

Direct Laser Photocoagulation of the Retinal Pigment Epithelium: A Novel Method to Seal Retinal Breaks during Pars Plana Vitrectomy for Retinal Detachment

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Background: This study evaluates the clinical effectiveness of employing direct retinal pigment epithelium (RPE) laser photocoagulation as a technique for achieving chorioretinal adhesion to effectively seal retinal breaks.

Methods: A total of 20 eyes from 20 patients were enrolled in the study; all selected eyes exhibited either rhegmatogenous or combined rhegmatogenous-tractional retinal detachment. During vitrectomy, direct RPE laser photocoagulation was executed, employing a power range of 100–150 mW and a duration of 120–200 ms, targeting the peripheries where the edges of each retinal break were anticipated to settle post-reattachment. This treated area's neuroretina thickness was compared to measurements obtained after conventional transretinal laser photocoagulation.

Results: Patients were followed for an average duration of 24 months, with a range of 11–46 months. A visible pigmentary reaction in the ophthalmoscopic examination was evident in the treated regions for all but one eye, where the retinal break was situated amidst myelinated nerve fibers. The study encountered no severe complications, and successful retinal reattachment was achieved in all 20 eyes. The mean best-corrected visual acuity (BCVA) at the final follow-up showed a statistically significant improvement compared to preoperative levels ($p < 0.0001$). A noteworthy difference in neuroretinal thickness was observed one-month post-surgery between areas treated with direct RPE and those treated with transretinal photocoagulation, measuring 217 μm and 104 μm , respectively.

Conclusions: Our findings suggest that direct RPE laser photocoagulation is an effective therapeutic intervention for sealing retinal breaks.

Keywords: retinal detachment; vitrectomy; direct RPE laser photocoagulation; ocular endoscopy

Introduction

Retinal detachment (RD) develops when fluid vitreous infiltrates the subretinal space through a retinal tear [1] or when preretinal (or more rarely, subretinal) traction forces exceed those maintaining the retinal attachment. The counteraction of traction and the sealing of the retinal tear, most commonly through photocoagulation, are pivotal for successful retinal reattachment.

Laser energy is absorbed by melanin in the retinal pigment epithelium (RPE) cells and the hemoglobin in the blood vessels. This absorption results in a thermal effect, leading to tissue coagulation and necrosis. Subsequently, this forms an adhesion between the RPE and the overlying neuroretina, thereby sealing the retinal tear [2–4]. Laser photocoagulation also promotes the absorption of the subretinal fluid and can prevent the occurrence of retinal detachment once the adhesion reaches its full strength [5,6].

The laser energy utilized in transretinal photocoagulation must be calibrated precisely: sufficient to induce adhesion yet moderate enough to avoid damaging the overlying retinal fiber layer or insulating a retinal hole.

Undertreatment—defined as the use of insufficient laser power—diminishes the rate of successful retinal reattachment [7]. In particular, it is difficult for an effective laser spot to form in the presence of subretinal fluid. Furthermore, it is hard for the laser to penetrate any myelinated nerve fibers, should the retinal tear be located in such an area [5,6].

Overtreatment—defined as the use of excessive retinal laser energy—escalates the risk of subsequent retinal redetachment due to retinal necrosis, especially in cases of hypopigmentation (such as in high myopia), ocular trauma, endophthalmitis, or acute retinal necrosis-induced retinal thinning [8–10]. In hyperpigmented or thinned retinal ar-

eas, the risk of nerve fiber damage is notably elevated [9,10]. When employing standard transretinal delivery, calibrating the appropriate laser energy proves challenging in eyes with severe edema (as seen in diabetic retinopathy) or in areas with hemorrhage (as seen in vein occlusions) [11,12].

Particularly during scleral buckling surgery, and also during vitrectomy, residual subretinal fluid often remains at the retinal tear's posterior edge unless heavy liquid fills the eye. This residual fluid may compel the surgeon to amplify the laser energy [13–15], thereby heightening the risks outlined above.

We hypothesised that direct RPE photocoagulation during vitrectomy could offer equivalent efficacy to traditional transretinal delivery while permitting greater control over the energy administered, without exposing the patient to the risks associated with overtreatment. Here we present the outcomes of our initial trial aimed at evaluating this hypothesis.

