PRELIMINARY EFFICACY AND SAFETY OF A SILICONE OIL–FILLED FOLDABLE CAPSULAR VITREOUS BODY IN THE TREATMENT OF SEVERE RETINAL DETACHMENT

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Purpose: We previously invented a novel foldable capsular vitreous body (FCVB) in the treatment of severe retinal detachment. The purpose of this study was to determine its hydrolytic stability in vitro and further evaluate its efficacy and safety in human eyes.

Methods: The hydrolytic stability test proceeded according to State Food and Drug Administration guidelines about intraocular lenses of the ophthalmic implants. A standard three-port pars plana vitrectomy was performed, and FCVB was triple folded and sent into the vitreous cavity of three eyes; then silicone oil was injected into the capsule to support the retina. The treated eyes were examined using Goldmann applanation tonometry, fundus photography, optical coherence tomography, noncontact specular microscopy, and ultrasound biomicroscopy during a 12-month follow-up appointment.

Results: The mass of FCVB with silicone oil after 60-day accelerating aging temperature was equal to that at baseline. The FCVB can easily be implanted into the vitreous cavity through a 3-mm incision. The visual acuity and intraocular pressure after FCVB implantation show a slight elevation compared with those of preoperative eyes. The fundus and optical coherence tomography showed that the FCVB was well distributed in the vitreous cavity and evenly supported the retina. Retinal reattachment was found in 3 eyes at the 12-month examination. There was no statistically significant decrease in the density of corneal endothelial cells from baseline to 12 months after FCVB implantation. Ultrasound biomicroscopy showed that the FCVB smoothly contacted but not crushed the ciliary body.

Conclusion: Silicone oil–filled FCVB was shown to be effective and safe in 3 eyes as a vitreous substitute over a 12-month observation time.

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The vitreous body is a transparent gelatinoid structure that occupies four fifths of the volume of the eye. It consists of approximately 99% water and 1.0% inorganic salts, organic lipids, and hyaluronan, which can maintain a certain spatial relationship with dipolar water molecules.[1] The physiologic function of the vitreous body involves support of adjacent posterior segment structures, provision of an ocular refractive medium, and acting as a cell barrier to inhibit cell migration from the retina to the vitreous cavity.[2] Pars plana vitrectomy combined with artificial vitreous substitutes can treat severe retinal detachments (RDs), such as proliferative diabetic retinopathy, proliferative vitreoretinopathy, and endophthalmitis.[3–7]

A number of artificial vitreous substitutes (e.g., silicone oil [SO], heavy SO, and hydrogels) have been adopted.[8–16] Among these, SO, introduced by Cibis in

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1962, has been the most important adjunct for internal tamponade in the treatment of complicated retinal or choroidal detachment for the past 5 decades. However, SO is not always successful and an anatomic success rate of around 70% has been reported[11] with complications including cataracts, keratopathy, anterior chamber oil emulsification, and glaucoma.[12] Several reports have demonstrated the migration of SO droplets into the retina and the optic nerve, and others[17] have reported the widespread loss of myelinated optic nerve fibers owing to its free fluid characteristics within the eye. Therefore, despite half a century of effort to replace the vitreous body of the eye, an ideal and permanent vitreous body has yet to be found.[11,18]

In our previous studies,[19–22] we proposed a new strategy to avoid the above complications using a novel foldable capsular vitreous body (FCVB). The FCVB consists of a thin vitreous-shaped capsule with a tube–valve system made using computer and industrial technology. After foldable installation into the eye, an injectable medium such as a balanced salt solution (BSS) or SO could then be injected into the capsule and inflated to support the retina and control the intraocular pressure (IOP) through the tube–valve system (see **Figure 1, Supplemental Digital Content 1,** http://links.lww.com/IAE/A63).[19]

Interestingly, the FCVB with BSS changes the refraction very little when compared with SO and heavy SO, based on the Gullstrand–Emsley and Liou–Brennan schematic eyes.[20] Reports from the State Food and Drug Administration in China show that the FCVB has good mechanical, optical, and biocompatibility properties.[21]

Because the FCVB has never been used in eyes worldwide, we conducted an exploratory study of 11 patients implanted by FCVB with BSS in the treatment of severe RD at Zhongshan Ophthalmic Center and found it had good flexibility, safety, and efficacy during a 3-month study period.[22] Because SO is much more inert and preservative than BSS within the FCVB, the purpose of this study was to determine its hydrolytic stability of FCVB injected with SO in vitro and further evaluate its long-term (>3 months) efficacy and safety in human eyes.

Methods

In Vitro Study of the Hydrolytic Stability Test on Foldable Capsular Vitreous Body

The hydrolytic stability test proceeded according to State Food and Drug Administration guidelines about the biocompatibility standards of intraocular lenses of the ophthalmic implants. The mimicking immersion time was the actual test time multiplied by the coefficient of F. The formula for the coefficient of F is

$$F = 2.0^{(T_a - T_o)/10}.$$

T_a is the accelerating aging temperature (the actual water temperature) and T_o is the intraocular temperature (35°). The temperature of the thermal water bath (T_a) was set to 85°. According to the formula, the coefficient of F was 32. This means that immersion of 1 day at 85° in vitro is equivalent to immersion of 32 days at 35° in the intraocular environment.

The manufacture method of FCVB (Guangzhou Vesber Co, Ltd, Guangzhou, China) was previously described.[21] Six FCVBs were divided into two groups. Group 1 was injected with 4.0 mL of BSS via the drainage tube–valve (n = 3). Group 2 was injected with 4.0 mL of SO (n = 3). The FCVBs were immersed in distilled water in cups and placed into the thermal water bath. The temperature of thermal water bath was 85°, and the total observation period was 60 days. At the time points of baseline and 1, 6, 12, 24, 36, and 60 days, the FCVBs were weighed and their transparencies were recorded by camera.

Study Design

The study protocol was reviewed and approved by the Sun Yat-sen University Medical Ethics Committee (Zhongshan Ophthalmic Center Medical Ethics [2009] No. 07). The clinical trials strictly adhered to the principles of The World Medical Association Declaration of Helsinki and have been successfully registered with ClinicalTrials.gov (ClinicalTrials.gov ID: NCT00910702) and the Chinese Clinical Trial Register (ChiCTR-TNC-00000396).

To be included in the study, patients had to have a severe RD that could not be easily reattached with SO tamponade, such as posterior scleral ruptures with large disruptions of the retina or severe scleral ruptures with retinal and choroidal detachments or they had to have rigid retinal redetachments or inferior holes that occurred after silicone or heavy oil tamponade had been attempted. The independent expert committee confirmed that the RDs were not easily reattached by SO. The surgeon ensured this inclusion again during the FCVB surgery. If an eye could be injected with SO, the surgeon could deny the FCVB surgery.

