Hyperopia affects approximately 25% of the general population. Currently available surgical options for the correction of hyperopia have significant disadvantages. Laser in situ keratomileusis (LASIK) and photorefractive keratectomy (PRK) can only be used for low hyperopia and are accompanied by an increased risk of regression, repeated corrective surgery, and higher order aberrations, mainly due to...

**ABSTRACT**

**PURPOSE:** To evaluate a new non-ablative and adjustable procedure for laser ablative refractive corneal surgery in hyperopia using the injection of a biocompatible liquid filler material into a stromal pocket.

**METHODS:** A total of 120 stromal pockets were created using a clinical femtosecond laser system in 96 rabbit corneoscleral discs and 24 whole globes. Pockets were cut at a depth of 120 or 250 µm below the epithelial surface. Hyaluronic acid was injected manually into the pocket. To determine the refractive changes, three-dimensional optical coherence tomography images and a specifically developed picture recognition Matlab (The Mathworks) routine were used.

**RESULTS:** After injection, a steepening of the anterior and flattening of the posterior corneal surface was observed, which led to hyperopic correction. The two main factors determining the amount of correction were the pocket depth and the injected volume. After the pocket was homogeneously filled, an initial refractive increase was observed, followed by a linear relation between the injected volume and the refraction increase.

**CONCLUSIONS:** This possible clinical protocol for controlled refraction correction of hyperopia suggests a potential readjustable clinical application.

the relatively small optical zone and related functional centration issues. Pseudophakic intraocular lenses lead to a loss of accommodation, whereas phakic intraocular lenses are often unavailable to patients with hyperopia due to their narrow anterior chamber morphology. The current solid hydrogel corneal implants are approved only for low hyperopia and lead to higher order aberrations and a loss of contrast sensitivity.3,4

Solid lenses and solid but more permeable hydrogel implants were implanted into stromal pockets,3 resulting in failure due to insufficient permeability of salt and nutrients.6 The implantation of corneal grafts7 was later refined by lamellar approaches8 and resulted in the first clinical studies of small incision lenticule extraction (SMILE) lenticule transplantations in corneal pockets created by femtosecond laser.9,10 A major problem of this approach is the low predictability of the refractive result, due to changes in both the anterior and posterior curvature and individual biomechanics of the cornea and the missing adjustability.11 In addition, complications that arise from donor material are issues that should be avoided in refractive surgery.12

Because of the above-mentioned disadvantages, it is desirable to find alternatives to correct higher levels of hyperopia and to increase the optical zone area. The adjustability would overcome the issue of the low predictability, observed in corneal expansion surgery,11 by allowing subsequent corrections and would be a major advantage over the previously described methods. Therefore, we proposed a new treatment modality by injecting a biocompatible, transparent, viscous liquid filler material into a laser-generated corneal pocket for corneal refractive increase. Other groups have tried to use a peripheral corneal gel injection to demonstrate myopia correction13 and a pilot in vitro study in pig eyes demonstrated the feasibility of the central approach for hyperopia.14 Analogous to the previous studies, which used firm corneal extension materials, a change in both the anterior and posterior surfaces was observed to correct hyperopia. This study reports the first systematic evaluation of refractive changes after filler injection in 120 rabbit eyes and provides a quantitative analysis of the achieved surgical results and demonstrates the adjustability of the approach.

MATERIALS AND METHODS
Tissue Acquisition and Preparation

This was a study on 120 fresh mature New Zealand White rabbit cadaver eyes (Pel Freez Biologicals), which were used within 24 hours after death. A total of 96 whole globes and 24 corneoscleral discs (approximately 17 mm diameter) were obtained. For the corneoscleral discs, keratoplasty scissors and fine forceps were used to remove the iridociliary complex. Both the whole globes and the corneoscleral discs were placed in phosphate-buffered saline (PBS; Fisher Bio Reagents) containing 20% w/v dextran (Relative molecular mass: 450,000 to 600,000; Sigma) for at least 30 minutes. The corneoscleral discs were then mounted into a specially designed artificial anterior chamber (analogous to the Barron artificial anterior chamber, but with higher diameter at the base to support natural curvature). The pressure in the anterior chamber and in the whole globes was regulated by a water column to reach a physiological pressure of 17 to 25 mm Hg and was transiently increased to approximately 40 to 60 mm Hg for the laser-assisted pocket creation.

