aberrations on the simulated retinal image of the moon. For example, 1/8 D of equivalent defocus of spherical aberration has a large effect on the quality of the retinal image when added to a perfect emmetropic eye, as shown in the top row of images. .

However, the same aberration has very little effect when added to a myopic eye with 1 D of uncorrected spherical refractive error, as shown in the bottom row of images.

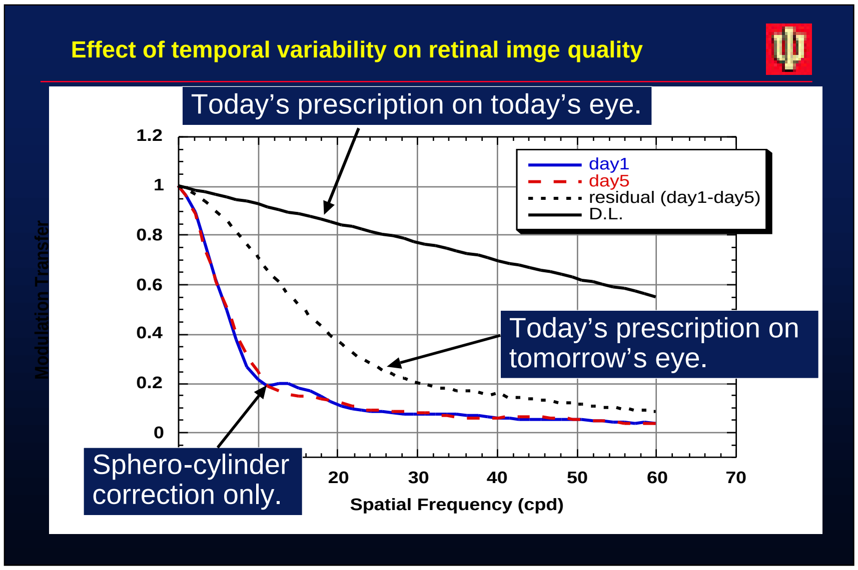
In other words, the visual effect of variability depends very much on the degree of aberration or refractive error present in an eye to begin with.



In the same way, we can expect variability in higher-order aberrations to be visually insignificant if the total amount of aberrations is large compared to the variability.

Indeed, this is the situation for our subjects as shown on this graph. The circles show the average amount of higher-order aberrations measured over 1 week for each of our 4 subjects. The error bars show the standard deviation of RMS measured that week. The error bars are only about 10% of the mean, which suggests that this amount of variability is negligible in the presence of the eye's normal level of aberrations.

However, one aim of refractive surgery is to correct the eye's higher-order aberrations, in which case variability of those aberrations will become important.

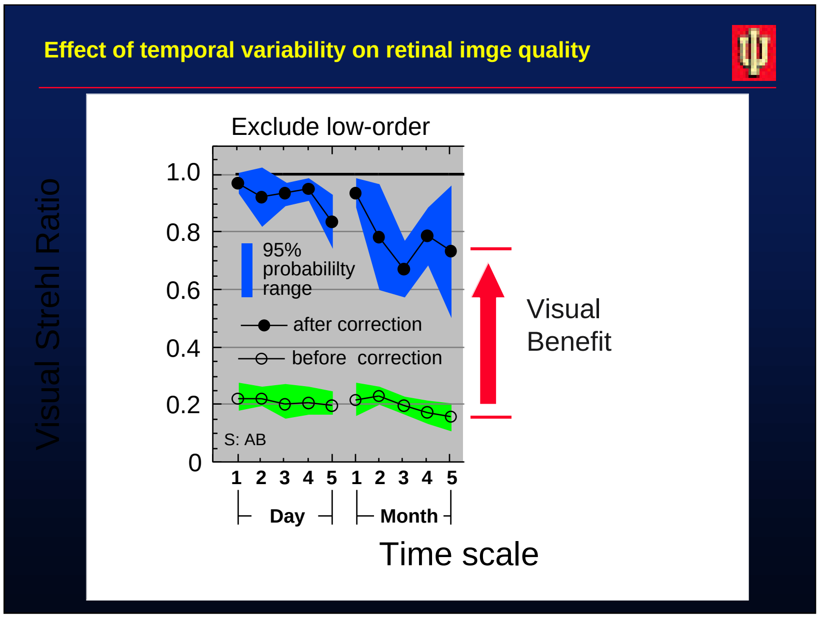


To emphasize this point, we used the data for one patient to compute the a modulation transfer function for that person's eye to quantify the eye's optical quality.

