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Twenty-three Gauge Cannula System with Microvitreoretinal Blade Trocar

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Running title: 23-gauge cannula with a MVR blade trocar

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Key words: 23-gauge vitrectomy, cannula, hypotony, postoperative complication, surgical instruments

Abstract

AIMS: To report on a 23-gauge cannula with a microvitreoretinal (MVR) blade trocar which improved wound closure after vitrectomy and reduced the incidence of postoperative hypotony.
METHODS: The resistance of inserting a 23-gauge MVR trocar-cannula through the porcine sclera was compared to that with the conventional 23-gauge trocar-cannula. The incidence of postoperative hypotony (intraocular pressure < 6 mmHg) was determined for 48 eyes that underwent vitrectomy with the 23-gauge MVR trocar-cannula and 30 eyes with the conventional 23-gauge trocar-cannula. The eyes were examined on postoperative days 1, 2, and 7. The closure of the sclerotomies was examined by optical coherence tomography in 9 eyes in each group on postoperative days 1, 3, and 7, and one month.
RESULTS: The resistance of inserting the MVR trocar-cannula was lower than that with the conventional trocar-cannula. In patients, a transient hypotony was found at postoperative day 1 after the vitrectomy in 2 eyes (4%) with the MVR trocar-cannula, and in 7 eyes (23%) with the conventional trocar-cannula (P= 0.023). An unclosed incision was detected in 9 sclerotomies (50%) with the MVR trocar-cannula and 16 sclerotomies (89%) with the conventional trocar-cannula (P= 0.028) on postoperative day 1, and the incidence of an opened incision was also significantly higher with the conventional trocar-cannula on days 3 and 7 but not after 1 month (P= 0.003, P= 0.008, P= 0.486, respectively).
CONCLUSION: The MVR trocar-cannula leads to better postoperative wound closure and reduces the incidence of postoperative hypotony.

Introduction

Small gauge vitrectomy instruments were developed to allow transconjunctival sutureless vitrectomy.[1] Although good results have been obtained with their use, hypotony, choroidal detachments, and endophthalmitis have been reported as postoperative complications.[2] An oblique sclerotomy or an angled incision was reported to minimize the incidence of wound leakage when the 25-gauge system was used.[3,4] Histological analysis of the angled incisions made by 25-gauge and 23-gauge systems showed better wound closure than with straight incisions.[5] The better closure reduced the leakage of intraocular fluid and blocked the entry of India ink on the surface of the eye into the vitreous.[5]

Twenty-three gauge vitrectomy, first described by Eckardt,[6] uses a slit-shaped blade that was similar to the microvitreoretinal (MVR) blade. The sclerotomy was made by inserting the blade at an angle of 30 degrees, and the blade was removed. The 23-gauge cannula with the inserter was then pushed through the sclerotomy into the vitreous. This two-step procedure had at least two disadvantages; the sclerotomy incision can be lost between the time of the incision and the insertion of the cannula, and the open incision between two-step procedure can enhance bacterial contamination although it is influenced by the sterile condition of the surgical field.

In an earlier study, we described the advantages of incorporating a MVR trocar in the 25-gauge cannula system so that the incision of the sclera by the trocar and insertion of the cannula could be done as a one-step procedure.[7] This reduced the incidence of postoperative hypotony.[7]

We have applied this principle to the 23-gauge system, and have investigated whether this system will have lower resistance during insertion, and whether this system will enhance the wound closure thus preventing postoperative hypotony.

Materials and methods

The resistance of inserting the MVR blade trocar-cannula through the sclera was measured in four isolated porcine eyes by a TENSILON Universal Tensile Instrument (RTC-1250A, A&D Co., Japan). The sclera was excised and a part of the sclera with a thickness of approximate 0.4 mm was used for the experiments. The resistance values obtained with the MVR blade trocar-cannula were compared to those obtained when a conventional solid-shafted 23-gauge

trocar system (Alcon Laboratories, Fort Worth, Texas, USA) was used (n=2).

To determine the effectiveness of the 23-gauge MVR trocar system in human eyes, vitrectomy was performed on 48 eyes with these instruments, and the results were compared to those obtained from 30 eyes that underwent vitrectomy with the standard 23-gauge trocar-cannula (Alcon Laboratories, Fort Worth, Texas, USA). A gas tamponade was used in 15 eyes with the MVR trocar-cannula and 16 eyes with the conventional trocar-cannula. The eyes were followed for at least 3 months in both groups. All patients were fully informed about the procedures and a signed written informed consent was obtained from all patients. The procedures conformed to the tenets of the Declaration of Helsinki and all federal laws.

