Initial Clinical Evaluation of an Intraocular Femtosecond Laser in Cataract Surgery

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ABSTRACT

PURPOSE: To evaluate femtosecond laser lens fragmentation and anterior capsulotomy in cataract surgery.

METHODS: Anterior capsulotomy and phacofragmentation procedures performed with an intraocular femtosecond laser (LenSx Lasers Inc) were initially evaluated in ex vivo porcine eyes. These procedures were then performed in an initial series of nine patients undergoing cataract surgery. In addition to standard intraoperative assessments (including capsulotomy diameter accuracy and reproducibility), optical coherence tomography was used to evaluate human procedures.

RESULTS: For an intended 5-mm capsulorrhexis in porcine eyes, average achieved diameters were 5.88±0.73 mm using a standard manual technique and 5.02±0.04 mm using the femtosecond laser. Scanning electron microscopy revealed equally smooth cut edges of the capsulotomy with the femtosecond laser and manual technique. Compared to control porcine eyes, femtosecond laser phacofragmentation resulted in a 43% reduction in phacoemulsification power and a 51% decrease in phacoemulsification time. In a small series of human clinical procedures, femtosecond laser capsulotomies and phacofragmentation demonstrated similarly high levels of accuracy and effectiveness, with no operative complications.

CONCLUSIONS: Initial results with an intraocular femtosecond laser demonstrate higher precision of capsulorrhexis and reduced phacoemulsification power in porcine and human eyes. [*J Refract Surg*. 2009;25:1053-1060.]

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Cataract surgery with intraocular lens (IOL) implantation is the most common ophthalmic surgical procedure worldwide. It is also the most common surgery that corrects refractive error, performed over five times more frequently than corneal refractive surgery.[1] Phacoemulsification is the dominant form of cataract surgery in developed countries, accounting for >90% of procedures.[2,3] Although a number of recent developments have occurred in IOL technology, the basic phacoemulsification procedure has remained largely unchanged over the past 20 years, involving a series of individual steps including corneal incision creation, capsulorrhexis, and phacofragmentation.

Although highly successful, each of these manual steps presents an opportunity for improvement in both safety and effectiveness. For example, manual capsulorrhexis results in capsular tears in approximately 1% of cases and has limited diameter predictability, which can affect IOL centration, postoperative anterior chamber depth, and posterior capsular opacification rates.[4-7] The surgical challenges posed by nuclear chopping techniques have hindered widespread adoption, despite evidence that they reduce ultrasound requirements relative to traditional phacoemulsification.[2,8]

Femtosecond lasers represent an important technological advance in ophthalmic surgery. Combined with computer-controlled optical delivery systems, femtosecond lasers can produce precise surgical incisions without collateral damage to surrounding tissues.[9-13] Since 2001, several femtosecond laser systems have been introduced clinically and more than 2 million ophthalmic procedures have been performed with femtosecond lasers, primarily for creation of a corneal flap in LASIK. The precision of femtosecond lasers exceeds that of

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highly sophisticated mechanical devices, with fewer likely collateral tissue effects.[14]

We evaluated a novel intraocular femtosecond laser to perform key steps of the traditional cataract procedure, including capsulotomy and lens fragmentation. Initial procedures were performed in ex vivo porcine eyes, with subsequent demonstration in human patients.

By improving the accuracy of the cataract procedure, this technology has the potential to reduce complications and improve visual outcomes.

PATIENTS AND METHODS

Ex Vivo Porcine Eyes

Capsulotomy Procedures and Diameter Measurements. The accuracy and reproducibility of femtosecond laser capsulotomy diameters was first compared to those of manual continuous curvilinear capsulorrhexis, with each procedure performed by an experienced cataract surgeon (M.S.) in a series of five ex vivo porcine eyes with an intended 5-mm diameter.

The LenSx laser system (LenSx Lasers Inc, Aliso Viejo, Calif) uses a curved contact lens to applanate the cornea. The location of the crystalline lens surface is determined following applanation using proprietary optical methodology. A 5-mm diameter capsulotomy procedure was performed by scanning a cylindrical pattern starting at least 100 µm below the anterior capsule and ending at least 100 µm above the capsule. Proprietary energy and spot separation parameters, which had been optimized in previous studies, were used for all laser procedures. Following the laser procedure, a corneal incision was created and the cut capsule was removed with forceps under a standard ophthalmic operating microscope.