Filler Material

Hyaluronic acid sodium salt from Streptococcus equi (Sigma) was chosen as a filler material. Hyaluronic acid was dissolved in phosphate-buffered saline at 1% w/v and stored at 4 °C.

Surgical Procedure

Total corneal volume was increased by injecting hyaluronic acid into a stromal pocket. This increase of central corneal volume steepens the anterior and flattens the posterior corneal surface. The procedure was performed as follows.

After stereo-microscopic inspection of the cornea, a three-dimensional optical coherence tomography (3D-OCT) image was acquired as detailed below, followed by gentle moistening of the cornea with a wet Merocel stile. A state-of-the-art commercially available femtosecond laser system (VisuMax; Carl Zeiss Meditec AG) was used to create circularly shaped stromal pockets. The cornea was aligned and attached to the patient interface (size S) by triggering the vacuum suction, which caused an increase of the corneal radius to 20 mm. After docking, the laser procedure for pocket creation was applied under microscopic control.

Cutting parameters were as follows. Deep anterior lamellar keratoplasty (DALK) mode was chosen, which allows a base cut parallel to the corneal surface. The depth of the pocket was chosen to be either 120 or 250 µm, and the diameter was 7 mm. The cutting procedure was manually discontinued before the side cut was started. After pocket creation, a tunnel (1 to 2 mm long) was manually created with an upward bent 28.5-gauge canula (U100 Insulin syringe; Becton Dickinson). The filler was injected using a blunt 28.5-gauge cannula (U100 Insulin syringe). Rarely, small tissue bridges needed removal through the injection canula. Due to the narrow and long
incision, there was no sealing required because no filler loss was observed. After filler injection, a 3D-OCT image was taken to document the changes of the corneal profile (Figure A, available in the online version of this article). Two types of injection schemes were performed: corneas were injected once with a random volume and the initially injected filler volume was consecutively reduced or increased to generate multiple filler volumes within a single cornea.

OCT SYSTEMS

OCT images were recorded using two different OCT systems. First, a modified Ganymed 10-μm OCT with a central wavelength of 930 μm (Thorlabs) had an axial resolution of 3.8 μm and a lateral resolution of 31.25 μm. The C-scan field of view measured 1.94 × 8 × 8 mm (z × x × y) and the scan speed was 30,000 A-scans/s. Second, the Telesto-II-SP15 OCT with a central wavelength of 1,300 μm (Thorlabs) had an axial resolution of 3.8 μm and a lateral resolution of 23.6 μm. The C-scan field of view measured 3.15 × 8 × 8 mm (z × x × y) and the scan speed was 76,000 A-scans/s. Eight A-scans were averaged with both platforms. The apex of the cornea was placed closest to the center of the x-y field of view.

OCT IMAGING PROTOCOL

The 3D-OCT C-scans of the whole filler pocket and surrounding cornea were taken before the creation of the pocket and after filler injection and after each consecutive release or refill of filler volume. The curvatures of each surface were semi-automatically determined by a self-developed picture recognition algorithm using Matlab (The MathWorks).

SEM-I-AUTOMATED DETERMINATION OF THE CORNEAL PROFILE

Scanning inaccuracies of the OCT system were corrected using a 1951 USAF resolution test chart (Edmund Optics Inc) and calibrated using spherical samples of known curvatures. The resulting corrected OCT images are still optically distorted and need further adaptation. The OCT A-scans generally neglect the refraction on optical surfaces and only show the optical length in the z direction. To display the geometric OCT, the image refraction and depth (z direction) need to be corrected:

\[ z_\circ = n \cdot z_g \]  
(1)

with the optical length \( z_\circ \), the geometrical length \( z_g \), and the refractive index \( n \).

To start the fitting process, the surfaces were fitted by a least-squares algorithm spherical fit (provided by Yury Petrov, Oculus VR) followed by a toroidal fit (MATLAB Curve Fitting Toolbox). Two tilted planes were added to simulate rotation of the torus. The 3D-ray tracing on each optical surface was performed using their toroidal surface fits and the vector Snell’s law on each A-scan using the geometrical length. This way each surface was corrected in a consecutive order from the outer to the inner surface of the cornea.

