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Effect of the Femtosecond Laser on an Intracorneal Inlay for Surgical Compensation of Presbyopia during Cataract Surgery: Scanning Electron Microscope Imaging

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ABSTRACT
Purpose: To investigate the effect of the femtosecond laser-assisted cataract surgery (FLACS) on porcine eyes implanted with a Kamra corneal inlay and to describe how the inlay may change the effect of the femtosecond laser on the lens.
Methods: FLACS was performed on six porcine eyes and a Kamra corneal inlay had been implanted, exploring the lens under the surgical microscope. Another Kamra corneal inlay was attached to the upper part of the transparent hemisphere used for calibration of the femtosecond laser. Capsulorhexis, arcuate incisions, and phacofragmentation were carried out. The Kamra corneal inlay was compared with a nontreated one using a scanning electron microscope (SEM), and the hemisphere was analyzed with a surgical microscope.
Results: Capsulorhexis and phacofragmentation were completed in all the porcine eyes, although accuracy to determine the exact effect on the lens was not possible to achieve. The effect of the femtosecond laser on the PMMA hemisphere through the Kamra corneal inlay showed the capsulorhexis was placed outside the outer margin of the inlay and a sharply sculpted fragmentation pattern with a three-dimensional (donut-shaped) annulus untreated beneath it. SEM images of the nontreated and the treated inlays were comparable. No ultrastructural changes were found in the treated Kamra corneal inlay.
Conclusions: FLACS can be performed with a Kamra corneal inlay for surgical compensation of presbyopia without the risk of damaging the inlay. The Kamra corneal inlay acts as a screen that avoids the laser to reach the areas beneath its shadow, but not the exposed areas of the lens.

Introduction
With the aging population and change in demographics, presbyopia and cataracts have probably become two of the most common problems the ophthalmologist have to manage daily in the clinical practice. According to recent estimates, more than 2 billion people worldwide are presbyopic, and cataract surgery remains the most commonly performed ophthalmic surgery with 18 million procedures performed globally every year. The World Health Organization estimates that this number will increase to 32 million by the year 2020 as the over-65-year population doubles worldwide between 2000 and 2020.

Presbyopia treatment with corneal inlays goes back to Barraquer, who implanted the first one in 1949. Since then, several designs and materials have been developed, and different surgical implantation techniques have been studied.

The Kamra intracorneal inlay (Acufocus, Inc., Irvine, CA, USA) utilizes the pinhole effect to increase the depth of focus in the implanted eye, restoring the intermediate and near vision without a significant impact in the distance visual acuity. Patients suitable for this technique are 40–65 years old presbyopes with no cataracts who seek for a reversible solution for their near vision problem. As well as those young LASIK patients operated decades ago have become presbyopes and now demand surgical solutions. Patients with corneal inlays will develop cataracts and will need surgery in the future, probably demanding the newest technology available for their pathology. At this point, femtosecond laser-assisted cataract surgery (FLACS) has rapidly evolved in the past few years, with several clinical studies supporting improvements in capsulotomy, lens fragmentation, incisions, macular thickness, and endothelial cell count when compared with traditional phacoemulsification.

In this study, we examined the effect of FLACS in porcine eyes where a Kamra corneal inlay was previously implanted, and in the PMMA (poly-methyl methacrylate) hemisphere used for femtosecond platform calibration after the inlay was adhered to the upper surface. Macroscopic and microscopic images of the porcine eyes and the PMMA hemisphere, besides scanning electron microscope (SEM) images from a nontreated Kamra corneal inlay and another one after the effect of the femtosecond laser, were analyzed.

Materials and methods
Porcine study
Six freshly enucleated porcine eyes obtained from animals sacrificed for human consumption in authorized facilities for
food industry were selected for the in vivo part of the study. The technique chosen to implant the Kamra corneal inlay was the creation of a corneal pocket. The first three eyes received a small corneal pocket (Pocket 1) that offered some difficulties to introduce the inlay, so a bigger pocket (Pocket 2) was programmed for the rest of the eyes in order to reduce manipulation and therefore, corneal edema. Depth of the dissection plane selected for all cases was 200 μm. Parameters required by the femtosecond laser (Intralase™ FS Laser, Abbot Medical Optics, Inc., Abbot Park, IL, USA) to perform the corneal cut are summarized in Table 1.

The Kamra corneal inlay was inserted through the corneal incision into the pocket and centered in the pupil, so as to leave enough space between the border of the inlay and the pupillary margin to fit a 5 mm capsulorhexis in all cases. Air bubbles accumulated in the interface were extracted by rubbing gently with a spatula over the epithelium. Corneal edema in the incision appeared in all cases, but did not interfere with femtosecond laser effect over the lens in any of the eyes.

