# Clinical Device-Related Article
# Evaluation of morphology and functions of a foldable capsular vitreous body in the rabbit eye

**Jiajia Chen,[1] Qianying Gao,[1] Yaqin Liu,[1] Jian Ge,[1] Xianwu Cao,[2] Yan Luo,[1] Danping Huang,[1] Gege Zhou,[2] Shaofen Lin,[1] Jianxian Lin,[1] Chi Ho To,[3] Andrew W. Siu[3]**

[1]State Key Laboratory of Ophthalmology, Zhongshan Ophthalmic Center, Sun Yat-Sen University, Guangzhou 510060, China
[2]The National Engineering Research Center of Novel Equipment for Polymer Processing, South China University of Technology, Guangzhou, 510641, China
[3]School of Optometry, The Hong Kong Polytechnic University, Hong Kong, China

Received 23 April 2010; revised 25 October 2010; accepted 30 November 2010
Published online 25 March 2011 in Wiley Online Library (wileyonlinelibrary.com). DOI: 10.1002/jbm.b.31812

**Abstract:** We previously proposed a new strategy to replace a vitreous body with a novel foldable capsular vitreous body (FCVB). In this study, the FCVB was designed to mimic natural vitreous morphology, and evaluate its physiological functions compared with traditional silicone oil substitutes, in an established rabbit model of proliferative vitreoretinopathy. We found that FCVB was a very good replacement for closely mimicking the morphology and restoring the physiological functions, such as the support, refraction, and cellular barriers, of the rabbit vitreous body. The study has provided us with a novel research and therapy strategy that could effectively mimic the morphology and physiological function of the rabbit vitreous body. © 2011 Wiley Periodicals, Inc. J Biomed Mater Res Part B: Appl Biomater 97B: 396–404, 2011.

**Key Words:** vitreous substitute, device, PVR, rabbit

## INTRODUCTION

The vitreous body is a transparent gelatinoid structure that occupies four-fifths of the volume of the eye. It consists of about 99% water and 1.0% inorganic salts, organic lipids, and hyaluronan, which can maintain a certain spatial relationship with dipolar water molecules.[1] The physiological function of the vitreous body involves support of adjacent posterior segment structures, provision of an ocular refractive media, and acting as a cell barrier to inhibit cell migration from the retina to the vitreous cavity.[2]

Pars plana vitrectomy (PPV) is a surgical procedure to remove the pathological vitreous in a number of ocular diseases, for example, proliferative diabetic retinopathy, proliferative vitreoretinopathy (PVR), and endophthalmitis that would previously have been regarded as untreatable.[3–7] Since the vitreous body cannot regenerate, the vitreous cavity resulting from PPV must be filled with suitable artificial materials that can keep the retina in place and prevent it from detaching.

A number of artificial vitreous substitutes, for example, silicone oil, heavy silicone oil, and hydrogels, have been adopted.[8–16] Among these, silicone oil, introduced by Cibis in 1962, has been the most important adjunct for internal tamponade in the treatment of complicated retinal or choroidal detachment during the past five decades.[8–10] However, it has been associated with complications including cataracts, keratopathy, anterior chamber oil emulsification, and glaucoma.[11] Some reports have demonstrated the migration of silicone oil droplets into the retina and the optic nerve; others have found that the widespread loss of myelinated optic nerve fibers is owing to its free fluid characteristics within the eye.[12] Recently, heavy oil has been used as an internal tamponade in retinal detachment surgery. It is a solution of perfluorohexyloctane and silicone oil that can induce complications similar to those from silicone oil, such as emulsification and inflammatory reaction.[13,14] A number of gel-form vitreous substitutes have been proposed that include silicone gel, crosslinked poly (vinyalcohol), and crosslinked poly (1-vinyl-2-pyrrolidinone). These materials are still in their experimental stages, and their long-term toxicity is unknown.[15,16]

In spite of half a century of effort to replace the vitreous body of the eye, an ideal and permanent vitreous body has yet to be found.[17,18] The natural vitreous has a thin, membrane-like structure that continues from the ora serrata to the posterior pole, a structure that corresponds to the vitreous cortex.[1] Inspired by this, in our previous studies, we proposed a new strategy to fabricate, using computer and industrial technology, a vitreous substitute in the form of a novel foldable capsular vitreous body (FCVB).[19–22] The FCVB consisted of a thin, vitreous-like capsule with a tube-valve system. After installation into the eye while folded, a balanced salt solution (BSS) could then be injected into the capsule and inflated to support retina and control the intraocular pressure (IOP) through the tube-valve system.[19] Reports from the State Food and Drug Administration in China show that the FCVB has good mechanical, optical, and

**Correspondence to:** Q. Gao; e-mail: gaoqy@mail.sysu.edu.cn
Contract grant sponsor: National High-tech R&D Program of China; contract grant numbers: Program 863, 2009AA2Z404

biocompatibility properties.[20] In addition, FCVB changes the refraction very little compared with silicone oil and heavy silicone oil,[21] and can be also used as drug delivery system (DDS) via the 300 nm mili apertures in the FCVB's capsule.[22]

In this article, the FCVB was designed to mimic natural vitreous morphology, to further evaluate its physiological functions compared with traditional silicone-oil substitutes, in an established animal model of PVR.

