

REFRACTIVE SURGERY

Softening the Presbyopic Lens With a Femtosecond Laser

BY LINDA ROACH, CONTRIBUTING WRITER FOR EYENET AND OUTLOOK
INTERVIEWING OMID KERMANI, MD, RONALD R. KRUEGER, MD, AND SUNIL SHAH, MD

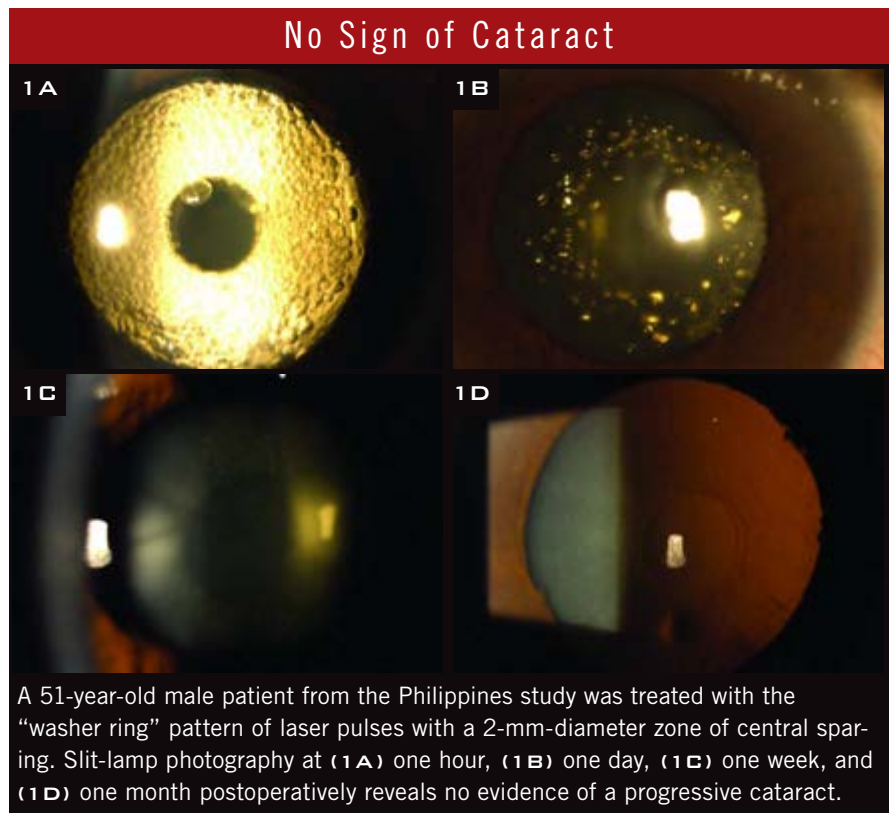
The femtosecond laser is the latest device to be explored as a solution to the refractive problem that eventually afflicts every aging eye: presbyopia. Unlike previously explored methods, which commonly try to manipulate the visual system through pseudoaccommodation, this new approach to presbyopia is aimed at re-enabling natural accommodation.

Two companies, Lensar (Orlando, Fla.) and Rowiak (Hanover, Germany), have ongoing clinical trials investigating the use of their femtosecond lasers to soften the presbyopic crystalline lens. With fewer than 200 eyes treated so far, investigators in this field say they are cautiously optimistic.

“The bottom line is that some results are promising, but reproducible, consistent efficacy has not yet been demonstrated. So investigations are continuing,” said Ronald R. Krueger, MD, at the Cleveland Clinic.

The principal investigator in the latest Lensar trial, Sunil Shah, MD, at the Birmingham and Midland Eye Centre in Birmingham, United Kingdom, agreed. “We’re still trying to work out how this works. It’s difficult to draw conclusions yet,” he said.

But the biomechanical underpinnings of this proposed solution to presbyopia are strong, Rowiak cofounder Omid Kermani, MD, of Cologne, Germany, emphasized at the 2013 annual meeting of the International Society of Refractive Surgery (ISRS). “We know that lens stiffness is the single



A 51-year-old male patient from the Philippines study was treated with the “washer ring” pattern of laser pulses with a 2-mm-diameter zone of central sparing. Slit-lamp photography at (1A) one hour, (1B) one day, (1C) one week, and (1D) one month postoperatively reveals no evidence of a progressive cataract.

factor that limits the accommodative amplitude at any age and ultimately leads to a complete loss of accommodation,” Dr. Kermani said. “The ciliary muscle continues to contract in the presbyopic eye, and the lens capsule stays elastic far beyond the onset age of presbyopia.”

Two Approaches

Lensar: retooling an existing device.

Clinical trials currently under way employ a modified version of the company’s existing femtosecond laser, which

is approved for cataract surgery in Europe and the United States. The first clinical trial using the laser for lens softening was performed in 2011 by cataract and refractive surgeon Harvey Uy, MD, of Makati City, Philippines. This feasibility study was performed in 80 eyes of patients one month prior to their scheduled cataract surgery. The pulse energy in the study was approximately 10 microjoules (μJ).

