Accommodation amplitudes after an accommodating intraocular lens refilling procedure: In vivo update

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PURPOSE: To evaluate whether a new capsular bag–refilling procedure provides some accommodation in monkey eyes and to assess the difference in accommodation with different volumes of capsular bag refilling.

SETTING: Jinshikai Medical Foundation, Nishi Eye Hospital, Osaka, Japan.

DESIGN: Experimental study.

METHODS: A central 3.0 to 4.0 mm continuous curvilinear capsulorhexis was created, after which phacoemulsification was performed in the usual manner. A new accommodating-membrane intraocular lens (IOL) for sealing the capsular opening was implanted in the capsular bag. Silicone polymers were injected beneath the IOL into the capsular bag through the delivery hole. In 3 study groups, each with 6 monkey eyes, the lens capsule was refilled with 0.080 mL of silicone polymers, corresponding to a 65% bag volume; 0.100 mL, corresponding to an 80% bag volume; or 0.125 mL, corresponding to a 100% bag volume. To calculate the accommodation amplitudes achieved, automated refractometry was performed before and 1 hour after topical pilocarpine 4.0% application preoperatively and 4 weeks postoperatively.

RESULTS: The refilling technique was successful without polymer leakage in all monkeys. Four weeks after surgery, the mean accommodation amplitudes were 2.56 diopters (D) $\pm$ 0.74 (SD), 2.42 $\pm$ 1.00 D, and 2.71 $\pm$ 0.63 D, respectively, in the 3 study groups.

CONCLUSIONS: The technique provided some accommodation in young monkey eyes. Leakage of the injectable silicone polymers and anterior capsule opacification in the visual axis were avoided. The results suggest that the capsular bag–refilling procedure warrants further study for possible clinical application.

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Refilling the lens capsule with an injectable malleable material that would restore ocular accommodation has long been the goal of cataract surgeons. However, 2 persistent problems with capsular bag–refilling methods have hampered the clinical application of the procedure.[1–11] The first is leakage of the injected material, usually a mix of 2 silicone compounds, from the capsular bag before the material's transformation into a gel-formed polymerized consistency. The second is capsule opacification. Despite these problems, previous studies[2,4,5,8,11] have achieved from 2.0 to 8.0 diopters (D) of accommodation in monkey eyes, although for a relatively short postoperative period, and have attempted to prevent leakage of the injected material. These methods include use of precured silicone gel,[1–3] an endocapsular balloon,[4,5] endocapsular polymerization by applying ultraviolet light,[6] a capsule-sealing plug,[7–10] or an expansible full-size intraocular lens (IOL).[11] Capsule opacification has proven to be extensive,[12] although in some instances it was minimized by treating residual lens epithelial cells (LECs).[10] None of these techniques has been proved to be clinically useful.

To address the problems of silicone leakage and capsule opacification, we recently developed a new accommodating IOL that serves as an optic as well

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as a plug that seals the capsular opening. In our previous studies using rabbit eyes and pig cadaver eyes,[13] the accommodating IOL sealed the large central 3.0 to 4.0 mm continuous curvilinear capsulorhexis (CCC) opening and successfully prevented silicone leakage. Posterior capsule opacification in the visual axis was prevented by the creation of a posterior CCC, which was sealed by an inversely implanted posterior accommodating IOL. Silicone polymers were injected between the 2 IOLs to fill the capsular bag. Thus, capsule opacification, at least in the visual axis, was prevented in the rabbit eyes by creating anterior and posterior CCCs, which were sealed using 2 accommodating IOLs.[13]

In the current study, we applied this technique in young monkey eyes to determine whether it can provide some accommodation. We also evaluated the difference in accommodation with different volumes of capsular bag refilling. The study design was based on our previous experimental in vitro study,[7] in which the accommodation amplitudes varied with different volumes of bag filling and a capsular bag with approximately 70% volume provided the optimum accommodation amplitude. In this study, a posterior CCC was not performed. The goal was to attain a high degree of surgical reproducibility because of the high cost of monkey experiments and because the primary purpose was to confirm whether the capsular bag–refilling procedure provides some accommodation in young monkey eyes.

MATERIALS AND METHODS

This study was performed at the Japan Life Science Center in Gifu prefecture. It adhered to the Association for Research in Vision and Ophthalmology statement for the Use of Animals in Ophthalmic and Vision Research and the rules of the Primate Society of Japan. Eighteen young Macaca fascicularis monkeys aged 3 to 5 years weighing 5.5 to 6.3 kg were used.

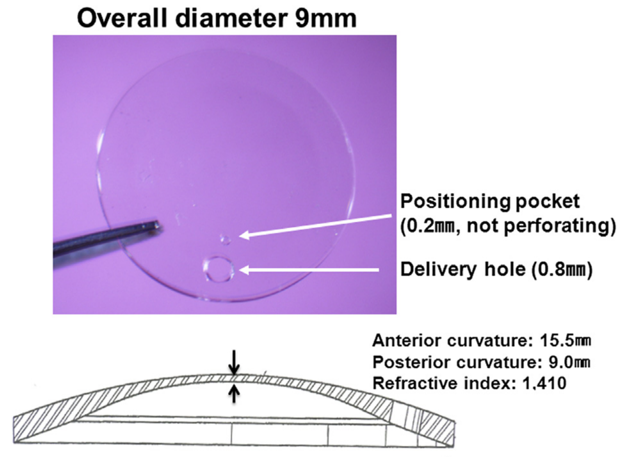

Figure 1. Foldable silicone accommodating-membrane IOL. The central part is between the 2 arrows.

Anesthesia

Animals were anesthetized with intramuscular ketamine chloride 0.5 mg/kg (Ketalar) and xylazine chloride 2.0 mg/kg (Selactar). Additional corneal anesthesia was provided with lidocaine hydrochloride 1.0% eyedrops (Xylocaine) before and during surgery.