For manual capsulorrhexis procedures, a round corneal marker was initially used to aid the surgeon in creating the correct size and shape capsulorrhexis. The porcine eye negligibly magnifies images at the pupillary plane (approximately 1.06×) due to its flat keratometry and shallow anterior chamber.[15-17] For this reason, a 5-mm corneal marker was used to guide the planned 5-mm capsulorrhexis. Continuous curvilinear capsulorrhexis was performed with the aid of a standard ophthalmic operating microscope and a cystotome. After creation of the capsulotomy by each method, the cornea was excised and the diameter of the capsular aperture was measured directly using digital calipers (Mitutoyo Corp, Aurora, Ill).

Scanning Electron Microscopy (SEM). The capsular edge morphology of standard capsulorrhexis and femtosecond laser capsulotomy procedures was also compared by SEM. Five procedures were performed with each device as described above, after which, the majority of the anterior lens capsule (inclusive of the capsulotomy) was carefully excised with scissors. This anterior lens capsule specimen was then fixed in Karnovsky Fixative (2% paraformaldehyde/2.5% glutaraldehyde in 0.1 M phosphate buffer). Samples were then subjected to successive dehydration steps and prepared for SEM.

Capsular Edge Strength. To compare capsular edge strength following femtosecond laser capsulotomy and manual capsulorrhexis, the diameter at which rupture occurred was determined for each procedure.[18] Following capsulotomy creation by each method as described above, the lens material was removed using an irrigation/aspiration device (Legacy 2000; Alcon Laboratories Inc, Ft Worth, Tex) in a series of porcine eyes. Castroviejo caliper (Rhein Medical, St Petersburg, Fla) with rounded tips was then introduced into the capsular aperture and the unstretched diameter recorded. Because the capsule aperture created by manual capsulorrhexis was not uniformly circular, the average of x- and y-diameters was used for this analysis. The tips were then slowly opened to stretch the capsular tissue. The diameter at which the capsule edge ruptured was then recorded and the circumference stretching ratio (R) between the stretched and unstretched circumference was computed. Analysis was performed with a minimum of eight eyes for each group, with a planned 5-mm central, anterior capsulotomy aperture.

Lens Fragmentation. Porcine eyes from animals at least 5 years of age were used to compare ultrasonic time and power requirements between traditional divide-and-conquer phacoemulsification methods and phacofragmentation using laser segmentation of the lens nucleus. The lens nucleus in the eyes from these older animals is consistently dense, requiring ultrasound power for complete lens removal. In the first group of eyes (n=12, manual group), grooves were created with an Alcon Legacy 2000 in perpendicular meridians. The lens was then divided into quarters and removed with a combination of phacoemulsification and irrigation/aspiration. In the second group of eyes (n=12, femtosecond group), the lens was subjected to a cross-pattern femtosecond laser treatment to create four equal segments. The laser pattern consists of two ellipsoidal planes (6 mm in length) that intersect at the center at depths starting 1000 µm above the posterior capsule and continuing anteriorly, to less than 1000 µm below the anterior capsule. Proprietary energy and spot separation parameters, which had been optimized in previous studies, were used for all laser procedures. Following introduction of the phacoemulsification probe, the fragmented lens quadrants were removed with a

TABLE 1

Baseline Characteristics of Nine Eyes That Underwent Femtosecond Laser Cataract Surgery

	Mean±SD	Median	Range
Spherical equivalent refraction (D)	−0.30±2.60	0.0	−4.70 to 2.50
Axial length (mm)	23.6±1.1	23.5	22.3 to 26.1
Central corneal thickness (μm)	534±30.2	535	491 to 593
Anterior chamber depth (mm)	3.4±0.5	3.5	2.6 to 4.0
Lens thickness (mm)	4.2±0.4	4.3	3.4 to 4.7
Nuclear density	1.7±0.3	1.5	1.5 to 2.0

combination of phacoemulsification and irrigation/aspiration, with ultrasonic power and time recorded for each sample.