The filler volume was calculated by counting the voxel volumes between the pocket surfaces. Pachymetry of the whole cornea, the pocket, the filler bed, and the cap were measured as the distances between related toroidal fits (Figure B, available in the online version of this article). Spherical and torical corneal radii \( r \) were used to calculate the refractive power \( P \) using the refractive indices \( n_1 \) and \( n_2 \) at the OCT wavelength:

\[ P = \frac{\left(n_2 - n_1\right)}{r} \]  
(2)

EXPERIMENTAL GROUPS

Six different groups were established to determine the refractive changes after filler injection. Pocket depth below the corneal surface was chosen to be either a superficial (120 μm) or a deep (250 μm) pocket. Depending on the group, corneas were either (1) injected once with a random volume and the refraction was determined, or (2) injected with a high volume to start, followed by a sequential filler reduction or increase and measurement of the refraction (Table 1).

STATISTICAL ANALYSIS

Statistical comparison between two different experimental groups was achieved by the \( t \) test and an analysis of variance (ANOVA) with a Bonferroni post hoc test for more than two groups. For all analyses, a \( P \) value of less than .05 was considered statistically significant with a 95% confidence interval. All graphs and all regressions (Pearson, \( r^2 \)) were plotted with GraphPad Prism 8 software (GraphPad Software, Inc), and the calculations were done using Excel 2016 (Microsoft Corporation) or Matlab software. Error bars represent the standard deviation. All statistical analysis was performed by SPSS software version 24.0 (IBM Corporation).

RESULTS

In all six experiments, we determined that after the injection of the filler there was an increase of corneal refractive power, correcting an assumed hyperopic refractive error (Figure 1). The total refractive change was determined as the sum of the anterior and posterior interface refractive changes. The results delib-
erately excluded the analysis of the two additional optical interfaces of the filler pocket, because no final choice of filler material for a clinical application has been made and the refractive index of the filler material is thus not yet known.

**Refractive Changes of a Single Volume Injection (Groups 1 and 2)**

In groups 1 and 2 (120 and 250 µm, respectively), in which corneas were injected once with a single volume, the refractive power of the whole cornea increased with the volume injected. A linear correlation between filler volume and refractive change ($r^2 = 0.06$ for superficial and $r^2 = 0.6$ for deep injections) was found. The ordered pairs of volume injected and resulting refraction gained were scattered in a high variability around this linear regression. The error (deviation from the line) in refractive gain for individual corneas was found to be up to approximately ±3 dpt in the 120 µm deep pocket and up to ±2 dpt in the 250 µm deep pocket. The linear regression did not intersect through the origin in the superficial pockets (Figure 1A), whereas the y-intercept was 2.6 ± 0.7 dpt but did interact in the deeper pockets at 0 ± 0.3 dpt. There was less refractive gain in the deeper pockets when compared to the superficial pocket.

**Refractive Changes in Consecutive Volume Adjustments (Groups 3 and 4)**

Due to the high variability of corneal tissue, a single volume injection seems to not be clinically feasible. Therefore, in the second step, a series of corneas were evaluated using a consecutive adjustment of filler material in the pocket (120 and 250 µm). A decent linear correlation between volume and refractive gain was observed for each individual cornea (mean $r^2 = 0.93 ± 0.10$ for superficial and $0.87 ± 0.18$ for deep pockets) (Figures 1B-1C) with a high interindividual difference. The linear regression lines of each cornea did not intersect through the origin, implying a high, more than linear unpredictable refractive gain at the beginning of the filling process, which we termed refraction offset. This refraction offset was on average 1.9 ± 1.3 dpt in the superficial pockets and a significantly lower 0.5 ± 0.8 dpt in the deep pockets ($P < .001$).

**Refractive Changes in Whole Eyes (Groups 5 and 6)**

Comparable results were achieved in whole eyes. We also determined a relevant linear correlation between volume and refractive gain for each individual cornea (mean $r^2 = 0.88 ± 0.09$ for superficial and $0.92 ± 0.04$ for deep pockets) and a refractive offset of 1.7 ± 0.9 dpt in the 120 µm group (group 5) and -0.2 ± 0.6 dpt in the 250 µm group (group 6), which again was statistically significantly different ($P < .001$) (Figure 1D). This highlights the importance of the pocket depth for the amount of correction achieved. The slopes of the linear regression lines were not significantly different between the different groups ($P > .05$ in all comparisons). In addition, if compared between the single samples, the slope did present with a certain variability, adding to the low predictability (corneoscleral discs, 120 µm: 0.20 ± 0.05 dpt/µL and 250 µm: 0.16 ± 0.05 dpt/µL; whole eyes, 120 µm: 0.16 ± 0.05 dpt/µL and 250 µm: 0.15 ± 0.03 dpt/µL) (Figure 1).