To begin, the MVR blade trocar was pushed through the sclera at an angle of about 45 degrees. This direction was parallel to the corneal limbus, and the direction was then changed so that the tip of the blade was directed to the center of the globe. The standard 23-gauge trocar-cannula was inserted in the same fashion. At the end of the surgery, the cannula was removed and the sclerotomy site was gently wiped with cotton swabs to close the opening and was not sutured. Eyes that had sutures because of silicon oil tamponade or simultaneous placement of encircling buckle were excluded from the study. The intraocular pressure (IOP) was adjusted to be between 10 to 20 mmHg by palpation by injecting balanced salt solution into the anterior chamber through a corneal paracentesis or gas into the vitreous cavity with a 30-gauge needle.

The selection of the patients was consecutive and not randomized, and the methodology was not masked. The IOPs were measured preoperatively and postoperatively on days 1, 2, and 7, and the incidence of hypotony (IOP <6 mmHg) was determined. Eyes with previous vitrectomies were excluded.

The sclerotomy incisions were examined by optical coherence tomography (OCT3, Carl Zeiss Meditec, Dublin, CA). Eighteen sclerotomy ports were made on the temporal and nasal sides in 9 eyes with the MVR blade trocar-cannula and 18 corresponding sclerotomy ports were made in 9 eyes with the conventional trocar-cannula. All of these sites were scanned with the OCT3 on days 1, 3, 7, and 1 month postoperatively. The direction of the OCT scan was parallel to the corneal limbus which was the same direction as the incision made by the trocar to create the sclerotomy. The number of eyes in each group that had open scleral wounds in the OCT images was determined. An open scleral wound was detected in the OCT3 image by the lack of signals within the sclera in the obliquely scanned images. Eyes with a postoperative IOP <6

mmHg were excluded from the wound scanning study.

Results

Insertion resistance of trocar-cannulas

The trocar-cannula with a MVR blade trocar is shown in Figures 1A. The width of the MVR blade was 0.65 mm, and the inner and outer diameters of the cannula were 0.66 mm and 0.77 mm, respectively. The tip of the cannula was sharpened to decrease the inserting resistance (Fig. 1A) compared to that of the conventional trocar-cannula (Fig. 1B). The inserting resistance of the MVR blade trocar-cannula though the porcine sclera had two peaks as the trocar and cannula passed through the sclera. The force was 0.24 N at 4.6 mm and 1.72 N at 6.7 mm. The values were lower than that with the conventional trocar-cannula which were 0.51 N at 4.8 mm and 2.16 N at 6.9 mm (Fig. 2).

Incidence of postoperative hypotony

The MVR blade trocar could be easily inserted through the sclera, and the cannula could be oriented so that it could be inserted into the middle of the vitreous. All of the incisions were angled (Fig. 1C, D), and the cannula was not retracted from the sclerotomy during the surgery. The sclerotomy was not sutured at the completion of the surgery in both groups.

The sclerotomies after vitrectomy with the MVR blade trocar-cannula were observed to be linear-shaped and those with the conventional trocar-cannula were V-shaped according to the shape of the tip of the trocar even with the angle incisions (Fig. 1E, F). The mean preoperative IOP in the eyes on which the MVR blade trocar-cannula was used was 12.7 ± 3.8 mmHg, and the mean postoperative IOPs were 13.1 ± 5.0 mmHg on day 1, 13.5 ± 4.9 on day 2, and 13.0 ± 3.3 on day 7. The postoperative IOPs were not significantly different from the preoperative IOPs (P = 0.891, 0.078, and 0.074, respectively; Wilcoxon signed rank test). The mean preoperative IOP in the eyes that had vitrectomy with the conventional trocar-cannula was 12.8 ± 3.8 mmHg, and the postoperative IOPs were 9.9 ± 6.2 mmHg on day 1, 12.8 ± 5.3 on day 2, and 13.1 ± 3.1 on day 7. The IOP was significantly lower only on postoperative day 1 (P = 0.019, 0.943, and 0.722, respectively; Wilcoxon signed rank test).