Once the Kamra corneal inlay was correctly placed in the pocket and nicely centered, the femtosecond laser suction ring (Catalys® Precision Laser System, Abbot Medical Optics, Inc.) was fixated and filled with balanced saline solution (BSS® Balanced Salt Solution, Alcon Laboratories, Inc., Fort Worth, TX, USA), and docked into the laser lens. Besides the 5 mm capsulorhexis already mentioned above, the fragmentation pattern selected was “octants” with a 300 μm grid (softening). The inlay was extracted from the cornea and the eye was analyzed under the surgical microscope to check for capsulorhexis and fragmentation.

### PMMA hemisphere study

The femtosecond laser platform used for the study works with a noncontact or fluid-filled interface system. If the Kamra corneal inlay would have been just placed over the PMMA hemisphere and not fixated, when the saline solution was poured, the corneal inlay would have floated. In order to avoid this situation, it had to be attached to the hemisphere surface with glue (Loctite, Henkel Ibérica S.A., Barcelona, Spain) in the four cardinal points right in the edges so as to preserve its structure. Once it was correctly placed, fixated, and centered, the suction ring was applied, filled with BSS, docked into the system and treated (Figure 1). The intraoperative optical coherence tomography (OCT) that is integrated in the femtosecond platform recognized the border of the Kamra corneal inlay as the pupillary margin. Corrections were needed in order to fit the capsulorhexis outside of the inlay with a 5 mm intended diameter. A simulated posterior corneal surface and lens had to be designed and introduced in the system so the treatment could be performed as if it was a real eye (Figure 2). Two arcuate incisions in the 180° axis were programmed to mark the Kamra corneal inlay (Figure 3). This way, we could later distinguish the treated corneal inlay from the nontreated one during SEM analysis.

Fragmentation pattern chosen in this part of the study was “quadrants” with a 300 μm grid (softening). The treatment was completed successfully, and the glass hemisphere was analyzed under the surgical microscope to describe

![Figure 1. Kamra inlay attached to the upper part of the PMMA hemisphere with the suction ring ready to be docked in the system.](image1)

![Figure 2. Optical coherence tomography (OCT) of the femtosecond laser platform shows modifications required to begin the treatment on the PMMA model.](image2)

<table>
<thead>
<tr>
<th>Pocket 1</th>
<th>Lamellar depth: 200 μm</th>
<th>Posterior depth: 230 μm</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Diameter: 4.0 mm</td>
<td>Diameter: 4.7 mm</td>
</tr>
<tr>
<td></td>
<td>Energy: 1.50 mJ</td>
<td>Energy: 2.50 mJ</td>
</tr>
<tr>
<td></td>
<td>Method: Raster</td>
<td>Cut angle: 90°</td>
</tr>
<tr>
<td>Pocket 2</td>
<td>Lamellar depth: 200 μm</td>
<td>Posterior depth: 230 μm</td>
</tr>
<tr>
<td></td>
<td>Diameter: 6.5 mm</td>
<td>Diameter: 7.2 mm</td>
</tr>
<tr>
<td></td>
<td>Energy: 1.50 mJ</td>
<td>Energy: 2.50 mJ</td>
</tr>
<tr>
<td></td>
<td>Method: Raster</td>
<td>Cut angle: 70°</td>
</tr>
</tbody>
</table>

### Table 1. Parameters required by the femtosecond laser (Intralase™ FS Laser) to perform the corneal pocket to insert the intracorneal inlay for presbyopia correction.
details about the effect of the femtosecond laser on the glass through the Kamra corneal inlay.

**Kamra corneal inlay specifications**

The Kamra corneal inlay used in this study was the latest model (ACI 7000PDT). It is made up of polyvinylidene fluoride (PVDF) and nanoparticles of carbon. The outer and inner diameters of the inlay are 3.8 and 1.6 mm, respectively, and it is 5 μm thick. In order to allow nutrient flow through the cornea, but to diminish photic phenomena, there are 8400 perforations, 5–11 μm wide, with higher concentration in the center of the annulus than in the periphery and randomly distributed. The microperforations allow a 5% light transmission rate through the inlay into the eye (Acufocus, Inc.

**Scanning electron microscope imaging**

Two Kamra corneal inlays were prepared according to the SEM technician indications (metalization with gold) to be analyzed: “Kamra 1,” a nontreated inlay brought directly for us from the supplier with no previous clinical use, and the “Kamra 2,” treated with the Catalys platform over the PMMA hemisphere. Order of magnification and description of the images are summarized in Table 2.