## MATERIALS AND METHODS

### Mimicking the shape of the natural vitreous body

The FCVB consists of a modified liquid silicone material that was shown in our previous study to have good oxygen permeability, good mechanical and optical properties, and biocompatibility.[20] It was a major challenge to produce an irregular vitreous-shaped thin capsule and to connect it smoothly to a 1.5 mm diameter tube and a pressure-control valve. Our previously reported FCVB was formed using a dipping technology,[19] but was unable to closely mimic the shape of the rabbit vitreous. In this study, the FCVB was fabricated by an injection forming technology, which used a specially designed mirror steel mold that consisted primarily of an upper composite die, a lower composite die, and the core.[23] The core shape could be manipulated via computer according to the vitreous parameters of a rabbit. The gaps between the dies and the core could be adjusted to control the thickness of the FCVB's capsule (Figure 1).[23]

### Animals

Twenty New Zealand albino rabbits (both males and females at 2–3 kg each) were involved in this study. The animals were raised in a 12-h day/night facility. They were kept in separate cages and fed with regular chow. All animals were examined ophthalmologically before the study to exclude ocular diseases. Preoperative IOP was measured using Goldmann tonometry. The procedures had been approved by the Hospital Animal Research Review Committee and were performed in accordance with the ARVO's Statement for the Use of Animals in Ophthalmic and Visual Research.

### Proliferative vitreoretinopathy model

All surgical procedures were performed by one investigator. The rabbits were anesthetized by an intramuscular injection of ketamine HCl (25 mg/mL; 1 mL/kg body weight) and chlorpromazine HCl (50 mg/mL; 1 mL/kg body weight) mixture. The right pupils were dilated with topical applications of 0.5% tropicamide and 2.5% phenylephrine HCl eye drops. The right eyes were immobilized by retraction of the eyelids. A 100 μL Hamilton Microsyringe was used to puncture the eye at a site 4 mm away from the corneal limbus in the upper temple quadrant. A small local retinal detachment was created by injecting 20-μL proteolytic enzyme dispase (0.02 units in phosphate-buffered saline; pH 7.4) into the subretinal space. A retinal break was also made in the area of the dispase bleb.[24] The left eyes did not receive any treatment, and they served as contralateral controls. The PVR were monitored regularly using ophthalmoscopy and B-scan ultrasonography for eight weeks.

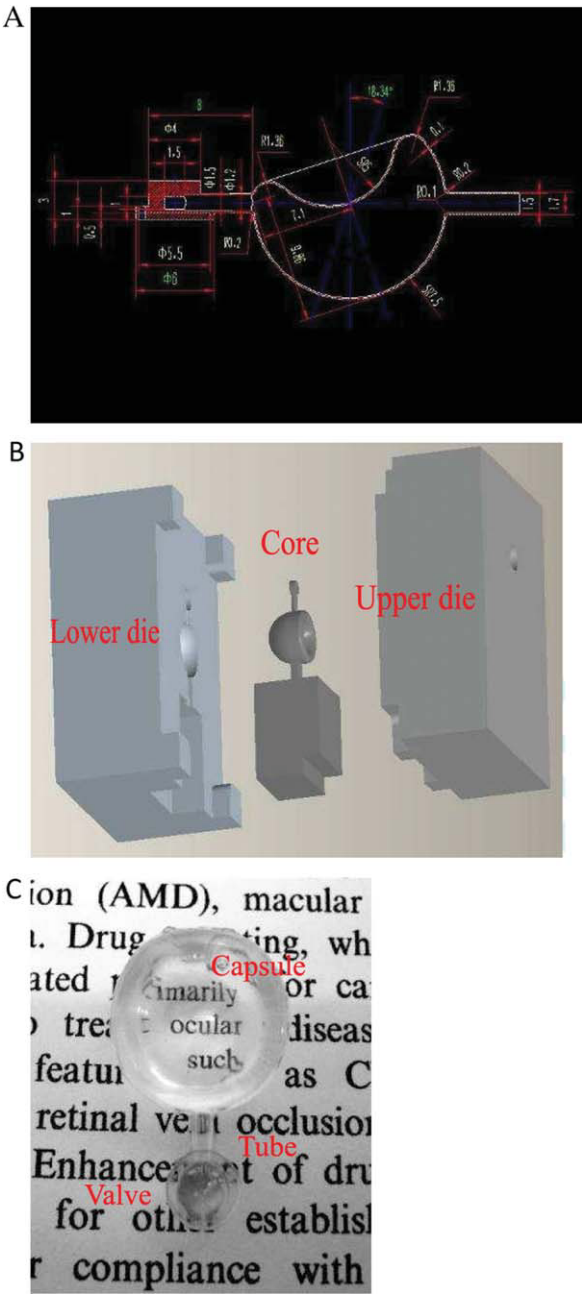


**FIGURE 1.** Fabrication process of a FCVB in a rabbit. A: Mimicking of the vitreous parameters. B: Three-dimensional design of the vitreous mould. C: Rabbit eye sample. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

### Surgical pars plana vitrectomy procedure

At the end of eight weeks, PVR had been established in the treatment eyes. With general anesthesia, the treatment eyes were immobilized by eyelid retraction, and the pupils were dilated. A routine, three-port PPV (with sclerotomy 4.0 mm posterior to the limbus) was performed using the Geuder vitrectomy unit (Germany). The animals were then equally divided into two groups, and the treatment eyes received either FCVB implantation or silicone oil substitution.

