One-Year Safety and Efficacy Results of a Hydrogel Inlay to Improve Near Vision in Patients With Emmetropic Presbyopia

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ABSTRACT

PURPOSE: To conduct a feasibility study of the safety and efficacy of a corneal contouring inlay as a treatment for emmetropic presbyopia.

METHODS: The Raindrop corneal inlay (ReVision Optics, Inc., Lake Forest, CA) was implanted on the corneal stromal bed beneath a keratotomy flap in 20 nondominant eyes of 20 patients. The implant is designed to cause a change in the curvature of the overlying cornea, with a subsequent multifocal change in refractive power. Efficacy outcome was defined as at least 75% of eyes with uncorrected near visual acuity of 0.3 logMAR (20/40 Snellen) or better at 6 months. Main safety outcomes were retention of preoperative best-corrected distance visual acuity and reports of adverse events. Other outcome measures included contrast sensitivity; near, intermediate, and distance visual acuities; patient satisfaction; spectacle use; and complications.

RESULTS: All implanted eyes achieved uncorrected near visual acuity of 0.3 logMAR (20/40 Snellen) or better by the 1-week postoperative examination and remained so throughout the 1-year follow-up period, also averaging less than 0.1 logMAR (20/25 Snellen) monocularly and binocularly throughout that period. Mean binocular uncorrected distance visual acuity remained within 0.02 logMAR of the preoperative mean throughout the study. One patient who was dissatisfied with the resulting vision underwent explantation. At 1 year, 16 of 19 patients seldom or never wore glasses and all 19 were satisfied or very satisfied with their overall vision.

CONCLUSIONS: The hydrogel corneal inlay improved uncorrected near and intermediate visual acuity in patients with emmetropic presbyopia, with high patient satisfaction and little effect on distance visual acuity.

PATIENTS AND METHODS

Informed consent was obtained from each patient before any study-specific procedures were performed. The study was approved by the institutional review board of the Universidad de Monterrey, Division de Ciencias de la Salud, Comite de Investigacion y Etica, and adhered to the tenets of the Declaration of Helsinki. Patients were included if they required a near add between +1.50 and +2.50 diopters (D), had a stable manifest spherical equivalent refraction between -0.5 and +1.00 D, and had best-corrected distance and near visual acuities of 0.1 logMAR (20/25 Snellen) or better. A monovision trial was performed and patients were implanted only after expressing satisfaction with their vision and confidence that they could conduct their lives normally after wearing a contact lens to correct the near vision of the nondominant eye for at least 5 days. The treated eye had to have a corneal thickness of 500 μm or greater and an age-appropriate minimum estimated endothelial cell density (2,000 cells/mm² for patients 45 to 55 years; 1,500 cells/mm² for patients 56 years and older). Exclusion criteria included previous ocular surgery; ocular or eyelid pathology, infection, or inflammation; corneal topographic irregularities; systemic disease or therapies that could affect wound healing or visual outcomes (e.g., diabetes, lupus, cancer); and any condition, such as pregnancy, associated with hormone fluctuations that could lead to refractive changes.

TESTING

Eye dominance was determined in all patients before surgery. Patients rapidly aligned a distant object, such as a letter on the visual acuity chart, so that they could see it through a 1-inch hole in the center of a card held with arms extended. The eye framed by the hole when the card was moved close to the face was considered the dominant eye.

Other assessments included manifest and cycloplegic refractions, intraocular pressure, slit-lamp examination, corneal pachymetry, visual acuities, contrast sensitivity, patient questionnaire, endothelial cell counts at the central cornea, and visual symptoms. Corrected and uncorrected near (40 cm) and distance (6 m) visual acuities were assessed using Early Treatment of Diabetic Retinopathy Study (ETDRS) charts with the Optec 6500 Vision Tester (Stereo Optical Co., Inc., Chicago, IL). Contrast sensitivity was measured preoperatively and at the 6- and 12-month postoperative visits under photopic and mesopic conditions using Functional Acuity Contrast Test (FACT) charts and the Optec 6500 system. A significant change in contrast sensitivity was defined as a greater than 0.30 log unit change at two or more spatial frequencies.