In Vivo Human Studies

The study was conducted in compliance with the Declaration of Helsinki, as well as with applicable country and local requirements regarding ethics committee/institutional review boards, informed consent, and other statutes or regulations regarding protection of the rights and welfare of human subjects participating in biomedical research.

The objective of this study was to evaluate the ability of the intraocular femtosecond laser to successfully perform an anterior capsulotomy and phacofragmentation during cataract surgery. Nine eyes of nine patients (four men, five women) scheduled to undergo cataract/IOL surgery were enrolled in this preliminary study following preoperative screening for eligibility and informed consent. Patients with active ocular disease, poorly dilated pupils, previous ocular surgery, or known zonular weakness were excluded from the study. Mean patient age was 61 years (range: 48 to 77 years). Preoperative refractive data, axial length, corneal thickness, anterior chamber depth, lens thickness, and lens density (0=very soft, 1=semisoft, 2=medium, 3=hard, 4=very hard) are shown in Table 1.

After pupillary dilation (1 drop of tropicamide 0.5% every 15 minutes × 3) and instillation of topical anesthesia (proparacaine HCl 0.5%) or retrobulbar anesthesia (using 1.5 to 2.0 cc of 2% lidocaine and 0.5% marcaine 50/50 mixture), the following nine procedure combinations were performed: lens fragmentation only (n=3), anterior capsulotomy only (n=3), and combined lens fragmentation and anterior capsulotomy (n=3). All laser procedures were performed using the LenSx laser system. The lens fragmentation laser pattern consists of two ellipsoidal planes that intersect at the center with the height of the cross-pattern programmed to provide a 1-mm clearance from the posterior and anterior lens surface. The height of the cylindrical pattern to perform capsulotomy was programmed at least 100 µm below and above the anterior capsule, with a diameter setting of 4.5 mm for both patterns. Proprietary energy and spot separation parameters, which had been optimized in previous studies, were used for all laser procedures. After programming, the surgical pattern was centered by the surgeon (Z.N.) in the dilated pupil and initiated using the footswitch, with combined fragmentation and capsulotomy laser procedures performed in approximately 1 minute. Immediately after the laser procedure, patients were evaluated with optical coherence tomography (Visante OCT; Carl Zeiss Meditec, Fremont, Calif) to assess the laser incisions.

The patient was then prepped and draped for surgery, which was performed using standard sterile techniques and instrumentation. Upon removal of the laser-created anterior capsulotomy, the specimen was laid over the cornea and flattened. The diameter was directly measured at two perpendicular axes using a Barraquer caliper (Asico, Westmont, Ill). Standard phacoemulsification was then performed to complete the procedure. In cases where laser phacofragmentation was performed, the nucleus was separated into four pieces using gentle pressure from the phaco probe. For non-lasered lens treatments, a two-section divide-and-conquer nucleofractis technique was performed to allow segmentation into four quadrants and subsequent emulsification. Ultrasound power and time were recorded for each case. Following removal of the lens cortex, an IOL was implanted in the capsular bag.

Patients followed a standardized postoperative regimen consisting of one drop of tobramycin 0.3% and dexamethasone 0.1% ophthalmic suspension four times a day for 7 to 10 days. Postoperatively, patients were seen at the standard intervals following cataract surgery at day 1, 1 week, and 1 month.

TABLE 2

Capsulotomy Diameter Comparison for 5-mm Intended Capsulorrhexis in Ex Vivo Porcine Eyes

	Mean±SD (Range) [95% CI]	
Measured Axis	**Manual Capsulorrhexis (n=12)**	**LenSx Femtosecond Laser (n=10)**
X-diameter	5.76±0.72 (4.71 to 6.80) [5.30-6.21]	5.02±0.04 (4.94 to 5.07) [4.99-5.05]
Y-diameter	6.00±0.81 (4.90 to 7.39) [5.48-6.51]	5.02±0.04 (4.94 to 5.07) [4.99-5.05]
Mean diameter	5.88±0.73 (4.88 to 6.83) [5.42-6.34]	5.02±0.04 (4.94 to 5.07) [4.99-5.05]
Mean error (%) (mm)	0.88 (17.6)	0.02 (0.4)