A temporary hypotony was found in 2 eyes (4%) on the day after vitrectomy in eyes that had vitrectomy with the MVR blade trocar-cannula but the IOP returned to normal levels on the

second day (Table 1). A temporary hypotony was found in 7 eyes (23%) on postoperative day one in eyes that had vitrectomy with the conventional trocar-cannula. The higher number of eyes with hypotony with the conventional trocar-cannula instrument group was significant ($P = 0.023$, Fisher exact probability test). However, only 3 eyes remained hypotonic on the second day (0/48 eyes vs. 3/30 eyes; $P = 0.103$). The incidence of hypotony in the eyes without a gas tamponade was also significantly higher in the eyes that had the conventional trocar-cannular vitrectomy (6% vs 36%; $P = 0.018$), but was not in the eyes with a gas tamponade (0% vs 13%; $P = 0.484$). Two eyes developed uveitis after vitrectomy with the MVR blade trocar-cannula system, and two eyes developed proliferative vitreoretinopathy after vitrectomy with the conventional trocar-cannula system. However, these four eyes did not develop postoperative hypotony as was expected for these postoperative complications. The incidence of hypotony in eyes with an epiretinal membrane (none had gas tamponade) was 0% (0/15 eyes) in the MVR trocar-cannula group which was lower than that of 22% (2/9 eyes) in the conventional trocar-cannula group ($P = 0.130$). The incidence of hypotony in the MVR trocar-cannula was lower than that of the conventional trocar-cannula group in eyes with a macular hole (0/5 eyes, 1/3 eyes; $P = 0.375$), proliferative diabetic retinopathy (0/16 eyes, 2/9 eyes; $P = 0.120$), and retinal detachment (0/8 eyes, 1/5 eyes; $P = 0.385$).

None of the eyes in both groups had a leakage of intraocular fluid (positive for Seidel test), postoperative endophthalmitis, retinal detachment, or suprachoroidal infusion.

Incidence of wound closure determined by OCT3

Open sclera wounds were observed on postoperative day one in 9 ports after vitrectomy with the MVR blade trocar-cannula system and in 16 ports after vitrectomy with the conventional trocar-cannula system (Fig. 3). The lower incidence of open wounds with the MVR blade trocar-cannula was significant ($P = 0.028$, Fisher's exact probability test, Table 2). Signals were not always detected at the sclerotomy sites because of subconjunctival hemorrhage or chemosis, but the signals became clearer on postoperative day 3 and 7. The significantly lower incidence of open wounds in the eyes that had undergone vitrectomy with the MVR trocar-cannula was still present on postoperative days 3 and 7 but not at 1 month ($P = 0.003$, $P = 0.008$, $P = 0.486$, respectively).

In the conventional trocar-cannula vitrectomy group, the internal sites of the incisions were seen to be open with closure of the external sites, "internal open", in two eyes one month after

the surgery. A gape in the incision at the external entry site with closure of the internal site, "external open", was seen in one eye of the conventional group at postoperative one month although the IOP was in the normal range and all these three eyes were classified as closed wounds.

Discussion

The advantages of micro-incision vitrectomy surgery (MIVS) including 25-gauge and 23-gauge vitrectomy are the faster recovery, less invasiveness, and reduction of surgery-induced astigmatism.[8,9] The 23-gauge vitrectomy system creates a larger sclerotomy than the 25-gauge vitrectomy system, but the system also has similar advantages over the 20-gauge system in postoperative astigmatism and faster visual recovery. Vitrectomy with 23-gauge instruments is safe and effective for surgeries for a macular hole, epiretinal membrane, and other posterior segment surgeries.[8-11]

In a multicenter retrospective study, the intraoperative and postoperative complications of vitreal surgery for various posterior segment diseases were reported to be rare with the 23-gauge system, and the recovery time was significantly shorter.[12] A postoperative transient hypotony was the most common complication observed, which was resolved without intervention by one week after the surgery.[12] A prospective randomized trial comparing 23-gauge and 20-gauge vitrectomy also showed that retinal manipulation and overall surgical damage did not differ significantly with the two systems although the 23-gauge group had a shorter time for wound construction but longer vitrectomy time.[13] However, a significantly higher numbers of patients reported less pain during the conjunctival injection and less pain during the early postoperative period in the 23-gauge MIVS group.[13,14]