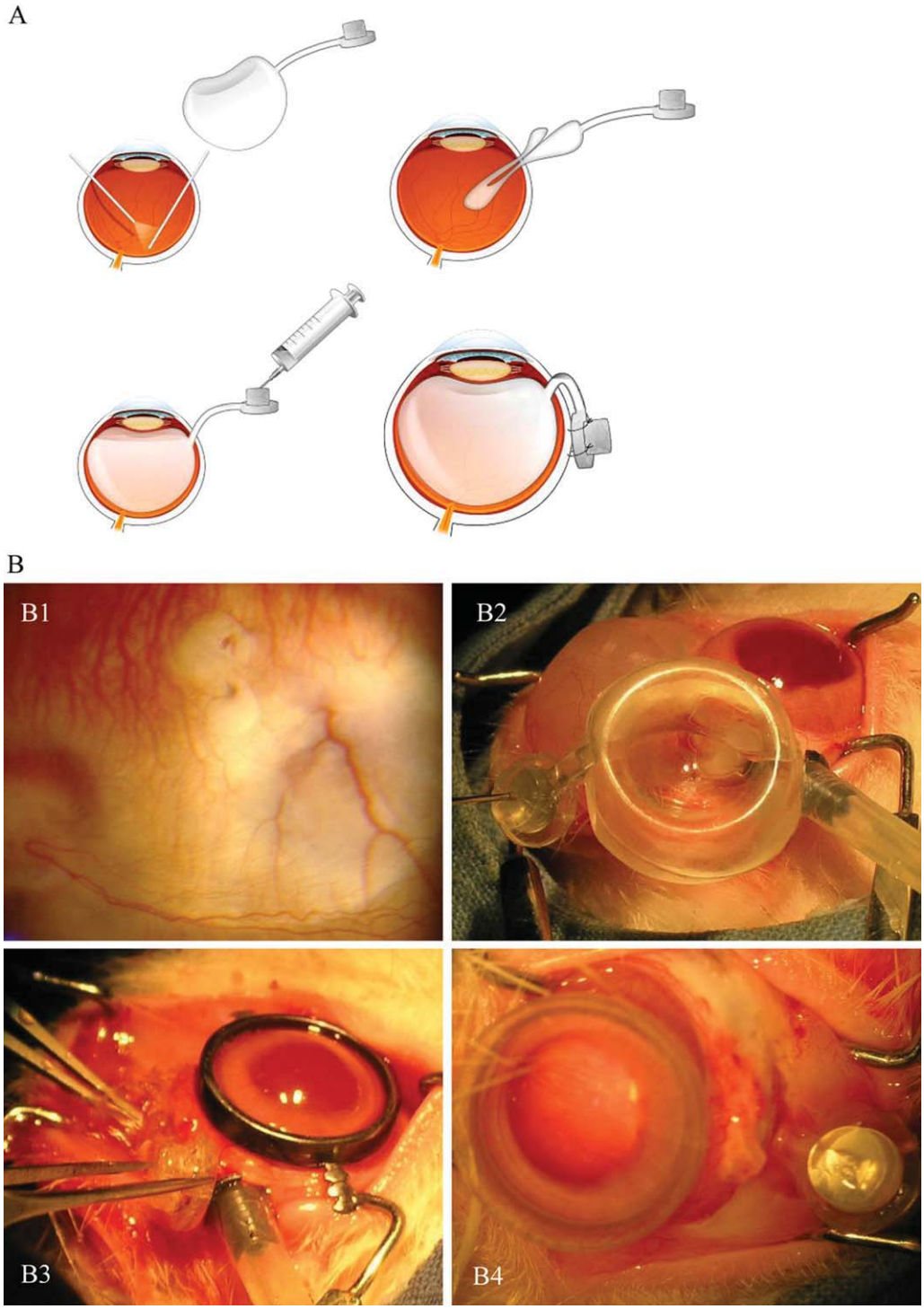


**FIGURE 2.** FCVB was folded and implanted into a vitreous cavity during PPV surgery. A: Illustration of FCVB implantation. B: FCVB implantation process in the rabbit PVR model. B1: The ocular fundus of the rabbit PVR model. B2: The FCVB cleaned before implantation. B3: The FCVB was folded into the vitreous cavity. B4: The ocular fundus, seen clearly after BBS was injected into the capsule. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

### Foldable capsular vitreous body implantation

The FCVBs were sterilized by boiling them for 2 h. Then, the FCVBs were folded and implanted into the vitreous cavity through a 2-mm incision aperture without fluid-air exchange (Figure 2). After the implantation, about 1.0 mL BSS was injected into the capsule through the tube-valve device fixed under the conjunctiva. The inflated capsule supported the eyeball, and the pressure was adjusted carefully by BSS injection.[19]

### Silicone oil substitution

The silicone oil control group received a routine intravitreal injection (1 mL) of silicone oil tamponade (Oxane 5700; Bausch & Lomb Inc., Ireland) after a fluid-air exchange.

### Post-PPV preparations

After the artificial vitreous replacement, the PPV was completed with 10-0 Vicryl sutures. The whole operation was concluded by subconjunctival injections of gentamycin and dexamethasone. The anterior surface received topical applications of tobramycin and atropine (1%) ointment. All animals were returned to the holding units afterwards.

### Ocular assessments

After PPV, all eyes were examined with slit-lamp biomicroscopy, ophthalmoscopy, and Goldmann tonometry weekly, over the following three months. B-scan ultrasonography (10 MHz probe; Cine Scan, BVI Inc., France) and optical coherence tomography (OCT; Stratus Carl Zeiss Inc., CA) were conducted at the end of three months.

### Refractive measures

Objective cycloplegic refraction was conducted both preoperatively and three months postoperatively using streak retinoscopy (three drops of 0.5% tropicamide; 10-min apart). The spherical-equivalent refractive errors were analyzed.

### Light microscopy and immunofluorescent staining

After the noninvasive ocular measurements, all animals were sacrificed by overdose injection of sodium pentobarbital. The anterior chambers, lenses, and vitreous substitutes were removed from the isolated eyeballs. The eyecups were fixed in 4% paraformaldehyde, embedded in paraffin, and sectioned (5 μm thickness). After hematoxylin and eosin (HE) staining, the tissue was examined under a light microscope.

For the immunofluorescent staining, paraffin sections were incubated overnight with the following antibodies: Griffonia simplicifolia (GSA) isolectin B4 (1:50; Sigma), macrophage (monoclonal, 1:50; Dako) and glial fibrillary acidic protein (GFAP; monoclonal, 1:50; BD Pharmingen). Photographs were taken with a fluorescence microscope.

### Statistical analysis

All data were presented as mean ± standard deviation (SD). Refractive data were analyzed using paired *t*-tests. IOP were analyzed using repeated measures analysis of variance (ANOVA). Statistical significance was set at $p < 0.05$.