SD = one standard deviation, CI= confidence interval

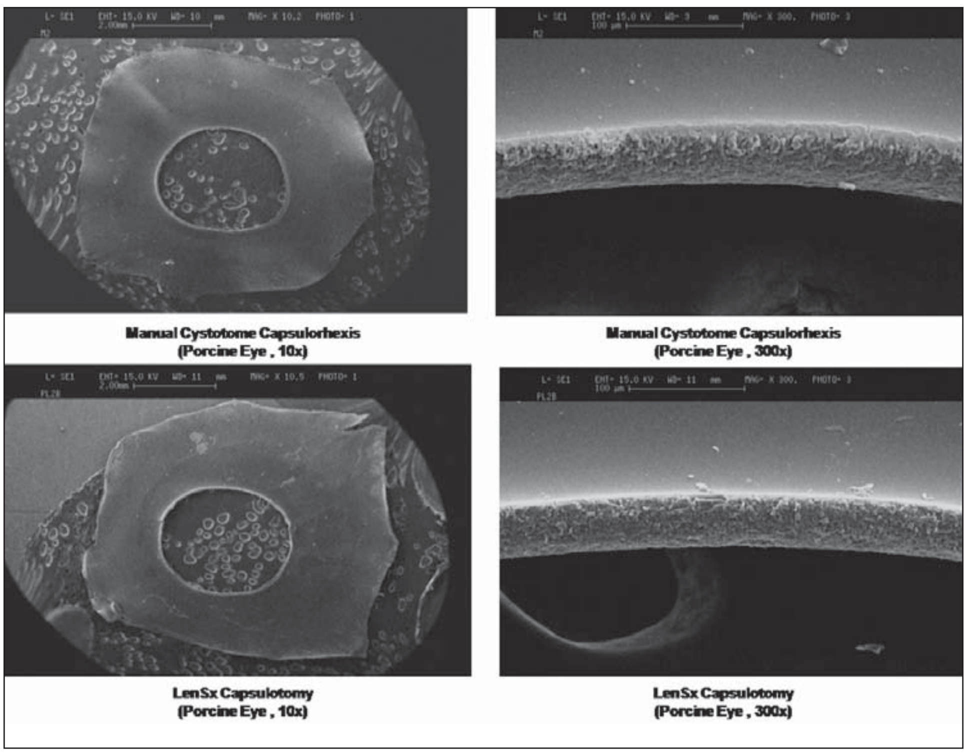

Figure 1. Scanning electron microscopy of capsulotomies in porcine eyes created manually by the surgeon and those created with the LenSx femtosecond laser.

RESULTS

Ex Vivo Porcine Studies

Capsulotomy Diameter Measurements. As shown in Table 2, reproducibility of capsulotomy dimensions created with the LenSx femtosecond laser was significantly higher than that of manual capsulorrhexis ($P<.001$, F-test). This significant difference was found despite physical marking of the desired capsulorrhexis diameter in manual procedures, a step that is generally not performed clinically. Capsulorrhexis produced noncircular capsulotomies, with an average difference of approximately 300 µm between the x- and y- diameters. Capsulotomies created by femtosecond laser were uniformly circular with no measurable difference between the x- and y-diameters. The accuracy of the anterior capsulotomies created with the femtosecond laser was also significantly higher than that for manual capsulorrhexis ($P<.001$).

Scanning Electron Microscopy. Recent studies suggest that edge morphology may predict capsular edge strength and resistance to capsular tears, with smooth regular edges being the most favorable.[18] As seen in Figure 1, which shows representative images of manual capsulorrhexis and LenSx capsulotomies (at 10× and 300× magnifications), the edge features of the laser capsulotomy were at least as smooth as those of the manual capsulorrhexis.

Capsular Edge Strength. Results of the stretching test for both capsulotomy techniques are shown in Table 3. The stretching ratio of capsule apertures created by the LenSx femtosecond laser was greater than that

TABLE 3

Tissue Stretching Test Results in Porcine Eyes for Capsule Apertures Created by Manual Capsulorrhexis and LenSx Femtosecond Laser

Group	Circumference Stretching Ratio (Mean±SD, Range)
Manual capsulorrhexis (n=8)	1.98±0.08 (1.84 to 2.09)
LenSx laser (n=10)	2.13±0.03 (2.07 to 2.17)

Note. More stretching means a stronger capsulorrhexis.

