Research Article
Ex Vivo Comparison of Intraocular Pressure Fluctuation During Pars Plana Vitrectomy Performed Using 25- and 27-Gauge Systems

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Short Title: 25G and 27G Vitrectomy Intraocular Pressure Fluctuation

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Abstract

Introduction: The purpose of this study was to compare intraoperative intraocular pressure fluctuation using different aspiration systems and 25- and 27-gauge vitreous surgery probes.

Methods: Ex vivo, pars plana, 25- and 27-gauge vitreous surgery was performed on four porcine eyes, and IOP fluctuations were evaluated. We performed three-port vitrectomy using the Constellation® Vision or the EVA® Phaco-Vitrectomy system. Each 20-s experiment was conducted five times for each set of conditions, each with the same substituted balanced salt solution. Real-time intraoperative intraocular pressure measurement was performed at the distal end of the infusion tube. Intraocular pressure was measured during core vitrectomy; core vitrectomy with fluid aspiration; peripheral vitreous shaving with scleral indentation; and fluid-gas exchange. The Mann-Whitney U test was used to evaluate statistical significance.

Results: Mean ± standard deviation intraoperative intraocular pressure fluctuation during 25- and 27-gauge core vitrectomy were 15.9 ± 1.6 mmHg and 11.9 ± 1.4 mmHg, respectively (P < 0.05), using the Constellation system; 23.2 ± 1.4 mmHg and 14.1 ± 0.7 mmHg, respectively (P < 0.001), using the EVA vacuum mode; and 15.0 ± 0.5 mmHg and 11.5 ± 1.4 mmHg, respectively (P < 0.05), using the EVA flow mode. The smallest intraoperative intraocular pressure fluctuations during core vitrectomy with fluid aspiration, peripheral vitreous shaving with scleral indentation, and fluid-gas exchange, were all achieved using the 27-gauge EVA flow mode; these values were 14.2 ± 0.4 mmHg, 35.7 ± 0.9 mmHg, and 6.4 ± 0.2 mmHg, respectively.

Conclusion: Regardless of the aspiration system, intraoperative intraocular pressure fluctuation was lower during 27-gauge than during 25-gauge vitrectomy. The 27-gauge EVA flow mode produced optimal intraoperative intraocular pressure stability.
Introduction

With the development of vitreous surgery, 27-gauge (27G) probes are increasingly being used because they are less invasive and result in better prognoses; however, intraocular pressure (IOP) fluctuations during pars plana vitrectomy (PPV) can cause expulsive choroidal hemorrhage, retinal ischemia, vitreous hemorrhage, choroidal detachment, and optic nerve ischemia [1-6]. In patients with proliferative diabetic retinopathy and retinal vein occlusion, the effects of IOP fluctuations are particularly pronounced, especially in eyes with impaired retinal and optic nerve blood flow [6, 7]. In short, detecting IOP fluctuation during PPV may improve the safety of the procedure.

Michelson et al. [8] were the first to demonstrate, in healthy volunteers, that a rapid rise in IOP leads to decreased blood flow in the retina and optic disc. Ex vivo experiments have also been performed in animal models [7, 9-12], one of which suggested that a rapid increase in IOP during PPV may lead to retinal ganglion cell damage [9]. To date, IOP fluctuations of up to 110 mmHg have been demonstrated during vitrectomy in an animal model [10], whereas, in vitrectomy of the human eye, IOP has proven to fluctuate in the range of 0-120 mmHg [6, 11]. These results were obtained using the Accurus® Surgery System (Alcon Laboratories, Inc., Fort Worth, TX, USA), which is dependent on vented gas forced infusion (VGFI). Yang et al. [13] compared the Accurus Surgery system to the Constellation® Vision system (Alcon Laboratories, Inc.) by directly monitoring IOP in vivo. IOP fluctuations were larger during vitrectomy using the Accurus than on the Constellation.