Excluded participants included patients with serious heart, lung, liver, or kidney dysfunction; patients with serious eye inflammation; patients with a single eye; patients with suitable SO-filled eyes; and patients with diseases that the researchers deemed unsuitable for this clinical trial. Adverse events to be recorded were unbearable foreign body sensations, abnormal bleeding,

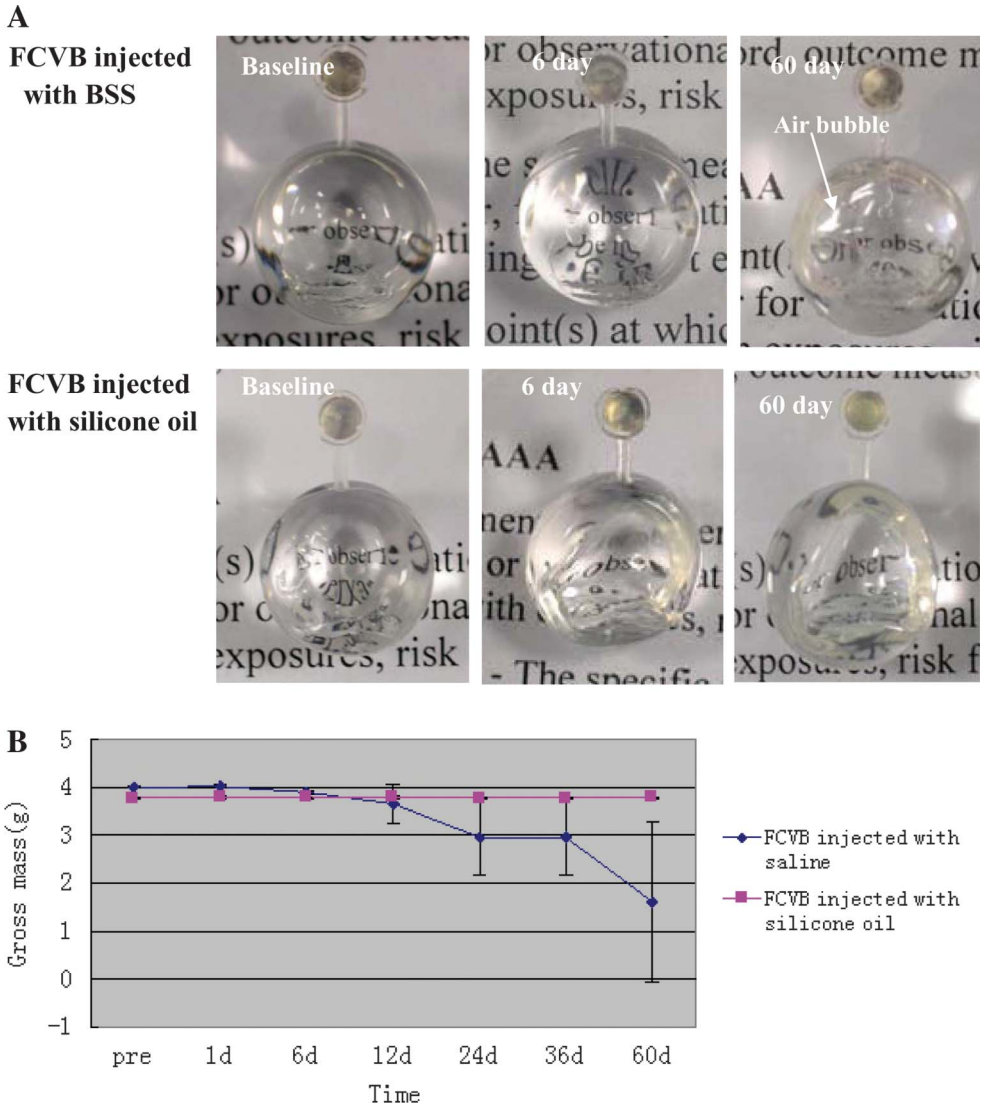


Fig. 1. The hydrolytic stability test of FCVB in vitro. Foldable capsular vitreous bodies injected with saline or SO maintained complete transparency and homogeneity. Foldable capsular vitreous bodies injected with SO were translucent when they were exposed to the air, but they soon recovered their transparency when cooled to normal temperature. There was no statistically significant difference in the mass of FCVB between baseline and 60 days later in these 2 groups.

severe inflammation, endophthalmitis, and sympathetic ophthalmia during clinical trials.

Study Treatment

Intervention procedures consisted of vitrectomy and FCVB implantation. A standard three-port pars plana vitrectomy was performed. Membrane peeling, retinotomies, and relaxing retinotomies were added if necessary. Perfluorocarbon liquid was totally removed. After an air–fluid exchange, incision was circumferentially prolonged to 3 mm, and then connected by a 0.5-mm radial incision toward cornea limbus. The FCVB was triple folded and implanted into the vitreous cavity. Some 4.0 mL to 5.5 mL of

Table 1. Demographic and Ocular Characteristics of 3 Patients at Baseline Examination

Patient	Age (Years)	Sex	History of Ophthalmic Surgery	Diagnosis
1	22	Female	Scleral wound exploration and repair	Ocular rupture (OS): 1. Scleral laceration 2. Choroidal detachment 3. RD
2	53	Male	Pars plana vitrectomy + SO tamponade	Ocular contusion (OD): 1. RD 2. SO eye
3	19	Male	Pars plana vitrectomy + SO tamponade + SO removal + scleral cryosurgery + C_3F_8 tamponade	Penetrating ocular injury (OD): 1. RD 2. Choroidal detachment

OS, left eye; OD, right eye.

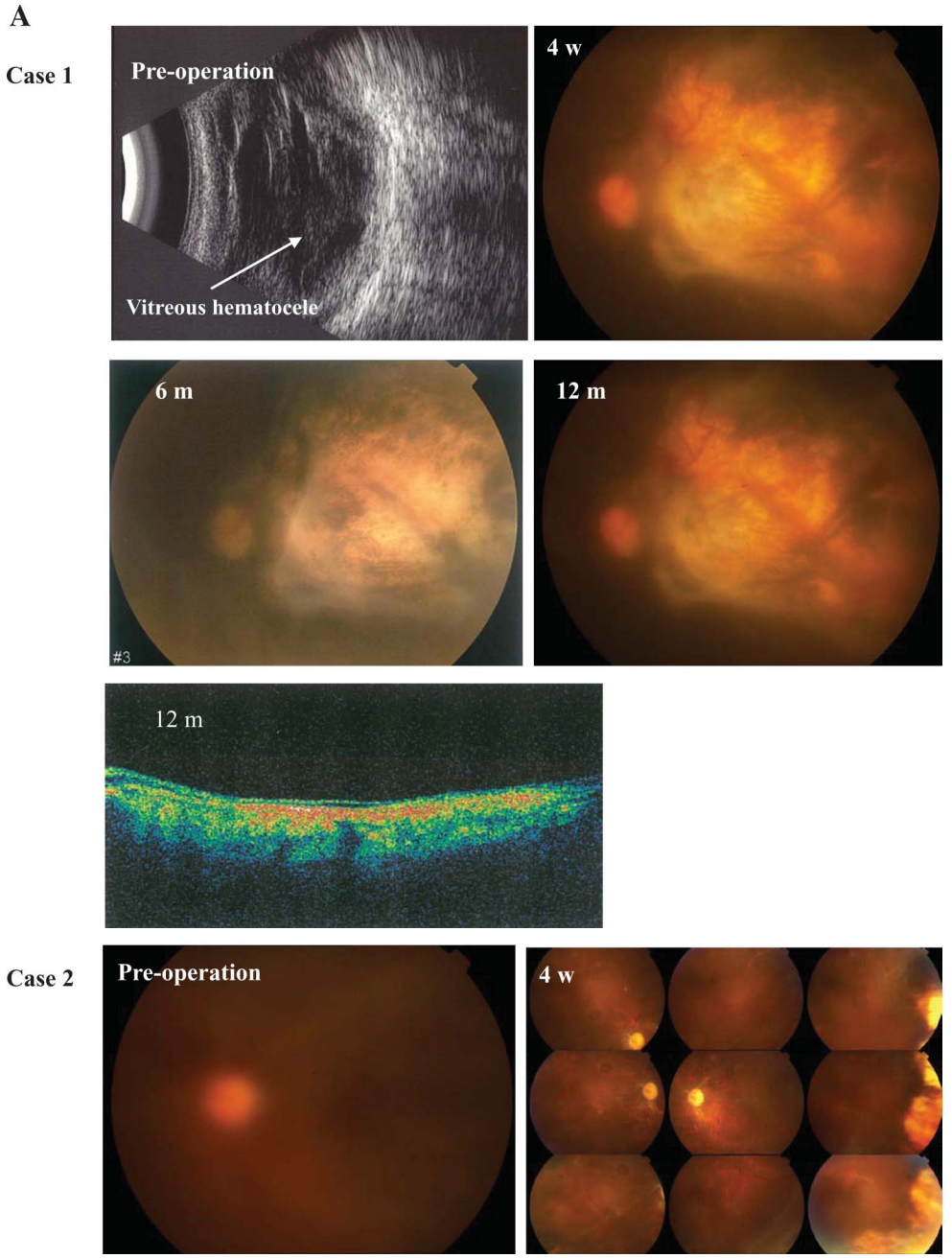


Fig. 2. Efficacy of 12-month FCVB with SO implantation in 3 cases. **A.** The fundus and optical coherence tomography images. Three cases have severe RDs at baseline. The retina was reattached, and the FCVB capsule supported the retina well, without any wrinkles at 4 weeks, 6 months, and 12 months implantation time. Optical coherence tomography also showed a similar result; the 60-μm-thick capsular membrane could evenly support the retina at 12 months' time. **B**. The graded scores of visual acuity at each time point after FCVB implantation show a slight increase compared with those at baseline. **C**. Intraocular pressure values. The IOPs at each point in time after FCVB implantation show a significant elevation compared with those at baseline in Cases 1 and 3 and a steady value in Case 2.