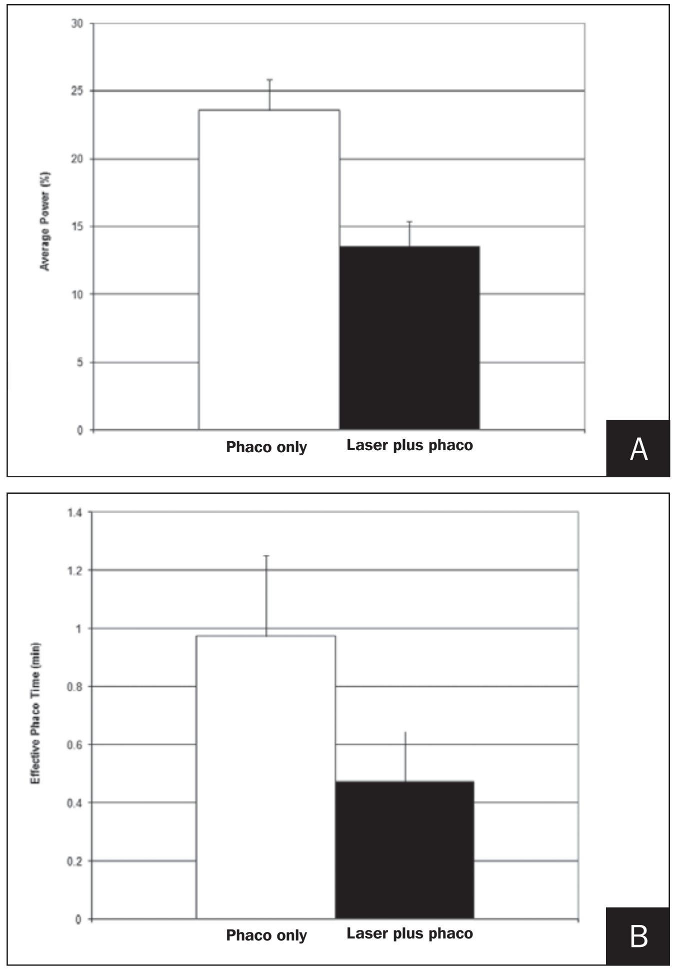

Figure 2. A) Comparison of average phaco power between the two groups of porcine eyes showed a 43% reduction in the eyes pre-treated with the LenSx femtosecond laser ($P<.001$). **B)** Comparison of effective phaco time between the two groups of porcine eyes showed a 51% reduction in the eyes pre-treated with the LenSx femtosecond laser ($P<.001$). Error bars indicate one standard deviation.

created by manual anterior capsulotomy ($P<.001$), with the values for manual capsulorrhexis similar to those found in other reports.[18]

Phacofragmentation. As seen in Figure 2, average phaco power was reduced 43% ($P<.001$) in eyes undergoing phacofragmentation, with a 51% reduction in effective phaco time ($P<.001$).

In Vivo Human Procedures

Capsulotomy Creation. Isolated capsulotomy was performed in three eyes, with an additional three eyes undergoing combined laser capsulotomy and fragmentation procedures. Laser capsulotomy procedures used the same cylindrical pattern as evaluated in porcine eyes. Optical coherence tomography performed immediately after laser treatment revealed a complete cut edge in all scanned meridians, with slight retraction of the cut edge (Fig 3).

The anterior capsulotomy was complete in all eyes and did not require the use of scissors to cut any intact portion. No radial tears were observed after any of the procedures. In all cases, the achieved diameter of the specimen (in both axes) equaled the intended diameter to within the accuracy of the caliper, producing a mean diameter error of 0.0 mm.

Phacofragmentation. Laser procedures were performed in three eyes, with an additional three eyes undergoing combined laser capsulotomy and fragmentation procedures. Laser fragmentation procedures used the same cross-pattern as evaluated in porcine eyes. Optical coherence tomography performed immediately after laser treatment (see Fig 3) demonstrated that the laser fragmentation pattern was effectively delivered, with division of the nucleus into smaller segments easily performed prior to phacoemulsification (Fig 4).