Accommodating-Membrane Intraocular Lens and Injectable Silicone Polymers

The foldable silicone accommodating-membrane IOL used in previous rabbit eye and pig cadaver eye experiments[13] was modified for the monkey experiment. The modified IOL serves as an optic as well as a plug for sealing the capsule opening to prevent leakage of the injected silicone polymers until their polymerization. The IOL is silicone and has a thin, plate, disk–shaped haptic with a 9.0 mm overall diameter (Figure 1). At the margin, there is a 0.8 mm delivery hole for insertion of a 22-gauge needle. More central to the optic is a 0.2 mm positioning pocket (not perforating the plug) through which the IOL can be positioned using a Sinskey hook. The IOL, which is thick at its margins, tapers to a 100 μm center. The most significant modification of the original IOL[13] is the absence of a transition zone between the optic and the haptic. This region is now a disk-shaped IOL. The anterior curvature is 15.5 mm and the posterior curvature, 9.0 mm. The refractive index of the silicone is 1.410. Accordingly, the refractive power of the membrane in the air calculated using ray tracing is +19.5 D.

Using a dynamic mechanical analyzer, the injectable silicone was formulated with an optimized mix ratio of silicone polymer part A to part B to achieve a modulus of 100 Pa, mimicking the natural lens of young humans. The refractive index in air after polymerization is 1.397.

Primary Treatment: Total Iris Removal

The entire iris of each monkey eye was removed 2 weeks before the capsular bag–refilling procedure to

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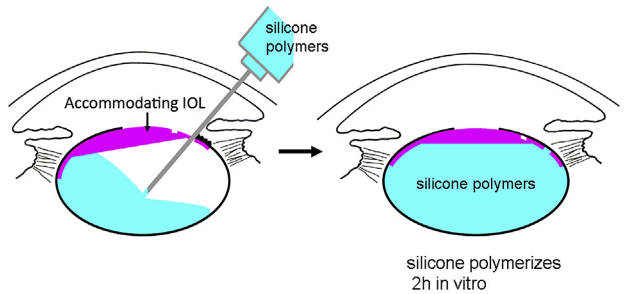

Figure 2. Capsular bag–refilling technique. The cross-section of the accommodating IOL is different than in Figure 1 because Figure 1 shows the modified IOL (reprinted with permission of the Journal of Cataract & Refractive Surgery).

facilitate postoperative observation of the refilled lens capsule and permit accurate measurement of the refraction. A 2.0 mm corneal limbal incision was created. A fine forceps was used to grasp the iris root and slowly and carefully pull the iris tissue away from the iris root insertion, resulting in an iridodialysis at the iris periphery. When the iridodialysis reached approximately one fourth of the iris circumference, the iris root at the corneal incision was regrasped. This procedure was repeated until total iridodialysis was obtained. This technique[10] resulted in an anterior chamber hemorrhage that ceased spontaneously when the intraocular pressure was raised for 1 to 2 minutes.

Surgical Technique

The refilling technique has been described[13] (Figure 2). In brief, phacoemulsification was performed and a 3.0 to 4.0 mm CCC created in the middle of the anterior capsule. Sodium hyaluronate 2.3% (Healon5) was injected into the capsular bag, and the foldable accommodating-membrane IOL was implanted. After the ophthalmic viscosurgical device (OVD) was removed from the capsular bag, in particular from underneath the IOL, a small amount of OVD was injected above the IOL. The injectable silicone polymer mixture was then injected beneath the IOL into the capsular bag using a purpose-designed dispenser[13] that delivers an arbitrary preset amount of the silicone material. The blunt needle of the dispenser containing the silicone polymers was inserted through the delivery hole, while the CCC edge was pulled slightly aside. The silicone mixture polymerized within 2 hours in vitro. After a certain amount of the silicone material was injected, the needle was withdrawn. The CCC edge returned, covering the delivery hole. The IOL was centered using a Sinskey hook.

Next, 0.2 mL of atropine sulfate 0.5% was applied to the lower subconjunctiva at the beginning of surgery in an attempt to make the injected silicone material conform to the disaccommodated capsular bag shape after polymerization of the material. This was done because according to a previous study,[4] the disaccommodated form may yield more accommodation. Gentamicin 4.0 mg and dexamethasone 0.33 mg were applied subconjunctivally at the end of surgery. Topical levofloxacin 0.5% (Clavid), diclofenac sodium 0.1 % (Diclod), and fluorometholone 0.1%, were applied 3 times a day for 3 days after surgery.

Preoperative and Postoperative Examinations

A slitlamp examination and anterior segment photography were performed before surgery and 2 and 4 weeks after surgery. Scheimpflug photography (EAS 1000, Nidek, Inc.) and measurement of refraction using an automated refractometer (ARK-10000, Nidek, Inc.) were performed before and 1 hour after application of topical pilocarpine 4.0% before surgery and 4 weeks after surgery. (Longer follow-up was not possible because the monkey facility was closed.)

In the Scheimpflug photography, 5 microphotographs were analyzed for the anterior chamber depth (ACD), lens thickness, and anterior and posterior capsule curvature. The 5 values of each parameter were averaged.

For the measurement of refraction, 5 to 7 consecutive dioptric power values were obtained. These were averaged to obtain the final value. The equivalent value in each eye was calculated from the spherical and cylindrical powers. The difference between the refractions, measured in spherical equivalence before and 1 hour after topical pilocarpine 4.0% application, was considered the accommodation amplitude. The ratio of the accommodation amplitude before surgery to that after surgery was also calculated.