SO was injected into the capsule to support the retina through the valve subsequently fixed onto the scleral surface 10 mm away from the corneal limbus (see **video 1, Supplemental Digital Content 3,** http://links.lww.com/IAE/A65 **and Figure 1, Supplemental Digital Content 1,** http://links.lww.com/IAE/A63). As shown in **Supplemental Digital Content 3** (see **video 1;** http://links.lww.com/IAE/A65), the valve can match the SO syringe well and can be automatically closed after syringe removal.

Ocular examinations were performed using Goldmann applanation tonometry (Haag-Streit BM 900; Haag-Streit, Bern, Switzerland), slit-lamp biomicroscopy, direct ophthalmoscopy, and fundus photography (TRC-50EX; Topcon, Tokyo, Japan) at baseline; 3 days; 1, 2, 4, 6, and 8 weeks; and 3, 6, and 12 months after FCVB implantation surgery. Optical coherence tomography (Visante; Carl Zeiss Meditec, Dublin, CA), noncontact specular microscopy (SP-3000P, Topcon), and ultrasound biomicroscopy (SW-3200 Kinscan; Suoer, Tianjin, China) were performed at

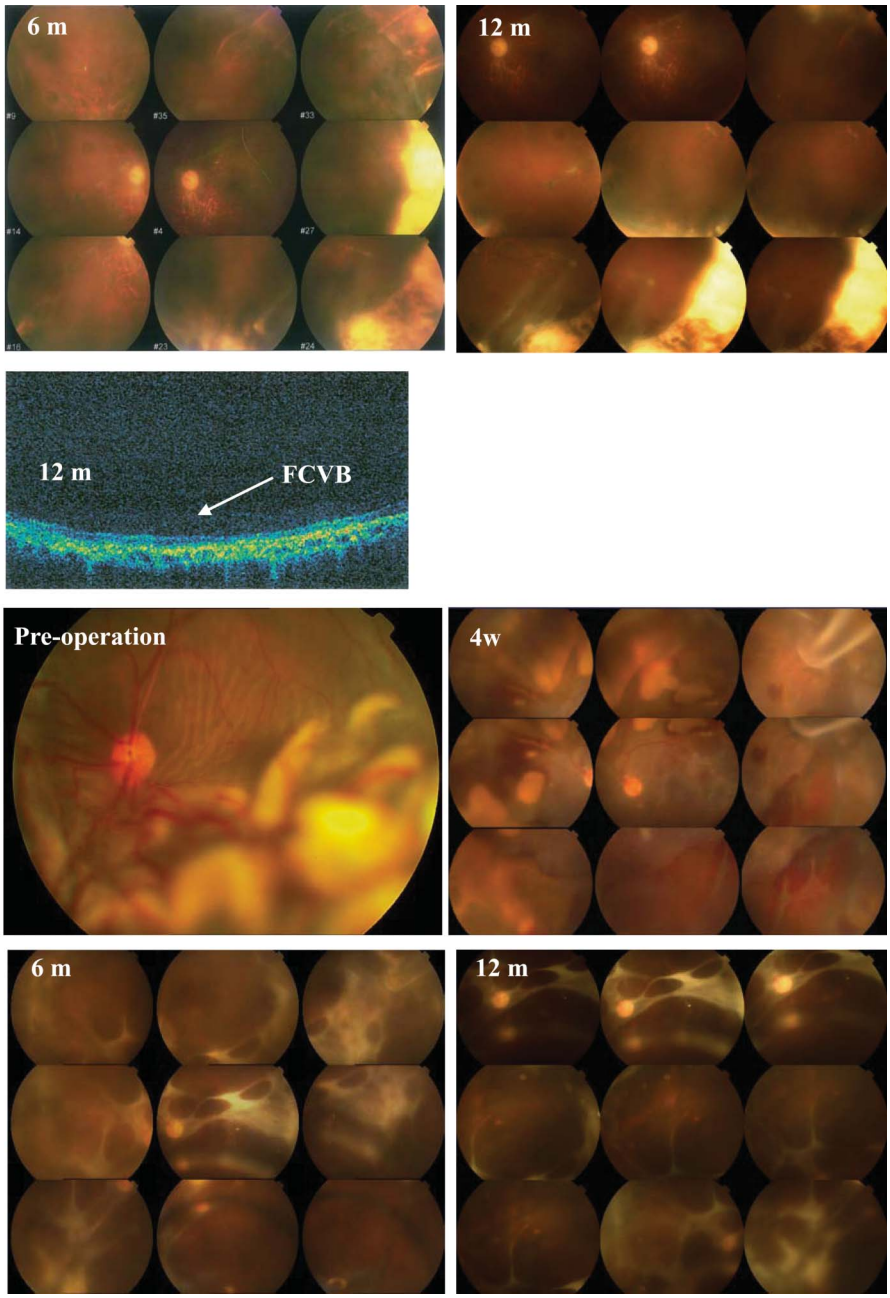


Fig. 2. Continued

baseline and at 6 months and 12 months. Postoperative IOP could be increased with a 2-mL syringe with BSS. An intraocular YAG laser was used if the membrane occurred in the capsule.

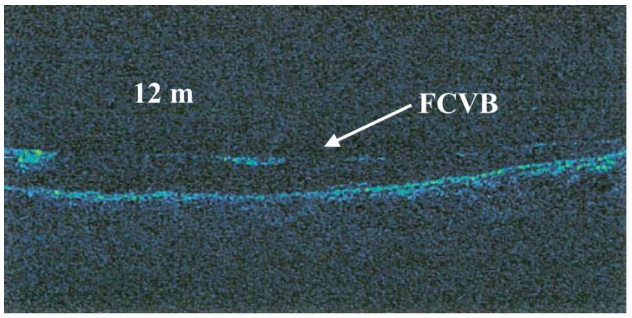
Outcome Measures

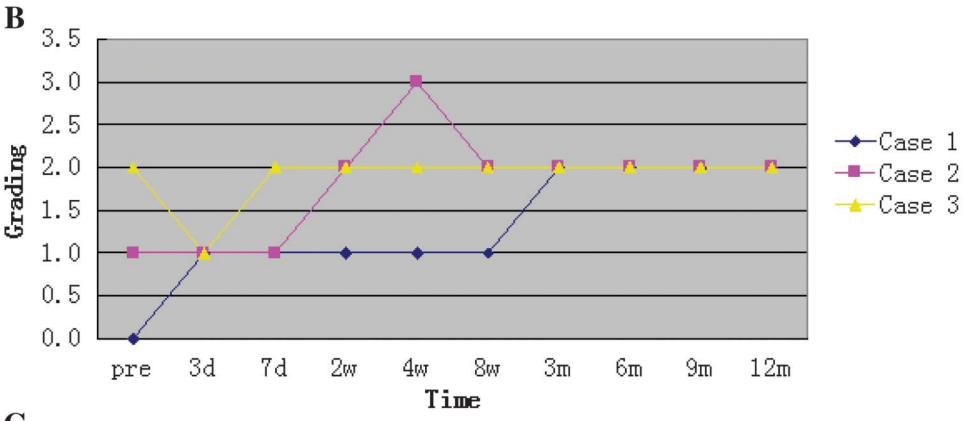
The primary outcome measure was complete retinal reattachment at 12 months after implantation of the FCVB, as determined by the fundus examination and optical coherence tomography. The secondary outcome measures included visual acuity and IOP. Visual acuity was graded according to the following system: no light perception was scored as 0, light perception was scored as 1, hand motion was scored as 2, finger count was scored as 3, ≥0.05 was scored as 4, and ≥0.1 was scored as 5.