In a 2010 pilot study, Oshima et al. [14] demonstrated the initial feasibility and safety of a novel 27G microincision vitrectomy surgery (MIVS) system. Since then, the use of 27G sutureless vitrectomy surgery has been on the increase, mostly for the treatment of macular disease [15-18]. In 2019, we reported the results of a retrospective multicenter study where we concluded that 27G PPV is a safe and effective treatment for primary retinal detachment [19]. Currently, more than half of the surgeons in Japan use 25G and 27G systems because they are minimally invasive. The most commonly used systems for MIVS are the Constellation and the EVA Phaco-Vitrectomy (D.O.R.C. Dutch Ophthalmic Research Center [International] B.V., Zuidland, The Netherlands) systems. Both are equipped with distinctive pressure control systems that can maintain IOP at a fixed value: in the case of the Constellation system, it is the IOP control (IOPc) feature, and in the case of the EVA system, it is the Automatic Infusion Compensation (AIC) feature. In our previous study, mentioned above, all surgeons performed 27G vitrectomy with either the Constellation or the EVA systems [19].

A limited number of studies have revealed, using 23G and 25G probes, that the IOPc feature of the Constellation system more effectively reduced IOP fluctuation than did the VGFI system [20, 21]. To
the best of our knowledge, IOP fluctuation during 27G PPV performed with various vitrectomy systems has not been investigated. The objective of the present study was to compare IOP fluctuation during vitrectomy with a 25G probe with that during vitrectomy with a 27G probe, on two different vitrectomy instruments.

Materials and Methods

In this study, we used four fresh porcine eyes, which were kept at 4°C, from a slaughterhouse within one day after death. The set-up of vitreous surgery was prepared according to general clinical standards. For the first eye, 25G vitrectomy was conducted using the Constellation system, with IOPc pressure set to 30 mmHg, cutting rate set to 7500 cuts per minute (cpm), and aspiration pressure set to 650 mmHg. For the second eye, 27G vitrectomy was performed under the same conditions. For the third eye, 25G vitrectomy was conducted using the EVA system, with AIC pressure set to 20-40 mmHg, cutting rate set to 8000 cpm, aspiration pressure set to 400 mmHg using the vacuum mode, and flow rate set to 15 ml/min using the flow mode. For the fourth eye, 27G vitrectomy was conducted using the EVA system under the same conditions, apart from the aspiration pressure, which was set to 600 mmHg. A summary of the settings is displayed in Table 1.

In each case, we performed standard three-port vitrectomy. Trocars (25G or 27G) were inserted perpendicularly into the pars plana. We performed core vitrectomy for all four eyes, extensively removing vitreous gel around the irrigation cannula with the 25G or 27G cutter, as vitreous gel impairs IOP measurement. Thereafter, the infusion tube was inserted into the vitreous cavity 3.5 mm posterior to the limbus. After confirming that the balanced salt solution (BSS) flowed freely through the cannula, we performed real-time measurement of IOP at the distal end of the infusion tube, using an invasive blood pressure monitor (LifeSource® UB-104U, Auto Control Medical Inc., Mississauga, Ontario, Canada). The infusion tube and pressure monitor were positioned at the same level as the eye during evaluation. The data were immediately sent to the UAS-308S data collection system (Unique Medical Co., Ltd., Tokyo, Japan). The experimental set-up is portrayed in Figure 1.

We measured real-time IOP for all four sets of conditions, conducting each 20-s experiment five times. Each experiment was initiated only after pressure fluctuation due to injection of the BSS had subsided. We continuously monitored the IOP to detect fluctuations, at an acquisition rate of 250 samples/min, and calculated mean values. First, IOP was monitored during core vitrectomy, where the foot pedal was fully pressed down (vitreous cutter on) 5 s after the start of IOP measurement, and released (vitreous cutter off) 15 s after the start of measurement. Second, IOP was monitored during core vitrectomy with fluid aspiration, with the same intervals as above. Third, IOP was monitored during peripheral vitreous shaving with scleral indentation, where the foot pedal was
pressed down fully for the entire 20 s of measurement. In this case, we initiated scleral indentation 5 s after the start of IOP measurement and terminated it 15 s after the start of measurement. Fourth, IOP was monitored during fluid-gas exchange, where the foot pedal was pressed down fully and fluid aspiration initiated 5 s after the start of IOP measurement. The foot pedal was released and fluid aspiration switched to gas aspiration 15 s after the start of measurement. Real-time IOP data were imported into Microsoft® Excel® 2016 (Microsoft Corp., Redmond, WA, USA), and graphs were plotted. We defined IOP fluctuation as the difference between maximum and minimum IOP values.

