Materials Science and Engineering C 62 (2016) 233–241

Contents lists available at ScienceDirect

Materials Science and Engineering C

journal homepage: www.elsevier.com/locate/msec

# The efficacy and safety of a novel posterior scleral reinforcement device in rabbits

Yongguang Yuan [a], Yao Zong [a], Qishan Zheng [a], Garrett Qian [b], Xiaobin Qian [a], Yujie Li [a], Wanwen Shao [a], Qianying Gao [a,*]

[a] State Key Laboratory of Ophthalmology, Zhongshan Ophthalmic Center, Sun Yat-sen University, Guangzhou, China
[b] University of New South Wales, Australia

ARTICLE INFO

*Article history:*
Received 2 September 2015
Received in revised form 14 November 2015
Accepted 19 December 2015
Available online 14 January 2016

*Keywords:*
PSR
Myopia
Axial length
Retina

ABSTRACT

*Purpose:* To evaluate the efficacy and safety of posterior scleral reinforcement (PSR) device for myopia suppression in rabbits' eyes.
*Methods:* PSR surgery was performed on the normal 12 8-week-old New Zealand white rabbits' right eyes. To determine efficacy of the device, ophthalmic examination would be taken at pre-operation and post-operation (1 week, 1 month, 3 months, 6 months, and 1 year), such as A-ultrasound, diopter and B-ultrasound. Evaluation of safety were based on the following indicators: intraocular pressure (IOP), slit lamp, fundus photography, fundus fluorescein angiography and pathological examination after surgery. The efficacy and safety of PSR device were evaluated by comparison (treated eyes and contralateral eyes) of pre and post-operation.
*Results:* The novel PSR device could significantly shorten axial length (preoperative axial length: 16.36 ± 0.14 mm, postoperative 1 week, 1 month, 3 months, 6 months and 1 year axial lengths: 15.03 ± 0.28 mm, 15.23 ± 0.32 mm, 15.39 ± 0.31 mm, 15.45 ± 0.22 mm and 15.45 ± 0.22 mm; $P = 0.00037 < 0.001$) in the treated eyes (right eyes) after surgery. At different postoperative time points, the B-ultrasound images showed that the PSR located in appropriate position and supported the posterior sclera very well. At the same time, IOP of treated eyes kept a relatively stable level (preoperative IOP: 12.56 ± 2.01 mmHg, postoperative IOP: ranging from 11.33 ± 1.23 mmHg to 13.44 ± 2.19 mmHg, $P > 0.05$) post-operation 1 year. During observation period, there was no significant inflammatory reaction and complications such as anterior chamber flare, empyema, endophthalmitis, vitreous hemorrhage, retina detachment and retinal choroid neovascularization by slit lamp, fundus photography and fundus fluorescein angiography. In addition, there were no pathologic changes be found by comparison treated eyes group and contralateral group eyes based on pathological examinations.
*Conclusions:* In vivo study, effectively and safely, the novel PSR device can inhibit rabbits' axial length elongation during postoperative 1 year. This study demonstrates that this novel PSR could be a potential treatment approach for myopia.



## 1. Introduction

Myopia is a major cause of legal blindness, affecting 20%–40% of adults, especially in Asian populations [1–3]. A part of people with myopia have degenerative change, which is characterized by a progressive elongation of the eyeball, scleral thinning, and formation of posterior staphyloma result in fundus lesion, such as retinochoroidal atrophy, choroidal neovascularization (CNV), macular retinoschisis, macular hole and retinal detachment.

The sclera plays a very important role in the mechanical support layer of the eye, which is comprised of avascular fibrous connective tissue containing various collagens and proteoglycans in mammalian and primate eyes. In mature and normal sclera, collagen shows an obvious gradient in different fiber layer, with the smallest fibers found innermost toward the retina. That gradient can not be found in high myopia [4,5], and result in strength of myopia sclera reduction. That is the reason why axial length lengthening is very difficult to restrict in degenerative myopia.

