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## 27.1 Introduction

Most of the retinal diseases are associated with occlusion of retinal vessels. However, we have not established surgical approach for retinal vessels yet because of its extremely small size. Retinal endovascular surgery (REV) is an exciting new avenue for retinal surgeons, and researchers are making efforts to develop effective REV techniques. An experimental study of REV was started during the 1990s. In the late 1990s, REV treatment first began as an insertion of a microcannula into branches of the retinal vasculature with injection of pharmacologic agents such as t-PA for eyes with central retinal vein occlusion [1, 2]. Some previous reports on visual acuity in CRVO patients suggested that REV can lead to recovery of vision; however, other reports showed little benefit [3, 4]. One thing that was the most challenging for REV was the retinal endovascular procedure itself. In this capture, the principle, a surgical procedure, and results of REV we have developed are noted.

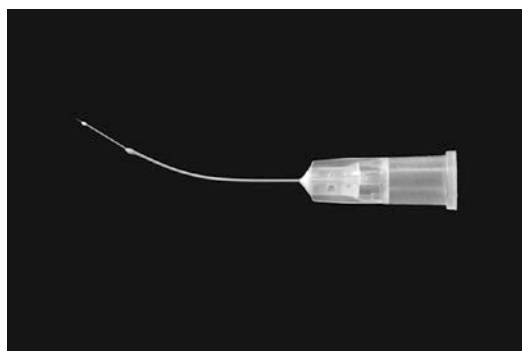
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## 27.2 Development of Endovascular Surgery with a Microneedle

Endovascular surgery involves three main variables: which instruments are used; how the vessels are pierced; and where the needle is placed. A micropipette had been used for a long time for retinal endovascular surgery manually, and it had been pierced into the central retinal vein.

However, we developed a technique for endovascular surgery which involves using a special needle to pierce the central retinal vein, and bimanually inject tPA at 2014 [5] (Fig. 27.1). We feel that the microneedle we have developed is an important instrument for cannulation. In recent years, microneedles have been fabricated



**Fig. 27.1** A picture of a microneedle which is made of stainless steel; its outer diameter is 50 microns and inner diameter is 20 microns

based on tools from the microelectronics industry, and they have been assessed as effective devices to facilitate administration delivery [6]. Fabricated microneedles are sharp and rigid, making them capable of serving as tools for microvascular surgery [6, 7]. We compared the capabilities of microneedles and conventional micropipettes for use in a microvascular procedure in porcine eyes and assessed the performance of microneedles as tools for retinal endovascular surgery [5]. As a result, we confirmed that microneedles are more feasible than micropipettes.

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### 27.3 Surgical Indication of Endovascular Surgical Procedure

CRVO is an important cause of vision loss [8, 9]. The only proven treatment for CRVO in the past was the central vein occlusion study which showed neither improvement with grid laser treatment for macular edema nor prophylactic effect of panretinal photocoagulation [10]. Recently the use of ranibizumab was also reported in a prospective, randomized study to improve visual acuity for eyes with macular edema due to CRVO [11]. When considering the pathogenesis of CRVO, the inciting event is thought to be thrombosis within the central retinal vein, which was supported by a previous pathological study [12]. Occlusion of the major outflow channel for retinal circulation obviously increases venous pressure, resulting in the macular edema and hemorrhages typical of the disease. These persistent macular edema and/or hemorrhages have irreversible adverse effects on essential retinal cells including photoreceptors. If the eye simultaneously has closure of a substantial proportion of the perifoveal capillaries, vision is severely impaired. One pathological study showed that the venous thrombus was present at the level of the lamina cribrosa in eyes with CRVO.