A higher incidence of postoperative endophthalmitis has been reported after 25-gauge vitrectomy than after 20-gauge vitrectomy.[15,16] In those studies, vertical incisions were performed in 0% to 27% of the subjects to create sclerotomy, but a more recent study with angled incisions reported no significant difference in the incidence of postoperative endophthalmitis between 25-gauge MIVS and 20-gauge vitrectomy.[17] Histological analysis of cadaver or animal eyes showed that angled incision led to a better wound closure then vertical incisions.[18,19]

However, the transient postoperative hypotony after MIVS may allow entry of ocular

surface fluid that increases the risk of bacterial contamination and endophthalmitis.[18,20-22] Because the conventional solid shaft-type trocar-cannula creates a V-shaped sclerotomy, the angled incision with a bevel-side down insertion has been suggested to lead to a better sealing of the wound.[4] Thus, we hypothesized that a slit-shaped incision with less resistance of insertion would lead to a better self-sealing wound.[7,23] We found less resistance of the MVR trocar-cannula in a porcine sclera and lower incidence of postoperative hypotony in the MVR trocar-canula group. We also found opened scleral ports even one month after surgery with the conventional solid shaft-type trocar-cannula system. This was probably because the V-shaped scleral tunnel would offer an easier passage of vitreous into the scleral tunnel. The opened wound was observed as an empty, non-reflective space in the OCT images. Nagpal and associates[24] described a significant amount of vitreous blocking the inner lip of the sclerotomy ports of 23-gauge conventional systems that was detected by endoscopy in uncomplicated cases of vitreous hemorrhage due to diabetic retinopathy.

OCT examinations of the anterior segment showed an occasional opened external incision at the entry site on postoperative days 1and 8 in the eyes after 23-gauge conventional vitrectomy without postoperative hypotony.[25] OCT has the advantage as a non-contact examination to evaluate postoperative surgical wounds compared to high-frequency ultrasound biomicroscopy which requires direct contact with the wound surface. We used an OCT with a shorter wavelength light source with lower penetrating power through the sclera, and we found significantly better wound closure with MVR blade troocar-cannula system from earlier postoperative period although we examined only a limited number of cases. The evaluation of wound closure in sclerotomy with OCT may have a disadvantage by mistaking hemorrhage or fibrin within the gap of the scleral wound as a wound closure. However, none of the eyes were misclassified as having wound closure after the absorption of hemorrhage or fibrin. In addition, we did not find any choroidal detachments as has been reported as a complication of 23-gauge vitrectomy.[25]

We conclude that this new trocar-cannula is effective in obtaining better wound closure, and the incidence of postoperative hypotony was significantly lower. However, more cases are needed to determine the value of this surgical instrument.

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Table 1. Comparison of the 23G MVR trocar-cannula vitrectomy and the conventional 23G vitrectomy

Surgical procedure	Total eyes with postop hypotony	Procedure details (eyes) with postop hypotony	Surgical Indications (N)
23G MVR trocar-cannula vitrectomy	2/48 (4%)*	No exchange: 2/33 (6%)† Gas exchange: 0/15 (0%)‡ Cataract surgery: 2/23 (8%)§ Vitrectomy alone: 0/25 (0%)‖	Epiretinal membrane: 15 Macular hole: 5 PDR: 16 Retinal detachment: 8 Uveitis: 2 Vitreous opacity: 1
Conventional 23G trocar-cannula vitrectomy	7/30 (23%)*	No exchange: 5/14 (36%)† Gas exchange: 2/16 (13%)‡ Cataract surgery: 3/17 (18%)§ Vitrectomy alone: 2/13 (15%)‖	Epiretinal membrane: 9 Macular hole: 3 PDR: 9 Retinal detachment: 5 DME: 1 PVR: 2

23G: 23-gauge, PDR: proliferative diabetic retinopathy, DME: diabetic macular edema, PVR: proliferative vitreoretinopathy. *$P = 0.023$, †$P = 0.018$, ‡$P = 0.484$, §$P = 0.634$, ‖$P = 0.111$; The statistics were to compare the distribution of the procedure details between the two groups. With significant P values, we assume that the procedure details are not balanced (Fisher exact probability test).