**Refractive Changes of the Outer and Inner Corneal Surface in Detail**

Both the anterior and posterior curvature of the cornea were influenced by the volume injection but reacted in a different way (Figure C, available in the online version of this article). The total change in refraction is the sum of anterior and posterior change in surface refraction. Due to the lower difference of refractive indices at the posterior interface, more spatial displacement is needed to gain the same amount of correction. One of the main characteristics, the above-mentioned refraction offset, of the correction is determined by the anterior interface. That is the above-described higher refractive change (refractive offset) in the beginning of the injection process, which also leads to the statistically significant difference.

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**TABLE 1**

Overview of the 6 Experimental Procedures Applied to Different Groups

<table>
<thead>
<tr>
<th>Group</th>
<th>Pocket Depth (µm)</th>
<th>Experimental Set-up</th>
<th>Injection Scheme</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>120</td>
<td>Corneoscleral disc mounted on an artificial anterior chamber</td>
<td>Injection of one single random volume</td>
</tr>
<tr>
<td>2</td>
<td>250</td>
<td>Corneoscleral disc mounted on an artificial anterior chamber</td>
<td>Injection of one single random volume</td>
</tr>
<tr>
<td>3</td>
<td>120</td>
<td>Corneoscleral disc mounted on an artificial anterior chamber</td>
<td>Multiple volumes in one single cornea</td>
</tr>
<tr>
<td>4</td>
<td>250</td>
<td>Corneoscleral disc mounted on an artificial anterior chamber</td>
<td>Multiple volumes in one single cornea</td>
</tr>
<tr>
<td>5</td>
<td>120</td>
<td>Whole globes</td>
<td>Multiple volumes in one single cornea</td>
</tr>
<tr>
<td>6</td>
<td>250</td>
<td>Whole globes</td>
<td>Multiple volumes in one single cornea</td>
</tr>
</tbody>
</table>
in change in refraction between the superficial and deep pockets \( (P < .001) \). The posterior interface instead determines the volume-based increase of refractive changes. The depth of the pocket did not matter for the correction of the posterior surface because both the slope \( (P = .15) \) and the offset \( (P = .11) \) of the linear relationship between refraction gained and volume injected was statistically equal in both pocket depths.

**ASTIGMATISM**

The use of corneoscleral discs in the artificial anterior chamber has several methodological advantages,
Figure 2. (A) Corneal astigmatism in whole globes (WG) and corneoscleral discs (CD) are shown before filler injection and the change afterward. The depth is given as 120 μm and 250 μm. (B and C) The mean change in astigmatism after filler injection over all volumes in the multiple volume corneas are depicted. Two representative topographies of a (D) whole globe and (E) corneoscleral disc before filler injection highlight the difference in astigmatism, which is higher in the corneoscleral disc.
mainly the stabilization of thickness through dehydration in dextran solution from both sides. Yet, the use of the artificial anterior chamber was connected to a high but regular artificially induced astigmatism (Figure 2). No correlation between the amount of astigmatism and the resulting spherical correction could be observed in any group ($r^2 < 0.25$ in all comparisons). The change in astigmatism was measured across groups 3 and 4 with multiple filler injections and did not change significantly after filler injection ($P > .10$ in all comparisons). No significant change was expected because we did not intend to correct astigmatism.

OTHER FACTORS THAT INFLUENCE THE REFRACTIVE CORRECTION

A better understanding of factors apart from the volume and the filler depth that could influence the refractive change was obtained by calculating several regressions. To rule out a change of refraction due to the surgical procedure itself on the refractive offset, we created the channel, removed all gas bubbles, and, after entering the pocket with the injection canula, the procedure was aborted and no filler was injected to measure the refractive change of that procedure. There was no statistically significant mean change in refraction due to the procedure (-0.5 ± 0.4 dpt) ($P = .40$). The slope and the refractive offset were not dependent on the central corneal thickness before the filler injection ($r^2 < .27$ in all comparisons), nor was the corneal spherical radius before injection ($r^2 < .3$ in all comparisons). The plots show a comparable experimental result between the whole globes and the corneoscleral discs (Figures 1C-1D), but with the slope in the 120 µm pocket being slightly but significantly lower in the whole eyes ($P = .01$).