Measurement of Crystalline Lens Volume and Refilled Capsular Bag Volume

Using Scheimpflug photography, the crystalline lens volume in each monkey eye was measured before surgery. First, the curvature of the anterior and posterior lens capsules delineated by Scheimpflug photography was represented as a part of a circle line by manually plotting 3 points on the capsule contour so that both lines of the anterior and posterior capsule meet at both sides, delineating and extrapolating a simulated crystalline lens. The crystalline lens volume was calculated by adding the volume of each of the 2 hemispheric cones, which was determined by drawing a straight line between the 2 cross points of each curvature line. The height of the hemispheric cone was mathematically determined from the crystalline lens thickness.

The ACD and crystalline lens thickness were corrected for the distortion caused by the cornea and aqueous humor using ray tracing. However, the measurement of the crystalline lens curvature was performed using the dedicated software for the anterior corneal curvature measurement and was not corrected for the distortion caused by the cornea and aqueous humor. Postoperatively, the refilled capsular bag volume was also measured in the same manner.

Research Design

The experiments comprised 18 eyes of 18 monkeys in which total iris removal was performed. Two weeks after iris removal, all eyes had the capsular bag–refilling procedure using the accommodating-membrane IOL. In 3 groups of 6 Macaca monkeys each, the lens capsule of each eye was refilled, respectively, with 0.080 mL of silicone polymers, corresponding to 65% of the mean capsular bag volume (Group A); 0.100 mL of silicone polymers, corresponding to 80% of the mean capsular bag volume (Group B); and 0.125 mL of silicone polymers, corresponding to 100% of the mean capsular bag volume (Group C). The mean crystalline lens volume of the monkeys was defined as 0.125 mL (see Results).

Table 1. Preoperative measurements of ACD, lens thickness, and capsule curvatures using Scheimpflug photography.

	Mean (mm) ± SD				
Group/Time	ACD (mm)	Lens Thickness (mm)	Anterior Capsule Curvature (mm)	Posterior Capsule Curvature (mm)	Capsular Bag Volume (mL)
A					
Before pilo	2.67 ± 0.17	3.07 ± 0.10	10.99 ± 0.80	7.52 ± 0.68	0.126 ± 0.008
1 h after pilo	2.19 ± 0.21	3.81 ± 0.12	7.23 ± 0.54	5.78 ± 0.40	—
B					
Before pilo	2.83 ± 0.07	2.89 ± 0.17	11.81 ± 0.79	8.53 ± 0.58	0.124 ± 0.007
1 h after pilo	2.40 ± 0.11	3.47 ± 0.09	8.41 ± 0.58	6.91 ± 0.39	—
C					
Before pilo	2.64 ± 0.09	3.01 ± 0.16	11.07 ± 0.64	7.35 ± 0.36	0.124 ± 0.073
1 h after pilo	2.29 ± 0.12	3.33 ± 0.14	8.31 ± 0.76	6.58 ± 0.56	—

ACD = anterior chamber depth; pilo = pilocarpine 4.0%

Statistical Analysis

The Kruskal-Wallis test was used for statistical evaluation of the accommodation amplitudes before surgery and after surgery as well as for the accommodation ratio.

RESULTS

Preoperative Scheimpflug Analysis and Crystalline Lens Volume

Table 1 shows the mean ACD, lens thickness, anterior and posterior capsule curvatures, and crystalline lens volume in the 3 groups.

The Scheimpflug photography before surgery showed 3 characteristic findings after pilocarpine 4.0% eyedrops: shallowing of the anterior chamber, thickening of the crystalline lens, and steepening of the anterior lens curvature (Figure 3). The calculated mean crystalline lens volume before surgery in the 3 groups was 0.125 ± 0.029 mL. From the results, the mean crystalline lens volume in the monkey eyes was determined to be 0.125 mL.

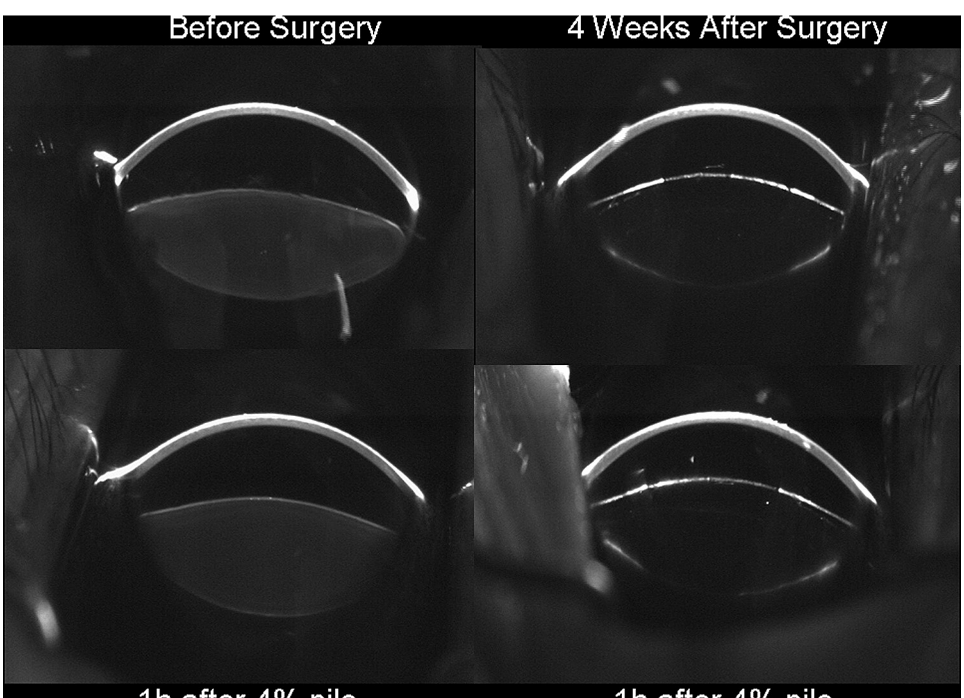

Figure 3. Scheimpflug photography of a Macaca monkey eye in Group B. Note that the lens capsule after surgery is optically empty due to the silicone polymers.