Table 2. The incidence of absence of signals of oblique scleral wounds

	Scleral ports	day 1	day 3	day 7	1 month
MVR	temporal				
trocar-cannula	(n=9)	6	3	0	0
	nasal				
	(n=9)	3	1	0	0
Conventional	temporal				
trocar-cannula	(n=9)	9	9	6	2
	nasal				
	(n=9)	7	5	1	0
P-value		0.028	0.003	0.008	0.486

Figure Legends

Figure 1. Microphotographs and intraoperative and postoperative photographs of the MVR trocar-cannula

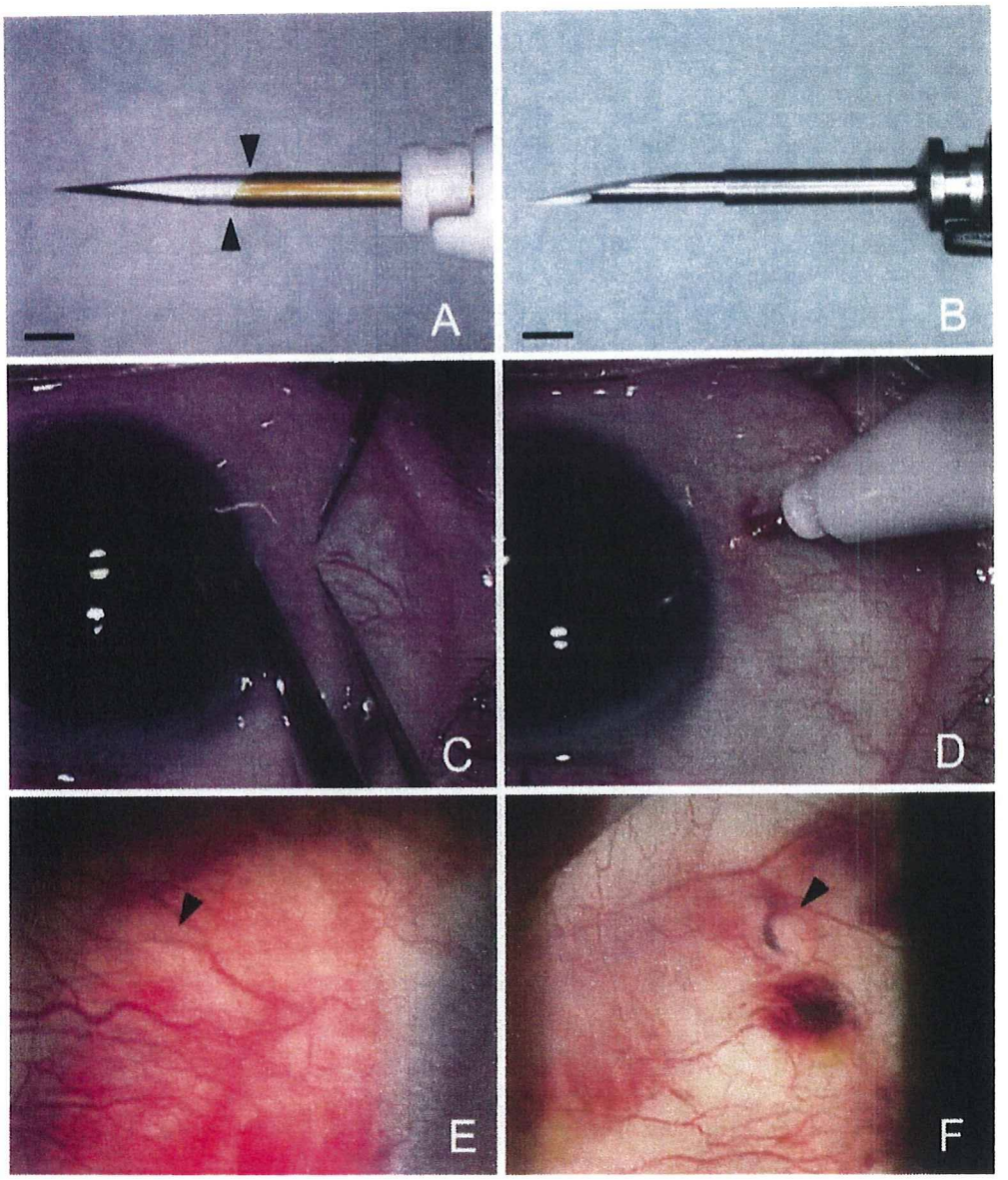
(A) Side view of the MVR trocar-cannula and (B) side view of the conventional trocar-cannula (Alcon, Bar: 0.5 mm). The tip of the cannula was sharpened to decrease the inserting resistance (A: arrowheads). (C) The head of the microvitreoretinal (MVR) blade trocar can be seen as it penetrates the globe at a 45 degree angle and parallel to the corneal limbus. (D) The direction of the trocar is turned to the vertical direction. (E) The sclerotomies after vitrectomy with the MVR blade trocar-cannula is linear-shaped (arrowhead) on the postoperative day 1. (F) The sclerotomies after vitrectomy with the conventional trocar-cannula is V-shaped (arrowhead) on the postoperative day 1.