Patients and Methods

Patients

Twenty patients, each with one eye affected by retinal detachment, were prospectively enrolled in the study at our hospital (LiXiang Eye Hospital of Soochow University) between January 2015 and October 2017. The retinal detachment was either rhegmatogenous or combined rhegmatogenous-tractional. This study was approved by the Suzhou LiXiang Eye Hospital of Soochow University Committee for Research Ethics (20150109-1), conducted in accordance with the official regulations for clinical research and the Declaration of Helsinki. We have obtained signed informed consent from each patient for participation in this study and consent to publish the findings.

The inclusion criteria included eyes in which the subretinal fluid was impossible to completely remove or where the retinal transparency was seriously affected due to intraretinal hemorrhage, severe edema, or myelinated nerve fibers. Excluded criteria were eyes where the traditional transretinal, rather than the direct RPE, photocoagulation constituted the main force in creating a chorioretinal seal.

Patients were followed for an average duration of 24 months, with a range of 11–46 months. Each patient underwent a comprehensive eye exam, including non-contact intraocular pressure (IOP), best-corrected visual acuity (BCVA), slit lamp, B-ultrasound, and fundus examination.

All twenty eyes underwent vitrectomy (Surgical Microscope, OPMI Lumera T, Carl Zeiss-Strabe 73446 Oberkochen, Baden-Wuerttemberg, Germany), retinal reattachment, air-fluid exchange, and gas- or silicone oil implantation; 11 eyes had a retinectomy for traction release. Each eye received direct RPE laser, and 13 cases received partial (less than 50% of the edge) supplementary tradi-

tional transretinal laser treatment as well; the wavelength used was 532 nm (Purepoint Laser Alcon laboratories, INC, Fort Worth, TX, USA).

Postoperative visits were performed at 1 week, 1 month, 3 months, 6 months, 1 and 2 years after surgery. At each follow-up visit, the BCVA was taken, a complete anterior segment examination was performed, and the IOP was measured. After fully dilating the pupil, the fundus was evaluated using a 90 D lens, and binocular indirect ophthalmoscopy was also performed. When possible, optical coherence tomography (Cirrus HD-OCT, 5160 Hacienda Drive, Dublin, CA, USA), and fundus photography were employed to document the status of the posterior retina. All Snellen visual acuities were converted to LogMAR (logarithm of the minimum angle of resolution) for statistical analysis; “counting fingers” was defined as 2.3 logMAR, “hand movement” to 2.6 logMAR, and “light perception” to 2.9 logMAR.

Surgical Procedure

All procedures were performed by the same surgeon (X.Y.) under general or local (retrobulbar) anesthesia. A 23- or 25 g three-port vitrectomy (20 g in the case of endoscopy use) was performed to achieve complete vitreous removal, including the previously undetached posterior cortical vitreous. For visualization, either the surgical microscope (19 eyes) or an ocular endoscope (E2 Compact MicroProbe Laser and Endoscopy, ENDO OPTIKS, INC. Little Silver, NJ, USA) (one eye) was employed. All traction forces were removed, and if necessary, a heavy liquid was used to aid in removing the subretinal fluid and reattach the retina. Retinectomy was performed in areas with severely fixed folds, retinal stiffness, or shortened, thickened, or curled areas that could not be flattened. The retinectomy's extent depended on the lesion's size, and varied between 45 degrees and 360 degrees.

Direct RPE photocoagulation was performed in the area where the edge of the subsequently reattached retina was to settle. Three to four rows of laser spots were delivered. The power of the laser for direct RPE photocoagulation was in the range of 100 to 150 mW, with a duration between 120 and 200 ms, spaced at half the diameter of the spots. The laser's energy was high enough to create pale yellow spots while avoiding the formation of bubbles during laser delivery. After air-fluid exchange or heavy-liquid use and retinal reattachment, the pale yellow area subjected to direct RPE laser could still be seen through the retina in most cases. If the retina settled so the laser effect near the edge of the break was deemed insufficient, the conventional retinal laser was used to supplement the treatment. If the area of conventional laser reached 50% of the break's margin or the retina's edge lay in an untreated area, and conventional laser treatment was needed, the case was excluded from this series.

Table 1. Basic characteristics of patients (n = 20) with retinal detachment.