Results

The Hydrolytic Stability Test

No change in gross appearance, transparency, or emulsification of SO was observed in these two groups. The mass of FCVB with SO after 60-day





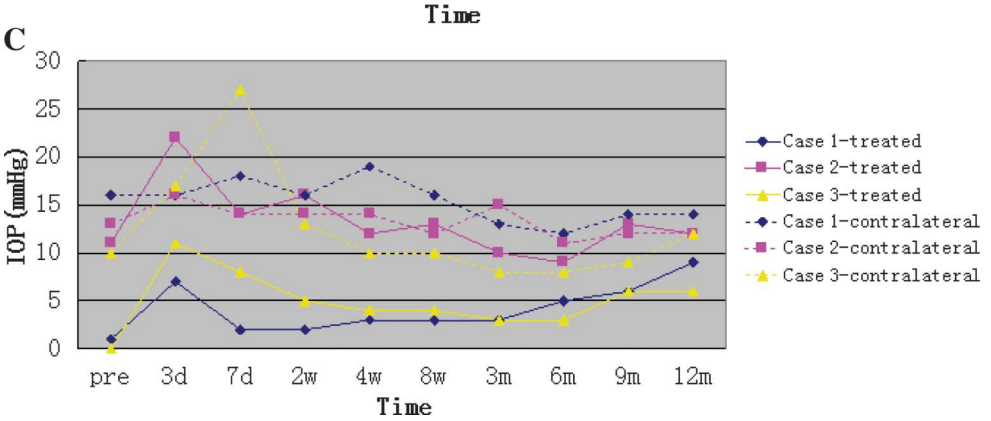


Fig. 2. Continued

accelerating aging temperature was equal to that at baseline. However, the mass of FCVB with BSS after 60 days showed a slight decrease when compared with that at baseline (Figure 1). These data indicate that the FCVB injected with SO is more inert and preservative than FCVB injected with BSS over the course of 5 years (60 days × 32 = 1,920 days). But there was no statistical significant difference in the mass of FCVB between baseline and 60 days in these 2 groups ($T = 2.460$, $P = 0.133$; $T = -0.238$, $P = 0.834$).

Study Patients

Between December 2009 and July 2010, 3 patients (3 eyes) were enrolled in this study. The demographic and ocular characteristics of the patients at baseline examination are shown in Table 1. The mean age of the patients was 31.3 years (SD, 19–53 years), and 2 of the 3 patients were men. Case 1 had severe ocular rupture with retinal and choroidal detachments. Case 2 had redetachment with subretinal SO after SO tamponade. Case 3 had redetachment with anterior chamber SO after SO and C_3F_8 tamponade. All three patients gave written informed consent.

Efficacy Evaluations

The FCVB can easily be implanted in the vitreous cavity through a scleral mini-incision (see **video 1, Supplemental Digital Content 3;** http://links.lww.com/IAE/A65). After FCVB tamponade, the fundus was clearly visible and the retina was reattached. Foldable capsular vitreous body was well distributed in the vitreous cavity, and the FCVB capsule supported the whole retina well, without any wrinkles during the 12-month implantation time, as

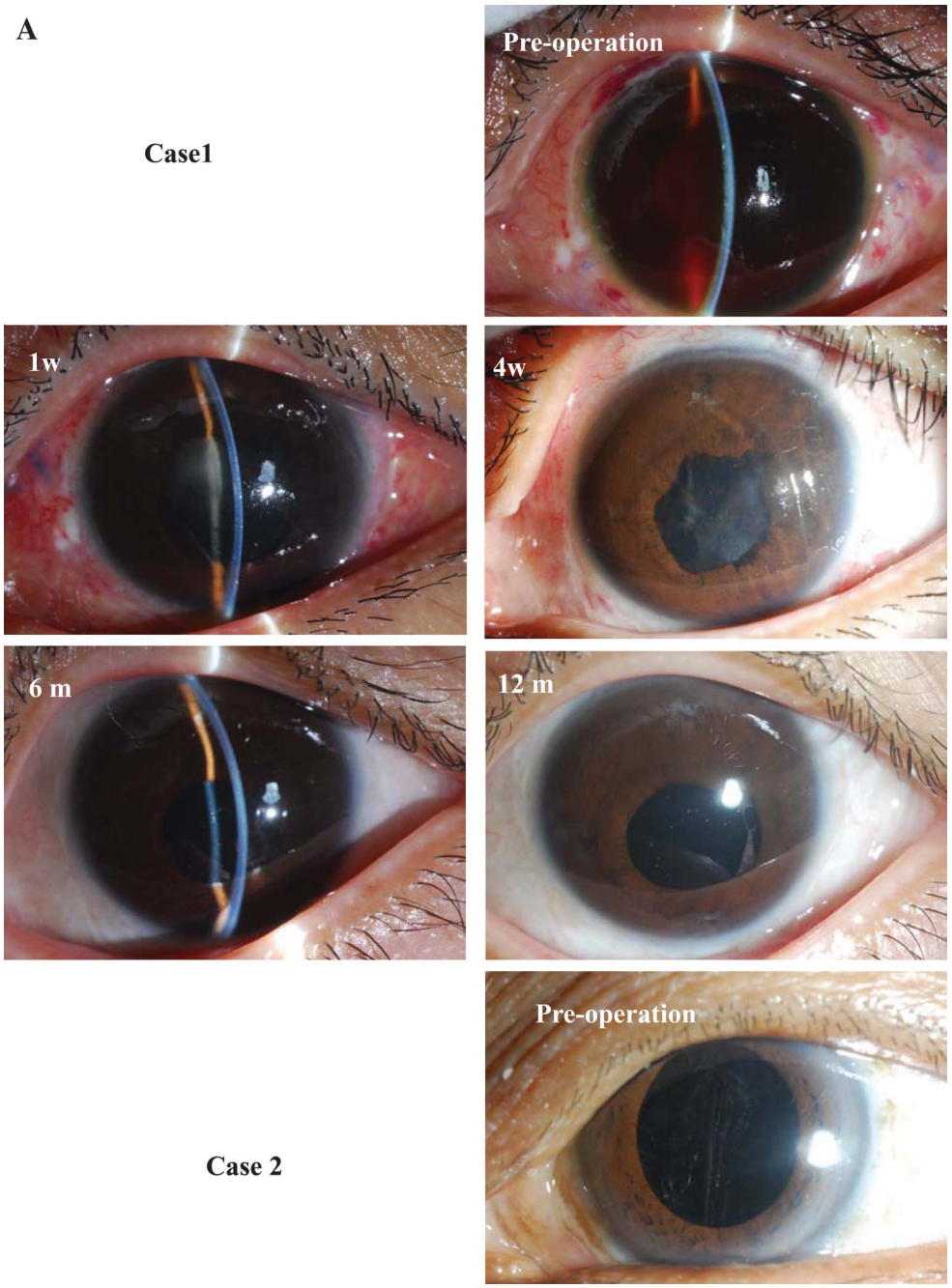


Fig. 3. Safety of 12-month FCVB with SO implantation in 3 cases. **A.** Anterior segment photography showing no obvious inflammation. **B**. There was no statistically significant conjunctival congestion, corneal edema, keratic precipitate, or aqueous flare. The Wilcoxon signed rank test was used to test for conjunctival congestion (P = 0.180), corneal edema (P = 0.317), keratic precipitate (P = 1.000), and aqueous flare (P = 1.000). **C**. Corneal endothelial numbers. There was no statistically significant difference in density of corneal endothelial cells between baseline and 12 months after FCVB implantation (Wilcoxon signed rank test: P = 0.180). **D**. Ultrasound biomicroscopy showed that the FCVB smoothly contacted but not crushed the ciliary body. No edema or atrophy of ciliary bodies was observed.

shown in Figure 2A. Optical coherence tomography at 12 months indicated that the 60-μm-thick capsular membrane could evenly support the retina. Retinal reattachments were observed in all 3 eyes by the fundus at 12 months after implantation. A good appearance of the eyes was found in the FCVB implantation eye. Based on the above data, it appears that FCVB can be well distributed in the vitreous cavity and can evenly support the retina.