Dr. Shah’s clinical trial in Britain included 30 patients, all of whom were scheduled for refractive lens exchange

surgery one month later. However, the results are not directly comparable to those of the earlier study because of differences between the patient groups, and modifications in the spot size and energy of the laser pulses after conclusion of the study in the Philippines, Dr. Shah said.

Femtosecond laser softening of the lens has proved to be a “very quick, simple technique,” he said. “A typical treatment takes about 7 or 8 seconds, and the patients are usually turning around afterward and asking us, ‘Is that it?’ So if we can get this to work, this is much better than an accommodating intraocular lens.”

Rowiak: a single-procedure laser.

This German company is new to ophthalmology but not to femtosecond lasers. It has been making lasers and imaging systems for tissue processing and cell manipulation since 2003. Two years later, Rowiak-affiliated scientists began reporting on a series of preclinical studies in support of using a femtosecond laser to soften the presbyopic lens.¹⁻⁴ The scientists call the procedure fs-lentotomy.³

The Rowiak laser was designed at the outset to have a “delicate” intralenticular impact, Dr. Kermani said at the 2013 annual meeting of ISRS. Each pulse delivers less energy (<2 μ J), with a smaller focal spot size and faster repetition rate than is the case for cataract surgery, he said.

“For cataract surgery, we need effectiveness, so the cutting process is driven by the mechanical forces of the expanding gas bubbles and the energy ranges from 5 to 20 μ J per pulse. For presbyopia we need more delicate cuts, and therefore pulses should be no more than 2 μ J, with a much higher repetition rate.”

The company conducted a pilot clinical study in 16 patients last year, which it is following with a small phase 2 trial at two sites in Cologne and Rosstock, Germany, he said.

Early Outcomes

Variable effect. Ex vivo studies of donor lenses, in vivo animal studies, and finite element modeling suggest that

laser-softened lenses might produce up to 2.0 D of accommodation. But in early clinical studies, the refractive impacts have ranged widely for unknown reasons, Dr. Krueger said.

“At the moment, there appears to be some inconsistency in getting the same kind of results in everybody. Maybe that’s because of our patient selection,” he said. “The initial treatments were in eyes in which we were planning on extracting the lens in a month. In the refractive lens exchange patients, some of them may have had early cataracts, and maybe that affects the kind of results they get.

“And some of the variability probably has to do with the algorithms—we’re still defining the exact pattern so we can get reproducible results. All of this is new information that we still need to uncover,” he said.

In the Philippines trial, 40 percent of 80 participants had improved distance-corrected near visual acuity (DCNVA) in the treated eye. The maximum gain in subjective near acuity was 2.33 D, but the mean improvement, compared to baseline, was 0.72 D. One-third of the subjects had improved objective accommodation, Dr. Shah said.

This trial also showed that the treatment should not be performed in the center of the crystalline lens. Among eyes in which pulses were placed within the central 1 mm of the lens, more than 70 percent lost two or more lines of best spectacle-corrected visual acuity at one month.⁵

Because of the subsequent modifications to the laser, the results in the current British study are not directly comparable to those in the Philippines, Dr. Shah said. However, in the 30 patients treated so far, “We’ve had very encouraging results—good enough that if we had a choice we’d follow them for longer,” he added. (The study protocol limited follow-up to one month.)

The data hint that laser softening of the presbyopic lens might work best in emmetropes, he added. He gave the example of one emmetrope, a 57-year-old woman, whose posttreatment defocus

curve showed a gain in accommodative range of 1.75 D. Also, he said, all emmetropes had a DCNVA of 20/40 or better after treatment, compared with 38 percent of the nonemmetropes, and their mean improvement in binocular preferred viewing distance was 8.66 cm, compared with 3.92 cm for the nonemmetropes.

In the Rowiak pilot clinical trial, fewer patients have been treated, and the company is releasing little information about the outcomes. When Dr. Kermani spoke at the ISRS 2013 meeting, he said he could only say that “a lot of” the 16 patients in the pilot study gained accommodative power “comparable to what we have seen in the experimental results.”

Lack of complications. “Whenever you put energy someplace, you want to make sure you’re not doing harm,” Dr. Krueger said. And, so far, investigators have not reported seeing the potential complication about which they are often asked: cataract formation.⁵

However, some micro-opacities were visible in Scheimpflug imaging of the eyes, and the investigators concluded that the per-pulse energy should be lower than they had used (~10 μ J). They noted that no such micro-opacities occurred in previous animal studies using pulses of approximately 2 μ J.⁵

At lower pulse energies, the lines of cavitation bubbles created by the laser usually fade within 24 hours, and patients have not complained of visual distortions or light scatter from the residual intralenticular lines, the investigators reported.