No.	Principal diagnosis	Special conditions	Preoperative Snellen	Six months Snellen	Final Snellen	Photocoagulation
			BCVA	BCVA	BCVA	
1	RRD	Medullated fibres, Retinectomy	20/50	20/25	20/20	RPE
2	RRD; myopia	Retinectomy	FC/10 cm	20/800	20/667	RPE + Retina
3	LRD; HIM	Retinectomy	LP	FC/20 cm	FC/30 cm	RPE
4	RRD; HIM	Giant retinal tear	20/63	20/50	20/40	RPE + Retina
5	VH	Giant retinal tear	HM/40 cm	20/40	20/40	RPE + Retina
6	LRD		HM/10 cm	20/32	20/32	RPE + Retina
7	RRD	Giant retinal tear	20/20	20/20	20/20	RPE + Retina
8	RRD	Retinectomy	20/800	20/25	20/25	RPE
9	RRD	Giant retinal tear	20/80	20/32	20/32	RPE + Retina
10	PVR	Retinectomy	HM/10 cm	20/250	20/250	RPE + Retina
11	DR; TRD	Intraoperative iatrogenic retinal breaks	HM/10 cm	20/100	20/100	RPE
12	RRD; HIM		20/25	20/100	20/100	RPE + Retina
13	RRD	Giant retinal tear	FC/50 cm	20/40	20/40	RPE + Retina
14	RRD; MH; HIM	Retinectomy	HM/50 cm	20/200	20/200	RPE + Retina
15	LRD; HIM	Retinectomy	FC/30 cm	20/20	20/20	RPE
16	ReRD; HIM	Retinectomy	20/1000	20/40	20/32	RPE
17	RRD; HIM; MH	Retinectomy	20/333	20/63	20/63	RPE + Retina
18	ReRD; Myopia	Retinectomy	20/50	20/32	20/32	RPE + Retina
19	VH; Oculartrauma; LRD		LP	FC/30 cm	FC/30 cm	RPE
20	RRD; MH; HIM	Retinectomy	20/400	20/250	20/200	RPE + Retina

BCVA, best-corrected visual acuity; RRD, Rhegmatogenous retinal detachment; RPE, retinal pigment epithelium; FC, finger counting; HIM, high myopia; LRD, long-standing retinal detachment; LP, light perception; VH, vitreous hemorrhage; HM, hand movements; PVR, proliferative vitreoretinopathy; DR, diabetic retinopathy; TRD, traction retinal detachment; MH, macular hole; ReRD, recurrent retinal detachment.

If transretinal laser photocoagulation was used, the settings were: 100–250 mW power with a duration between 150 and 300 ms.

One eye (case 3) had concurrent cataract removal via phacofragmentation but without the implantation of an intraocular lens.

At the conclusion of the operation, the vitreous cavity was filled with silicone oil or gas (C₃F₈ or SF₆), as demanded by the patient's history and the intraoperative findings. The silicone oil was removed 3 to 6 months after the operation.

Statistical Analysis

Wilcoxon matched pairs test analyzed the LogMar BCVA in GraphPad Prism (version 9, GraphPad Software, Boston, MA, USA) (The data followed a non-normal distribution). If the total difference was statistically significant ($\alpha = 0.05$), the Bonferroni method would be used to compare the difference of each timepoint ($\alpha = 0.0167$).

Results

Our study enrolled 20 eyes from 20 distinct patients, 12 males, and 8 females. Their mean age was 47 years, ranging from 24 to 69. The patients characteristics, including ocular characteristics are summarized in Table 1.

Out of the total, 11 eyes exhibited fresh, primary rhegmatogenous retinal detachment (cases 1, 2, 4, 7–9, 12–14, 17 and 20). Notably, three of these (cases 14, 17 and 20) also had macular holes, although these were not the initiating factors for the retinal detachment. Two eyes (cases 16 and 18) had recently redetached, while four eyes presented with chronic retinal detachment (cases 3, 6, 15, and 19, Figs. 1,2). The remaining eyes had a combined rhegmatogenous-tractional type of retinal detachment. In terms of refractive errors, eight eyes were classified as highly myopic, two as moderately myopic, and one as mildly myopic. One eye featured myelinated nerve fibers near the optic disc, with the retinal break situated within this myelinated region. Five eyes exhibited a giant retinal break.

Surgically, no major intraoperative complications were observed, and postoperatively, all retinas remained attached. No cases of redetachment were recorded, and apart from silicone oil removal, no additional surgeries were performed. Only one eye experienced a postoperative vitreous hemorrhage, likely originating from the scleral incision site, which resolved spontaneously within a month.