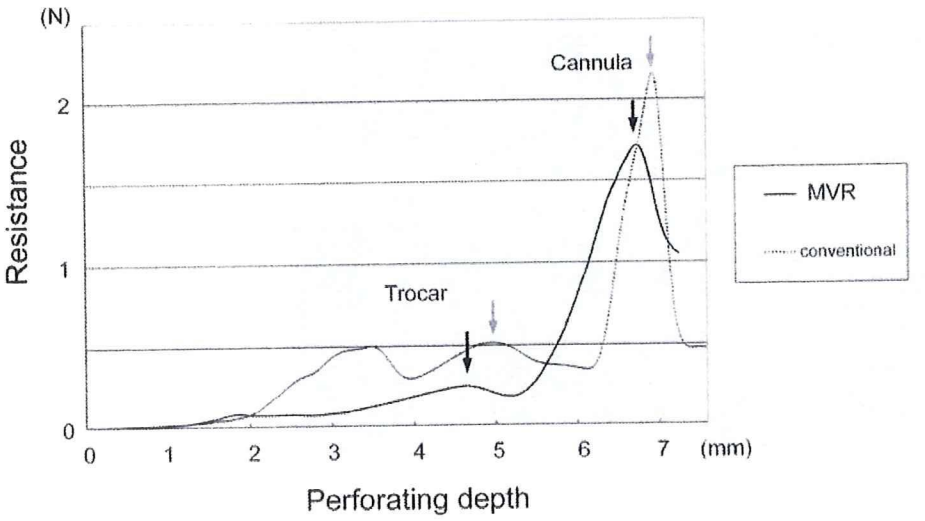
Figure 2. Resistance of insertion of each trocar-cannula through the sclera of an isolated porcine eye.

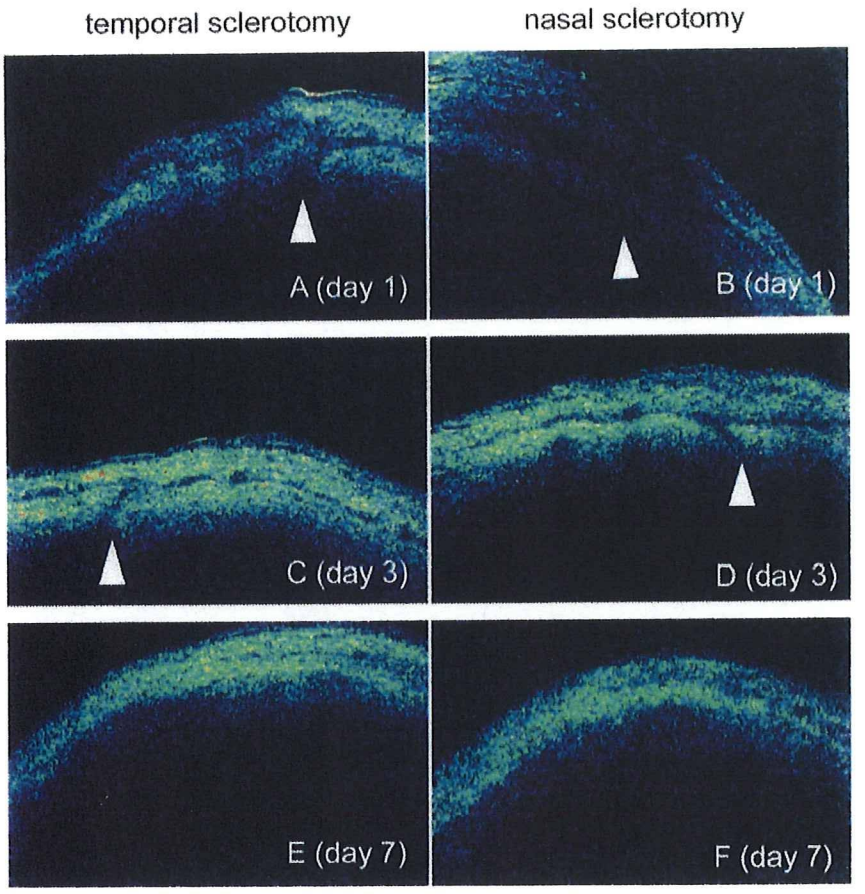
The resistance of insertion of the MVR blade trocar-cannula was less than that of the conventional trocar-cannula when the trocar and the cannula were pushed through the sclera as indicated by black arrows (MVR) and gray arrows (conventional). (MVR: MVR trocar-cannula, conventional: conventional trocar-cannula).