## RESULTS

### Dimensions of the foldable capsular vitreous body

The capsular shape of the inflated FCVB was very similar to that of the vitreous of the rabbit eye. The capsule was thin, with a thickness of 30 μm-only one-fifth that of the retina. The outside and inside diameters of the tube were 1.5 ± 0.2 mm and 1.2 ± 0.2 mm, respectively. The tube length was 4.0 ± 0.5 mm. The bottom diameter of the valve was 6.0 ± 0.2 mm, and the top diameter was 4.0 ± 0.2 mm. The total thickness of the valve was 3.5 ± 0.2 mm. The FCVB's capsule, drainage tube, and valve were formed in one all-encompassing procedure, which produced an FCVB that was seamlessly connected (Figure 1). The standard weight of this FCVB for rabbits was 0.21 ± 0.005 g.

To test the physiological functions of the FCVB, we evaluated its supporting, refraction, and cellular barrier functions.

### Supporting function

In the two groups, there was a slight conjunctival hyperaemia by day 7 after surgery in both the FCVB implanted eyes and the silicone oil-treated control eyes. Over the three-month observation time, the ocular fundus in the FCVB eyes was clearly visible from the second week, the retina was reattached, and the capsule of the FCVB supported the retina and whole eye well, without any wrinkles, among all the 10 PVR models, as shown in Figure 3(A). No serious complications, such as corneal opacity, intraocular inflammation, or retinal hemorrhage or detachment, were observed. Only two out of ten animals in the FCVB group developed cataracts in the implanted eye. But the fibers of the lenses seemed much more bulky and less uniformly organized than those in silicone oil and contralateral control eyes (Figure 4). The peripheral fundus showed that the FCVB was well distributed in the vitreous cavity [Figure 3(A)], indicating that the FCVB effectively supported the retina The silicone oil-filled eyes now had an interface between the water and silicone oil. The emulsification of the silicone oil was observed [Figure 3(B)]. The B-scan's reflected signal showed that a capsule-shaped arc was supporting the retina [Figure 3(C)]. OCT indicated that the 30 μm-thick capsular film was able to support the retina evenly. In addition, there was a very thin gap between the film and the retina that prevented sticking [Figure 3(D)].

In contrast, at the same time, five of the 10 rabbits that had been treated with silicone oil showed lens opacity. The fibers of the lenses had a slight abnormity when compared with those in the contralateral control eyes (Figure 4). Retinal detachment recurred in 50% of the silicone oil-filled PVR eyes. Both the B-scan and the OCT showed recurring retinal detachment [Figure 3(C,D)]. The redetachment rate of the silicone oil-filled PVR eyes seemed higher than it was for cases previously seen in the clinic, which had been due to a lack of laser, cryotherapy and/or electric coagulation equipment to block the hole. On the basis of the above results, the support function of the silicone oil was significantly inferior to that of the FCVB under the same conditions.

The valve, with its pressure-sensitivity crevice, can modulate the pressure of the capsule when it is higher than 30 mmHg. Gross examination of eye specimens showed that the FCVB eyes could evenly fill the vitreous cavity, support the retina, and maintain a good eye profile. IOP is essential for sustaining the profile of the eye. The tonometric measurements showed the treatment's main effect on IOP was not significantly different between the FCVB and the silicone oil-filled eyes [Figure 3(E)].