Lens removal was uneventful in all eyes, with successful IOL implantation. The IOL was centered in all study eyes, and no posterior capsule tears were observed. The surgeon determined that all capsulotomies were well-centered based on visual inspection with the operating microscope. Lenses that received laser fragmentation were easily divided into segments, with decreased phaco power/time requirements to complete the lens removal than eyes not undergoing laser phacofragmentation.

Postoperative Slit-lamp Findings. Trace to mild corneal edema was observed in seven of the nine study eyes at day 1, consistent with standard procedures performed by the same surgeon. In each of these cases, edema was completely resolved at 1-week follow-up. No corneal abrasions were observed following the laser procedure or during postoperative follow-up.

Trace anterior chamber cells and flare were present in six eyes at day 1 follow-up. These observations were again consistent with standard procedures performed by the same surgeon, with complete resolution by 1 week in all eyes. Preoperatively and through

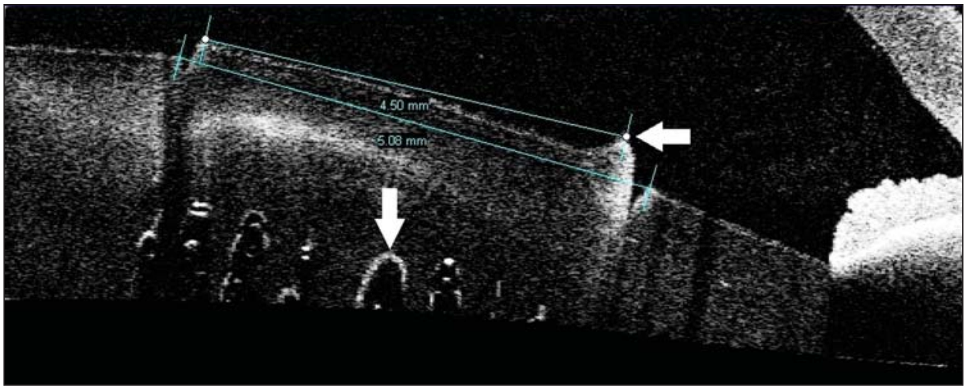

Figure 3. Optical coherence tomography of an eye immediately following femtosecond laser capsulotomy and phacofragmentation with the LenSx laser. Intralenticular bubbles are seen at the nuclear cleavage plane (down arrow). Accurate diameter and complete separation of the anterior capsule without residual adhesion is also shown (left arrow).