In 19 of the eyes, postoperative ophthalmoscopy revealed a distinct pigmentary reaction around the laser-

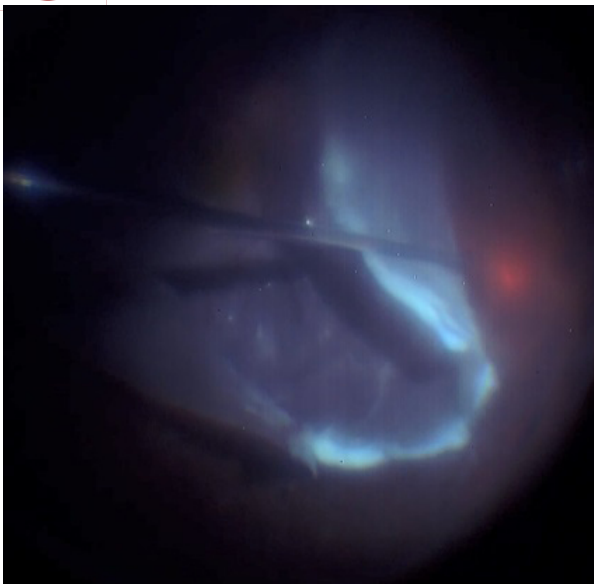


Fig. 1. Direct retinal pigment-epithelial laser photocoagulation in the midperiphery. Intraoperative image (case 3) showed 360-degree retinal pigment-epithelial photocoagulation was being performed after 360-degree retinectomy. Traditional retinal photocoagulation was not considered due to the peripheral retina being very thin in this highly myopic eye.

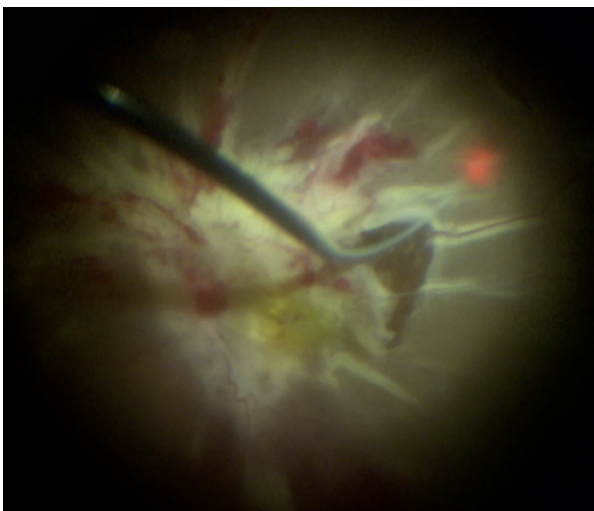


Fig. 2. Direct retinal pigment-epithelial laser photocoagulation in the posterior pole. Within this eye (intraoperative image; case 11), the curvable laser probe was employed to seal an iatrogenic break that occurred during the removal of extensive posterior proliferative membranes in diabetic retinopathy. RPE on the area where the edges of the retinal break were anticipated to settle post-reattachment was photocoagulated by inserting the curvable laser probe under the edge of the break. The retina was not transparent enough to allow transretinal photocoagulation.

treated retinal tear. However, in the eye with myelinated nerve fibers, this pigmentary response was challenging to visualize.

The mean preoperative intraocular pressure (IOP) was 11 mmHg (7–15 mmHg range), and the mean postoperative IOP at the 6-month follow-up—after silicone oil removal—was 18 mmHg (9–22 mmHg range). Topical therapy was necessary to control the IOP in two eyes.

Preoperatively, the median LogMAR BCVA was measured at 2.0, ranging from light perception to 20/20. At 6 months post-operation, the median LogMAR BCVA improved to 0.35 and further refined to 0.3 at the final follow-up. The 6-month and final follow-up BCVA were statistically higher than preoperative values ($p < 0.0001$ for both). No significant difference was found between the 6-month and final follow-up BCVA ($p = 0.0625$). The main changes in the vision before and after surgery are shown in Table 1 and Fig. 3.