Figure 3. Optical coherence tomography images of temporal and nasal sclerotomies.

The absence of scleral signals (white arrowheads) in the eyes that were operated on with the MVR trocar-cannula can be seen on each side of the sclerotomy on postoperative day 1 and day 3, but not on postoperative day 7.







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Review

Implantable CMOS Biomedical Devices

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Abstract: The results of recent research on our implantable CMOS biomedical devices are reviewed. Topics include retinal prosthesis devices and deep-brain implantation devices for small animals. Fundamental device structures and characteristics as well as *in vivo* experiments are presented.

Keywords: biomedical devices; retinal prosthesis; image sensors; CMOS; brain implantation

1. Introduction

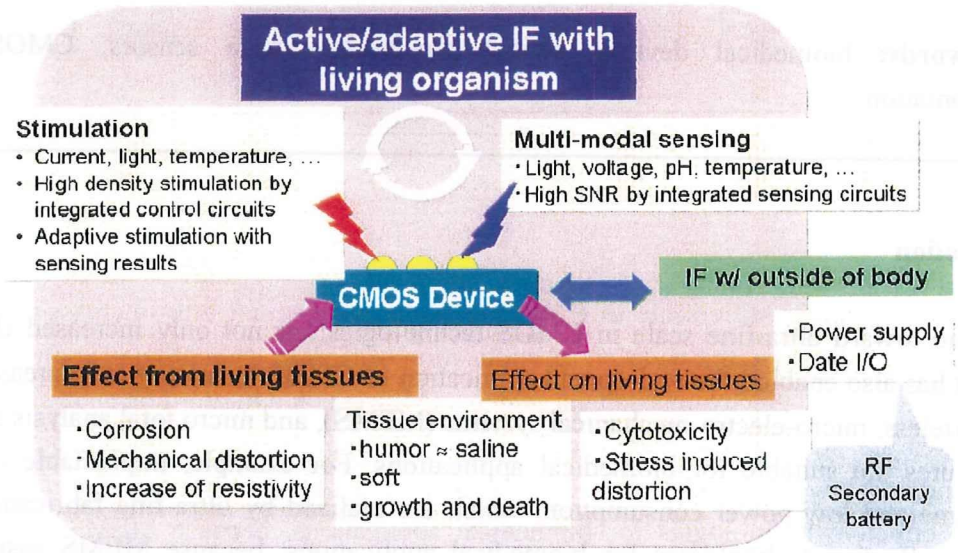
The trend toward ultra-fine scale in CMOS technologies has not only increased chip integration density but has also enabled the widespread application of CMOS technologies in areas such as image sensors, wireless, micro-electro-mechanical systems (MEMS), and micro total analysis system (μTAS). These features are suitable for biomedical applications. For example, implantable devices require small volume and low power consumption, which are realized by ultra-fine fabrication technology. MEMS are effective technologies for biomedical applications, because MEMS easily form three-dimensional structured which are useful in the applications. Image sensor technology is also very efficient for biotechnology applications in which fluorescence is frequently used for labeling specific cells or detecting neural activity. CMOS technologies are thus highly suitable for implantable devices for biomedical applications and have been used in various types of devices.

In this review, two typical examples of implantable CMOS devices from our research are described: retinal prosthesis devices [1-5] and brain-implantable devices based on CMOS technologies [6-9]. In retinal prosthesis devices, MEMS technologies with CMOS circuits have been used to realize a retinal stimulator based on a microchip array, and in brain-implantable devices, image sensor technology and MEMS have been combined to realize an ultra-compact device to be implanted in the deep brain of experimental small animals. The present review describes the results of recent research on retinal prosthesis devices and brain-implantable devices. In Chapter 2, we discuss the advantages and problems associated with the *in vivo* implantation of CMOS devices. In Chapter 3, we describe retinal prosthesis devices that we have developed. We also describe a multiple microchip architecture that we developed in order to realize a retinal stimulator that uses a large number of stimulus electrodes while bending the stimulator to match the curvature of an eyeball. Chapter 4 describes brain-implantable CMOS imaging devices for measuring the neural activity in the deep brain of a small experimental animal, such as a mouse. Chapter 5 briefly addresses areas for future research and summarizes the present review.