Table 2. Refractions and accommodation amplitudes in Group A (65% bag volume filling).

	Mean ± SD						
	Before Refilling			After Refilling			
Monkey/Time	Sph (D)	Cyl (D)	Equ (D)	Sph (D)	Cyl (D)	Equ (D)	Ratio (%)
A1							
Before pilo	−0.35 ± 0.12	−0.75 ± 0.00	−0.73 ± 0.23	−0.33 ± 0.12	−2.56 ± 0.11	−1.48 ± 0.25	—
1h after pilo	−12.00 ± 0.00	−2.86 ± 0.13	−13.50 ± 0.09	−1.40 ± 0.24	−3.25 ± 0.42	−3.93 ± 0.45	—
Accommodation	—	—	−12.75 ± 0.32	—	—	−2.48 ± 0.42	19.6 ± 1.3
A2							
Before pilo	+0.10 ± 0.00	−0.70 ± 0.19	−0.19 ± 0.12	+1.10 ± 0.12	−1.90 ± 0.12	−0.15 ± 0.09	—
1h after pilo	−12.80 ± 0.77	−3.50 ± 0.27	−14.63 ± 0.73	−1.05 ± 0.10	−1.70 ± 0.10	−1.90 ± 0.05	—
Accommodation	—	—	−14.51 ± 0.77	—	—	−2.09 ± 0.05	14.6 ± 1.4
A3							
Before pilo	+1.00 ± 0.16	−0.95 ± 0.56	−1.54 ± 0.17	+2.13 ± 0.38	−6.63 ± 0.13	−1.13 ± 0.50	—
1h after pilo	−13.50 ± 0.27	−2.00 ± 0.16	−14.50 ± 0.35	+0.75 ± 0.00	−4.25 ± 0.70	−2.36 ± 0.47	—
Accommodation	—	—	−12.97 ± 0.22	—	—	−1.73 ± 0.47	13.4 ± 1.1
A4							
Before pilo	+0.40 ± 0.12	1.70 ± 0.73	−0.45 ± 0.23	+2.58 ± 0.12	−2.75 ± 0.20	+1.25 ± 0.10	
1h after pilo	−11.95 ± 0.10	−1.30 ± 0.33	−12.60 ± 0.12	+1.63 ± 0.11	−2.19 ± 0.45	−2.66 ± 0.29	
Accommodation	—	—	−12.15 ± 0.32	—	—	−3.92 ± 0.50	32.1 ± 1.3
A5							
Before pilo	−0.25 ± 0.16	−1.45 ± 0.10	−0.73 ± 0.05	NA	NA	NA	—
1h after pilo	−10.25 ± 0.27	−1.86 ± 0.38	−11.30 ± 0.26	NA	NA	NA	—
Accommodation	—	—	−11.92 ± 1.70	—	—	—	
A6							
Before pilo	−1.25 ± 0.12	−0.25 ± 0.00	1.50 ± 0.00	−1.60 ± 0.12	−2.05 ± 0.10	−2.63 ± 0.11	—
1h after pilo	−15.25 ± 0.00	−0.40 ± 0.12	−15.50 ± 0.06	−4.95 ± 0.10	−0.45 ± 0.10	−5.20 ± 0.10	—
Accommodation	—	—	−13.85 ± 0.06	—	—	−2.58 ± 0.19	18.6 ± 0.6
Overall							
Before pilo	−0.06 ± 0.69	−0.97 ± 0.48	−0.86 ± 0.50	+0.78 ± 1.55	−2.31 ± 2.37	−0.83 ± 1.31	—
1h after pilo	−12.63 ± 1.54	−1.99 ± 1.00	−13.67 ± 1.40	−1.00 ± 2.27	−5.71 ± 3.44	−3.21 ± 1.20	—
Accommodation	—	—	−13.02 ± 0.91	—	—	−2.56 ± 0.74	19.7 ± 6.6

Equ = equivalant power; NA = not applicable; pilo = pilocarpine 4.0%; Ratio = accommodation amplitude after refilling:accommodation amplitude before refilling; Sph = sphere

Preoperative Refractions and Accommodation Amplitudes

Table 2, Table 3, and Table 4 show the preoperative and postoperative refractions and accommodation amplitudes in Group A, Group B, and Group C, respectively.

Surgical Outcomes

The surgical time required was 20 to 30 minutes for each monkey. In some cases, when the injection needle was withdrawn, small silicone spheres were released outside the capsular bag. This occurred when the CCC edge was pulled aside and then returned to cover the delivery hole of the IOL within 1 to 2 seconds. Because of their cohesiveness, the fine silicone globules could be distinctly recognized and easily removed by aspiration. During the injection and the course of surgery, no silicone leakage occurred in any eye. Posterior capsule rupture occurred during phacoemulsification in 1 monkey (C-1) (Table 4); the postoperative Scheimpflug analysis and the refraction and accommodation measurements could not be performed in this case, and the monkey was excluded from the postoperative analysis. Once phacoemulsification was completed, there were no cases of capsule rupture during or after injection of the silicone polymers.

Two weeks and 4 weeks after surgery, all the lens capsules in all 3 groups remained well filled and showed no silicone leakage. However, some eyes had a tiny, very thin silicone particle attached to the delivery hole at the CCC margin. This did not involve the central optic of the IOL.

Slight to mild capsule opacification of the remaining anterior capsule was observed 4 weeks after surgery. Lens epithelial cells did not reach the central area of the posterior capsule in any eye 4 weeks after surgery.

