Experimental Application of Piezoelectric Actuator-Driven Pulsed Water Jets in Retinal Vascular Surgery

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Purpose: To report on the effectiveness and safety of an ophthalmic piezoelectric actuator-driven pulsed water jet (ADPJ) system adapted for intraocular use.

Methods: First, we determined the highest ADPJ flow rate that did not cause an unsafe rise in intraoperative intraocular pressure (IOP) in rabbits ($n = 4$). Next, we determined the most effective ADPJ frequency (in hertz) at that flow rate. Finally, we visualized the ADPJ stream, measured its pressure, and determined the minimum voltage and distance between the ADPJ needle and retinal veins to induce intravenous displacement of the blood column (DBC) through massage of the outer retinal vessels ($n = 3$) while not causing retinal tearing or hemorrhage.

Results: We found that a 0.05 mL/min ADPJ flow rate caused IOP to rise above 40 mm Hg after 1 minute, but that at 0.025 mL/min, IOP stayed below 40 mm Hg even after 3 minutes. Moreover, we found that a 0.025 mL/min ADPJ stream was stable at a pulse frequency of 10 Hz and that at this flow rate/frequency the ADPJ pressure was closely correlated with the applied voltage ($P < 0.001$, $r^2 = 0.9991$). The minimum voltage and distance to achieve intravenous DBC without causing retinal tearing or hemorrhage were 40 V and 0.5 mm, respectively.

Conclusions: With an appropriate flow rate and surgical time, ADPJ successfully induced massage of the retinal vessels and intravenous DBC while maintaining safe IOP and not causing retinal complications.

Translational Relevance: The ADPJ system has promise as a safe and minimally invasive instrument for the intraocular surgical treatment of human retinal vascular diseases.

Introduction

Retinal vessel occlusion is a condition that remains difficult to treat for ophthalmologists, but it is very common, occurring in 2% to 3% of individuals over 40 years of age.¹ Among types of retinal vessel occlusion, retinal vein occlusion (RVO), which can cause macular edema, retinal cell death, and vision loss,^{2,3} has become a major problem affecting quality of life worldwide.^{4,5} These factors have led to the investigation of a variety of novel pharmacological and surgical approaches to RVO treatment.^{6–13} Pharmacological treatments for RVO have become available and are simple to use, but have a number of serious drawbacks

related to the method of drug delivery, recurrence, and side effects such as endophthalmitis. Surgical treatments for RVO are a promising alternative, but they remain challenging due to their technical difficulty. There is thus a need for easier and safer techniques to open occluded retinal vessels.

Recently, piezoelectric actuator-driven pulsed water jet (ADPJ) systems have been used experimentally and clinically in nonophthalmological fields of medicine.^{14–18} Surgeries using ADPJ systems have had remarkable results due to the system's ability to make incisions in internal organs while preserving blood vessels. Tissue incisions can be made with ADPJ systems without affecting vessels larger than

Figure 1. Photograph of the ophthalmic pulse jet surgery system (A). The system consists of a control unit, syringe pump, actuator-driven pulsed water jet generator, foot switch, handgrip (B), and microtube needle (C). Only the needle is inserted into the eye.

approximately 100 μm or causing heat injury and use only a small volume of ejected water.

Here, we investigated the possibility of using ADPJ systems in the eye. We developed an intraocular ADPJ surgical system and evaluated the effectiveness and safety of this novel surgical approach in vivo.

Materials and Methods

Pulse Jet Device

Figure 1 is a photograph of the ADPJ system developed for this study. The system consists of a

control unit, syringe pump, ADPJ generator, and foot switch (Fig. 1A). An intraocular irrigating solution (0.0184% BSS Plus 500; Santen Corp., Osaka, Japan) was injected at 0.000 to 0.100 mL/h through a capillary (inner diameter: 0.3 mm) by a syringe pump. An ADPJ generator (containing a piezoelectric element), regulated by a foot switch on the control system, controlled the pulsing of the fluid stream. The piezoelectric actuator had dimensions of 5 mm $\times$ 5 mm $\times$ 18 mm (Model PSt 150/5 $\times$ 5/20; Piezomechanik GmbH, Munich, Germany), with a displacement of 20 μm (without payload) at an input voltage of 150 V. The piezoelectric actuator was glued to an

aluminum disk (diameter: 8.7 mm; thickness: 1.5 mm) that acted as a piston. This piston, in turn, was glued to a stainless steel diaphragm (thickness: 0.02 mm), which was fixed at its margin to the metal wall of the device. The center of the diaphragm was separated from the wall by 0.2 mm to allow water to be fed into the chamber (height: 0.2 mm). A connecting pipe (inner diameter: 1.1 mm) reached to the actuator. The handgrip of the device (Fig. 1B) had a needle-shaped nozzle (Fig. 1C; SUS304 30G stainless steel tube, 0.14 mm internal diameter, 0.30 mm external diameter, length 20 mm).