Ocular discomfort (pain, dryness, and discomfort) and visual symptoms (glare, halos, blurred vision, double vision, and fluctuations in vision) were self-reported and rated from 0 (absent) to 4 (severe). The ability to perform tasks requiring vision at distance, intermediate, or near focus was assessed by patient survey. There were five tasks at each distance, and patients were asked how difficult it was to perform each task. Patient answers were scored as follows: 0 = not at all, 1 = with difficulty, and 2 = with ease. The points were added to obtain the cumulative task score at each distance.

Examinations were performed pretreatment, on the day of surgery, and at 1 day, 1 week, and 1, 3, 6, 9, and 12 months postoperatively. Examination windows increased with time (e.g., 5 to 9 days at 1 week and 11 to 14 months at 12 months).

CORNEAL INLAY

The Raindrop corneal inlay is made of a clear, permeable hydrogel material with approximately the same refractive index as the cornea (1.376), making it virtually invisible in the eye (Figure 1).

The inlay has a positive meniscus shape, with a diameter of 2 mm and a center thickness of 32 μm. The inlay has no intrinsic power because the index of refraction is the same as that of the surrounding corneal tissue; it alters the eye’s refractive power by increasing the central radius of curvature of the cornea overlying the implant. Because the inlay is thinner at the edge than in the center, the increase in anterior corneal height transitions from the region anterior to the inlay diameter, through an intermediate region, and back to the unaltered cornea. Gentle epithelial remodeling aids the smoothing between the altered and unaltered regions of the cornea.
A refraction map obtained from an iTrace wavefront aberrometer (Tracey Technologies, Houston, TX) is shown in Figure 2A. Radial annular and zonal refraction plots pertaining to the same scan are shown in Figure 2B. Both scans show the gradual change in refraction from the inlay region in the center to the largely unchanged region of the cornea beyond a diameter of approximately 3 mm, best illustrated by the annular refraction plot in Figure 2B.

**SURGICAL PROCEDURE**

The nondominant eye was prepared for keratotomy according to the site’s standard clinical procedures. A flap with a diameter of greater than 8 mm and a depth of 150 μm was created using a femtosecond laser (Intralase; Abbott Medical Optics, Santa Ana, CA). Once the flap was made, the cornea was well irrigated with chilled balanced salt solution and the patient’s eye was closed and patched for 15 minutes to allow the cornea to quiesce. The Raindrop corneal inlay was placed in the inserter according to the manufacturer’s guidelines. At the end of the 15-minute wait time, the flap was retracted and the inlay delivered from the inserter to the stromal bed. The inlay was positioned over the center of the pupil and allowed to dry for approximately 1 minute before the flap was replaced on the corneal bed.

For the first week, the following medications were prescribed: moxifloxacin hydrochloride ophthalmic solution 0.5% (Vigamox; Alcon Laboratories, Inc., Fort Worth, TX), difluprednate ophthalmic suspension 0.05% (Durezol; Alcon Laboratories, Inc.), cyclosporine ophthalmic emulsion 0.05% (Restasis; Allergan, Inc., Irvine, CA), carboxymethylcellulose sodium 0.5% (Refresh Plus Artificial Tears; Allergan, Inc.), and TheraTears Nutrition Capsules (Advanced Vision Research, Lake Forest, IL).

In one case, the inlay shifted in position postoperatively. The flap was opened and the inlay replaced approximately 1 month after the original procedure. Data shown here are relative to the exchange date.

**STATISTICAL METHODS**

Descriptive statistics were used to calculate the frequency of events defined by the primary safety and effectiveness end points for this study using the R open-source software environment for statistical computing and graphics.

The primary efficacy end point was 75% of eyes achieving 0.3 logMAR (20/40 Snellen) or better uncorrected near vision (UNVA) at 6 months or beyond. Safety measures included loss of best-corrected distance visual acuity (CDVA) and incidence of adverse events in the treated eye.

Data were found to be normally distributed when analyzed as a distribution of total letters read.