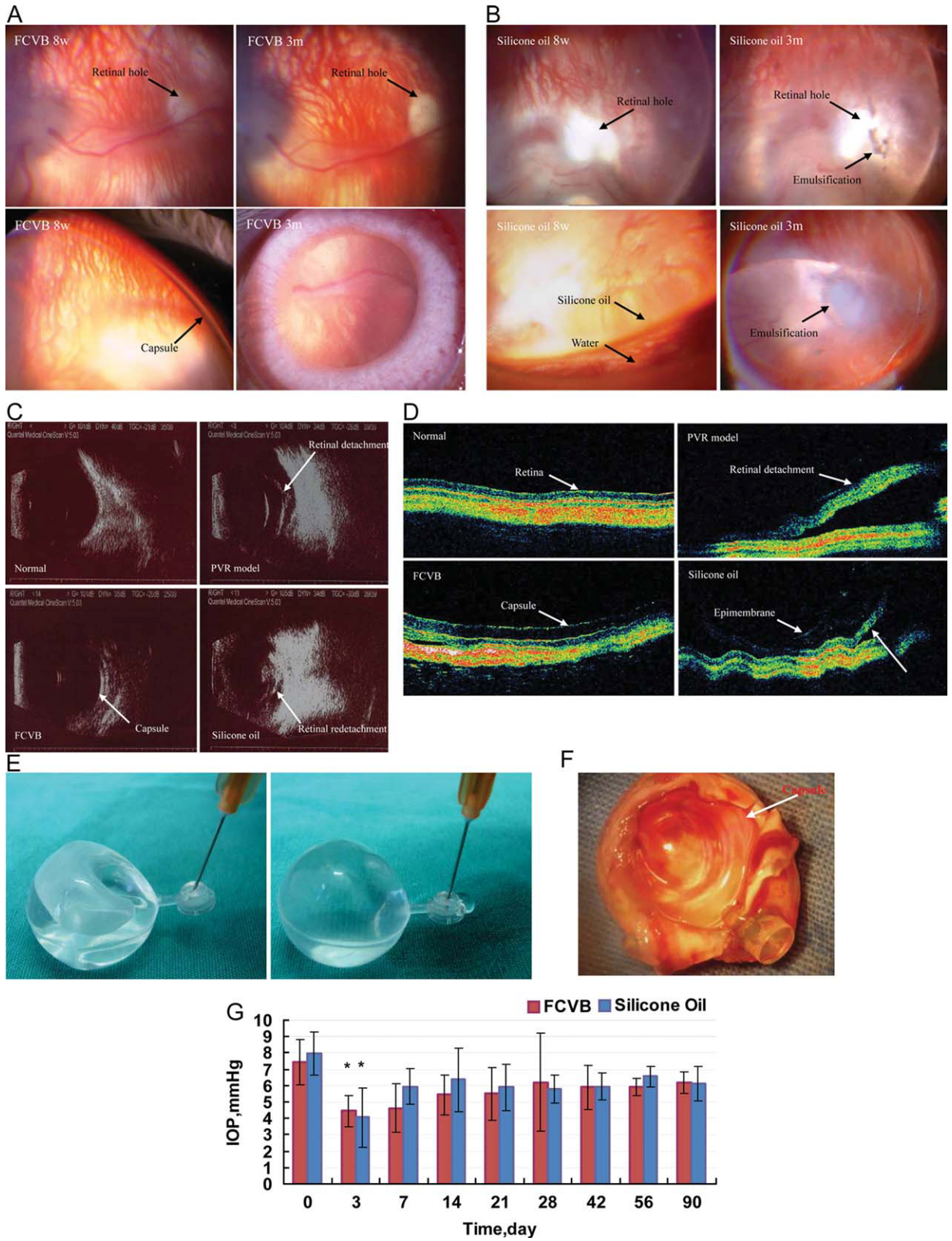


**FIGURE 3.** FCVB, in place of silicone oil, apparently supporting the retina and the eye well by providing a solid arc in rabbit PVR eyes after PPV surgery over the three-month observation period. A: The ocular fundus in the FCVB eyes was clearly visible from the second week; the retina was reattached and the capsule of the FCVB supported the retina and whole eye well, without any wrinkles. B: The silicone oil was unable to adequately support the retina by interfacial surface tension alone, especially the inferior retina. Silicone oil emulsification and retinal redetachment were observed. C: The B-scan showed that a capsule-like arc reflective signal was supporting the retina of the FCVB eyes, while a retinal detachment signal was recurring in the silicone oil-treated eyes. D: OCT indicated that the 30-μm-thick capsular film could evenly support the retina of the FCVB eyes, while retinal detachment was recurring in the silicone oil-treated eyes. The blue arrows denote the capsule film of the FCVB, the red arrows denote the detached retina and proliferative membrane. E: The valve of the FCVB with a pressure-sensitivity crevice can modulate the pressure of the capsule when it was more than 30 mmHg. F: Gross examination of eye specimens showed that the FCVB eyes could evenly fill the vitreous cavity, support the retina, and maintain a good eye profile. G: The tonometric measurements showed that the IOP was not significantly different between the FCVB and the silicone oil-filled eyes, except on day 3.


**FIGURE 4.** HE staining of the lens in FCVB, and the silicone oil-filled and contralateral eyes. The fibers of lenses in FCVB eyes seemed much more bulky and less uniformly organized than those in silicone-oil and contralateral control eyes. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

These results indicated that the FCVB apparently supported the retina and the eye well by providing a solid arc, while silicone oil was unable to adequately support the retina or the eye by interfacial surface tension alone, especially the inferior retina, due to its low density.

### Refraction function

Previously, Stefansson et al. reported that human eyes filled with silicone oil alone after PPV will acquire a refraction shift of + 9.30 D.[25] However, we previously found that the FCVB had much less effect on the refraction in the eye after PPV surgery, when compared with a silicone oil tamponade.[21]

Figure 5 depicts the refractive errors of the FCVB and silicone oil-treated eyes. Before treatment, all rabbits exhibited moderate hyperopia (+3.68 ± 0.41 D), and the refractive errors were not significantly different between the right and left eyes ($p = 0.79$). Three months after PPV, a significant hyperopic shift of 2.00 ± 1.17 D was observed in the silicone oil-treated group ($p = 0.029$). In the FCVB group, the average refractive change was +0.20 ± 0.45 D, and the difference was not significant ($p = 0.73$).

From the schematic eye and animal model data, we therefore concluded that the patients with FCVB could almost fully retain their normal refraction condition after FCVB surgery.

### Cellular barrier function

In the FCVB implanted eyes, HE staining showed that the retinal holes were enclosed by a flat contour and no proliferative membranes were observed in the vitreous cavities of all 10 eyes [Figure 6(A)]. Immunofluorescent data showed that glial cells, collagen IV, and microglia were activated in the healing process [Figure 6(B)]. There was no formation of preretinal membranes, nor was there recurrent retinal detachment. These results indicated that the FCVB formed a

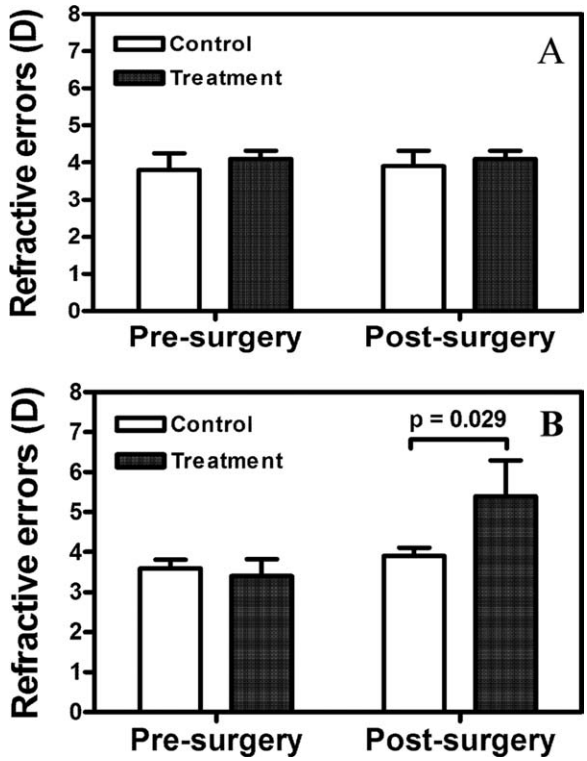


**FIGURE 5.** Refraction shifts in FCVB (A) and silicone oil (B) treated eyes at the end of a three-month treatment period. Before the treatments, all rabbits exhibited moderate hyperopia (+3.68 ± 0.41 D), and the refractive errors were not significantly different between the right and left eyes ($p = 0.79$). Three months after PPV, a significant hyperopic shift of 2.00 ± 1.17 D was observed in the silicone oil-treated group ($p = 0.029$). In the FCVB group, the average refractive change was +0.20 ± 0.45 D, and the difference was not significant ($p = 0.73$).