Animal Subjects

All experimental procedures conformed to the ARVO (Association for Research in Vision and Ophthalmology) Statement for the Use of Animals in Ophthalmic and Vision Research and were conducted with approval from the Experimental Animal Management Committee of Tohoku University School of Medicine. This study used male Japanese white rabbits (2.5–3.0 kg; Kitayama Labes Co. Ltd., Ina, Japan). Before surgery, the animals were anesthetized intramuscularly with a mixture of ketamine hydrochloride (60 mg/kg; Sankyo, Tokyo, Japan) and xylazine (10 mg/kg; Bayer, Munich, Germany). Before treatment with the ADPJ system, vitreous surgery was performed under a microscope with a specialized device (Accurus; Alcon, Fort Worth, TX) and a kit of disposable components (AccuPak Vitrectomy Set with Accurus 2500 Probe; Alcon). Briefly, three trocars were inserted near the cornea in the conjunctiva-sclera. An infusion bottle filled with intraocular irrigating solution (0.0184% BSS PLUS 500; Alcon Japan Ltd., Tokyo, Japan) was set 35 cm above the treated eye and attached to one of the cannulas. A light guide and a vitreous cutter were inserted into the two other cannulas. Core vitrectomy was then performed for 5 seconds before the use of the ADPJ system.

Evaluation of Intraocular Pressure (IOP) Increase During Intravitreal Fluid Injection

Seeking to understand the effect of intraocular irrigation on IOP and determine the safety of different ADPJ flow volumes, we performed intraocular surgery in rabbits ($n=4$) using our ADPJ system and evaluated the resulting increase in IOP. The eyes underwent core vitrectomy in which one of the three trocars was closed with a cap and the infusion valve was kept open in order to stabilize IOP, a procedure that is also used in clinical vitreous surgery. A continuous water jet was

used, with flow rates of 0.010, 0.025, 0.050, and 0.100 mL/min, after the animal had been gently moved into a prone position. The IOP was measured three times with a tonometer (icare TONOVET TV01; M.E. Technica, Tokyo, Japan) before insertion of the surgical device. The IOP was then measured three times every 30 seconds for 5 minutes, while the position of the device, the animal, and the flow rate, were held steady. After 5 minutes of IOP measurement, the device was removed. If IOP exceeded 60 mm Hg before the end of the 5-minute measurement period, the device was immediately removed and the experiment was stopped. The flow rate was gradually increased as testing continued.

Evaluation of the Deflection Pressure of the ADPJ

The deflection pressure of the generated ADPJ was evaluated in an aqueous solution at various voltages using the intraocular irrigation flow volume that had been chosen as the most appropriate in the previous experiment. The distance between the pressure sensor and the tip of the ADPJ device was fixed at 0.5 mm, and the pulse rate was fixed at the maximum frequency that allowed the emission of a stable ADPJ at the chosen flow volume. A pressure sensor (Amplifier Type 5018 and Pressure Sensor Type 601A; Kistler Japan Co., Ltd., Tokyo, Japan) was used to measure the deflection pressure.

Visualization of the ADPJ Stream in an Aqueous Solution with a High-Speed Camera

The changing shape of the ADPJ stream in an aqueous environment was visualized over time with a high-speed camera (30,000 frames per second) to confirm that a 30-gauge needle allowed the emission of a stable stream at the chosen flow volume and frequency. The irrigating solution used in this experiment was 4% methylene blue.