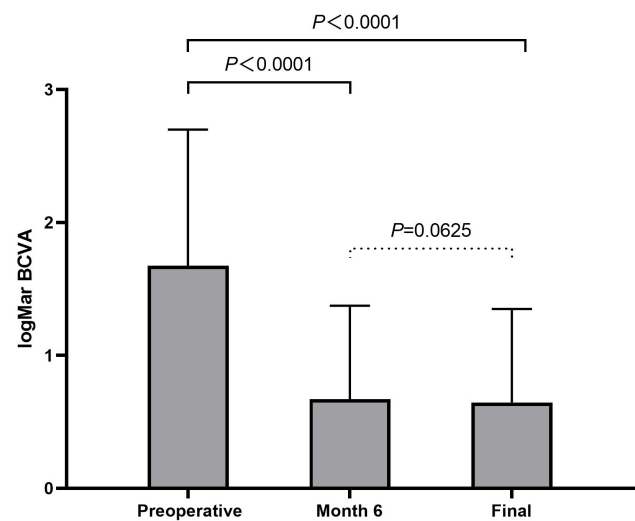


Fig. 3. Visual acuity changes before and after vitrectomy. Total twenty eyes, the postoperative visual acuity in our study was statistically significantly greater at 6 months than the preoperative values. There was no significant change in the visual acuity during the follow-up period past 6 months ($\alpha = 0.0167$). LogMAR, logarithm of the minimum angle of resolution.

Regarding retinal thickness, in three eyes with posterior retinal breaks identifiable via optical coherence tomography (OCT), we measured the postoperative neuroretinal thickness in areas treated with both direct RPE and transretinal photocoagulation. At one month postoperation, the mean thickness was 217 μm (181–280 μm range) in areas treated with direct RPE photocoagulation and 104 μm (55–133 μm range) in those treated with transretinal photocoagulation (Figs. 4,5). These values shifted from 189 μm and 124 μm to 148 μm and 94 μm , respectively, nearly 4 years post-operation (case 17; Fig. 5).