In these 3 cases, visual acuity of 1 patient improved from no light perception to hand motion, 1 patient from light perception to hand motion, and 1 patient was preserved as hand motion (Figure 2B). Intraocular pressure is essential to sustaining the appearance of the eyes. During observation time, IOP can be adjusted using a 2-mL syringe with BSS. Two of 3 eyes received 0.2 mL of BSS additional injection at 2 weeks. The IOPs at each time point after FCVB implantation show a significant elevation compared with those at baseline in Cases 1 and 3 and a steady value in Case 2 (Figure 2C). It seems that the FCVB injected with SO can restore the IOP well.

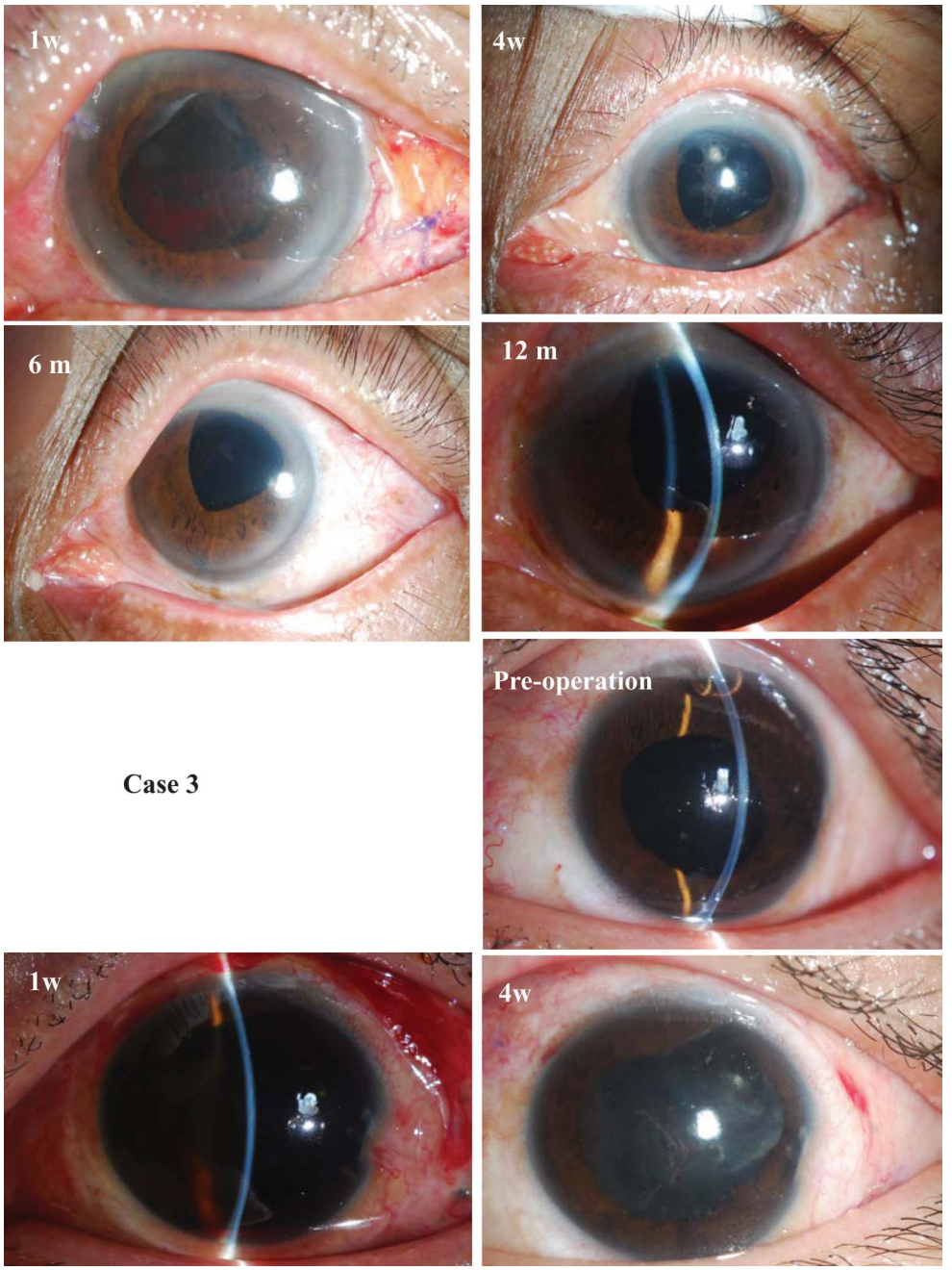
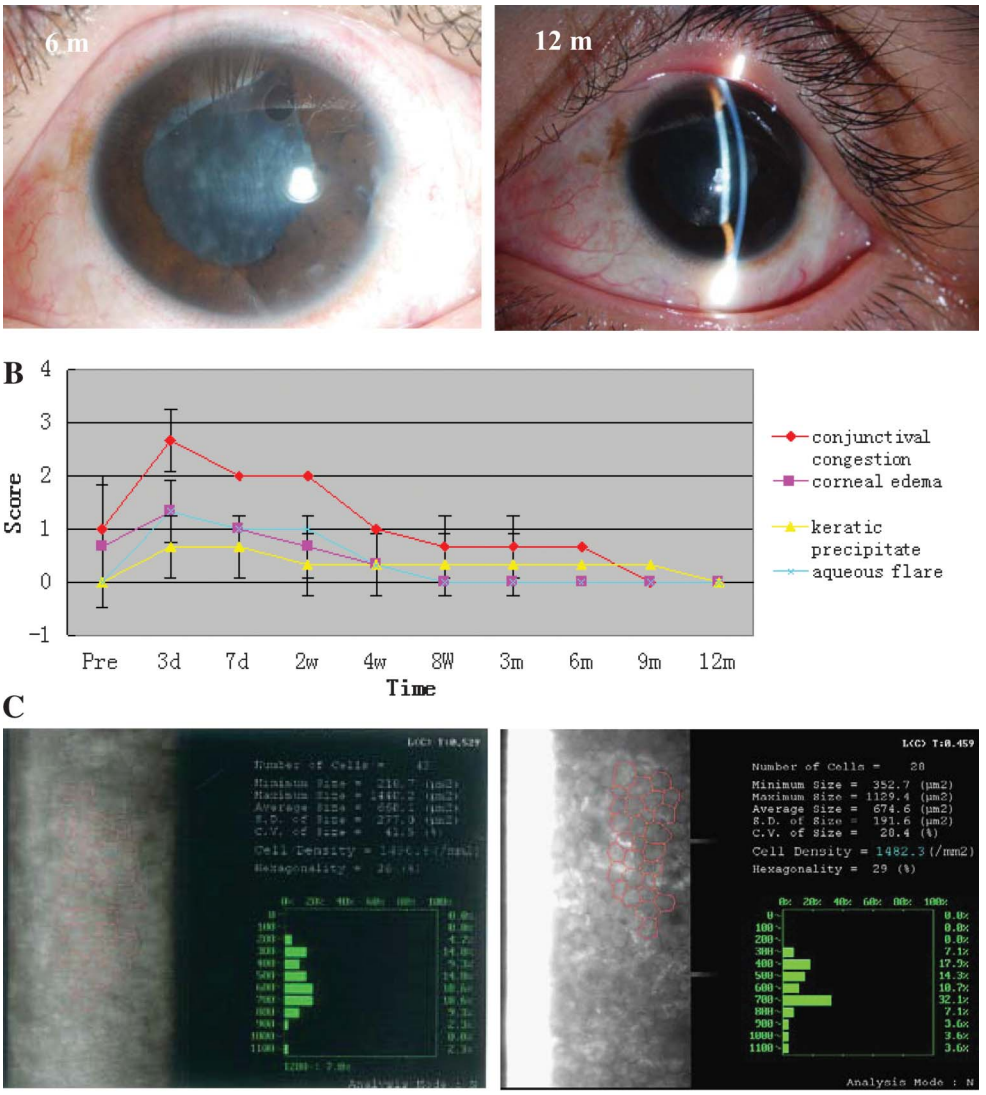