Evaluation of the Retinal Vessel Massage Effect of ADPJ Surgery

To investigate the retinal vessel massage effect induced by ADPJ surgery, intravenous displacement of the blood column (DBC) was evaluated at various ADPJ voltages and at various distances of the ADPJ needle tip to the retina. Surgical retinal complications were also evaluated during this experiment, including retinal hemorrhaging and tearing. Each measured effect of the ADPJ on the retina, including intravenous DBC, retinal damage, and hemorrhaging, was assigned a score of 0 (–), 0.5 ($\pm$), or 1 (+) in each experimental

Figure 2. Influence of different water jet flow rates on intraocular pressure over time during vitreous surgery ($n = 3$, error bar = SD). The data shown are the average values of three experiments performed under the same conditions.

condition, that is, the distance to the retina and the voltage. In all tests, the flow rate and frequency were set at the values that had been previously determined to be most appropriate. In this experiment, ADPJ surgery was performed in three rabbit eyes. Finally, we determined the minimum voltage/distance at which the massage effect was clearly achieved (score ≥ 0.5) and retinal damage or hemorrhaging did not occur.

Statistics

A one-tailed unpaired t -test, a one-tailed paired t -test, a nonparametric analysis, and the Bonferroni-adjusted P value test were used in the statistical analysis, which was performed with spreadsheet software (Microsoft Excel 2008 for Mac, Ver. 12.2.9; Microsoft, Santa Rosa, CA).

Results

Evaluation of IOP Increase during Intravitreal Fluid Injection

The IOP rose to more than 60 mm Hg after 1 minute of surgery with an ADPJ flow rate of 0.1 mL/min (Fig. 2) and to more than 40 mm Hg after 1 minute of surgery with a flow rate of 0.05 mL/min.

Figure 3. Pressure generated by the pulse jet in an aqueous solution at various voltages.

However, IOP did not exceed 40 mm Hg after 3 minutes of surgery with a flow rate of 0.025 mL/min and did not exceed 30 mm Hg after 5 minutes of surgery with a flow rate of 0.01 mL/min.

Evaluation of the Deflection Pressure of the ADPJ

The flow rate was fixed at 0.025 mL/min, reflecting the results of the previous IOP experiment. At this flow rate, stable emission of the ADPJ was only possible at a frequency ≤ 10 Hz because of the limited available volume of fluid. At 0.025 mL/min and 10 Hz, the pressure induced by the ADPJ was closely correlated with the voltage (Fig. 3; $P < 0.001$, $r^2 = 0.9991$), indicating its stability.

Visualization of the ADPJ Stream in Aqueous Solution with a High-Speed Camera

This experiment used an ADPJ flow rate of 0.025 mL/min and a frequency of 10 Hz, as determined in the previous experiments on safe IOP levels, deflection pressure, and frequency. The visualized ADPJ stream was stable at 40 V (Fig. 4).

Evaluation of the Retinal Vessel Massage Effect of ADPJ Surgery

Table shows the average scores for various effects of the ADPJ on the retina, including

Figure 4. Series of consecutive images of the generated pulse jet obtained with a high-speed camera. The stream used for the visualization had a flow rate of 0.025 mL/min, a voltage of 40 V, and a frequency 10 Hz. The ejected fluid was 4% methylene blue solution.

Table. Summary of Retinal Changes Caused by Pulse Jet Surgery under Various Conditions

Distance to targets [mm]	Voltage [V]	Intravenous DBC Score	Retinal hemorrhage Score	Retinal tear Score
5	30	0	0	0
	40	0	0	0
	50	0	0	0
	60	0	0	0
	70	0	0	0
	80	0	0	0
	90	0	0	0
2	30	0	0	0
	40	0	0	0
	50	0	0	0
	60	0.17	0	0
	70	0.17	0	0
	80	0.67	0	0
	90	0.83	0	0
1	30	0	0	0
	40	0	0	0
	50	0.33	0	0
	60	0.83	0	0.33
	70	0.83	0.33	0
	80	1	0	0
	90	1	0.67	0.17
0.5	30	0	0	0
	40	0.5	0	0
	50	0.83	0	0
	60	1	0.17	0
	70	1	0.67	0.33
	80	1	0.67	1

Figure 5. Pulse jet surgery for intraocular retinal vessel massage. The intravenous blood column, marked by ellipses (A), was displaced (B) and subsequently recovered (C) during treatment with a 50-V, 10-Hz pulse jet at 0.5 mm from the retina with a flow volume of 0.025 mL/min without retinal hemorrhage.

intravenous DBC (shown in Fig. 5), retinal damage, and hemorrhaging, in each experimental condition. The ADPJ flow rate and frequency were set to 0.025 mL/min and 10 Hz, respectively. Intravenous DBC was achieved at a relatively small distance between the needle and retina (2.0 mm) and at a relatively high voltage (40 V). Retinal hemorrhaging and tearing began to occur at distances smaller than 1.0 mm and at voltages higher than 60 V. We found that the minimum ADPJ power and distance to achieve intravenous DBC while avoiding retinal hemorrhaging and tearing were 40 V and 0.5 mm, respectively.