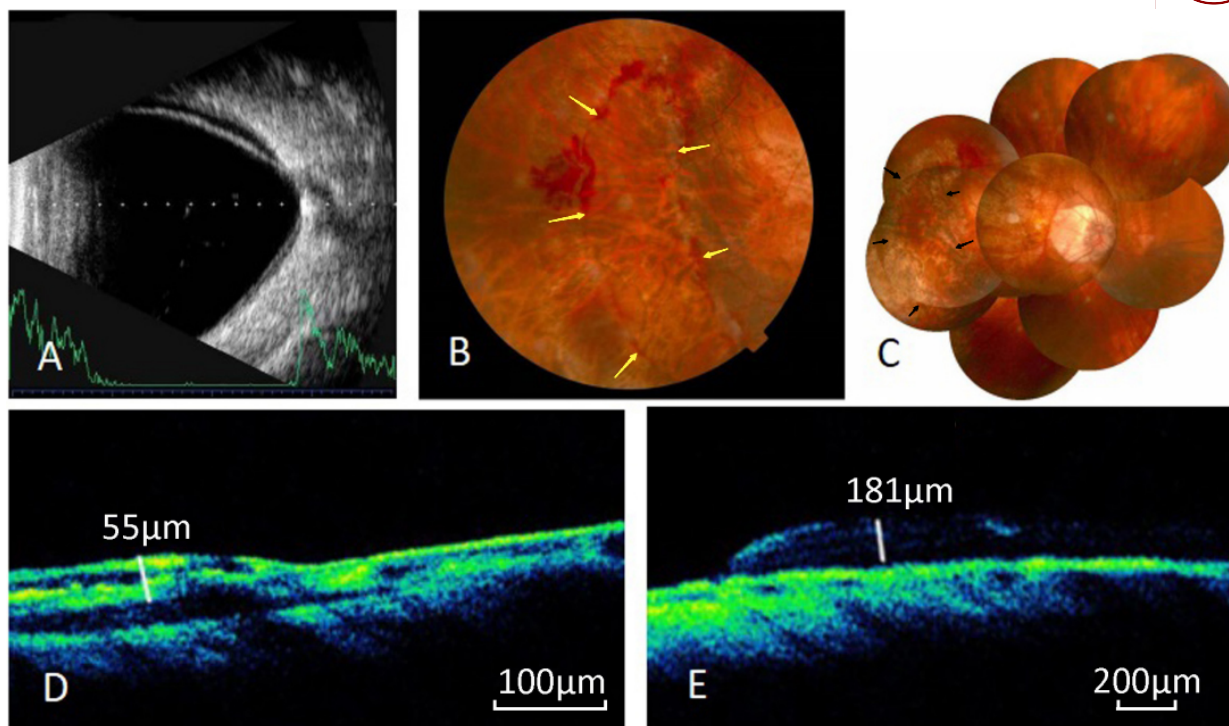


Fig. 4. Direct retinal pigment-epithelial laser photocoagulation in an eye with rhegmatogenous retinal detachment. This eye had high myopia and a macular hole (case 14). (A) Preoperative B-scan ultrasonography showed the retinal detachment and a longer-than normal axial length. (B) Intraoperative image with the yellow arrows pointed to the line of retinectomy. Direct retinal pigment-epithelial laser photocoagulation was then applied along the incision. (C) One month postoperatively, visible pigmentation was at the laser site (arrows). (D,E) (D) Optical-coherence-tomography images one month postoperatively. The thickness of the neuroretina in the area of transretinal photocoagulation was 55 μm ; (E) in the area of direct retinal-pigment-epithelial photocoagulation, the thickness of the neuroretina was 181 μm .

Discussion

The goals of surgery in eyes with retinal detachment include sealing the edge of the retinal break to prevent access of the intravitreal fluid to the subretinal space. Today, such a seal is created almost exclusively through the use of laser.

During traditional laser treatment, energy is delivered through the neuroretina, but the desired effects mainly occur in the retinal pigment epithelium (RPE) and choroidal melanocytes, leading to coagulation necrosis. Increased laser energy intensifies thermal effects, potentially causing significant damage to the neuroretina. This underscores the importance of delivering laser energy at an “ideal” level to produce effective chorioretinal adhesion without causing undue damage to the neuroretina.

Direct, rather than transretinal, photocoagulation of the RPE avoids both problems: the effect on the pigmented cells can be clearly visualized, and the neuroretina sustains no damage during laser delivery. The desired adhesion to the underlying RPE layer will still develop if the retina is reattached soon after the laser treatment. Our preliminary study shows that the laser at the settings we employed (100–150 mW, 120 and 200 ms) while achieving proper chori-

oretinal adhesion around the break (bonding the two tissues like a glue), results in reduced retinal damage. Furthermore, the retinal thickness remained normal in direct RPE laser photocoagulation while reduced by almost two-thirds in the traditional transretinal laser treatment area, where the fusion is achieved by a thermal effect [16]. Since glial and RPE cells may play an important role in the closure of retinal break [17], preserving the integrity to the extent possible of both the neuroretina and RPE may enhance the formation of the seal. The effectivity of the direct RPE laser photocoagulation is shown by the fact that the retinal reattachment rate remained 100% after a long follow-up, even without supplementary traditional photocoagulation.

The power of the laser during direct RPE delivery is not substantially lower as compared to that used during traditional photocoagulation: the neuroretina cannot inflict its insulating effect during direct RPE lasering as it is replaced by fluid, which carries away the heat generated by the laser. The distance between two laser spots can be reduced to half the diameter of the spot since, with direct RPE lasering, the spot size barely grows with time, showing an added benefit in eyes in which the laser pathology is employed is close to the fovea.