“In this pilot study we could show that the laser lesions do clear up rapidly, within hours, and far vision stays unchanged. There were no clinical complications, no significant technical complications,” Dr. Kermani said.

However, he said that longer-term studies are needed to rule out late opacification and other possible complications.

Patterns of Pulses

The Philippines trial showed that placing pulses in the center of the lens led to a loss of BCVA. Consequently, the

various treatment algorithms now being tested have one thing in common, Dr. Krueger said: They leave the central 2 mm of the lens undisturbed. But the optimal locations for the laser pulses around the lens center remain undetermined, he said.

“Some of our patterns have included what we call a washer ring pattern [Fig. 1A], which basically is an inner clear zone and an annulus of very intense energy all the way out to an outer diameter. So you might have a 2-mm clear zone, and from 2 to 5 mm there are coincident rings of light that make a very dense-looking bubble pattern, which then dissipates later,” Dr. Krueger said. “We also have a waffle pattern. It has little checkerboards of patterns that go outward around the center.”

As Dr. Kermani showed in his 2013 presentation, the initial pulse pattern favored by Rowiak investigators looked like a steering wheel: an inner ring of laser spots and an outer ring, with several spoke-like connections between them. Previous finite element modeling indicated that this pattern would alter the lens biomechanics by creating “sponge-like compression joints” and “sliding joints” at key locations, he explained.

What Lies Ahead?

At Lensar, Dr. Krueger said the immediate goal is to settle on an algorithm for the treatment. “If we can titrate our pulse patterns to come up with the best response and the most consistency, then we can do a real formal clinical trial and have results that clearly show efficacy. I think in five years we may have something that is being done

internationally,” he said.

Dr. Kermani, too, expressed optimism about the ultimate outcome of the Rowiak trials. “Our goal is to restore accommodation and to gain up to 2 diopters of additional refractive power,” he said. “Hereby we could be able to postpone the need of refractive lens exchange by five to 10 years. And I am personally convinced that we will be able to achieve this goal and make femtosecond laser–assisted presbyopia reversal available for all our patients by the end of this decade.” ■

- 1 Krueger RR et al. *J Cataract Refract Surg.* 2005;31(12):2386-2394.
- 2 Gerten G et al. *Ophthalmologie.* 2007;104(1):40-46. [In German.]
- 3 Schumacher S et al. *J Refract Surg.* 2008;24(9):991-995.
- 4 Lubatschowski H et al. *Klin Monbl Augenheilkd.* 2009;226(12):984-990. [In German.]
- 5 Krueger RR et al. *Trans Am Ophthalmol Soc.* 2012;110:130-165.

Omid Kermani, MD, is cofounder of Rowiak in Cologne, Germany. Financial disclosure: Has equity interest in Rowiak.

Ronald R. Krueger, MD, is medical director of refractive surgery at the Cleveland Clinic's Cole Eye Institute, in Cleveland. Financial disclosure: Has equity interest in Lensar, is a consultant to the company, and serves on its medical advisory board.

Sunil Shah, MD, is in practice at the Birmingham and Midland Eye Centre in Birmingham, United Kingdom. Financial disclosure: Has received travel expense payment from Lensar, is medical director for CustomVis, and is a consultant for or has received research funding from Alcon, AMO, Bausch + Lomb, Lenstec, Oculentis, PhysIOL, Refocus, and Topcon Europe.

INSIDE REFRACTIVE SURGERY OUTLOOK. EyeNet is pleased to bring its readers the above article from the May *Refractive Surgery Outlook*. This is the online monthly member publication of the International Society of Refractive Surgery (ISRS), a partner of the American Academy of Ophthalmology. ISRS membership offers access to the latest in refractive, cataract, cornea, and lens-based clinical and research developments via its publications, meetings, and Multimedia Library. Through its clinical forum, members can connect with the world's leading surgeons for discussion of specific clinical case questions and issues.

For more information or to join ISRS, visit www.aaopt.org/isrs/membership.



Coming in the next EyeNet

Feature

OCT Interpretation

Despite major improvements in OCT technology, artifacts can still lead you—and your patients—down the wrong path. Tricks for avoiding the traps.

Clinical Update

Cornea An update on glues for the ocular surface.

Oncology Expert discussion about a case of melanocytic lesion: nevus or melanoma?

Refractive Surgery Toric IOL calculations—taking posterior corneal astigmatism into account.

Practice Perfect

How to protect (and promote) your online reputation.

Destination AAO 2014

Chicago meeting essentials.

EyeNet Extra

Get more from your EHR.

For Your Convenience

These stories also will be available online at www.eyenet.org.

FOR ADVERTISING INFORMATION

Mark Mrvica or Kelly Miller
M. J. Mrvica Associates Inc.
856-768-9360
mjmrvica@mrvica.com