**RESULTS**

Twenty patients with presbyopic emmetropia were enrolled and implanted, although one patient left the study after the 6-month visit following inlay explantation. The study population was Hispanic, with 55% men and 45% women. The average age was 50 years, ranging from 48 to 55 years (standard deviation [SD] = 1.9). Preoperatively, mean manifest spherical equivalent was +0.07 D (SD = 0.3 D) and mean add power was +1.83 D (SD = 0.2 D).
VISUAL ACUITIES

The Raindrop implant achieved the effectiveness end point from 1 day postoperatively and was shown to be a statistically significant improvement relative to preoperatively \( (P = 1.1 \times 10^{-7}) \). Mean acuity was between 0.04 and 0.07 logMAR \((20/22 \text{ to } 20/23 \text{ Snellen})\) at all visits from 1 week onward (Figure 3). Statistical analysis again showed improvement relative to preoperatively \( (P < 10^{-10} \text{ for all visits}) \). When chronologically adjacent visits were compared, near vision was shown to have stabilized at 1 week because the \( P \) value for the 1-week to 1-month acuity change was greater than .5, as were all subsequent comparisons.

By 1 week postoperatively, mean uncorrected distance visual acuity (UDVA) was 0.14 logMAR \((20/28 \text{ Snellen})\) \( (SD = 0.1) \) and remained less than 0.2 logMAR \((20/32 \text{ Snellen})\) at all subsequent preoperative visits (Figure 3B). By 1 month postoperatively (first measurement), mean uncorrected intermediate visual acuity was 0.1 logMAR \((20/25 \text{ Snellen})\) \( (SD = 0.06) \) and remained less than 0.2 logMAR \((20/32 \text{ Snellen})\) at all subsequent postoperative visits.

Mean binocular near and distance visual acuities are shown in Figure A (available as supplemental material in the PDF version of this article). By 1 month postoperatively (first measurement), mean binocular UNVA was 0.03 logMAR \((20/21 \text{ Snellen})\) \( (SD = 0.1) \) and remained less than 0.1 logMAR \((20/25 \text{ Snellen})\) at all subsequent postoperative visits. By 1 month postoperatively (first measurement), mean binocular UDVA was 0.01 logMAR \((20/20 \text{ Snellen})\) \( (SD = 0.05) \) and remained at this level or better at all subsequent postoperative visits.

At the 12-month visit, all patients \((19 \text{ of } 19)\) had achieved CDVA of 0.05 logMAR \((20/22 \text{ Snellen})\) or better, and this was also true for best-corrected near visual acuity (CNVA). The findings showed that 42\% of patients lost at least 0.02 logMAR CDVA, and on average, patients lost 0.02 logMAR CDVA \( (SD = 0.04) \). In addition, 68\% of patients lost at least 0.02 logMAR CNVA and, on average, patients lost 0.02 logMAR \( (SD = 0.04) \). No patient lost 0.2 logMAR corrected visual acuity at near or distance in the implanted eye during any examination (including the patient who underwent explantation).

CONTRAST SENSITIVITY

Mean photopic contrast sensitivity in the implanted eye was similar to preoperative levels at both 6 and 12 months postoperatively (Figure 4). The mean change in contrast sensitivity from preoperatively was less than 0.30 log units at all frequencies, suggesting that the mean change in photopic contrast sensitivity was not clinically significant. In Figure 4, error bars indicate one standard deviation, and their overlap strengthens this conclusion, although there is some indication that losses may appear more significant with larger patient populations at higher spatial frequencies. Additionally, the 6- and 12-month postoperative contrast sensitivity values were well within the normal range for phakic eyes.10,11

SPECTACLE WEAR AND SATISFACTION

Patients completed a spectacle use and satisfaction questionnaire at the preoperative examination and at all postoperative visits. Preoperatively, 7\% \((1 \text{ of } 14)\) of patients seldom or never wore corrective lenses; 12 months postoperatively, 84\% \((16 \text{ of } 19)\) of patients reported that they seldom if ever used corrective lenses.