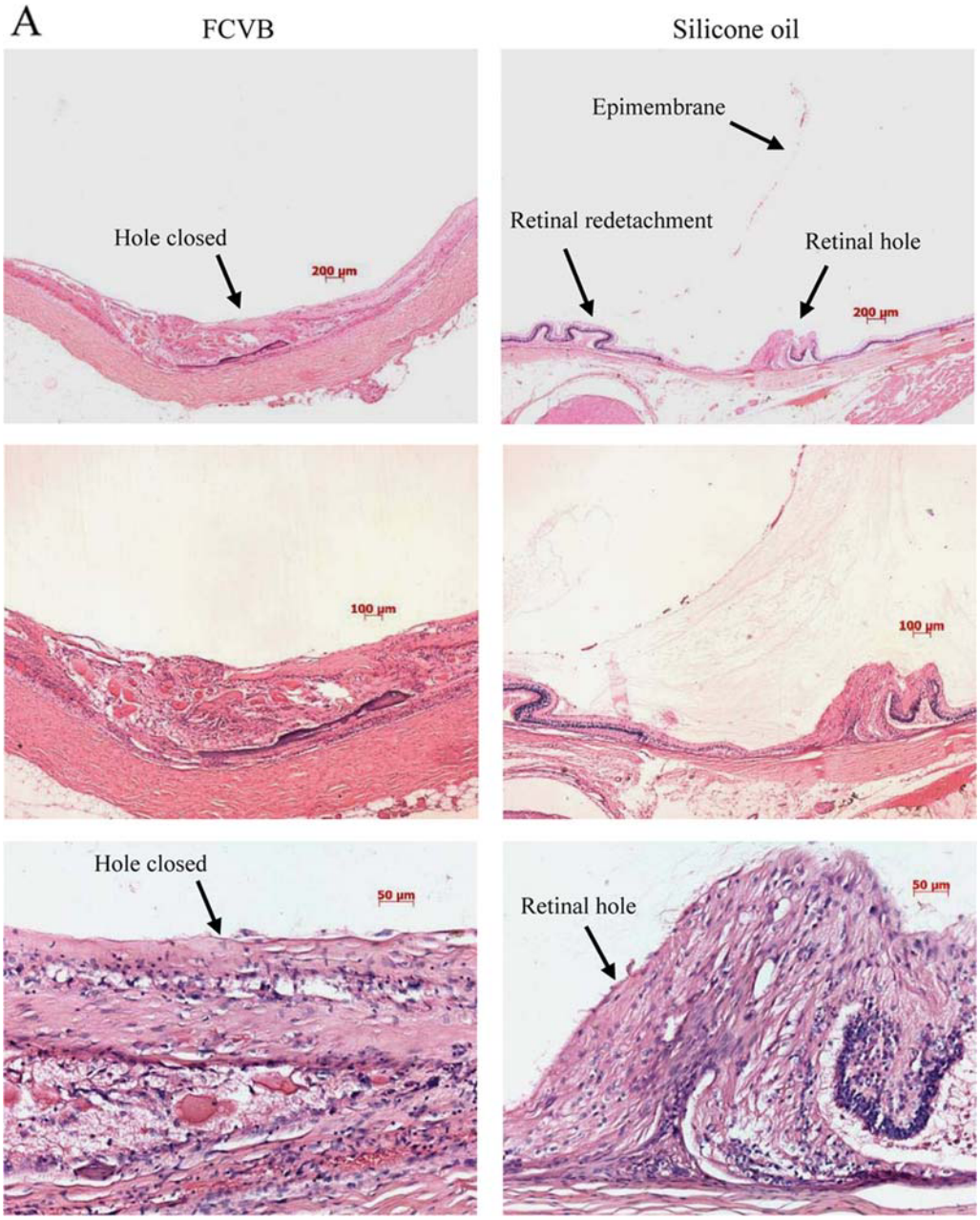


**FIGURE 6.** FCVB can restore the cellular barrier function in rabbit eyes after PPV surgery at the end of a three-month observation period. A: HE staining. In the FCVB eye, the retinal hole was closed, the retina was flat around the hole, and no proliferative membranes occurred in the vitreous cavity. In the silicone oil-filled eye, the retinal hole was not sufficiently closed, the retina projected into the vitreous cavity, and membrane formation and vitreoretinal traction were observed. B: Immunofluorescence detection of the retina near the hole at the end of a three-month observation period in FCVB (A1, A2), silicone oil (a1, b2) and contralateral eyes (n1, n2). A1, a1, n1: GFAP (red), the collagen IV (green); A2, a2, n2: macrophage (red), GSA isolectin B4 (green). [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

barrier to retinal cell migration and proliferation. In the silicone oil-treated eyes, however, HE staining showed that the retinal holes were not closed completely, and the surrounding retinal tissue penetrated into the vitreous cavity in five out of ten eyes. Preretinal membrane formation and vitreoretinal traction were observed in the vitreous cavity in five out of ten eyes [Figure 6(A)]. Immunofluorescent data showed that glial cells and macrophages were active in the tissues [Figure 6(B)].