The model of SEM utilized for the Kamra analysis was JEOL JSM 6400 placed in the National Centre of Electronic Microscopy (ICTS, Universidad Complutense de Madrid, Madrid, Spain) that works with a thermoionic cathode electron spotlight with tungsten filament. The image resolution with secondary electron detection (25 kV) is 3.5 nm with 8 mm work distance and 10.0 nm with 39 mm work distance. With retrodispersed electron detection, the image resolution is 10.0 nm with 8 mm work distance (ICTS Centro Nacional de Microscopía Electrónica. Data available at www.cnme.es).

### Table 2. Order of magnification and description of the scanning electron microscope (SEM) imaging of Kamra 1 (non-treated) and Kamra 2 (treated).

<table>
<thead>
<tr>
<th>Magnification</th>
<th>Kamra 1 (non-treated)</th>
<th>Kamra 2 (femto-treated)</th>
</tr>
</thead>
<tbody>
<tr>
<td>25×</td>
<td>General view: arcuate incisions and damage in the borders (manipulation)</td>
<td>General view: arcuate border visible</td>
</tr>
<tr>
<td>80×</td>
<td>General view: inlay margins and hole distribution Caliper: 7 mm</td>
<td>General view: arcuate border visible Caliper: 100 μm</td>
</tr>
<tr>
<td>400×</td>
<td>Precise image of a hole Caliper: 10 μm</td>
<td>10 μm</td>
</tr>
<tr>
<td>2000×</td>
<td>Hole width from border to border: 11.5 μm Caliper: 10 μm</td>
<td>Hole width from border to border: 10.4 μm Caliper: 10 μm</td>
</tr>
<tr>
<td>4000×</td>
<td>Inclined image to see the hole material accumulated in the margins Caliper: 100 μm</td>
<td>High-magnification image of the surface of the non-treated Kamra. Precise image of two holes. Caliper: 20 μm</td>
</tr>
<tr>
<td>5000×</td>
<td>Hole width from border to border: 10.4 μm Caliper: 10 μm</td>
<td>High-magnification image of the surface of the nontreated Kamra; particles of the saline solution used for the femtolaser treatment can be seen Caliper: 10 μm</td>
</tr>
</tbody>
</table>

### Results

#### Porcine study

The Kamra corneal inlay could be implanted in the cornea of the six porcine eyes with no complications. Manipulation of the incision needed to introduce the inlay in the pocket was higher in porcine eyes than in real cases of human patients, probably due to the lower intraocular pressure of animal enucleated eyes. Corneal edema appeared in the incision area but did not interfere with femtosecond laser application during capsulorhexis and phacofragmentation. Figure 4 shows
one of the porcine eyes docked in the femtosecond platform with the Kamra inlay implanted in the cornea, capsulorhexis being performed around the inlay, and phacofragmentation visible inside and around the inlay.

Once the treatment was completed, each porcine eye was analyzed under the surgical microscope. The cornea was extracted to acquire a general view of the lens with the capsulorhexis and fragmentation. We could confirm capsulorhexis had been performed in all the eyes, with incomplete cut and adhesions left only in the area beneath the Kamra inlay implantation and FLACS) were performed simultaneously. In two clinical cases where a Kamra inlay had been implanted the inlay created a pocket 80 μm below a previous LASIK flap, with a reported improvement in near vision without significant impact on distance vision. According to these promising results, it is presumable that the number of patients receiving this type of implants will increase every year, and many of them will develop cataracts.

Phacoemulsification with a corneal inlay poses some questions about technical difficulties, biometry, and visual outcomes. Surgical technique has already been described by Tan et al.18 in two clinical cases where a Kamra inlay had been previously implanted. Besides the need for some ocular rotations during capsulorhexis and phacoemulsification to improve visualization, no other modifications to their usual technique were required. According to their results, biometry readings were reliable and the SRK-T formula was accurate for intraocular lens power calculation.

In our study it was possible to perform the capsulorhexis and fragmentation in porcine eyes and in the PMMA hemisphere used for calibration of the femtosecond platform. SEM images from the nontreated (Kamra 1) and treated (Kamra 2) inlays showed in detail the structure of both inlays. Further than the arcuate incisions (Figure 6a) of the treated Kamra (that allowed to distinguish macroscopically Kamra 1 from Kamra 2) and some saline particles accumulated on the surface of Kamra 2 (Figure 6b), we found no more differences with SEM images up to 5000×. The random distribution of the holes appeared to be comparable and the diameters of the holes were pretty much alike ranging from 10 to 11.5 μm (Figure 6c, d).