Table 3. Refractions and accommodation amplitudes in Group B (80% bag volume filling).

	Mean ± SD						
	Before Refilling			After Refilling			
Monkey/Time	Sph (D)	Cyl (D)	Equ (D)	Sph (D)	Cyl (D)	Equ (D)	Ratio (%)
B1							
Before pilo	−10.05 ± 0.49	−2.33 ± 0.57	−11.28 ± 0.67	−13.56 ± 0.32	−6.13 ± 0.28	−16.63 ± 0.23	—
1h after pilo	−23.20 ± 0.48	−9.65 ± 0.12	−27.93 ± 0.47	−16.00 ± 0.00	−6.44 ± 0.11	−19.70 ± 0.06	—
Accommodation	—	—	−16.65 ± 0.81	—	—	−3.08 ± 0.27	18.5 ± 1.5
B2							
Before pilo	−8.10 ± 0.12	−7.20 ± 1.00	−11.70 ± 0.30	15.75 ± 0.00	−8.25 ± 0.00	−19.88 ± 0.00	—
1h after pilo	−20.25 ± 1.25	−10.12 ± 0.11	−25.58 ± 1.25	−16.25 ± 0.00	−9.75 ± 0.00	−21.38 ± 0.00	—
Accommodation	—	—	−13.14 ± 1.00	—	—	−1.25 ± 0.00	9.5 ± 1.3
B3							
Before pilo	−5.50 ± 0.00	−0.75 ± 0.00	−5.88 ± 0.00	−12.25 ± 0.20	−5.00 ± 0.00	−14.75 ± 0.20	—
1h after pilo	−8.02 ± 0.12	−5.85 ± 0.12	−11.08 ± 0.09	−15.25 ± 0.22	−1.60 ± 0.75	−16.04 ± 0.17	—
Accommodation	—	—	5.64 ± 0.09	—	—	−1.85 ± 0.49	32.6 ± 1.2
B4							
Before pilo	−5.50 ± 0.16	−0.45 ± 0.10	−5.73 ± 0.12	+3.25 ± 0.00	−8.95 ± 0.10	−1.23 ± 0.05	
1h after pilo	−17.15 ± 0.20	−0.56 ± 0.11	−17.93 ± 0.37	−4.95 ± 0.10	−0.75 ± 0.00	−5.20 ± 0.10	
Accommodation	—	—	−12.33 ± 0.44	—	—	−4.04 ± 0.10	32.8 ± 1.1
B5							
Before pilo	−3.17 ± 0.31	−0.40 ± 0.12	−3.38 ± 0.29	−4.50 ± 0.00	−3.13 ± 0.13	−6.05 ± 0.06	—
1h after pilo	−9.75 ± 0.11	−2.63 ± 0.13	−11.06 ± 0.09	−6.25 ± 0.00	−3.20 ± 0.10	−7.95 ± 0.05	—
Accommodation	—	—	−7.68 ± 0.250	—	—	−1.88 ± 0.10	24.5 ± 1.0
B6							
Before pilo	−5.65 ± 0.20	−2.70 ± 0.10	−7.00 ± 0.19	NA	NA	NA	—
1h after pilo	−11.23 ± 0.20	−5.44 ± 0.21	−13.60 ± 0.46	NA	NA	NA	—
Accommodation	—	—	−6.54 ± 0.55	—	—	—	
Overall							
Before pilo	−6.33 ± 2.19	−2.31 ± 2.37	−7.50 ± 3.03	−8.56 ± 7.02	−6.92 ± 2.13	−11.71 ± 6.96	—
1h after pilo	−14.93 ± 5.63	−5.71 ± 3.44	−17.86 ± 6.73	−11.74 ± 5.04	−4.35 ± 3.33	−14.05 ± 6.41	—
Accommodation	—	—	−10.33 ± 3.98	—	—	−2.42 ± 1.00	23.6 ± 8.9

Equ = equivalant power; NA = not applicable; pilo = pilocarpine 4.0%; Ratio = accommodation amplitude after refilling:accommodation amplitude before refilling; Sph = sphere

In some eyes, fibrin deposits were observed 2 weeks after surgery but absorbed after 4 weeks (Figure 4).

Postoperative Scheimpflug Photography Analysis

After surgery, changes in the ACD, lens thickness, and anterior and posterior capsule curvatures were present but were much less marked than before surgery. The results are shown in Table 5 and Figure 3.

Postoperatively, the ACD became shallower with increasing bag volume in all 3 groups. The mean lens thickness became thinner in Group A but was thicker in Groups B and C. The mean anterior curvature was significantly steeper with increasing bag volume in all 3 groups. The mean posterior curvature was significantly flatter in Group A after surgery. The mean posterior curvature in Group B was similar to the preoperative value. In Group C, the entire posterior capsule could not be photographed on Scheimpflug imaging because it was pushed too posteriorly.

The mean refilled capsular bag volume in Group A ranged from 0.075 to 0.081 mL. The mean refilled lens volume in Group B could be measured in 3 eyes and ranged from 0.100 to 0.117 mL.

Postoperative Refractions and Accommodation Amplitudes

In Group A (Table 2), the spherical power ranged from −1.60 to +2.58 D. The equivalent dioptric power ranged from −2.63 to +1.25 D.

In Group B (Table 3), the spherical power ranged from −15.75 to +3.25 D. The equivalent dioptric power ranged from −19.88 ± 0.00 to −1.23 ± 0.05 D.

Table 4. Refractions and accommodation amplitudes in Group C (100% bag volume filling).