Discussion

We set out to develop an ophthalmic ADPJ system to treat intraocular diseases and to evaluate its effectiveness and safety in vivo. We began by determining the effect of intraocular irrigation flow volumes on IOP and found that 0.025 mL/min was the highest flow volume that could be used while maintaining a safe IOP. Next, we confirmed that an ADPJ stream ejected through a 30-gauge microneedle was stable at this flow volume and that the pressure of this stream was correlated with the applied voltage at a pulse frequency of 10 Hz. Finally, we determined that intravenous DBC was possible without retinal complications at a minimum voltage of 40 V and a tip distance of 0.5 mm.

The ADPJ surgery, an innovation created at Tohoku University in 2004, has found wide clinical use in nonophthalmological fields of medicine. Its effectiveness has been confirmed in a number of studies.^{14–18} Pulsed water jets, such as those used in our ADPJ system, can make tissue incisions while preserving vessels larger than approximately 100 μ m, do not cause heat injury, and require only a small volume of ejected water. These advantages of ADPJ technology, particularly the ability to make incisions in internal organs while preserving blood vessels, have enabled surgeons to use it to obtain remarkable surgical results. An additional advantage of ADPJ technology is the dramatically shorter surgery times it allows in comparison with other techniques. This is especially beneficial because of the consequent reduction in bleeding, a particular benefit in surgeries of the cranial nerve and liver, which are highly susceptible to intraoperative bleeding. We considered that these properties of ADPJs would also be useful in certain vitreous surgeries and thus launched the current investigation of the ability of ADPJs to preserve and massage the retinal vessels, thereby improving retinal circulation.

Despite the clear surgical advantages of water jet devices, it is very challenging to use them in vitreous surgery. Modern vitreous surgery is a closed procedure that is performed in an operating volume of only about 6 mL, and as water jet techniques involve the injection of fluid, elevated IOP is a significant risk. This can cause corneal edema, obscuring the surgeon's view, and can impair retinal nerve fibers in the optic nerve head, leading to glaucoma. Extremely elevated IOP can also block circulation in the retinal artery, leading to central retinal artery occlusion.

However, instruments using a pulsed rather than a continuous water jet use a remarkably lower volume of water, which we believed made them feasible for consideration, even in the restricted operating volume of modern, closed vitreous surgery. The results of our investigation showed that the most suitable ADPJ flow rate for vitreous surgery was 0.025 mL/min. A flow rate of 0.05 mL/min caused IOP to rise to above 40 mm Hg after only 1 minute and above 50 mm Hg after only 2 minutes of surgery. However, at 0.025 mL/min, IOP stayed below 40 mm Hg for 3 minutes and below 45 mm Hg for 5 minutes of surgery, leading us to conclude that this was the most suitable flow rate for ophthalmic ADPJ procedures. Thus, we continued our investigation using this flow rate. Interestingly, ADPJ surgery at 0.025 mL/min for 3 minutes and 0.05 for 1.5 minute inject an equal quantity of fluid into the eye, but we found that they led to different increases in IOP, that is, to below 40 mm Hg and to above 45 mm Hg, respectively. We speculate that this was related to intraoperative fluid leakage from the 25-gauge cannulas at a fixed rate, meaning that more leakage occurred during the longer procedure, leading to a smaller effect on IOP.

An important finding of this study was that it was possible to successfully emit the ADPJ through a 30-gauge needle, which creates considerable resistance to the flow of fluid due to its small size. The advantages of smaller instrument gauges for microincision vitrectomy surgery (MIVS) have led surgeons to shift to 25-gauge systems, and 27-gauge or smaller systems may soon become common. Thus, the successful use of 30-gauge instruments in our procedure ensures that it should remain a practical option for many years. Furthermore, the successful emission of an ADPJ through such a small system indicates that ADPJs could also be stably emitted with larger MIVS systems.