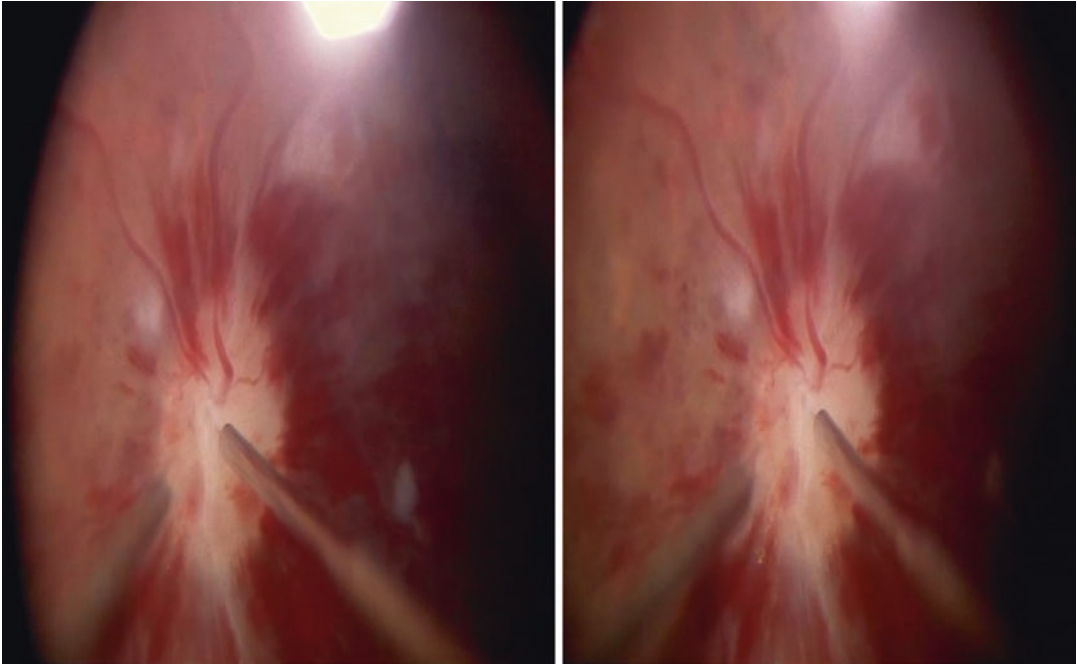
We consider that eyes with CRVO are well indicated for REV and its timing should be an

earliest intervention to avoid macular structure infarction. And also, eyes with refractory macular edema after many injections of anti-VEGF drug are also indicated for REV in which a cannulation procedure is the only method to improve refractory macular edema.

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### 27.4 Surgical Procedure

All surgical procedures were performed using a 25-gauge microincisional vitrectomy system with the Constellation Vision System (Alcon Laboratories, Fort Worth, Texas). After displacement of the conjunctiva, a total of four trocars were inserted, with one trochanter used for chandelier illumination with a light source (Brightstar, DORC Company, Holland). After a core vitrectomy, both the posterior hyaloidal membrane and the internal limiting membrane around the macular region were removed. To pierce the dilated retinal vein, a microneedle with an outer diameter of 50  $\mu\text{m}$  was used (Fig. 27.2). This instrument, which has been developed and manufactured solely for retinal endovascular surgery, is sharp and stiff enough to perform piercing procedures in very small vessels. The needle was connected to a 10 cc syringe containing tissue plasminogen activator (tPA) (Criactor, Eisai pharmaceutical com., Japan) with balanced saline solution (BSS plus, Alcon Laboratories, Fort Worth, Texas) (Fig. 27.3). The concentration of tPA is 43  $\mu\text{g}/\text{mL}$  which is prepared just before cannulation in an operating room. The volume of BSS with tPA injected was in proportion with the pressure of the syringe connected to the viscous fluid control system, which was controlled by the surgeon using a pedal. To manage any sudden hemorrhages during the piercing, a bimanual procedure was used, with the surgeon holding the microneedle in the right hand, and a flute needle for the suction of possible bleeding in the left hand. When accurately piercing the dilated retinal vein close to the optic nerve in an eye with CRVO, a slight sensation of loss of resistance occurs, indicating that BSS can be slowly



**Fig. 27.2** A picture of retinal vein cannulation. The microneedle is pierced into the central retinal vein using a 3D system

injected into the retinal vein with a pressure of about 4 psi. After confirming that the vessel has turned white, the pressure is elevated to 40 psi. The time of injection is roughly 3 min, and during this period the flow of BSS in the retinal vessel can be clearly observed as a streamline. After removal of the microneedle, the vessel is checked for any bleeding.