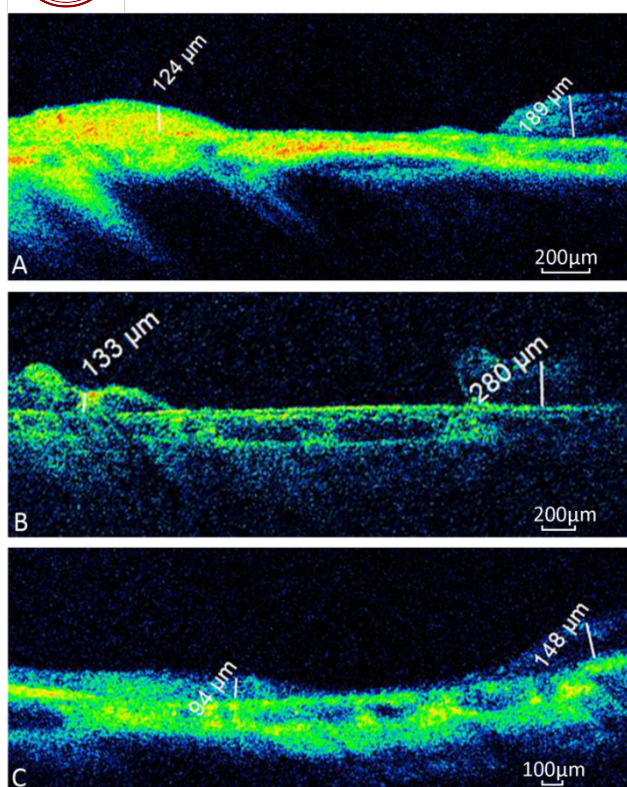


Fig. 5. Postoperative optical-coherence-tomography images. (A) In this highly myopic eye (case 17), the thickness of the neuroretina in the transretinal photocoagulation area was 124 μm , as opposed to a thickness of 189 μm in the direct RPE retinal-pigment-epithelial photocoagulation laser treatment. (B) The same relevant numbers in case 20 was 133 μm and 280 μm , respectively, one month postoperatively. (C) Almost 4 years postoperatively, the same area as A (case 17).

In addition to a complete vitrectomy, attention was paid to removing all traction forces [18] during surgery. Nevertheless, retinectomy was still necessary in 11 eyes due to various factors such as retinal shortening such as in eyes with high axial length [16,18,19] or proliferative tissues prove impossible to separate from the retina [20–24].

Finally, it appears that direct RPE photocoagulation may also reduce the tendency of RPE cells to migrate and proliferate: although the proliferative vitreoretinopathy (PVR) development was a rather significant risk [25–29] in our cohort, not a single case has occurred. The lack of distant adverse effects is shown by the fact that the visual acuity improved in all eyes, and all eyes reached their maximum visual potential within 6 months postoperatively.

In summary, direct laser photocoagulation of the RPE has several possible advantages of RPE photocoagulation in sealing retinal breaks: (1) the process does not generate heat on any layer of the neuroretina, thereby eliminating the risk of causing atrophic retinal holes; (2) even in eyes with reduced transparency of the neuroretina, the laser energy can be kept to the minimum since the laser light does not

have to traverse the neuroretina; (3) there is proper visual feedback from RPE to allow precise titration of the laser energy, irrespective of retinal transparency; (4) it appears that bypassing the retina with the laser reduces the risk of post-laser retinal thinning; (5) since the laser spots barely grow post-treatment, direct RPE laser is advantageous in eyes with a pathology close to the fovea.

Direct laser photocoagulation of the RPE also poses technical difficulties. (1) The surgeon must rely on experience to predict the position of the reattached retinal breaks and deliver the laser spots accordingly; if the prediction is incorrect, either traditional laser treatment must be used to supplement the direct photocoagulation (which is what we did in 13 eyes in this study) or the retina be redetached and the direct RPE laser repeated at the verified location. (2) The laser spots may be difficult to visualize if retinal transparency is severely compromised. In such cases, again, either additional transretinal laser treatment is needed or the direct RPE laser application is to be repeated after retinal redetachment. (3) Finally, especially when the retinal break is small, very peripheral, and the pupil narrow, endoscopy may be necessary to complete the photocoagulation of the break.

Despite the promising findings, this study has significant limitations, notably being a case series without controls and involving a limited number of eyes. As indicated in our preliminary findings, a larger, controlled study is needed to confirm the benefits and lack of adverse effects of direct RPE laser in retinal detachment surgery.

Conclusions

Direct RPE laser photocoagulation offers an alternative method for effectively sealing retinal breaks, and it may reduce some of the side effects commonly associated with traditional retinal photocoagulation in selected cases.

Availability of Data and Materials

The data are available upon request from the corresponding author.

Author Contributions

XY designed the study and performed all surgeries. SD, YYZ and JZ made substantial contributions to acquisition of data. SD, YYZ and XC analysed the data. XC prepared the original draft, YYZ, JZ revised the original draft; XY, SD contributed to all the revision of the manuscripts. FK participated the design and rewrote the manuscript with significant revisions. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

This study was approved by the Suzhou LiXiang Eye Hospital of Soochow University Committee for Research Ethics (20150109-1), and conducted in accordance with the official regulations for clinical research and the Declaration of Helsinki. We have obtained signed informed consent from each patient for participation in this study and consent to publish the findings.

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Conflict of Interest

The authors declare that there is not any conflicts of interest regarding the publication of this paper, and none of the authors have any proprietary interests or conflicts of interest related to this submission.

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