**Statistical Analysis**

Continuous variables were indicated as the mean ± the standard deviation. Where appropriate, the Mann-Whitney U test was used to evaluate statistical significance. Statistical analysis was performed using IBM SPSS® Statistics 24.0 (IBM Corp., Armonk, NY, USA). A P-value of < 0.05 was considered statistically significant.

**Results**

Figure 2A is a plot of the mean dynamic change in IOP during core vitrectomy. Mean IOP fluctuation during 25G and 27G core vitrectomy were: 15.9 ± 1.6 mmHg and 11.9 ± 1.4 mmHg, respectively (P < 0.05), using the Constellation system; 23.2 ± 1.4 mmHg and 14.1 ± 0.7 mmHg, respectively (P < 0.001), using the EVA vacuum mode; and 15.0 ± 0.5 mmHg and 11.5 ± 1.4 mmHg, respectively (P < 0.05), using the EVA flow mode.

Figure 2B is a plot of the mean dynamic change in IOP during core vitrectomy with fluid aspiration. Mean IOP fluctuation during 25G and 27G vitreous aspiration were: 82.0 ± 2.6 mmHg and 31.5 ± 1.0 mmHg, respectively (P < 0.001), using the Constellation system; 35.3 ± 1.0 mmHg and 19.6 ± 0.5 mmHg, respectively (P < 0.001), using the EVA vacuum mode; and 26.1 ± 0.6 mmHg and 14.2 ± 0.4 mmHg, respectively (P < 0.001), using the EVA flow mode.

Figure 2C is a plot of the mean dynamic change in IOP during peripheral vitreous shaving with scleral indentation. Mean IOP fluctuation during 25G and 27G peripheral vitreous shaving were: 92.4 ± 2.4 mmHg and 82.9 ± 2.3 mmHg, respectively (P < 0.001), using the Constellation system; 53.6 ± 2.0 mmHg and 43.6 ± 0.8 mmHg, respectively (P < 0.001), using the EVA vacuum mode; and 47.1 ± 1.0 mmHg and 35.7 ± 0.9 mmHg, respectively (P < 0.001), using the EVA flow mode.

Figure 2D is a plot of the mean dynamic change in IOP during fluid-gas exchange. Mean IOP fluctuation during 25G and 27G fluid-gas exchange were: 36.3 ± 0.7 mmHg and 28.1 ± 1.0 mmHg, respectively (P < 0.001), using the Constellation system; 30.6 ± 1.1 mmHg and 19.6 ± 0.8 mmHg,
respectively (P < 0.001), using the EVA vacuum mode; and 14.6 ± 0.4 mmHg and 6.4 ± 0.2 mmHg, respectively (P < 0.001), using the EVA flow mode. All the above results are presented in Table 2.

Figure 3 is a plot of mean IOP fluctuations using 25G and 27G vitrectomy for the various vitreous conditions. Mean IOP fluctuation was 39.4 ± 24.7 mmHg during 25G vitrectomy, and 26.3 ± 20.4 mmHg during 27G vitrectomy. The range of IOP fluctuation was smaller during 27G vitrectomy than during 25G vitrectomy, with a mean difference of 13.0 ± 22.5 mmHg (P < 0.001).

Discussion/Conclusion

In the present study, we conducted an experiment using the Constellation and EVA systems, the main instruments in use for various types of vitreous surgery in Japan. Other studies have been conducted to describe IOP fluctuations during vitrectomy with 23G and 25G probes using the IOPc feature of the Constellation system [20, 21]. However, to the best of our knowledge, IOP fluctuation during 27G PPV has not been investigated. Furthermore, many Japanese surgeons use 27G probes even for difficult cases such as retinal detachment [19]. Therefore, we conducted experiments using 25G and 27G probes.

The Constellation system was the first vitrectomy instrument to incorporate an IOP compensation feature, which they termed “integrated pressure injection with IOP control.” It utilizes noninvasive flow sensors to measure injections into the eye and corrects IOP in real time to maintain the desired pressure. The EVA system has the AIC feature, similar to IOPc, which stabilizes IOP by progressively increasing infusion via bottle pressure.