	Mean ± SD						
	Before Refilling			After Refilling			
Monkey/Time	Sph (D)	Cyl (D)	Equ (D)	Sph (D)	Cyl (D)	Equ (D)	Ratio (%)
C1							
Before pilo	+2.25 ± 0.40	−2.50 ± 0.00	−1.00 ± 0.40	NA	NA	NA	—
1h after pilo	−9.92 ± 0.68	−9.25 ± 0.81	−14.63 ± 0.61	NA	NA	NA	—
Accommodation	—	—	−15.46 ± 0.49	—	—	—	—
C2							
Before pilo	+1.81 ± 0.48	−2.65 ± 0.20	+0.35 ± 0.41	−1.44 ± 0.11	−4.19 ± 0.21	−3.53 ± 0.05	—
1h after pilo	−4.23 ± 0.11	−8.06 ± 1.62	−8.47 ± 070	−3.25 ± 0.18	−7.56 ± 0.54	−7.05 ± 0.14	—
Accommodation	—	—	−9.10 ± 0.46	—	—	−3.48 ± 0.17	38.1 ± 1.0
C3							
Before pilo	−7.05 ± 0.10	−1.05 ± 0.10	−7.58 ± 0.10	−12.50 ± 0.18	−5.10 ± 0.57	−15.13 ± 0.38	—
1h after pilo	−18.60 ± 0.19	−1.40 ± 0.20	−19.10 ± 0.49	−14.13 ± 0.22	−8.56 ± 0.21	−18.56 ± 0.26	—
Accommodation	—	—	−11.54 ± 0.52	—	—	−3.43 ± 0.27	29.8 ± 1.3
C4							
Before pilo	−1.40 ± 0.22	−2.20 ± 0.37	−2.03 ± 0.56	−4.75 ± 0.00	−3.75 ± 0.00	−6.63 ± 0.00	
1h after pilo	−10.35 ± 0.20	−1.05 ± 0.10	−10.85 ± 0.19	−6.41 ± 0.20	−4.05 ± 0.37	−8.57 ± 0.56	
Accommodation	—	—	−8.85 ± 0.34	—	—	−1.94 ± 0.56	21.9 ± 1.3
C5							
Before pilo	−6.60 ± 0.12	−2.05 ± 0.48	−7.63 ± 0.21	−15.85 ± 0.20	−8.60 ± 0.12	−20.15 ± 0.24	—
1h after pilo	−13.94 ± 0.11	−2.50 ± 0.00	−15.19 ± 0.11	−18.90 ± 0.38	−6.90 ± 0.56	−22.50 ± 0.58	—
Accommodation	—	—	7.64 ± 0.10	—	—	−2.35 ± 0.50	30.7 ± 1.2
C6							
Before pilo	+1.70 ± 0.48	−2.65 ± 0.20	+0.35 ± 0.41	−6.35 ± 0.12	−4.65 ± 0.41	−8.72 ± 0.35	—
1h after pilo	−10.50 ± 0.27	−1.31 ± 0.11	−11.15 ± 0.23	−8.36 ± 0.42	−6.70 ± 1.74	−11.75 ± 1.02	—
Accommodation	—	—	−11.65 ± 0.27	—	—	−2.35 ± 1.18	20.2 ± 1.9
Overall							
Before pilo	−1.55 ± 3.92	−2.18 ± 0.55	−2.92 ± 3.41	−8.18 ± 5.25	−5.26 ± 1.73	−10.83 ± 6.01	—
1h after pilo	−11.26 ± 4.35	−3.93 ± 3.39	−13.23 ± 3.49	−10.21 ± 5.61	−6.75 ± 1.50	−13.69 ± 5.92	—
Accommodation	—	—	−10.71 ± 2.57	—	—	−2.71 ± 0.63	28.1 ± 6.5

Equ = equivalant power; NA = not applicable; pilo = pilocarpine 4.0%; Ratio = accommodation amplitude after refilling:accommodation amplitude before refilling; Sph = sphere

In Group C (Table 4), the spherical power ranged from −15.85 to −1.44 D. The equivalent dioptric power ranged from −20.15 to −3.53 D.

The refractions of monkeys A-5 and B-6 (Table 2 and Table 3) could not be measured due to cell deposits with posterior synechia on the anterior surface of the IOLs.

Table 2, Table 3, and Table 4 show the mean postoperative accommodation amplitudes and the accommodation ratios in Group A, Group B, and Group C, respectively. There was no statistically significant difference in the accommodation amplitude before or after surgery and in the accommodation ratios after surgery between the 3 groups.

DISCUSSION

This study confirmed that despite the creation of a large central CCC, our capsular bag–refilling technique prevented intraoperative and postoperative leakage of the injected silicone polymers, similar to the findings in our previous studies using pig cadaver eyes and rabbit eyes.[13] The injected polymers presses the IOL in the capsular bag against the CCC and anterior capsule, which is most likely the result of the buoyancy of the silicone. As a result, unless the IOL is forcibly pushed posteriorly, the injected cohesive silicone polymers with its high molecular weight does not leak through the space between the anterior capsule and IOL before it polymerizes in a consistent gel form.[13] This simple technique should be considered in future studies of capsular bag refilling to prevent silicone leakage from the capsular bag.