Fig. 3. Continued

Safety Evaluations

There was slight conjunctival hyperemia by Day 7 after surgery in FCVB-filled eyes. No serious complications (e.g., corneal keratopathy or intraocular inflammation) were observed. Slight hyphema from the vitreous was quickly absorbed within 1 week to 2 weeks after surgery. There was no statistically significant conjunctival congestion, corneal edema, keratic precipitate, or aqueous flare at baseline or at 12 months (Figure 3A). The Wilcoxon signed rank test was used to test for conjunctival congestion (P = 0.180), corneal edema (P = 0.317), keratic precipitate (P = 1.000), and aqueous flare (P = 1.000) (Figure 3B).

There was no statistically significant decrease in the density of corneal endothelial cells from baseline to 12 months after FCVB implantation, as shown in Figure 3C (Wilcoxon signed rank test: P = 0.180). Ultrasound biomicroscopy showed that the FCVB smoothly contacted but not crushed the ciliary body. No edema or atrophy of ciliary bodies was observed (Figure 3D). Fundus fluorescein angiography in Case



Baseline of Case 3 | 12 months after FCVB implantation

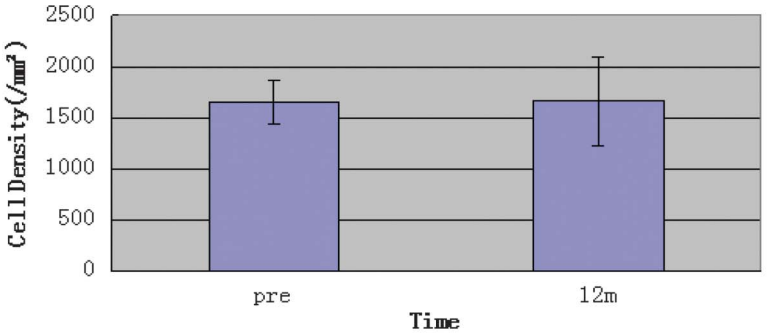
Fig. 3. Continued

3 shows that the capsule of FCVB does not cause ischemia to the retina (see **Figure 2, Supplemental Digital Content 2**; http://links.lww.com/IAEA64). No adverse events were observed during the study.

Discussion

The natural vitreous has a thin, membranelike structure that continues from the ora serrata to the posterior pole that corresponds to the vitreous cortex.[1] Inspired from this structure, we first used FCVB injected with SO as a novel vitreous substitute and demonstrated that the FCVB can restore the retinal structure and partial functions in the treatment of severe RD in human eyes. The present study shows that FCVB is an effective and safe artificial vitreous for severe RDs and can avoid complications induced by SO such as glaucoma, corneal degeneration, and SO emulsification during a 12-month implantation time.

Traditional SO is used for intraocular tamponade because of its buoyant force and high surface tension. Because SO is lighter than water, it is unable to adequately support the retina, especially the inferior retina. Foldable capsular vitreous body was designed to omnidirectionally support the retina by a 360° solid arc after it is injected with BSS or SO. The FCVB consists of liquid silicone rubber, which is a nontoxic and stable material.[21] Mechanical properties indicate that liquid silicone rubber has suitable hardness and high strain capability, which allows the 60-μm-thick FCVB to stretch its capsule to fill all the space of vitreous cavity, close the retinal holes, and evenly and gently support the detached retina.[21] No water–oil interface was observed in either BSS or SO-filled FCVB eyes. The



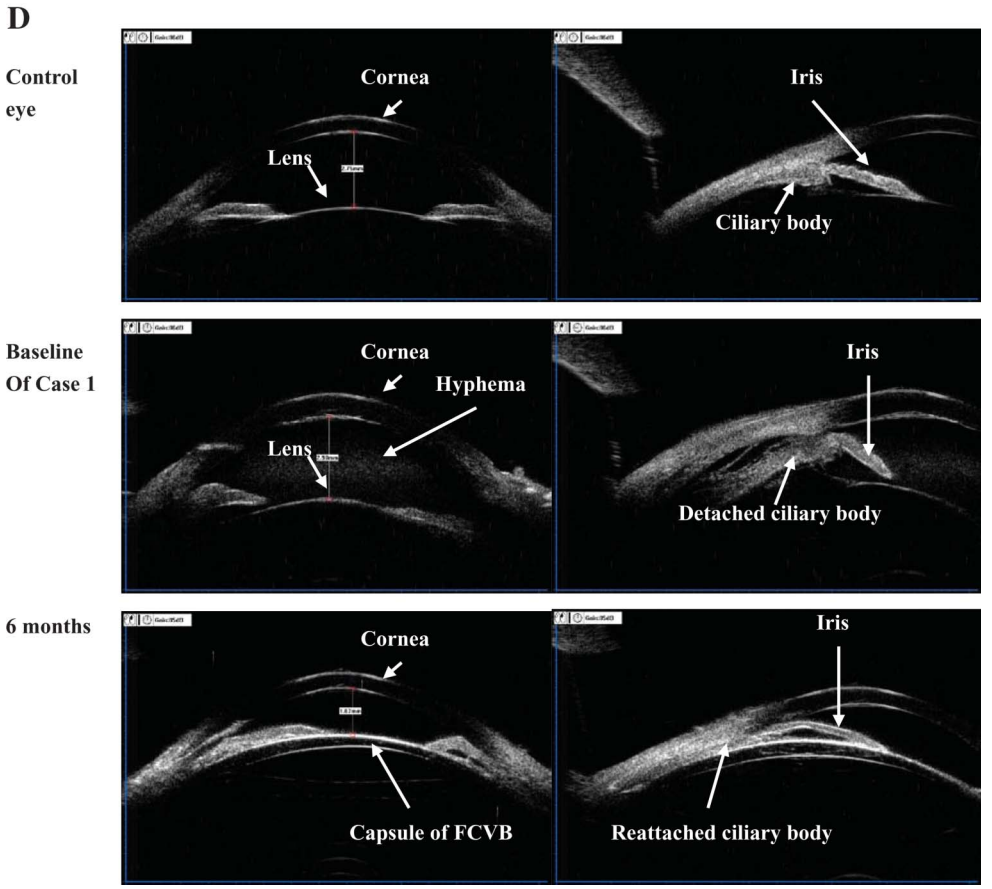


Fig. 3. Continued

heavy oil and hydrogels have the potential use in the tamponade in the FCVB. We also used magnetic resonance imaging to monitor the support of the FCVB and found that FCVB can fully fill the vitreous cavity.[23] Therefore, FCVB provides us with a new therapeutic theory and product for severe RD.

The eye in Case 1 had severe ocular rupture and retinal and choroidal absence. Cases 2 and 3 had already failed to respond to SO tamponade. It was very difficult to reattach these 3 eyes after SO tamponade. However, it is an inspiring result that, using FCVB with SO, all three eyes were reattached. The inferior detached retina was effectively sustained, as shown in Figure 2. Twelve months after FCVB implantation, we found that the structures of the human eyes were gradually restored.

