Objective Characterization of Haze Following Refractive Surgery

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APL has collaborated with the Wilmer Eye Institute since the beginning of the Biomedical Program at the Laboratory in the 1960s. Here we discuss recent efforts related to refractive surgery.

Argon fluoride excimer lasers operating at a wavelength of 193 nm are being used extensively in the United States and throughout the world for vision-correction procedures known technically as photorefractive and phototherapeutic keratectomies (PRK and PTK). In contrast with another very popular procedure called LASIK (laser *in situ* keratomileusis), PRK does not appreciably weaken the cornea and is less invasive; however, the mild wound healing response results in increased light scattering that gives the cornea a hazy appearance during the first months after surgery.

In standard clinical practice, haze is graded subjectively via slit-lamp examination by an experienced observer; however, comparisons of haze severity between different subjects or even between different times for the same subject are difficult with subjective methods. Consequently, at the request of Dr. Walter Stark at the Wilmer Eye Institute in 1993, we developed a simple instrument called a scatterometer to make objective measurements of haze. We also devised a standardized PTK treatment procedure in rabbits to evaluate the development of haze in a controlled manner. In early studies, the scatterometer was used with the standardized procedure to show that antioxidants and the drug mitomycin-C reduce corneal scattering after laser keratectomy. The scatterometer has also been used in clinical investigations. For example, we demonstrated that deeper PRK treatments necessary to correct high myopia (nearsightedness) result in greater levels of haze than the shallower treatments for low myopia.

The scatterometer has also been used to characterize light scattering after a new surgical procedure in which the back of the cornea is replaced (known as deep lamellar endothelial keratoplasty or DLEK). The light-scattering outcomes of DLEK were compared with those of standard penetrating keratoplasty, in which the whole cornea is replaced.[1] In another study, it was used to determine whether sterilization of eye bank donor corneas by irradiation alters their optical properties.

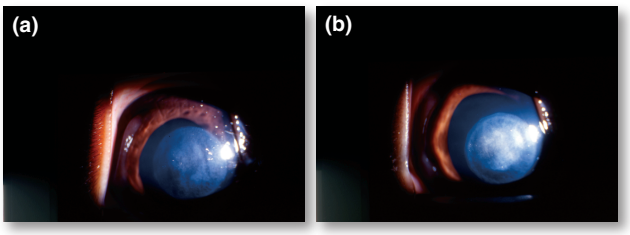

Figure 1. (a) A cornea in the low-scattering group 21 days after treatment. (b) An identically treated cornea in the high-scattering group at 21 days.

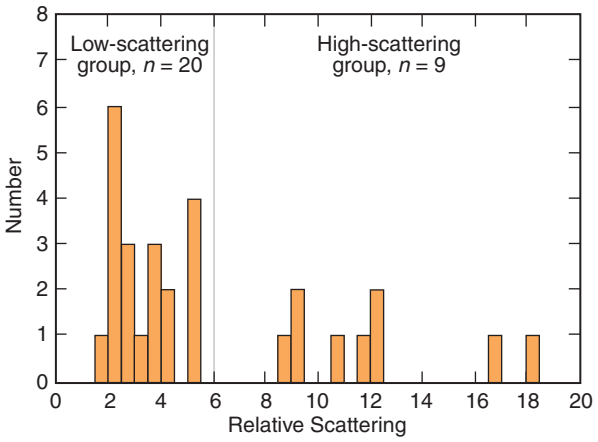

Figure 2. A histogram of the numbers of corneas as a function of relative scattering at 3 weeks after the identical PTK treatments. Relative scattering is defined as the ratio of the scattering at each posttreatment time to its pretreatment level. The histogram clearly shows that the data separate into distinct low- and high-scattering groups, with the high-scattering group showing greater variability.

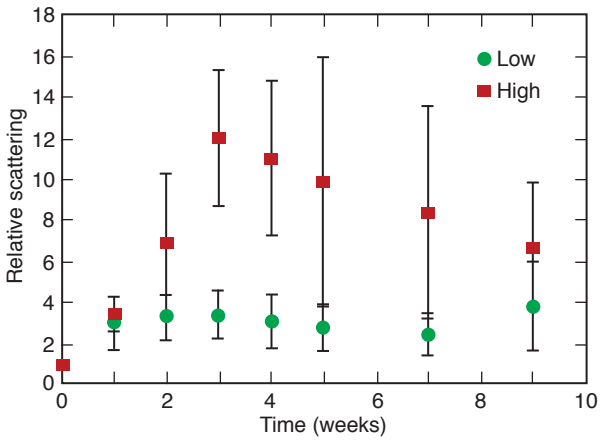

Figure 3. Mean relative scattering levels and standard deviations at various times after identical PTK treatments. After 2 weeks, the mean scattering levels split into distinct low- and high-scattering groups. The groups remain statistically distinct up to 7 weeks ($P < 0.005$).

A very interesting finding published recently is that identical PTK treatments in rabbits result in distinct low- and high-level light-scattering responses (Figs. 1–3).[2] The underlying mechanism for the distinct responses is not yet understood. However, several factors may play roles either collectively or individually. These include: the re-growth rate of the cornea's front cell layer, which is removed in the procedure; the behavior of the plasminogen-activator–plasmin system in the tear layer; programmed death (apoptosis) of cells called keratocytes, which are in the cornea's interior; and the relationship between a chemical growth factor known as transforming growth factor β (TGF-β) and the transformation of myofibroblasts, which are cells involved in the wound-healing process. Individual variations in healing may also be involved.

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For further information on the work reported here, see the references below or contact russell.mccally@jhuapl.edu.

[1]Hindman, H. B., McCally, R. L., Myrowitz, E., Terry, M. A., Stark, W. J., Weinberg, R. S., and Jun, A. S., "Evaluation of Deep Lamellar Endothelial Keratoplasty Surgery Using Scatterometry and Wavefront Analysis," *Ophthalmology* 114, 2006–2012 (2007).

[2]McCally, R. L., Connolly, P. J., Stark, W. J., Jain, S., and Azar, D. T., "Identical Excimer Laser PTK Treatments in Rabbits Result in Two Distinct Haze Responses," *Invest. Ophthalmol. Vis. Sci.* 47, 4288–4294 (2006).