If this patient's eye is perfectly corrected for sphere and cylinder but the higher-order aberrations are left uncorrected, then the eye's MTF is unaffected by variability in the higher-order aberrations, as shown by the blue and red curves in this graph which correspond to two different days. But if higher order aberrations are corrected as well, then a perfect eye is achieved, as shown by the solid line at the top. This is the idealized case of "perfect optics" using today's prescription to correct today's eye.

However, if we use today's prescription to correct tomorrow's eye, the aberration map would have changed enough to significantly reduce the amount of gain realized by correcting the higher-order aberrations. This gap between the solid curve and the dashed curve represents a loss of image quality caused by a seemingly trivial degree of variability amounting to only 1/100 of a diopter.

To pursue this result in greater depth, we determined a "prescription for perfection" based on aberration measurements taken on day 1. We then computed the MTF of the eye for multiple measurements on the same day, on different days, and on different months assuming this single, fixed prescription was implemented perfectly by refractive surgery. Each MTF was reduced to a single number, the Strehl Ratio, which served as a metric of image quality. The results are shown in the next slide.

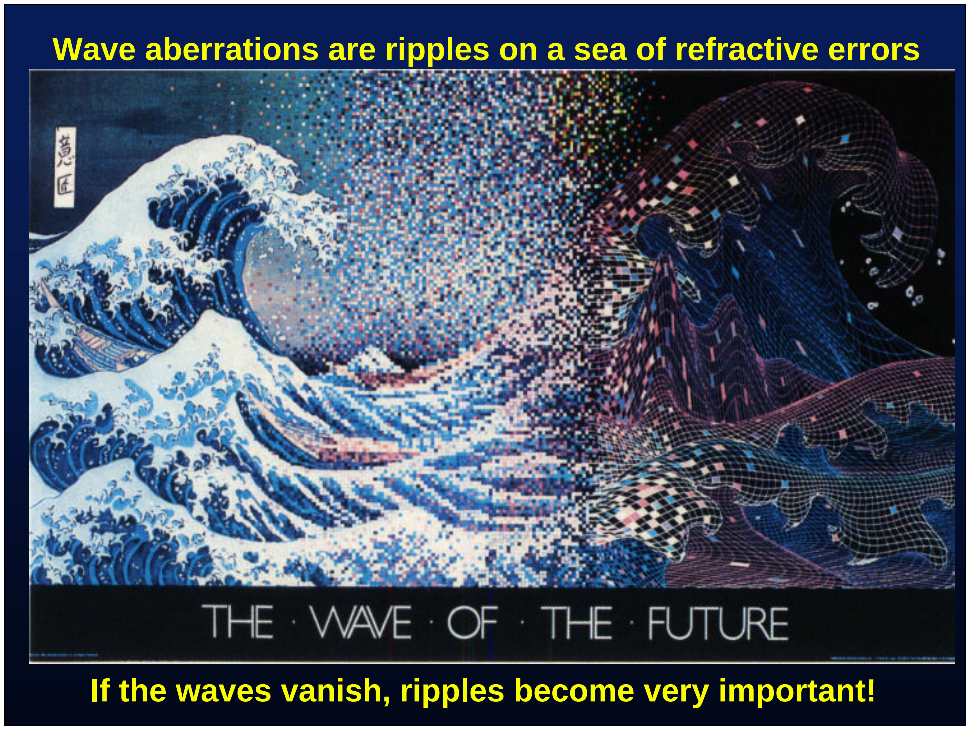


Imagine first that the eye's lower-order aberratons of sphere and cylilnder were perfectly stable and were perfectly corrected by the surgery. The variation in image quality computed over days and months is shown in the shaded region on the left side of this graph.