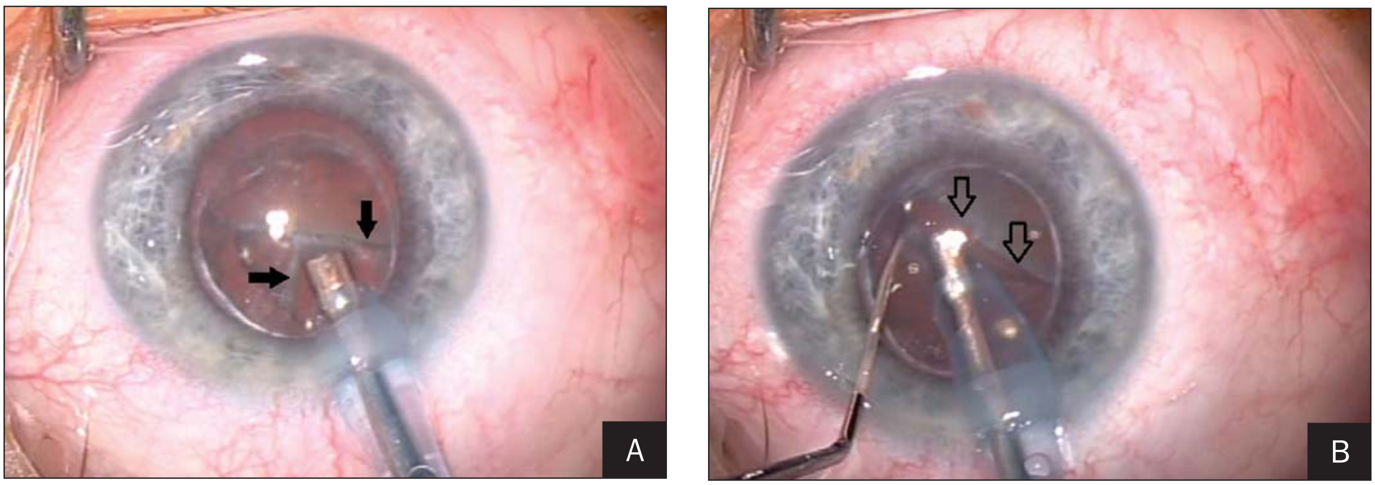

Figure 4. A) Intraoperative image showing the femtosecond laser phacofragmentation X-pattern (arrows) dividing the nucleus into four equal segments. **B)** Spreading of the cut segments demonstrate the straight cleavage (arrows) created by the LenSx femtosecond laser.

the course of follow-up, all patients had normal pupil examination, with no evidence of iris damage, atrophy, or transillumination defects observed in any eye during the course of the study.

Postoperative Visual Acuity Results. Visual acuity was measured at baseline and at 1 day, 1 week, and 1 month. Corrected distance visual acuity was 20/40 or better in seven (77.8%) of nine eyes at 1 day and in nine (100%) of nine eyes at 1 week. At 1 month postoperatively, all eyes were 20/20.

Intraocular Pressure (IOP). Mean IOP at baseline for the total population was 13.8 mmHg (range: 10 to 18 mmHg). Mean IOP at 1 day, 1 week, and 1 month was 16.1 mmHg (range: 12 to 19 mmHg), 16.0 mmHg (range: 15 to 18 mmHg), and 14.2 mmHg (range: 11 to 18 mmHg), respectively. None of the eyes had IOP >21 mmHg at any time point.

Complications and Adverse Events. No adverse events or complications occurred during the course of the study.

DISCUSSION

We evaluated the LenSx femtosecond laser for intraocular procedures, including incisions in the lens capsule and fragmentation of the lens nucleus. Laser-created anterior capsulotomies created ex vivo were more uniform, accurate, and predictable than those produced by manual capsulorrhexis. Interestingly, laser capsular edge strength, as indicated by the ratio of maximally stretched to unstretched circumference, was at least as great as that with manual capsulorrhexis. The presented ex vivo studies in porcine eyes also suggest that reductions in phaco power and time may be seen when laser phacofragmentation is performed in conjunction with phacoemulsification.

Initial procedures performed in humans further support the feasibility of the LenSx intraocular femtosecond laser system to enhance the safety and reproducibility of two of the most critical steps in the cataract surgery procedure, anterior capsulotomy and phacofragmentation. In contrast to previous attempts aimed at improving manual capsulorrhexis using physical or virtual calipers,[5,19,20] the precision of laser-created capsular incisions is largely surgeon independent and potentially more flexible in terms of size, shape, and positioning. Although refractive outcome was not the focus of this initial report, the importance of perfectly sized and symmetrically shaped capsulotomy in refractive performance is increasingly being recognized.[5,21,22] In comparison to earlier laser phacofragmentation techniques with Nd:YAG and erbium:YAG laser systems,[23-27] the femtosecond laser procedure can divide the nucleus with low-energy pulses and without the need to physically enter the eye, thereby simplifying the phacoemulsification procedure.

Although additional clinical studies are required to further evaluate the potential clinical advantages and limitations of femtosecond laser technology in cataract surgery, no safety issues were identified in this pilot study. Importantly, the laser wavelength is not absorbed by the cornea. Unlike the large shock and acoustic waves generated by the phacoemulsification device, which can be associated with endothelial cell damage,[28-31] those generated by femtosecond photodisruption dissipate within approximately 100 µm of the targeted lens tissue that is millimeters from the cornea.[9,32-36] Similarly, the maximum retinal fluence from the LenSx is approximately five times less than the multiple shot damage threshold determined by Schumacher et al.[37] These findings are consistent with the safety record established for femtosecond laser corneal surgery in over 2 million procedures over the past decade.

AUTHOR CONTRIBUTIONS

Study concept and design (Z.N., M.S.); data collection (Z.N., A.T., T.F.); interpretation and analysis of data (M.S.); drafting of the manuscript (Z.N., M.S.); critical revision of the manuscript (A.T., T.F., M.S.)

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