DISCUSSION

In this in vitro study, we demonstrated that a filler material injected into a corneal pocket can correct spherical hyperopia without removing corneal substance. The pocket can be created with a clinically used femtosecond laser platform. The whole procedure is feasible with the currently available technology but needs optimization as discussed below. We were successful in characterizing the relationship between the injected volume and the amount of refractive change. Moreover, the pocket depth is another major dosimetry parameter for hyperopia correction. To improve the predictability of the refractive correction, we propose either a three-step procedure in each patient to compensate for the individually different biomechanical conditions, or, alternatively, as a real-time determination of the refraction to control the filler injection procedure.$^{15}$

For the three-step procedure, the individual offset $p_{\text{offset}}$ and the linear relation rate $dR / dV$ between the refractive change $\Delta P$ and filler volume $V$ need to be taken into account (Equation 3):

$$\Delta P = p_{\text{offset}} + \frac{dR}{dV} \cdot V \quad (3)$$

The parameters $dR / dV$ and $p_{\text{offset}}$ need to be determined by using two pairs of $\Delta P$ and $V$ values (two filler injections). After having defined the parameters in Equation 3, a third injection can create the anticipated refractive change with a predetermined volume injection. Of note, a variation of pocket diameter will certainly change the metrics of the refraction correction and is an interesting direction for future investigation.

As observed in other procedures in which material was added into the cornea$^{9,10}$ different biomechanical properties of the corneas might also explain the reduced predictability that we encountered in our experiments.$^{11}$ We suspect that the different biomechanical properties result in an initial strong refractive increase, termed the refractive offset, that was individual for the anterior interface of each cornea. This offset might be a result of the specific non-linear stress-strain behavior of collagen.$^{16}$ It must be suspected that the refractive offset might be caused by a non-linear stretching of the anterior lamella, just before a certain minimal amount of filler material is present in the pocket to guarantee a complete and homogeneous filler distribution. Especially in the first “weak” phase, little stress is needed to cause a large strain, unlike linear elastic materials where the stress-strain relation is constant. This could explain the refractive offset. After the offset, the refraction increases linearly with higher volumes and with a slope between volume and correction that was only slightly different between each cornea. This was mainly determined by the posterior capsule. The posterior surface of the cornea does not follow the stress-strain curve of collagen, because it is compressed toward the posterior pole into the anterior chamber. In the case of a compression, the collagen does not undergo the two different stages of extending the spring-like molecular structure and the already stretched collagen molecule. Therefore, we might have observed a classic linear compression deformation.

With the given method, two factors caused a significant loss of experimental samples: the manually designed incision in our approach to reach the pocket and tissue bridges. During the experimental procedures, 51 of the eyes were excluded due to problems in creat-
ing the injection channel manually, 40 of them due to tissue, experimental, and laser problems and 19 more due to remaining tissue bridges. The tissue bridges at least were reduced substantially in later experiments, changing the energy settings and the spacing of the femtosecond laser focus. However, the positioning of the incision instead was surgically demanding. Due to the high expectations of reproducibility of our application, we suggest a self-sealing incision cut applied with the femtosecond laser. A precisely cut incision analogous to the cataract surgery and perfect corneal incisions would improve the procedure significantly.

As also observed in our experiments, there is a low predictability in procedures in which substance is added to the central cornea. Several earlier studies that used various approaches different from our method attempted to steepen the corneal profile by increasing total corneal volume for hyperopia correction. The most recent study examined the implantation of autologous corneal lenticules into the stroma, either below a flap (LIKE)17 or in a stromal pocket (sLIKE).18 A major issue is the reduced predictability in comparison to myopia surgery.9,19 A recent study showed that the refractive change was dependent on tissue depth of implantation, with being lower at deeper lenticule placement a finding that is consistent with our results in filler pockets of varying depth. The authors of this study attributed the low predictability to an unpredictable change of the posterior surface, which was difficult to compensate.11 This is in contrast to our findings, because we observed the anterior surface to have the highest impact on the low predictability. Although the corneal stromal filler injection is biomechanically different due to the liquid material in our approach, we encountered the same behavior. Fortunately, in comparison to a firm lenticule, a liquid material gives the advantage of individual adjustments to optimize refraction correction and a possible controlled method for refraction correction as described above.