Therefore, the use of FCVB could cut the migration pathway of retinal cells from the subretina to the vitreous cavity, further restricting cellular proliferation in the eyes, thereby acting as a cellular barrier.

## DISCUSSION

In this study, we found that the modified version of our previously reported FCVB, which was manufactured with industrial technology, could finely mimic the morphology and

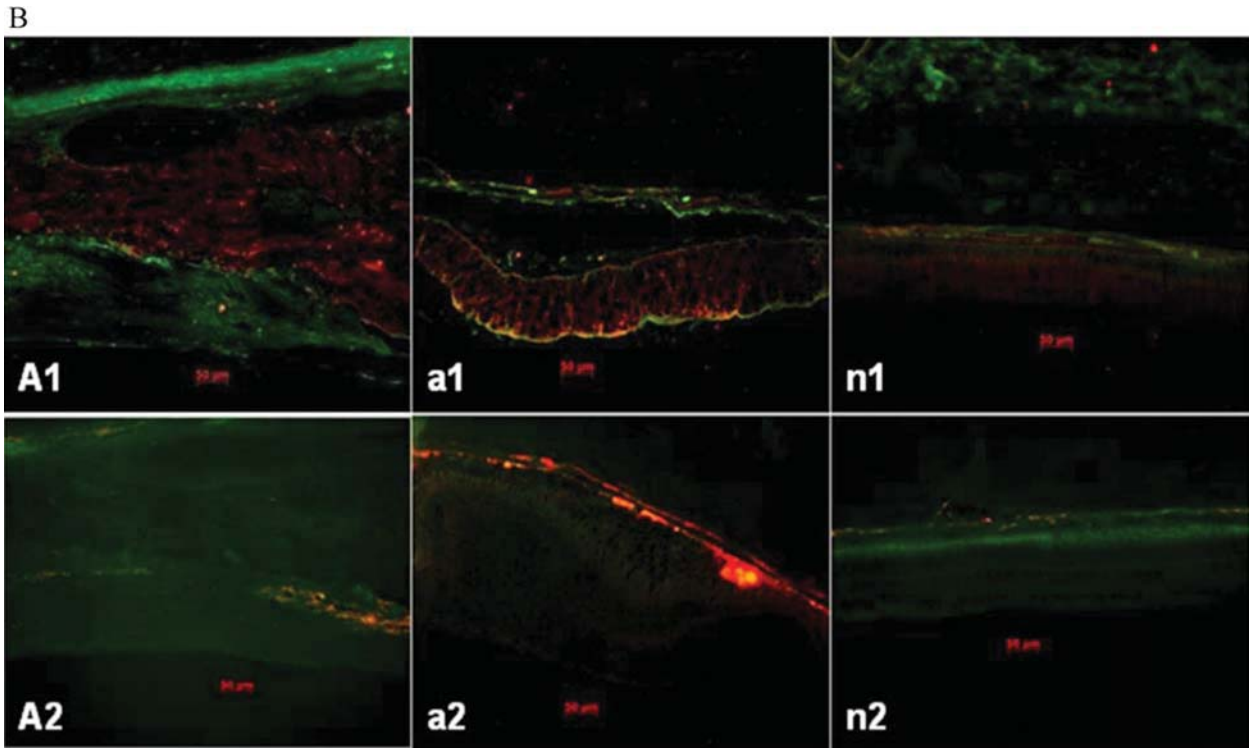


**FIGURE 6.** (continued)

restore the physiological function of the vitreous body during a three-month observation period.

**Physical characteristics**

Each FCVB can be made specifically before surgery, using a computer-aided program to match it with individual ocular characteristics. It can be made very fine and thin, and can be folded and inserted via a very small incision to support differently shaped eyes. Its thin (30 μm) and flexible nature allows FCVB implantation through a small surgical incision. Previously, our laboratory reported the first version of FCVB using a dip-formation technology. In this study, the FCVB was fabricated by an injection forming technology that produces the seamless connection of the capsule, drainage tube, and valve. In addition, there were numerous 300 nm mini-apertures located on the capsule.[22] These apertures allowed free metabolic and drug exchange between the retina and the other intraocular tissues.

**Supporting and barrier characteristic**

Our results indicate that FCVB supports the eye by forming a firm inner lining and maintaining the normal IOP. It also provides a scaffold for retinal repair and blocks the migration of retinal cells to the vitreous cavity. The low density silicone oil cannot support the inferior retina. The formation of preretinal membrane and retinal proliferation were observed in the silicone oil-treated group. Recurrent retinal detachment is a risk factor of PVR.[26] Reoperations are indicated clinically when recurrent retinal detachments are observed in silicone oil-filled eyes.[27] Based on these data, FVCB offers a new clinical strategy to resemble the natural vitreous body without obvious ocular complications.

**Refractive characteristics**

Our study showed that the refractive errors of the FCVB-treated eyes were comparable to those of the contralateral control eyes. However, the silicone oil-treated eyes experienced a significant hyperopic shift of approximately 2D in the rabbits. Compared with the silicone oil-treated group, the FCVBs induced only marginal refractive changes. In the Gullstrand-Emsley schematic eye, the silicone oil substitution is also expected to induce higher refractive shifts (+8.71 D) than the BSS-filled FCVB (−0.338 D).[21] Stefansson et al. also reported a 9.30 D hyperopic shift in human eyes with silicone-oil substitution.[25] If FCVB were applied clinically to the human eyes, the refractive outcome would be expected to result in emmetropia. If we could further manipulate the refractive index of BSS, we should be able to control the post-PPV refractive errors in humans. It would alleviate the perceptual difficulty induced by the drastic change in optical correction associated with silicone oil substitution.