### 27.4.1 Surgical Results

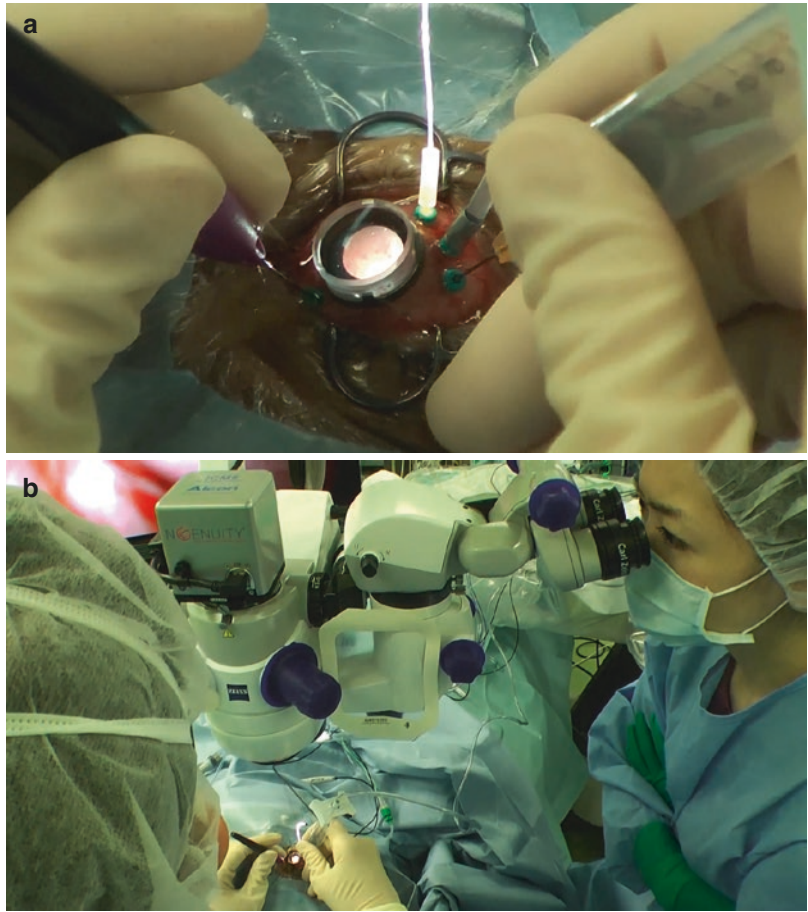
We reported the study published [13]. In this study, the BCVA of 9 of 12 patients had improved by more than 15 letters at 24 weeks after surgery compared with the baseline value. The mean VA had improved by 14.1 letters at 6 weeks, by 15.3 letters at 12 weeks, by 15.3 letters at 18 weeks, and by 16.3 letters at 24 weeks. The preoperative mean BCVA of 29.6 letters (20/250) had improved to 45.9 letters (20/125) at 24 weeks after surgery, and the mean decrease in central foveal thickness was 271.1  $\mu$ m.

### 27.4.2 Complications

In our report published, no neovascular glaucoma was observed in any of the patients when examined at 24 weeks. All surgical procedures were successful, as confirmed by the streamlined flow during the injection. Intraoperative complications developed in two patients and consisted of a mild vitreous hemorrhage in one eye and a small subretinal hemorrhage in one eye, neither of which impaired VA. No occurrences of retinal tears, endophthalmitis, retinal detachment, severe vitreous hemorrhage, or recurrence of macular edema were observed during the 24-week follow-up period.

However, we should carefully follow up patients with ischemic CRVO which has a relatively high risk of developing neovascular glaucoma with performing panretinal photocoagulation. The occurrence rate of macular edema is not so high; however when we see macular edema which usually occurs about a month after cannulation, we routinely inject steroid into a sub-Tenon's space.