Treatments for degenerative myopia intend to improve vision and reduce occurrence rate of aforementioned complications, however, the outcome is not desirable usually. The treatment of degenerative myopia mainly includes two aspects: optical correction operation and treatment of complications. Optical correction operations are made up of cornea surgery, intraocular lens implantation and posterior scleral reinforcement [6–8]. Therapy of complications (CNV, macular retinoschisis, macular hole and retinal detachment) primarily include the following

* Corresponding author.
*E-mail address:* gaoqy@mail.sysu.edu.cn (Q. Gao).

http://dx.doi.org/10.1016/j.msec.2015.12.046

methods: intravitreal anti-VEGF therapy for CNV, laser photocoagulation, verteporfin photodynamic therapy and vitrectomy [9]. Disappointingly, cornea and lens surgeries fail to prevent further eye stretching. PSR, which proposed by Shevelev and modified by Thompson et al., has the potential to control axial elongation [10–12].

To date, PSR has been applied to clinical therapy widely to treat high myopia and complications [8,12–17]. In the present study, materials of PSR mainly include fascia, lyophilized dura, synthetic materials (polymeric hydrogels, artificial pericardium and collagen coating fibrous capsule) [15–17], and autologous and homologous human sclera [16]. However, the therapeutic benefit of PSR is considered to be controversial because of disappointing results reported by Curtin and Whitmore [8]. Therefore, our study aims to evaluate the efficacy and safety of a new PSR device in rabbits' eyes during post-operation 1 year.

## 2. Methods

### 2.1. Materials

The rabbit PSR device (Guangzhou Vesber Biotechnology Co. Ltd., Guangzhou, China) was made of tailor-made modified liquid silicone rubber, which was considered as transformation of foldable capsule vitreous body (FCVB) [18]. The basic material was Dow Corning Class VI elastomers (Dow Corning Corporation, Midland, MI, U.S.A.). The device consisted of oblate capsule, a valve and two fixed bands, which was showed in Fig. 1. Accurate parameter information were summarized in Table 1 including each part of this device. The sterilized PSR devices were used to rabbits' surgery. Twelve New Zealand white rabbits were used in this study, each weighed between 2.5 and 3.5 kg. The right eye was the treated eye and the left eye served as the contralateral control. Regular examination, including examination of diopter, A-ultrasound, B-ultrasound, intraocular pressure (IOP), the anterior segment, fundus photography, and fundus fluorescein angiography (FFA) would be taken to record the baseline and exclude eye defects. All experiments were performed in accordance with the Association for Research in Vision and Ophthalmology (ARVO) statement regarding the use of animals in ophthalmic and vision research. The study protocol was reviewed and approved by the animal treated ethics committee of Zhongshan Ophthalmic Center, Sun. Yat-sen University, China (authorized number: 2013-006).

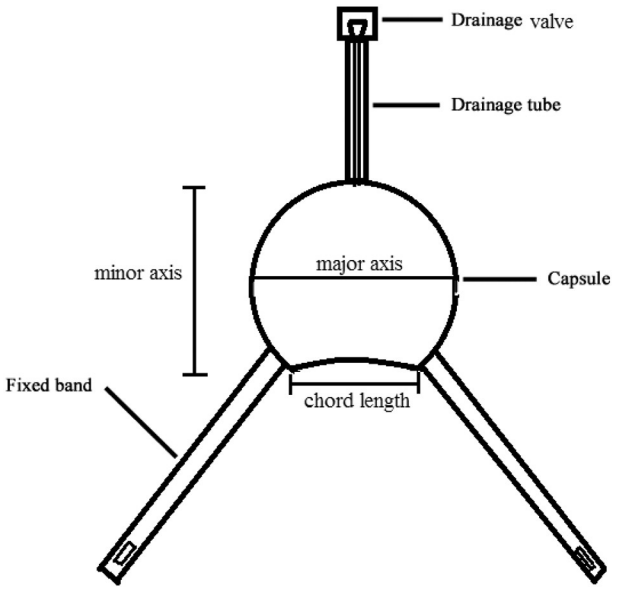


**Fig. 1.** Schematic drawing showing relative plan position about different parts of the PSR device labeled by black line.