**Effect of the femtosecond laser on an intracorneal inlay for surgical compensation of presbyopia during cataract surgery: Scanning electron microscope imaging**

Several authors have reported their results with intracorneal inlays for presbyopia treatment. Seyeddain,8 Dexl,9 and Yilmaz15 found the Kamra small-aperture inlay to be safe and effective for emmetropic presbyopic patients. Tomita16 implanted the inlay in combination with LASIK to treat both ametropia and presbyopia, reporting patient satisfaction with their decreased dependence on reading glasses regardless of the preoperative spherical equivalent range. In other study, the same author implants the inlay creating a pocket 80 μm below a previous LASIK flap, with a reported improvement in near vision without significant impact on distance vision. According to these promising results, it is presumable that the number of patients receiving this type of implants will increase every year, and many of them will develop cataracts.

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In our study it was possible to perform the capsulorhexis and fragmentation in porcine eyes and in the PMMA hemisphere used for calibration of the femtosecond platform. Manipulation of the incision needed to introduce the inlay in the pocket in porcine eyes was higher than in our real cases of human patients, probably due to the lower intraocular pressure of animal enucleated eyes. Corneal edema appeared in the incision area of the porcine eyes, but did not interfere with femtosecond laser application during capsulorhexis and phacofragmentation. Corneal edema during FLACS in a patient previously implanted with a Kamra corneal inlay could interfere with femtosecond laser due to corneal opacity. This complication could happen if both procedures (corneal inlay implantation and FLACS) were performed simultaneously, or if the patient had corneal edema not detected previous to surgery.

Microscopical examination of the model allowed us to describe in detail how the femtosecond laser would potentially strike the lens, with a perfectly shaped effect in all the exposed areas and an annular zone beneath the corneal inlay.

**PMMA hemisphere study**

Femtosecond arcuate incisions, 5 mm capsulorhexis and fragmentation, were successfully completed on the PMMA hemisphere. Application of the suction ring with the Kamra fixated on the surface and Catalys display image of the treatment planification are shown in Figures 1 and 3, respectively. OCT of the femtosecond laser platform with the changes required to begin the treatment in the PMMA model are displayed in Figure 2.

Once the treatment had finished, the hemisphere was analyzed under the surgical microscope to assess where and how the femtosecond had reached the PMMA material. Capsulorhexis was perfectly performed around the outer margin of the inlay. Fragmentation (quadrants with 300 μm grid softening) was visible but the accuracy to determine where and how it had reached the lens was not possible to assess. For this reason, we decided to perform the same study in the PMMA hemisphere used for calibration of the femtosecond platform.

**Figure 5.** Capsulorhexis and phacoemulsification are sculpted in the PMMA hemisphere. A three-dimensional annulus beneath the corneal inlay is not treated and remains clear.
that remains untreated. We believe that the Kamra corneal inlay acts as a “screen” that prevents the laser to reach the lens. Since capsulorhexis is outside of the inlay, it is not affected by this “screen” effect and therefore can be performed as usual.

The question about how the femtosecond laser would affect the inlay is well documented by the SEM images of the inlay before and after the treatment. The randomized distribution of the holes remains intact, the tissue in between them shows no additional damage in the treated sample, and no presumed femtosecond impacts can be found in all the surface. Both inlays are comparable, meaning that the femtosecond laser can be safely applied in our cataract patients without the risk of damaging the inlay and with the certainty that capsulorhexis and fragmentation can be performed as in a standard cataract procedure. Femtosecond lasers use ultrashort pulses of light ($10^{-15}$ s) that provide very high power in every pulse with low energy rates. One single pulse of 100 femtoseconds with a modest energy of 3 mJ (insufficient to raise in a millionth of a Celsius degree the temperature of a water drop) delivers a 30 mW peak power. The pulse transfers the energy to the focused point with such rapidity that the heat does not reach the areas that surround the edge of the treated zone, the effect is called cold ablation.\textsuperscript{19} Mita et al.\textsuperscript{20} reported the case of a patient implanted with a Kamra corneal inlay that developed a central serous retinopathy that required photodynamic therapy. One month later, degeneration and scar were observed at the location of the inlay due to the heat and burning. This complication is not expected to occur with FLACS because heat is not delivered to the tissue. In fact, no signs of burning or any other damage to the Kamra corneal inlay could be observed using SEM imaging.

To our knowledge, this is the first study to analyze the effect of the FLACS in a Kamra corneal inlay for surgical compensation of presbyopia during cataract surgery. However, future studies upon the clinical application of this technique are needed and should be conducted.

**Acknowledgments**

The authors thank Raquel Aguejas, member of the optometrist team of our clinic, for her ability to manage the femtosecond platform during the study, and also Juan Gabriel Ortiz, engineer, for his technical support.

**Declaration of interest**

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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