As in a previous report [7], intraoperative IOP fluctuation was the highest during peripheral vitreous shaving with scleral indentation in the present study. In the previous report, they concluded that there was no statistically significant difference in IOP fluctuations between 23G and 25G vitrectomy [7]. On the other hand, in another study, it was concluded that 23G probes lead to a lower IOP drop and smaller pressure overshooting than did 25G probes [21]. When using the Constellation system, the diameter of the cutter is smaller in the case of 27G vitrectomy, but the suction efficiency and the duty cycle are also lower. We hypothesize that the change in IOP was more stable due to the prevention of a rapid increase in the flow rate. The EVA system has a mechanism to adjust the pressure in response to the suction pressure, termed the “diafragma method” and “AIC.” Similar to that in the Constellation system, 27G vitrectomy lowers the suction efficiency in the EVA system, but IOP is more stable.

The EVA vacuum mode keeps the vacuum pressure constant, and the EVA flow mode keeps the flow volume constant. In this study, the 27G EVA flow mode produced optimal IOP stability when
compared the other conditions we investigated. In particular, IOP is most stable during fluid-gas exchange. A possible explanation is that, during the final stage of fluid-gas exchange, it is highly likely that, when aspirating the last drop of BSS, air will be aspirated. In a vacuum-based system, this can cause a large drop in IOP due to the difference in viscosity of BSS and air. By applying the EVA flow mode, a smooth fluid-gas transition is guaranteed, as the aspirated flow remains constant for both BSS and air.

It should be noted that the current study had some limitations. We used porcine eyes, as its scleral rigidity has been reported to be similar to that of the human eye [22]. However, experiments performed in porcine eyes are ex vivo, and the vitreous cavity in the human eye is smaller than that in the porcine eye; therefore, the results cannot be directly related to the human eye.

In conclusion, we confirmed that, regardless of the aspiration system, IOP fluctuation was lower during 27G vitrectomy than during 25G vitrectomy. In addition, the 27G EVA flow mode, with brief flow-rate control, produced optimal IOP stability when compared with the other conditions in the present study.
Statement of Ethics

This study was approved by the Committee for Safe Handling of Living Modified Organisms at the Kyoto Prefectural University of Medicine (Permission number: B2020-14) and carried out according to the guidelines of the committee.

Conflict of Interest Statement

The authors have no conflicts of interest to declare. The authors have no proprietary or commercial interest in any of the products described in this article.

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Author Contributions

Y.S. and K.Y. designed and performed the experiments. Y.S. analyzed the date. Y.S., K.Y., and C.S. generated the figures and tables, drafted and revised the manuscript, and approved the final manuscript.
References


Figure Legends

Fig. 1. Schematic of the experimental set-up to measure intraocular pressure fluctuation during pars plana vitrectomy with the EVA® Phaco-Vitrectomy system. The invasive blood pressure monitor and the liquid level in the bottle of balanced salt solution are positioned at the same level as the porcine eye.

Fig. 2. a. Intraocular pressure (IOP) fluctuations during core vitrectomy using various instruments and settings. We pressed the foot pedal down completely (vitreous cutter on) 5 s after the start of measurement and released it (vitreous cutter off) 15 s after the start of measurement.

Fig. 2. b. Intraocular pressure (IOP) fluctuations during core vitrectomy with fluid aspiration using various instruments and settings. We pressed the foot pedal down completely (vitreous cutter on) 5 s after the start of measurement and released it (vitreous cutter off) 15 s after the start of measurement.

Fig. 2. c. Intraocular pressure (IOP) fluctuations during peripheral vitreous shaving with scleral indentation. We pressed the foot pedal down completely (vitreous cutter on) for the entire 20 s. We initiated scleral indentation 5 s after the start of measurement and terminated it 15 s after the start of measurement.

Fig. 2. d. Intraocular pressure (IOP) fluctuations during fluid-gas exchange. We pressed the foot pedal down fully and initiated fluid aspiration 5 s after the start of measurement. We switched to gas aspiration 15 s after the start of measurement.