There has been a concern that sufficient accommodation cannot be achieved because a great portion of the middle of the anterior capsule (∼3.0 mm in

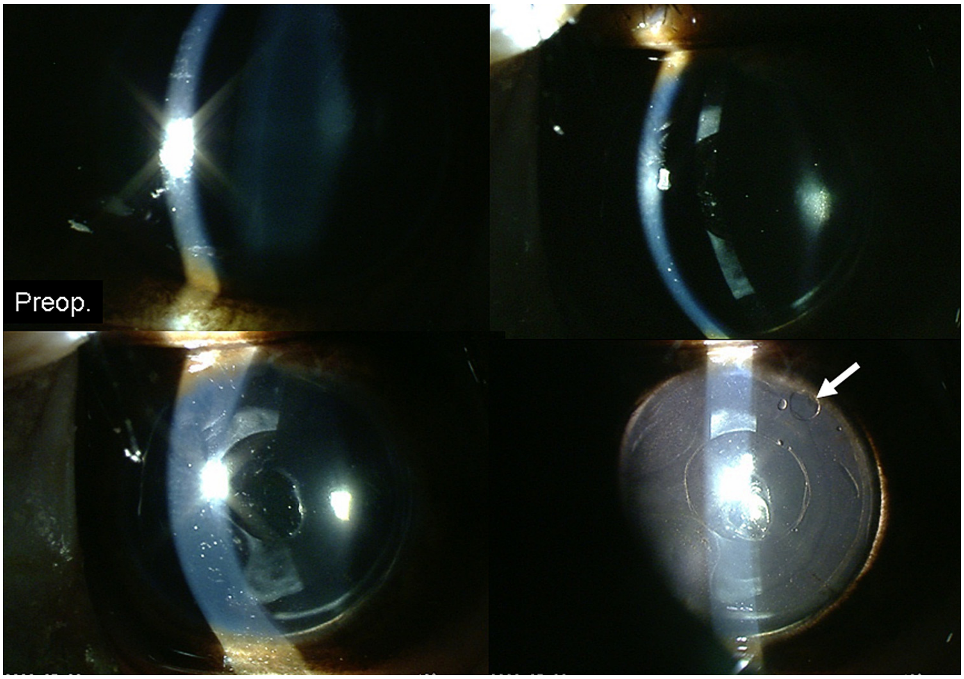

Figure 4. Slitlamp findings of the Macaca monkey eye shown in Figure 3. *Top left*: Preoperative view. *Top right*: Findings 2 weeks after surgery show a fine fibrinous membrane deposit in the CCC. The lens capsule is well filled with no obvious leakage of the injected silicone polymers. *Bottom left*: Findings 4 weeks after surgery show a slightly opacified peripheral posterior capsule due to LEC migration but a clear visual axis. *Bottom right*: On retroillumination, the CCC edge is clearly seen. The arrows show the delivery hole in the anterior membrane IOL, which is located behind the anterior capsule. There is no silicone leakage.

diameter), which contributes physiologically to ocular accommodation by substantial steepening, was removed to prevent anterior capsule opacification. In the current study, despite a large central capsule defect created by the CCC, mean accommodation amplitudes of approximately 2.5 D were obtained independent of the amount of filling, after a 4-week follow-up. The obtained accommodation amplitudes may be clinically useful for near vision because multifocal IOLs with a 3.0 D addition (add) allow patient's to read, and this 3.0 D add in vivo corresponds to approximately 2.5 D of accommodation if the amplitudes do not decline with time.

In this study, aged presbyopic monkeys should have been used to simulate the human condition that would require a capsular bag–refilling procedure for presbyopia. However, it was extremely difficult to find aged monkeys. We chose the monkeys mainly for facial contours that can make surgery easier to perform, such as a flatter nose, flatter forehead, and the absence of enophthalmos. Although these characteristics provided a better surgical approach, they also contributed to a higher incidence of myopia, as seen in Group B. Group B monkeys, however, had preoperative accommodation amplitudes comparable to those in the other 2 groups. Thus, the high myopia

Table 5. Postoperative measurements of ACD, lens thickness, and capsule curvatures using Scheimpflug photography.

	Mean ± SD				
Group/Time	ACD (mm)	Lens Thickness (mm)	Anterior Capsule Curvature (mm)	Posterior Capsule Curvature (mm)	Capsular Bag Volume (mL)
A					
Before pilo	2.52 ± 0.25	2.50 ± 0.17	7.74 ± 1.01	11.20 ± 1.54	0.079 ± 0.002
1 h after pilo	2.39 ± 0.24	2.66 ± 0.37	7.38 ± 0.92	10.65 ± 1.36	—
B					
Before pilo	2.43 ± 0.07	3.17 ± 0.34	7.35 ± 0.99	7.64 ± 1.26	0.106 ± 0.008
1 h after pilo	2.32 ± 0.05	3.35 ± 0.24	7.07 ± 0.84	6.91 ± 1.52	—
C					
Before pilo	2.14 ± 0.24	3.60 ± 0.15	6.28 ± 0.34	NA	—
1 h after pilo	2.02 ± 0.26	3.85 ± 0.27	6.09 ± 0.40	NA	—

ACD = anterior chamber depth; NA = not applicable; pilo = pilocarpine 4.0%

in Group B may not have adversely affected the results.

We were unable to find references to the crystalline lens volume in Macaca monkey eyes. We therefore tried to calculate it using Scheimpflug photography and a dedicated computer program. This may have resulted in errors in our calculations. The peripheral part of the crystalline lens was extrapolated using graphs with the curvatures and lens periphery; the calculated curvatures were not corrected for the distortion caused by the cornea and aqueous humor. However, 5 refilled capsules injected with 0.080 mL of silicone polymers (Group A) and 3 refilled capsules injected with 0.100 mL of silicone polymers (Group B) showed a mean calculated volume of 0.079 mL and 0.108 mL, respectively, values that were very close to the injected silicone volumes. Therefore, the calculated crystalline lens volume of 0.125 mL suggests no error occurred that would have significantly affected the results.