At 12 months, 95\% \((18 \text{ of } 19)\) of patients reported that they were satisfied or very satisfied with their near vision, and 95\% \((18 \text{ of } 19)\) were satisfied or very satisfied with their intermediate vision. All patients \((19 \text{ of } 19)\) reported that they were satisfied or very satisfied with their distance vision. Similarly, all patients \((19 \text{ of } 19)\) reported that they were satisfied or very satisfied with their overall visual outcome. Similar satisfaction scores were recorded at all postoperative visits at which the
questionnaire was used (1 month onward). No patient reported being very dissatisfied at any range at any visit, and no patients reported being dissatisfied at near, distance, or overall from the 9-month visit onward.

**Task Assessment**

Patient responses to task ability were scored as 0 = not at all, 1 = with difficulty, and 2 = with ease for five tasks for near, intermediate, and distance vision. The points were added to obtain a cumulative task score for each distance, with a maximum score of 10. The specific tasks are shown in Table 1.

Distance tasks were performed with ease preoperatively and throughout the postoperative period. There was a slight increase in the ease of performing intermediate tasks postoperatively compared with preoperatively, as well as a substantial increase in the patients’ ability to perform near tasks (Figure B, available as supplemental material in the PDF version of this article). Eleven patients (58%) reported being able to perform all 15 tasks “with ease” at 12 months.

**Visual Symptoms**

Patients rated their visual symptoms (glare, halos, blurred vision, double vision, and fluctuation in vision) on a scale of 0 (absent) to 4 (severe). All responses were added to obtain a total score between 0 and 20, and an average of these scores was taken to provide an indicator between 0 and 4. Similarly, a summary score was calculated for ocular discomfort (pain, dryness, and discomfort) that summed to a value between 0 and 12 that could be averaged to a score between 0 and 4. These averages are shown for each visit in Figure C (available as supplemental material in the PDF version of this article).

The mean ocular discomfort score hardly varied from preoperative levels (preoperative = 0.37, 12 months = 0.26), whereas the mean visual symptom score increased from preoperatively (0.18) to 1 month (0.58) but then reduced with time and at 12 months (0.22) was very close to the preoperative level.

At 12 months, no patients reported marked or severe visual symptoms in any category and only two patients reported moderate symptoms. Ten patients (53%) reported visual symptoms to be absent in all categories.

**TABLE 1**

<table>
<thead>
<tr>
<th>Near Tasks</th>
<th>Intermediate Tasks</th>
<th>Distance Tasks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Read medicine instructions</td>
<td>Find items on a kitchen shelf</td>
<td>Read street signs</td>
</tr>
<tr>
<td>Read a newspaper article</td>
<td>Read a computer screen</td>
<td>Identify people across a room</td>
</tr>
<tr>
<td>Examine their fingernails</td>
<td>Use a bathroom mirror</td>
<td>Judge car distances</td>
</tr>
<tr>
<td>Dial a cell phone</td>
<td>Use a wall calendar</td>
<td>Read house numbers</td>
</tr>
<tr>
<td>Read a magazine</td>
<td>Recognize framed photo portraits</td>
<td>Tell the time from a wall clock</td>
</tr>
</tbody>
</table>

Figure 4. Mean (A) photopic and (B) mesopic contrast sensitivity in the implanted eye. Error bars indicate one standard deviation.

<table>
<thead>
<tr>
<th>Spatial frequency (cycles/degree)</th>
<th>Mean Contrast Sensitivity (Log)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.5</td>
<td>2.0</td>
</tr>
<tr>
<td>1.0</td>
<td>1.5</td>
</tr>
<tr>
<td>1.5</td>
<td>1.0</td>
</tr>
<tr>
<td>2.0</td>
<td>0.5</td>
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<tr>
<td>2.5</td>
<td>0.0</td>
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AB
Complications/Adverse Events

One patient reported “severe” halos at the 6-month visit, which improved to “mild” after the 6-month visit. No other complications were reported.