In this study, we used hyaluronic acid as a filler material due to its frequent use in cataract, glaucoma, and refractive surgery, which results in an in-depth characterization of the biocompatible and pharmacological use in the cornea.20 Obvious advantages are the transparency in solution, a high molecular weight that limits diffusion into the corneal stroma, and high viscosity, which turns into low viscosity under the pressure of injection. Furthermore, hyaluronic acid naturally occurs in the stroma and was found to remain in a corneal stroma pocket for an extended period of time after accidental injection in case reports.21,22 However, the lenticular shape of the filler reduces the intended refractive increase because of its slightly lower refractive index compared to the corneal stroma. New filler materials are currently being tested and a special emphasis is laid on different options that have a similar matching refractive index to the stroma.

There might be a possible effect of eyelid pressure on a fluid-filled intrastromal pocket causing astigmatic changes to the intended correction. This was tested in 6 rhesus monkeys with an implanted intraocular telemetric pressure sensor.Transient pressure fluctuations occur 2,000 to 5,000 times per hour greater than 5 mm Hg above baseline from blinks, saccades, and ocular pulse amplitude.23 Those pressure increases in the globe are caused by the force exerted on the eye by the eyelid and lead to the conclusion that at least some force is acting on the filler pocket by blinking. No conclusion can be drawn about a possible effect on changes of the filler shape and future studies have to evaluate this problem in vivo. A possible strategy for stabilizing the filler shape would be cross-linking the filler material.

Corneas of different species vary in their response to corneal and refractive surgery, most likely due to their different anatomy and biomechanics.24,25 Due to a scarcity of human donor globes, we deliberately chose to develop this new surgical method with the widely abundant available rabbit eyes. In addition, the radius and corneal thickness of rabbit corneas are roughly comparable to those of humans. We were able to present a systematic evaluation of refractive changes in 120 eyes following corneal stromal filler injection. This was done by always keeping in mind that no clinically ready dosimetry can be obtained from the data and that the experiments have to be repeated on human eyes ex vivo and in clinical studies. Another problem lies in the different viscoelastic and elastic properties of the ex vivo corneas. To fully adjust for any changes in those properties is an inherent problem in an ex vivo model. There are many factors that determine biomechanics in the ex vivo situation that are not present ex vivo,25 such as corneal hydration and osmosis, which is altered due to a loss of corneal physiology (endothelial pump) ex vivo. To avoid experimental errors by these factors, we tried to simulate the corneal physiology ex vivo and keep these factors constant by carefully adjusting the experimental properties as described above.

These promising results and the understanding of the mechanics of the injection of liquid filler material into the cornea suggest a possible clinical application to treat hyperopia in a minimally invasive way. However, further studies are necessary to address the issues that have been discussed and are currently underway.
AUTHOR CONTRIBUTIONS
Study concept and design (CMW, SP, RRA, RB); data collection (CMW, KB, SK, CE, SAK, LP); analysis and interpretation of data (CMW, KB, SK, CE, SAK, HS-H, RB); writing the manuscript (CMW, SAK); critical revision of the manuscript (CMW, KB, SK, CE, SAK, LP, HS-H, SP, RRA, RB); statistical expertise (CMW, SK); administrative, technical, or material support (SAK, RRA, RB); supervision (CMW, SP, RB)

REFERENCES
Figure A. Scheme of anticipated postsurgical result. (A) Sagittal optical coherence tomography B-scan through the apical corneal region and the pocket center. (B) Sagittal central view and (C) frontal view. The 500 µm width of the channel is calculated from the needle circumference.

Figure B. Flowchart diagram showing the consecutive calculations using our Matlab algorithm (The Mathworks) to detect the geometric profile of the cornea to determine the corneal refraction after filler injection. OCT = optical coherence tomography

Figure C. Linear regression variation for the different corneoscleral discs (groups 3 and 4). The mean linear regression is shown with the standard deviation as shaded error areas. (C) The total refractive change is the sum of the changes in the (A) anterior and (B) posterior surface. The anterior surface is primarily responsible for the initial refraction-offset and the posterior surface mainly for the increased refractive gain, depending on the injected filler volume.