Because the anterior accommodating IOL used in this technique does not have a refractive power, the steepening of the anterior surface of the accommodating-membrane IOL shown by Scheimpflug analysis may have played the main role in achieving accommodation. The use of an IOL with a thinner, softer, and more elastic center that is more similar to the anterior capsule might achieve higher accommodation amplitude levels. Furthermore, more flattening of the anterior curvature might achieve higher accommodation because the flatter the lens and the smaller the volume of the anterior segment, the more potential energy is stored in the capsule for release by zonular relaxation.[14] The mean anterior curvature of the present accommodating-membrane IOL after surgery was 7.74 mm, 7.35 mm, and 6.28 mm in Group A, Group B, and Group C, respectively, and was significantly steep compared with not only its own anterior curvature of 15.5 mm but also with the mean preoperative anterior curvature values of 10.99 mm, 11.81 mm, and 11.07 mm, respectively. This may explain the high postoperative myopic shift in Groups B and C. Thus, controlling and restoring the preoperative original capsular bag shape is a must for achieving emmetropia and obtaining useful accommodation. This issue should be resolved in future studies.

The accommodation amplitudes in the 3 study groups, ranging from approximately 2.0 to 4.0 D with a mean of approximately 2.5 D, were independent of the volume of capsular bad filling. The Scheimpflug analysis showed analogous findings, with shallowing of the ACD, thickening of the refilled lens, and steepening of the anterior curvature of the IOL, although these changes were not great when compared with the preoperative values.

Results in previous in vitro studies[7,9] suggest that there is an optimum amount of filling to obtain greater accommodation. In these in vitro experiments, underfilling the capsular bag with a volume of 60% to 80% yielded significantly higher accommodation amplitudes. However, in the present study, there were no statistically significant differences before or after surgery in the accommodation amplitudes and accommodation ratios between the 3 amounts of filling. In other words, with this procedure, optimum accommodation amplitude was not dependent on the extent of capsular bag filling. The reason may be that in the previous in vitro experiment, the refilled capsule was stretched to generate accommodation, implying that the mechanism of accommodation was different.

Another explanation may be that the accommodating-membrane IOL was much thicker and stiffer than the anterior capsule and was not sufficiently thin and resilient; thus, the anterior curvature of the membrane did not change as much as the anterior capsule, and in fact changed very little, during accommodation. The membrane might have been too stiff to react sensitively to different amounts of silicone polymers and thus to exactly mimic the accommodation mechanism. Therefore, as discussed, making the membrane much thinner might result in greater accommodation amplitude but might also result in a different relationship between the accommodation amplitude and different amounts of filling. This might be advantageous because both factors do not need to be considered to achieve optimum accommodation amplitude and emmetropia if clinically useful accommodation can be obtained independent of the degree of capsular bag filling. If this were the case, the surgeon could concentrate on achieving emmetropia only, facilitating surgery.

The postoperative accommodation amplitudes attained were a small fraction of the preoperative values. This result is similar to the findings in our monkey experiments.[4,8] Koopmans et al.[10] report similar results (3.0 to 4.0 D of accommodation [up to 6.0 D]) in their rhesus monkey experiments using the plug-sealing technique; these values were far lower than preoperatively. The use of a thick (IOL-like) centrally located plug may be a cause. The structure of the polymerized silicone gel is different from that of the natural crystalline lens. Thus, the IOL may not be able to consistently follow the change in the shape of the capsular bag after pilocarpine application, as the normal crystalline lens capsule does. Another reason may be less adhesion between the lens capsule and polymerized silicone than is present preoperatively, which may result in less efficient transmission of the capsule forces.[4,10]

Regarding postoperative refraction, there was a significant tendency toward a myopic shift with increasing ACD, lens thickness, and anterior curvature that occurred with increasing bag volume after surgery. The results suggest that the postoperative refractive state depends, to a large degree, on the extent of capsular bag filling. Koopmans et al.[10] found that the postoperative refraction was influenced by overfilling and underfilling the lens capsule. The attainment of emmetropia is an important issue that must be solved before the potential clinical application of this procedure is determined.

Similar to the refractive error, the degree of the astigmatism increased with increased capsular bag filling. This may be caused by unwanted deformation of the accommodating-membrane IOL. Future studies must be performed to verify this finding and to offer a possible explanation for and to prevent the toric phenomenon.

As reported previously,[13] anterior and posterior CCCs eliminated capsule opacification for several weeks in the visual axis in rabbit eyes, which have a much higher propensity for LEC proliferation. Performing posterior CCCs might decrease the accommodation amplitude. However, we think the decrease would be limited because the posterior capsule does not play much of a role in accommodation. In fact, with 65% filling (Group A), the posterior capsule curvature became much flatter and was almost the same as with 80% filling (Group B) after surgery and similar accommodation amplitudes were attained. Apart from this series of experiments, we refilled 1 monkey lens in which both an anterior CCC and posterior CCC were created; an accommodation amplitude of 3.1 D was attained.

Although capsule opacification in the visual axis can be prevented by anterior and posterior CCCs, how and to what extent capsule opacification in other areas and residual LEC proliferation in the form of a Soemmerring ring affect accommodation have to be clarified. In the present study, we could not determine the answer to these questions because of the short follow-up. This remains a task for future studies.

In conclusion, our new capsular bag–refilling procedure, which required 20 to 30 minutes of surgical time, was highly reproducible in monkey eyes. There was no significant leakage of the injectable silicone polymers in young monkey eyes, as shown in numerous rabbit eye and pig cadaver eye experiments, and approximately 2.5 D of accommodation was obtained independent of the volume of capsular bag filling. These results suggest that this capsular bag–refilling technique warrants further studies to determine whether it has clinical application.

WHAT WAS KNOWN

- The new capsular bag–refilling procedure using an accommodating-membrane IOL prevented leakage of silicone polymers injected into the capsular bag in rabbit eyes. However, there was a concern that ocular accommodation cannot be obtained because the central part of the anterior capsule (3.0 to 4.0 mm CCC) is removed to avoid anterior capsule opacification.

WHAT THIS PAPER ADDS

- Despite creation of a central CCC in young monkey eyes, approximately 2.5 D of accommodation amplitude was obtained independent of the volume of capsular bag filling.

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