There were two adverse events. One patient was dissatisfied with postoperative distance vision and reported difficulty with playing tennis at night on a floodlit court. The corneal inlay was removed, and at 1 week postexplant, UDVA in the treated eye had improved from 0.4 to 0.1 logMAR (20/50 to 20/25 Snellen). By 1 month postexplant, it had returned to the preoperative level of 0.0 logMAR (20/20 Snellen). As discussed earlier, a second patient experienced a decentered inlay that required replacement.

Discussion

The current study shows the ability of the Raindrop corneal inlay to safely correct emmetropic presbyopia. Of the 19 eyes available for examination at 12 months, 100% (19 of 19) achieved UNVA of 0.2 logMAR (20/32 Snellen) or better in the operative eye. Binocularly, 100% of patients achieved UNVA of 0.18 logMAR (20/31 Snellen) or better. All patients maintained binocular distance vision from 3 months postoperatively onward. No eye lost two or more lines of CDVA or CNVA. The visual acuity results were echoed by task performance at different differences.

Reports of dry eye were minimal during the postoperative period. This is notable because implanting the Raindrop corneal inlay requires creation of a corneal flap similar to that created for LASIK procedures. During the first 6 months postoperatively, dry eye is a common side effect of LASIK and can be severe. It has been suggested that cutting the corneal nerves during flap creation is responsible for the dry eye. However, in this study, increased dry eye postoperatively was minimal, with some eyes even showing an improvement in dry eye symptoms postoperatively.

Halos and glare can also be problematic for patients after LASIK surgery, particularly affecting their comfort with night driving. Reports of halos and glare were minimal in this study, decreasing over time postoperatively until they approached preoperative levels by the 12-month visit. One report of “severe” halos at the 6-month visit resolved to “mild” at the 9- and 12-month visits. Overall, halos and glare were not an issue for this study group.

Monovision is probably the most popular form of presbyopia treatment. One eye, usually the nondominant eye, is corrected for near vision using contact lenses or surgically with LASIK. The fellow eye is corrected, if necessary, for distance. Durrie reported that UNVA for the “near” eye improved with increased contact lens power; mean UNVA with a +0.75 lens was 0.45 logMAR (20/56 Snellen), 0.29 logMAR (20/39 Snellen) with a +1.50 lens, and 0.11 logMAR (20/26 Snellen) with a +2.50 lens. Binocular UNVA was similar. Concomitantly, UDVA in the “near” eye decreased with increasing lens power, becoming worse than 0.6 logMAR (20/80 Snellen) with a +2.50 lens. Patients showed significant losses in both photopic and mesopic contrast sensitivity in the corrected eye. Unlike monovision, the Raindrop corneal implant creates a multifocal cornea to provide near through distance vision. Distance vision in the treated eye does not decrease to the levels seen in eyes treated with monovision. In this study, 85% of implanted eyes achieved UDVA of 0.22 logMAR (20/34 Snellen) or better by the 1-week visit. This may explain why mean changes between preoperative and postoperative photopic and mesopic contrast sensitivity are small (<0.3 log units) with the corneal inlay and are not considered clinically significant.

The one patient who was not satisfied during the course of the study because of problems pursuing a hobby had the inlay explanted, and her vision returned to preoperative levels within 1 month of the explant procedure. To date (currently 18 months post-explantation), there have been no adverse sequelae for this patient.

The clinical outcomes generated to date support both the preliminary safety and efficacy of the Raindrop corneal inlay for improvement of near vision in the patient with emmetropic presbyopia. No serious safety concerns were noted in this trial.

Author Contributions

Study concept and design (EBG, AC, JD); data collection (EBG, SG); analysis and interpretation of data (EBG, AC, JD, SG); drafting of the manuscript (EBG); critical revision of the manuscript (AC, JD, SG); administrative, technical, or material support (SG)

References

5. Mester U, Heimig D, Dardenne MU. Measurement and calcu-


Figure A. Binocular uncorrected (A) near and (B) distance visual acuity of the implanted eye relative to pretreatment acuity. Binocular acuities were not recorded before 1 month postoperatively.

Figure B. Patient assessment of ease of performing visual tasks at distance, intermediate, and near.

Figure C. Mean ocular discomfort and visual symptom scores.