**Table 1**
Parameters of each part of the PSR device.

| Different parts of PSR | | mm |
|---|---|---|
| Capsule | Major axis | 11.5 ± 1.0 |
| | Minor axis | 10.5 ± 1.0 |
| | Chord length | 6.0 ± 0.5 |
| Drainage tube | Length | 12.0 ± 1.0 |
| | Width | 2.5 ± 0.2 |
| | Height | 2.2 ± 0.2 |
| Drainage valve | Length | 6.0 ± 0.5 |
| | Width | 4.5 ± 0.5 |
| | Height | 3.5 ± 0.5 |
| Fixed bands | Length | 37.0 ± 1.0 |
| | Width | 2.3 ± 0.2 |
| | Height | 1.0 ± 0.2 |

### 2.2. PSR surgical procedures

All rabbits were anesthetized via a subcutaneous injection of a mixture of ketamine hydrochloride (30 mg/kg) and chlorpromazine hydrochloride (15 mg/kg). Under aseptic situation, the surgery steps were summarized as follows: bulbar conjunctiva and muscle separation, capsule vacuum, implantation, balanced salt solution injection, band and valve fixation and bulbar conjunctiva suture. To relieve postoperative inflammatory reaction and prevent infection, the surgery ended with a subconjunctival injection of tobramycin and dexamethasone (Fig. 2). After surgery, the eyes were treated with tobramycin dexamethasone eye drops (Tobradex; Alcon, Fort Worth, TX) and ofloxacin eye drops (Pranopulin; Senju, Osaka, Japan) three times a day for one week.

### 2.3. Postoperative examinations

To determine the efficacy of PSR device, diopter and A-ultrasound (Cine Scan; Quantel Medical Co., France) would be taken at 1 week, 1 month, 3 months, 6 months and 1 year postoperatively. B-ultrasound (Cine Scan; Quantel Medical Co., France) was applied to detect relative spatial position with sclera at 6 months and 1 year postoperatively. To confirm the safety, postoperative IOP was detected by Tono-Pen (Tonopen AVIA; Reichert Co., U.S.A.) at 1 week, 1 month, 3 months, 6 months and 1 year. A slit lamp (SL-D7; Topcon Co., Japan) and were used to examine and record the anterior segment at postoperative 1 week, 1 month, 3 months, 6 months and 1 year. Postoperatively, a fundus camera (TRC-50DX; Topcon Co., Japan) and FFA was used to judge vessels function about retina and choroid at 6 months and 1 year.

### 2.4. Histopathological and immunohistochemical analysis

Three rabbits from each group were executed at 1 month, 3 months, 6 months and 1 year postoperatively, and both eyeballs were enucleated for histopathological and immunohistochemical analyses. The eyeballs were fixed in 4% paraformaldehyde for 48 h and then embedded in paraffin. Sections were cut on a microtome (RM2235; Leica, Germany) at 5 mm and stained with hematoxylin and eosin (H&E) (C0105; HE kit, Beyotime, Beijing, China). The retinal sections were heated in a sodium citrate buffer at 95 °C for 30 min for antigen retrieval. After naturally cooling to room temperature, the sections were blocked in 3% hydrogen peroxide ($H_2O_2$) for 15 min, then blocked in 5% BSA for 30 min at 37 °C and then incubated with mouse monoclonal anti-VEGF antibody (15200; Abcam, Territories, Hong Kong) at 37 °C for 2 h. After washing with phosphate buffer saline with tween (PBST), the sections were incubated with horseradish-peroxidase-conjugated rabbit anti-mouse IgG antibody (IHC kit, NeoBioscience Technology Co., China) at 37 °C for 20 min. Then, the sections were stained with diaminobenzidine