The open symbols show the mean of repeated measures of optical quality of the uncorrected eye and the closed symbols show the mean image quality for the corrected eye. This analysis clearly indicates a large visual benefit of correcting the eye's higher-order aberrations <u>on average</u> when lower order aberrations are excluded. Furthermore, the range of individual Strehl ratio values, shown by the blue and green zones, is reasonably narrow, indicating a reliably good outcome.

The problem with this analysis is that it is overly optimistic because it assumed zero variability in the second-order aberrations. In fact, the lower-order aberrations also vary from day-to-day and when we take this variability into account the results are not nearly so optimistic.

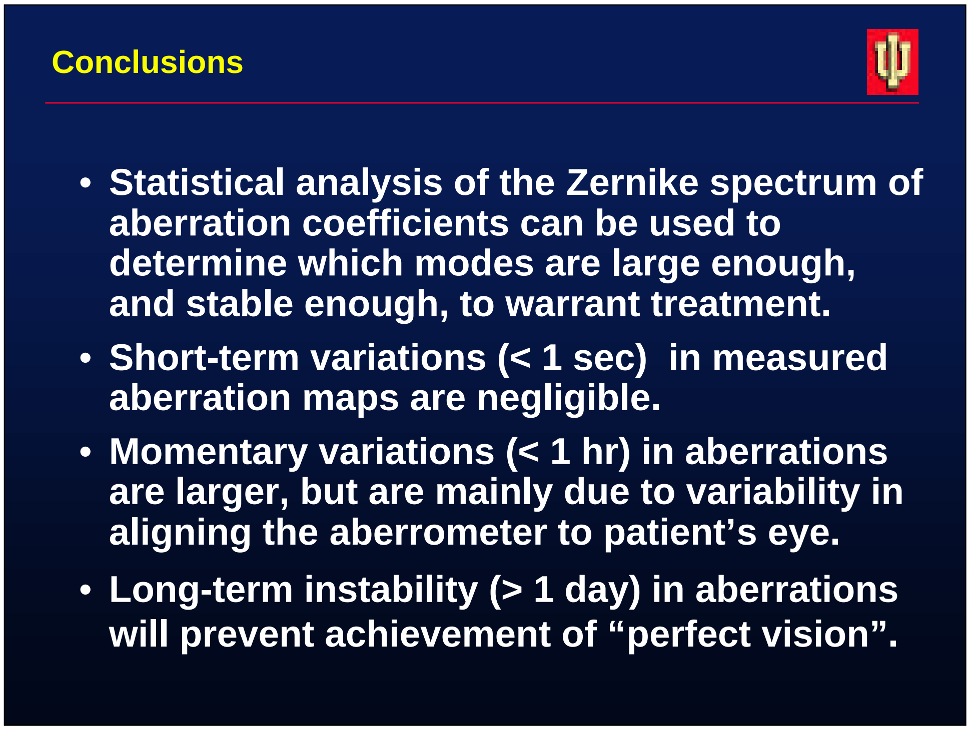
The right-hand side of this graph shows that when variabillity in lower-order aberrations is taken into account, the visual benefit of a perfectly-implemented, perfect-correction diminishes over time to the point that little, if any, benefit is evident after just a few months of normal variability in the eye's aberration structure.



Summarizing these results from a clinical perspective, the higher-order aberrations of the normal healthy eye are typically less than 1/4 diopter, which means they are of the same order of magnitude as the residual sphere and cylinder present in an eye that is well-corrected by clinical standards.

Variability in those higher order aberrations is an order of magnitude smaller, on any time scale from seconds to years. Thus, *the variability in wave aberrations is merely e a ripple on the sea of refractive errors*.

Although refractive surgery may be able to calm this sea of refractive errors significantly, the ripples of day-to-day variability are large enough to prevent a total becalming of the seas that would represent perfect optical correction.



In conclusion, we have found that:

Statistical analysis of the Zernike spectrum of aberration coefficients can be used to determine which modes are large enough, and stable enough, to warrant treatment.

Short-term variations (< 1 sec) in measured aberration maps appear negligible.

Momentary variations (< 1 hr) in aberrations are larger, but are probably due to variability in aligning the instrument to the patient's eye.

Daily, monthly, and yearly variations in aberration maps are large enough to prevent achievement of "perfect vision" even in the unlikely event that spherical and astigmatic refractive errors are corrected perfectly.