Fig. 3. Box plots of intraocular pressure (IOP) fluctuations with 25- and 27-gauge vitrectomy systems for the various vitreous conditions.
<table>
<thead>
<tr>
<th>Machines</th>
<th>IOP control (mmHg)</th>
<th>AIC (mmHg)</th>
<th>Cut rate (cpm)</th>
<th>Aspiration pressure (mmHg)</th>
<th>Flow (cc / min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Constellation25G</td>
<td>30</td>
<td></td>
<td>7500</td>
<td>650</td>
<td></td>
</tr>
<tr>
<td>Constellation27G</td>
<td>30</td>
<td></td>
<td>7500</td>
<td>650</td>
<td></td>
</tr>
<tr>
<td>EVA (25G vacuum mode)</td>
<td></td>
<td>20 · 40</td>
<td>8000</td>
<td>400</td>
<td></td>
</tr>
<tr>
<td>EVA (27G vacuum mode)</td>
<td></td>
<td>20 · 40</td>
<td>8000</td>
<td>600</td>
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<tr>
<td>EVA (25G Flow mode)</td>
<td></td>
<td>20 · 40</td>
<td>8000</td>
<td></td>
<td>15</td>
</tr>
<tr>
<td>EVA (27G Flow mode)</td>
<td></td>
<td>20 · 40</td>
<td>8000</td>
<td></td>
<td>15</td>
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</table>

AIC : Automatic Infusion Compensation
Table 2. The Results of the Intraocular Pressure Fluctuations during various settings

<table>
<thead>
<tr>
<th></th>
<th>IOP fluctuation</th>
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<tr>
<td></td>
<td>25 G</td>
<td>27 G</td>
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<tr>
<td>Constellation</td>
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<tr>
<td>Core Vitrectomy</td>
<td>15.9 ± 1.6</td>
<td>11.9 ± 1.4</td>
<td>&lt; 0.05</td>
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<tr>
<td>Aspiration mode</td>
<td>82.0 ± 2.6</td>
<td>31.5 ± 1.0</td>
<td>&lt; 0.001</td>
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<td></td>
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<tr>
<td>Scleral indentation</td>
<td>92.4 ± 2.4</td>
<td>82.9 ± 2.3</td>
<td>&lt; 0.001</td>
<td></td>
<td></td>
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<tr>
<td>Fluid-gas exchange</td>
<td>36.3 ± 0.7</td>
<td>28.1 ± 1.0</td>
<td>&lt; 0.001</td>
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<tr>
<td>EVA (vacuum)</td>
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<tr>
<td>Core Vitrectomy</td>
<td>23.2 ± 1.4</td>
<td>14.1 ± 0.7</td>
<td>&lt; 0.001</td>
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<tr>
<td>Aspiration mode</td>
<td>35.3 ± 1.0</td>
<td>19.6 ± 0.5</td>
<td>&lt; 0.001</td>
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<tr>
<td>Scleral indentation</td>
<td>53.6 ± 2.0</td>
<td>43.6 ± 0.8</td>
<td>&lt; 0.001</td>
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<tr>
<td>Fluid-gas exchange</td>
<td>30.6 ± 1.1</td>
<td>19.3 ± 0.6</td>
<td>&lt; 0.001</td>
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<td>EVA (Flow)</td>
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<tr>
<td>Core Vitrectomy</td>
<td>15.0 ± 0.5</td>
<td>11.5 ± 1.4</td>
<td>&lt; 0.05</td>
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<tr>
<td>Aspiration mode</td>
<td>26.1 ± 0.6</td>
<td>14.2 ± 0.4</td>
<td>&lt; 0.001</td>
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<tr>
<td>Scleral indentation</td>
<td>47.1 ± 1.0</td>
<td>35.7 ± 0.9</td>
<td>&lt; 0.001</td>
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<tr>
<td>Fluid-gas exchange</td>
<td>14.6 ± 0.4</td>
<td>6.4 ± 0.2</td>
<td>&lt; 0.001</td>
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</table>

Values are mean ± SD
Statistical analysis: Mann-Whitney U test
Intraocular pressure (mmHg)

Time (seconds)

- Constellation 25G
- Constellation 27G
- EVA 25G (Vacuum mode)
- EVA 25G (Flow mode)
- EVA 27G (Vacuum mode)
- EVA 27G (Flow mode)

Vit shaving on

Vit shaving off
Scleral indentation on

Scleral indentation off
* P < 0.001