**Clinical applications**

Since the FCVB implantation does not require a routine fluid-air exchange, it may reduce the surgical complications of PPV. Hence, the FCVB has provided us with a novel research and therapy approach that mimics the natural vitreous in the rabbit eye. In addition, it is also a new vehicle for ophthalmologic DDS delivered via 300 nm mili apertures

in the FCVB capsule. Therefore, FCVBs are a potentially new approach to providing both vitreous support and DDS delivery.

Because the FCVB has never been used in eyes worldwide, we conducted an exploratory study of 11 patients implanted via FCVB with BSS for the treatment of severe retinal detachment at Zhongshan Ophthalmic Center. The clinical trials adhered strictly to the principles of the World Medical Association Declaration of Helsinki, were approved by the Sun Yat-sen University Medical Ethics Committee (No. 07 [2009], Zhongshan Ophthalmic Center of Medical Ethics), and were successfully registered with ClinicalTrias.gov (NCT00910702) and with the Chinese Clinical Trial Register (ChiCTR-TNC-00000396). Exploratory results showed that the FCVB had good flexibility, safety, and efficacy during a 3-month study period.[28] We designed the fovea lentis in the FCVB ($r = 6.0$ mm) to match the lens,[20] but the effects of FCVBs on lenses should be further evaluated, since the lens fibers in FCVB eyes in this study seemed much more abnormal than did those in silicone-oil and contralateral control eyes, as shown in Figure 4. Further multiple center clinical trials in China are in progress, to ascertain its safety and efficacy in human eyes.

In conclusion, we found that FCVBs could effectively mimic the morphology and physiological function of the rabbit vitreous body. The study has provided us with a novel research and therapy strategy that could effectively mimic the morphology and physiological functions of the rabbit vitreous body.

## REFERENCES


1. Green WR, Sebag J. Vitreoretinal Interface. In: Ryan SJ, editor. Retina, 4th ed., Volume III, Chapter 114. Elsevier Mosby, Philadelphia, USA; 2006. pp 1921–1989.
2. Goff MM Le, Bishop PN. Adult vitreous structure and postnatal changes. Eye 2008;22:1214–1222.
3. Castellarin A, Grigorian R, Bhagat N, Del Priore L, Zarbin MA. 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, Gupta A, Yoshizumi MO, Kreiger AE, Schwartz SD. 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., Lai MY, Topping TM, Benati L, Trask DK, Rogus LA. Silicone oil in the repair of complex retinal detachments. A prospective observational multicenter study. Ophthalmology 1998;105:1587–1597.
11. Ichhpujani P, Jindal A, Jay Katz L. Silicone oil induced glaucoma: A review. Graefes Arch Clin Exp Ophthalmol 2009;247:1585–1593.
12. la Cour M, Lux A, Heegaard S. Visual loss under silicone oil. Klin Monbl Augenheilkd 2010;227:181–184.
13. Bhisitkul RB, Gonzalez VH. "Heavy oil" for intraocular tamponade in retinal detachment surgery. Br J Ophthalmol 2005;89:649–650.
14. Mackiewicz J, Mühling B, Hiebl W, Meinert H, Maaijwee K, Kociok N, Lüke C, Zagorski Z, Kirchhof B, Joussen AM. In vivo retinal tolerance of various heavy silicone oils. Invest Ophthalmol Vis Sci 2007;48:1873–1883.
15. Leone G, Consumi M, Aggravi M, Donati A, Lamponi S, Magnani A. PVA/STMP based hydrogels as potential substitutes of human vitreous. J Mater Sci Mater Med 2010;21:2491–2500.
16. Hong Y, Chirila TV, Vijayasekaran S, Shen W, Lou X, Dalton PD. Biodegradation in vitro and retention in the rabbit eye of cross-linked poly (1-vinyl-2-pyrrolidinone) hydrogel as a vitreous substitute. J Biomed Mater Res 1998;39:650–659.
17. Soman N, Banerjee R. Artificial vitreous replacements. Biomed Mater Eng 2003;13:59–74.
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, To CH, Hui Y, Liu A, Wang Z, Long C, Tan J. 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. Liu Y, Jiang Z, Gao Q, Ge J, Chen J, Cao X, Shen Q, Ma P. Technical standards of foldable capsular vitreous body regarding mechanical, optical and biocompatible properties. Artif Organs 2010;34:836–845.
21. Gao Q, Chen X, Ge J, Liu Y, Jiang Z, Lin Z, Liu Y. 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.
22. Liu Y, Ke Q, Chen J, Wang Z, Xie Z, Jiang Z, Ge J, Gao Q. Dexamethasone sodium phosphate sustained mechanical release in the foldable capsular vitreous body. Invest Ophthalmol Vis Sci 2010;51:1636–1642.
23. Gao Q. A novel method andomould for foldable capsular vitreous body, China patent No. 200810199177.3, 2008.
24. Frenzel EM, Neely KA, Walsh AW, Cameron JD, Gregerson DS. A new model of proliferative vitreoretinopathy. Invest Ophthalmol Vis Sci 1998;39:2157–2164.
25. Stefánsson E, Anderson MM, Jr, Landers MB, III, Tiedeman JS, McCuen BW, II. Refractive changes from use of silicone oil in vitreous surgery. Retina 1988;8:20–23.
26. Nagasaki H, Shinagawa K, Mochizuki M. Risk factors for proliferative vitreoretinopathy. Prog Retin Eye Res 1998;17:77–98.
27. Sharma T, Gopal L, Shanmugam MP, Bhende PS, Agrawal R, Badrinath SS, Samanta TK. Management of recurrent retinal detachment in silicone oil-filled eyes. Retina 2002;22:153–157.
28. Lin X, Ge J, Gao Q, Wang Z, Long C, He L, Liu Y, Jiang Z. Evaluation of the flexibility, efficacy, and safety of a foldable capsular vitreous body in the treatment of severe retinal detachment. Invest Ophthalmol Vis Sci 2010. Forthcoming.