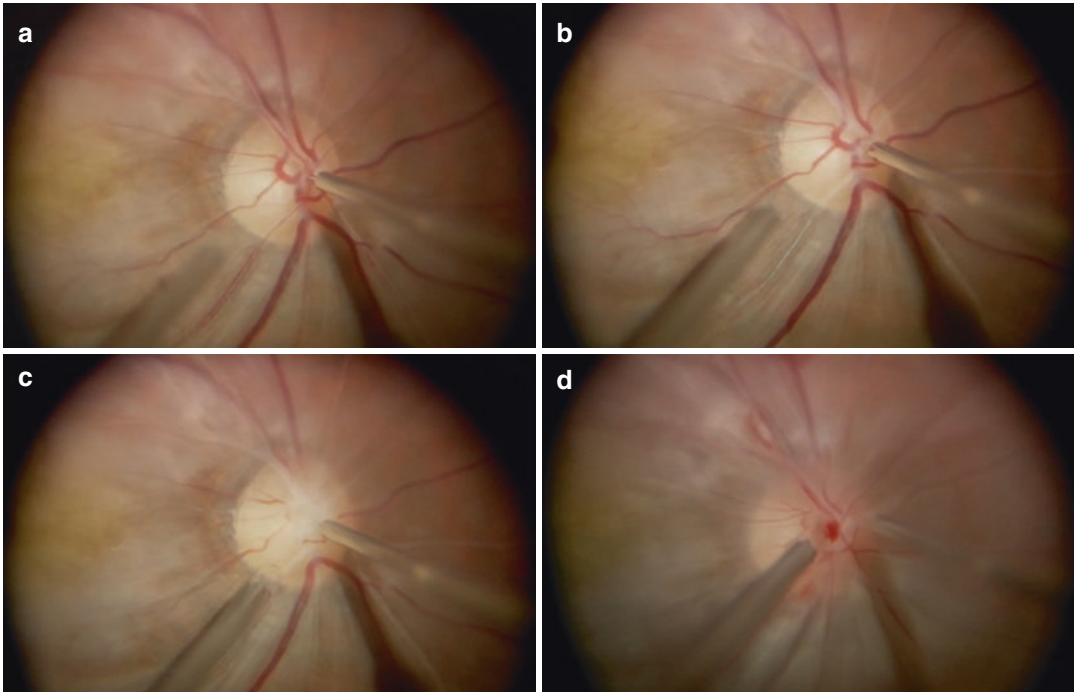
**Fig. 27.3** A picture of retinal endovascular surgery. A surgeon holds a microneedle in the right hand to get inside an eye for injection while holding a soft-tip cannula with the left hand (a). A cannula is connected with 10 cc syringe, which is controlled by a foot switch in a vitrectomy machine (b)



### 27.5 Recent Development of Cannulation for CRAO

Central retinal artery occlusion (CRAO) is caused by a thrombus or embolism in the central retinal artery. Mainly occurring in the optic nerve head, it is an ophthalmological emergency often resulting in blindness due to the resulting inner retinal ischemia [14]. If the embolism is resolved in an eye with CRAO by retinal endovascular surgery, we are able to confirm significant improvement of occluded blood flow, resulting in improved vision of a patient with CRAO. We routinely perform eyes with CRAO within 72 h or less after the onset. Patients with heart or brain problems

are excluded. Surgical procedure is same as that in CRVO (Fig. 27.4). The one point different from REV for CRVO is to pierce central retinal artery. It is sometimes difficult to distinguish which vessels are arterial because the diameter of vessels is quite different from the normal one. The risk of sudden bleeding from the pierced site is much lower than expected because an arterial vessel in an eye with CRAO is essentially occluded. If the bleeding happens in an artery during cannulation, it is a good sign demonstrating recanalization of vessels. In cases with sudden bleeding in cannulation, we passively aspirate the bleeding with a soft-tip cannula in the left hand.



**Fig. 27.4** A cannulation for an eye with CRAO. A cannula is pierced into a central retinal artery (a), and then tPA is injected into a vessel (b). The pressure of injection

is maximized (80 psi) (c). A needle is removed to simultaneously aspirate bleedings. (d) Any bleedings are aspirated with a soft-tip cannula

### 27.5.1 Results

Overall, results are good with an average rate of improvement of visual acuity which is approximately 80% in our initial study [15]. And also, a visual field with successful REV improves but relative central scotoma remains. The result showed that there is a significant association between improvement of visual acuity and severity of CRAO. For example, it is not expected that there is significant improvement of visual acuity in eyes with complete CRAO.

### 27.5.2 Complications

A small number of eyes can develop vitreous hemorrhages after REV, but there is low risk of severe surgical complications such as retinal detachment, endophthalmitis, and brain infarction.

### 27.6 Discussion

We demonstrated retinal endovascular surgery for eyes with CRVO as well as CRAO. The results obtained were quite good, leading to significant improvements in visual acuity. This surgical technique still has some inherent difficulties; it is a challenging procedure and requires a steep learning curve to master. However, recent advances in technology such as digitally assisted vitreoretinal surgery (3D) are able to assist surgeons in performing this procedure. Moreover, robotic surgery might provide further support to surgeons performing these types of surgeries in the future [16, 17].

In conclusion endovascular surgery is one of the latest techniques in the field of ophthalmology and has garnered significant interest from vitreoretinal surgeons since pioneers started to study this kind of surgery a decade ago. The combination of excellent skills as a surgeon, sci-

ence, objective clinical evidence, and cutting-edge technology will improve this surgical technique.

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