2. *In Vivo* Implantation of CMOS Devices

This section describes the advantages and problems associated with *in vivo* implantation of CMOS devices. Figure 1 summarizes these advantages and problems. The advantages include high performance and versatile functionality in the detection of bio-signals and the stimulation of living cells by on-chip integration of circuits. For example, an on-chip amplifier can detect weak signals with a high signal-to-noise (SN) ratio, and an on-chip multiplexer can be used for multi-site stimulation.

Figure 1. Advantages and problems associated with *in vivo* implantation of CMOS devices.

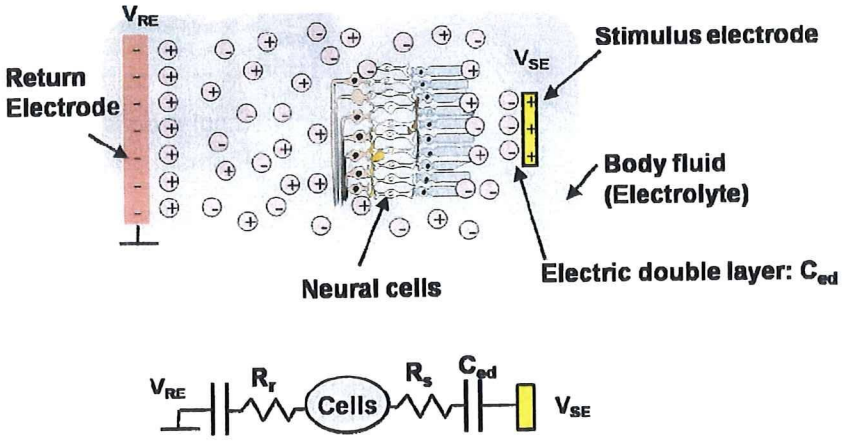


CMOS devices also have the advantage of multi-modal sensing of, for example, physical values such as the amount of light, voltage, and temperature, ions, and chemical entities such as enzymes. CMOS devices also enable multi-modal stimulation such as injection of charge and chemical

substances. The important point is that a CMOS device can configure a closed-loop of sense and stimulation. Neural cells can be actively and adaptively stimulated by detecting physical value(s) and analyzing spatio-temporal dynamics. For example, in retinal prosthesis, retinal cell stimulation is often adaptively controlled by monitoring the impedance value. In addition, for deep brain stimulation, such an implanted device is proposed that monitors the amount of dopamine emitted in a patient's brain, determines the optimum value of stimulation, and stimulates the deep brain before the onset of tremor is currently being developed [10]. This is a typical example of a closed-loop device.

Although implanted CMOS devices are expected to provide a highly sophisticated interface with the living body, there are many problems to be solved before realization because both stable and safe operation *in vivo* is required. Figure 1 shows these issues. An implanted device affects living tissues or cells, and these effects can include cytotoxicity and stress-induced distortion. As for cytotoxicity, packaging materials and/or electrode materials may be dissolved into tissue and affect cells. Many discussions including cytotoxicity and mechanical distortions appear in [11]. In addition, in stimulation, electrochemical reactions can occur when the stimulation voltage exceeds the voltage window, and pH changes and/or bubbling can have harmful effects on neural cells [12,13]. Moreover, implanted devices are also affected by the living environment. The living environment is composed primarily of saline solution, so that a CMOS chip with no coating may be damaged. Therefore, a highly water-tight packaging is necessary such as parylene. Of course, this material must be biocompatible. An implanted device is stressed by the living tissues so that it may be distorted or broken. For example, a thinned CMOS chip is easily implanted but may be broken by stress from tissues because Si is fragile when thinned. Living tissues may grow and die, and thus the configuration between the device and tissues may change gradually. This may cause an impedance change between an electrode and living cells. Implanted devices must be designed knowing that the configuration of the device may change.

Figure 2. Electrical stimulation of neural cells in body fluid (a) and its equivalent circuits (b).



Next, we consider the stimulation of neural cells in, for example, artificial cochlear and retinal prostheses. In these applications, stimulation is achieved by extra cellular stimulation, in which the potential between the inside and outside of the cell is changed through electrolytes such as a body fluid.