As shown in Figure 2 (B and C), visual acuity and IOP in FCVB postoperative eyes showed an increase, indicating that the retinal and ciliary body functions, to some extent, were rehabilitated. Although the retinas were apparently reattached, visual acuity was poor in each instance with no patient achieving better than hand motion vision. This may relate to the initial severity of the RDs.

Because tiny apertures existed in the capsule of the FCVB, some BSS leakage occurred. This was proven by 11 patients implanted by FCVB with BSS[22] and by in vitro study of the hydrolytic stability test as shown

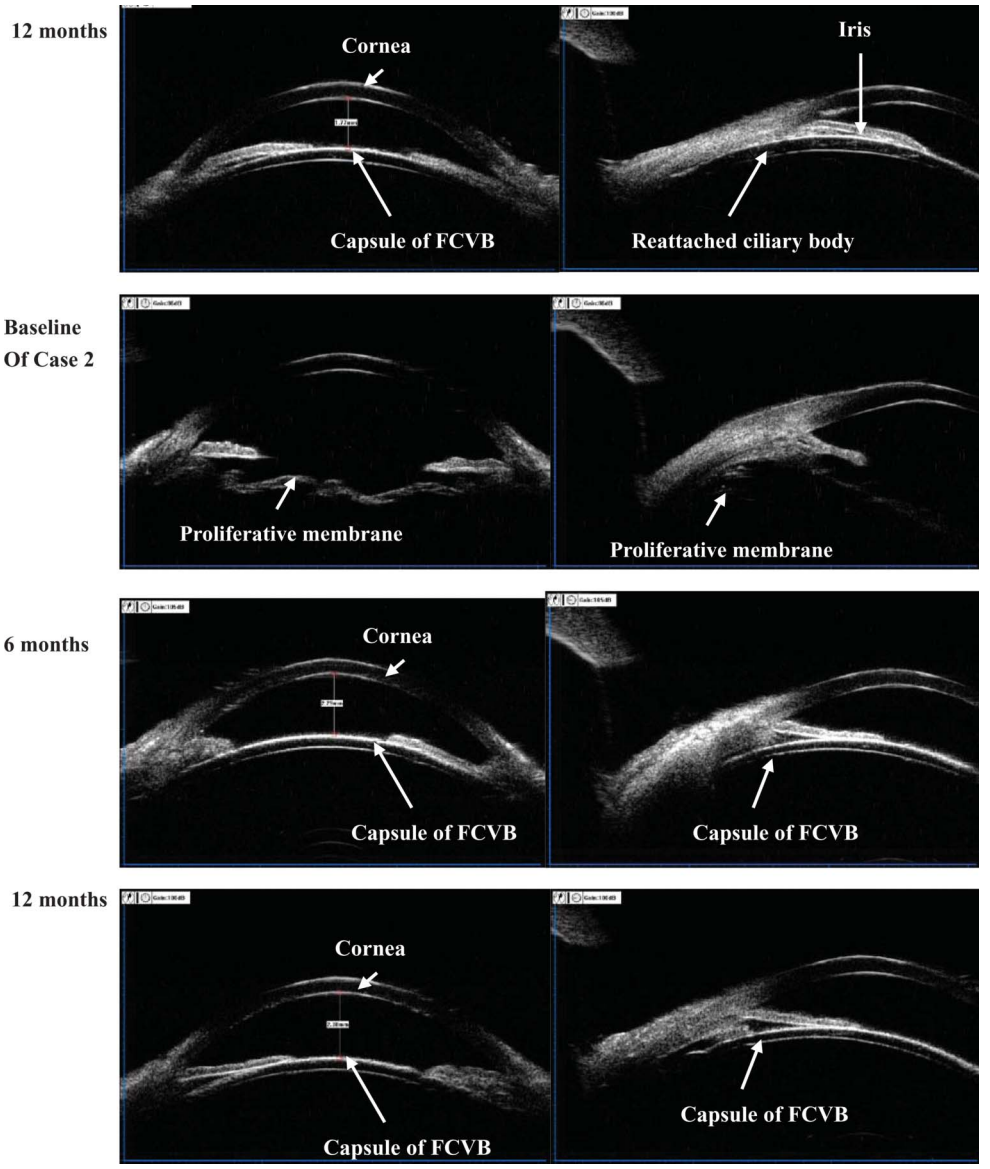


Fig. 3. Continued

in Figure 1. Foldable capsular vitreous body allows the addition of BSS to increase the IOP through the valve by syringe. This is a unique characteristic among all the clinical vitreous substitutes. In contrast, SO in the capsule of FCVB has no leakage, as is also shown in Figure 1. From these data, we can conclude that the FCVB with SO has shown good preservation and efficacy in this clinical trial.

In the rabbit model of proliferative vitreoretinopathy, we found that the FCVB with BSS very closely mimicked the morphology and restored physiological functions such as support, refraction, and cellular barriers during a 3-month observation period, without the obvious complications commonly induced with SO.[24] The FCVB capsule can provide the detached retina with a platform to form a flat scar and a barrier to block cell migration from the retina to the vitreous cavity.

Moreover, because of the constraints of the FCVB capsule, SO in the FCVB cannot flow into the anterior chamber or subretina or outside of the eye and does not easily emulsify with time, as shown in Figures 1 and 2. In SO-filled eyes, however, 11% to 49% of SO may migrate to the anterior chamber[25] and nearly 100% emulsifies at 12 months and subsequently induces complications such as glaucoma and corneal keratopathy.[26] Disordered flow out of the vitreous cavity and emulsification are the origin of SO complications.

Additionally, in our study, patients could maintain a normal position, regardless of the time of day. However, patients whose eyes are filled with SO need

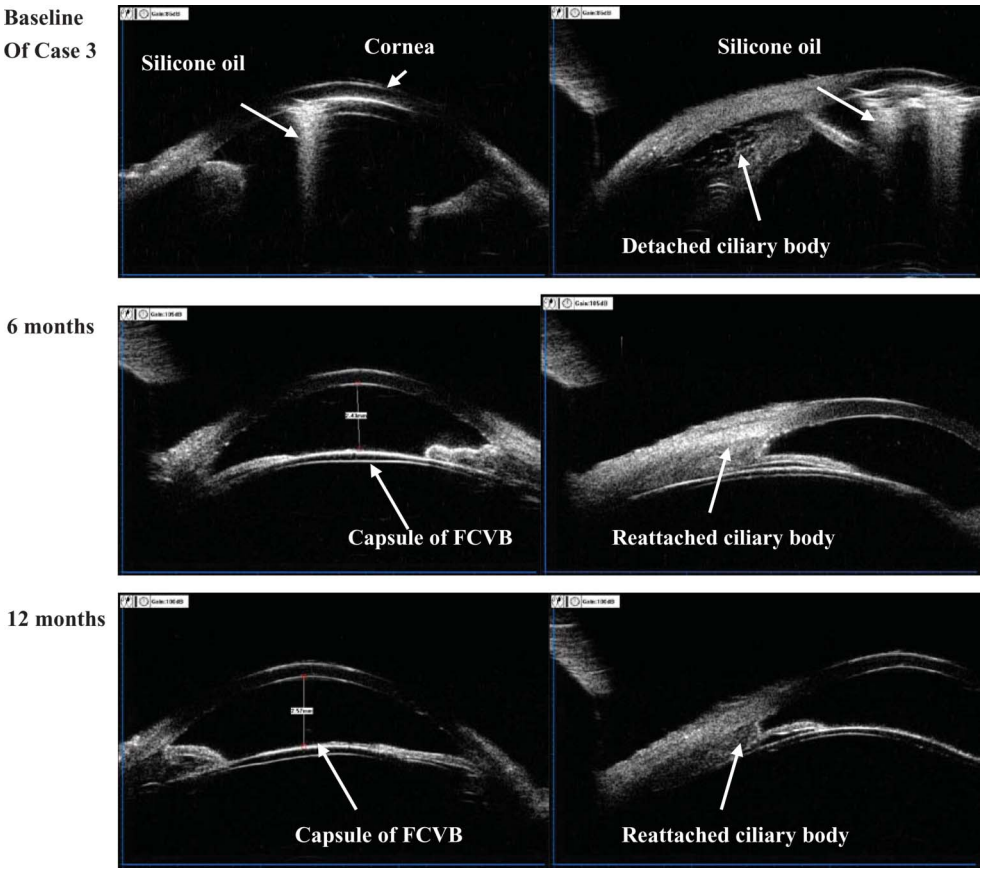


Fig. 3. Continued

to avoid supine positioning, which would be unnecessary with FCVB implant.

Optical properties indicate that the material has high light transmission and laser irradiation stability.[21] Laser irradiation stability tests demonstrated that FCVB can sustain 1,500-mW 0.2-second 532-nm green laser and 9-mW Nd:YAG laser. Laser therapy is an important method in ophthalmology. Good laser irradiation stability indicates that in patients with FCVB tamponade, if the proliferative membranes threaten the vision or the retina, associated laser therapy will eliminate the membranes' adherence to the capsule. An Nd:YAG laser successfully cleaned the front surface of FCVB in Case 1.

No obvious inflammation was observed in the three patients after FCVB implantation. Although a hemorrhage existed in the anterior chamber of one patient, this was because of a serious injury of the ciliary body and was not related to the FCVB tamponade. Ultrasound biomicroscopy showed that the FCVB can reattach the detached ciliary body and smoothly contact but not crush the ciliary body. Fundus fluorescein angiography shows that the retinal vessels are still open after FCVB implanted.

In addition, because tiny (300 nm) apertures exist in the capsule, the FCVB can release dexamethasone sodium phosphate sustainably and mechanically and can be used as an intravitreal drug delivery system in addition to serving as a vitreous substitute.[27] This dexamethasone sodium phosphate is a public vehicle for many drugs and factors and is very different from the current dexamethasone sodium phosphate such as liposome, biodegradable microspheres and nanospheres, high molecular polymers, and mechanical pumps.

These three cases are still under observation. Future studies will focus on >12-month safety and efficacy of FCVB. This study provides the basis for further multiple center clinical trials to evaluate the functions of FCVB. Based on this clinical trial, a nine-hospital clinical trial is in progress to ascertain FCVB safety and efficacy as a vitreous substitute in China.

In conclusion, FCVB filled with SO can be transplanted into the vitreous body easily and perform good efficacy and safety in the treatment of severe RD during a 12-month observation period.

Key words: foldable capsular vitreous body, retinal detachment, silicone oil.

Acknowledgments

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References

1. Green WR, Sebag J. Vitreoretinal interface. In: Ryan SJ, eds. Retina. 4th ed. Philadelphia, PA: Elsevier Mosby; 2006:1921– 1989.
2. Le Goff MM, Bishop PN. Adult vitreous structure and postnatal changes. Eye 2008;22:1214–1222.
3. Castellarin A, Grigorian R, Bhagat N, et al. Vitrectomy with silicone oil infusion in severe diabetic retinopathy. Br J Ophthalmol 2003;87:318–321.
4. Karel I, Kalvodová B. Long-term results of pars plana vitrectomy and silicone oil for complications of diabetic retinopathy. Eur J Ophthalmol 1994;4:52–58.
5. Pastor JC. Proliferative vitreoretinopathy: an overview. Surv Ophthalmol 1998;43:3–18.
6. Quiram PA, Gonzales CR, Hu W, et al. Outcomes of vitrectomy with inferior retinectomy in patients with recurrent rhegmatogenous retinal detachments and proliferative vitreoretinopathy. Ophthalmology 2006;113:2041–2047.
7. Yoon YH, Lee SU, Sohn JH, Lee SE. Result of early vitrectomy for endogenous. Klebsiella pneumoniae endophthalmitis. Retina 2003;23:366–370.
8. Cibis PA, Becker B, Okun E, Canaan S. The use of liquid silicone in retinal detachment surgery. Arch Ophthalmol 1962;68:590–599.
9. The Silicone Study Group. Vitrectomy with silicone oil or sulfur hexafluoride gas in eyes with severe proliferative vitreoretinopathy: results of a randomized clinical trial. Silicone Study Report 1. Arch Ophthalmol 1992;110:770–779.
10. Azen SP, Scott IU, Flynn HW Jr, et al. Silicone oil in the repair of complex retinal detachments. A prospective observational multicenter study. Ophthalmology 1998;105:1587–1597.
11. Soman N, Banerjee R. Artificial vitreous replacements. Biomed Mater Eng 2003;13:59–74.
12. Ichhpujani P, Jindal A, Jay Katz L. Silicone oil induced glaucoma: a review. Graefes Arch Clin Exp Ophthalmol 2009; 247:1585–1593.
13. Scott IU, Flynn HW Jr, Murray TG, et al. Outcomes of complex retinal detachment repair using 1000- vs 5000-centistoke silicone oil. Arch Ophthalmol 2005;123:473–478.
14. Bhisitkul RB, Gonzalez VH. ''Heavy oil'' for intraocular tamponade in retinal detachment surgery. Br J Ophthalmol 2005;89:649–650.
15. Hong Y, Chirila TV, Vijayasekaran S, et al. Biodegradation in vitro and retention in the rabbit eye of crosslinked poly (1-vinyl-2-pyrrolidinone) hydrogel as a vitreous substitute. J Biomed Mater Res 1998;39:650–659.
16. Maruoka S, Matsuura T, Kawasaki K, et al. Biocompatibility of polyvinylalcohol gel as a vitreous substitute. Curr Eye Res 2006;31:599–606.
17. la Cour M, Lux A, Heegaard S. Visual loss under silicone oil. Klin Monbl Augenheilkd 2010;227:181–184.
18. Steijns D, Stilma JS. Vitrectomy: in search of the ideal vitreous replacement. Ned Tijdschr Geneeskd 2009;153:A433.
19. Gao Q, Mou S, Ge J, et al. A new strategy to replace the natural vitreous by a novel capsular artificial vitreous body with pressure-control valve. Eye 2008;22:461–468.
20. Gao Q, Chen X, Ge J, et al. Refractive shifts in four selected artificial vitreous substitutes based on Gullstrand-Emsley and Liou-Brennan schematic eyes. Invest Ophthalmol Vis Sci 2009;50:3529–3534.
21. Liu Y, Jiang Z, Gao Q, et al. Technical standards of foldable capsular vitreous body regarding mechanical, optical and biocompatible properties. Artif Organs 2010;34:836–845.
22. Lin X, Ge J, Gao Q, et al. Evaluation of the flexibility, efficacy, and safety of a foldable capsular vitreous body in the treatment of severe retinal detachment. Invest Ophthalmol Vis Sci 2011; 52:374–381.
23. Zhang R, Wang T, Xie C, et al.Evaluation of supporting role of a foldable capsular vitreous body with magnetic resonance imaging in the treatment of severe retinal detachment in human eyes. Eye (Lond.) 2011;25:794–802.
24. Chen J, Gao Q, Liu Y, et al. Evaluation of morphology and functions of a foldable capsular vitreous body in the rabbit eye. J Biomed Mater Res B Appl Biomater 2011;97:396–404.
25. Honavar SG, Goyal M, Majji AB, et al. Glaucoma after pars plana vitrectomy and silicone oil injection for complicated retinal detachments. Ophthalmology 1999;106:169–176.
26. Federman JL, Schubert HD. Complications associated with the use of silicone oil in 150 eyes after retina-vitreous surgery. Ophthalmology 1988;95:870–876.
27. Liu Y, Ke Q, Chen J, et al. Dexamethasone sodium phosphate sustained mechanical release in the foldable capsular vitreous body. Invest Ophthalmol Vis Sci 2010;51:1636–1642.