Limitations of this study included the use of a normal animal model, a small sample size, and the lack of morphological and functional findings from a comparison between an ADPJ group and a non-ADPJ group. Additionally, the circulative benefit of ADPJ massage remains unclear. Nevertheless, our results show that ADPJs are a feasible option for vitreous surgery, despite the closed nature of modern procedures, and can be safely used in vivo. Additionally, ADPJ surgical systems have previously been noted for their ability to preserve large retinal vessels, that is, those approximately 100 μ m in size. This is a size similar to the vessels affected in RVO, suggesting that ADPJ surgery should be able to effectively

massage occluded retinal vessels without cutting them, positively affecting ocular blood circulation. Possibilities for future investigations into the ophthalmic use of ADPJs include their use in animal models of RVO and, eventually, their clinical use.

In conclusion, we developed and evaluated an ADPJ system that can be used in the field of ophthalmic surgery to treat intraocular diseases. The ADPJ stream ejected from a 30-gauge microneedle into an aqueous environment had a stable shape and pressure. With an appropriate flow rate, frequency, and surgical time, the ADPJ was able to massage the retinal vessels and achieve intravenous DBC while maintaining safe IOP and avoiding retinal complications. The ADPJ thus has promise as an easy and safe instrument for intraocular surgical treatment.

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Author involvement was as follows: design and conduct of the study (H.K., Y.T., and T.N.); preparation, management, analysis, and interpretation of the data (H.K., Y.T., N.A., and A.N.); and review or approval of the manuscript (T.T. and T.N.).

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References

1. Arakawa S, Yasuda M, Nagata M, et al. Nine-year incidence and risk factors for retinal vein

- occlusion in a general Japanese population: the Hisayama Study. *Invest Ophthalmol Vis Sci*. 2011; 52:5905–5909.
2. Sun C, Li XX, He XJ, Zhang Q, Tao Y. Neuroprotective effect of minocycline in a rat model of branch retinal vein occlusion. *Exp Eye Res*. 2013;113:105–116.
 3. Donati G, Kapetanios A, Dubois-Dauphin M, Pournaras CJ. Caspase-related apoptosis in chronic ischaemic microangiopathy following experimental vein occlusion in mini-pigs. *Acta Ophthalmol*. 2008;86:302–306.
 4. Zhou JQ, Xu L, Wang S, et al. The 10-year incidence and risk factors of retinal vein occlusion: the Beijing eye study. *Ophthalmology*. 2013; 120:803–808.
 5. Cugati S, Wang JJ, Rochtchina E, Mitchell P. Ten-year incidence of retinal vein occlusion in an older population: the Blue Mountains Eye Study. *Arch Ophthalmol*. 2006;124:726–732.
 6. Higashiyama T, Sawada O, Kakinoki M, Sawada T, Kawamura H, Ohji M. Prospective comparisons of intravitreal injections of triamcinolone acetonide and bevacizumab for macular oedema due to branch retinal vein occlusion. *Acta Ophthalmol*. 2013;91:318–324.
 7. Byun YJ, Roh MI, Lee SC, Koh HJ. Intravitreal triamcinolone acetonide versus bevacizumab therapy for macular edema associated with branch retinal vein occlusion. *Graefes Arch Clin Exp Ophthalmol*. 2010;248:963–971.
 8. Shimura M, Nakazawa T, Yasuda K, Kunikata H, Shiono T, Nishida K. Visual prognosis and vitreous cytokine levels after arteriovenous sheathotomy in branch retinal vein occlusion associated with macular oedema. *Acta Ophthalmol*. 2008;86:377–384.
 9. Yamamoto S, Saito W, Yagi F, Takeuchi S, Sato E, Mizunoya S. Vitrectomy with or without arteriovenous adventitial sheathotomy for macular edema associated with branch retinal vein occlusion. *Am J Ophthalmol*. 2004;138:907–914.
 10. Opremcak EM, Bruce RA. Surgical decompression of branch retinal vein occlusion via arteriovenous crossing sheathotomy: a prospective review of 15 cases. *Retina*. 1999;19:1–5.
 11. Brown DM, Campochiaro PA, Bhisitkul RB, et al. Sustained benefits from ranibizumab for macular edema following branch retinal vein occlusion: 12-month outcomes of a phase III study. *Ophthalmology*. 2011;118:1594–1602.
 12. Kumagai K, Furukawa M, Ogino N, Uemura A, Larson E. Long-term outcomes of vitrectomy with or without arteriovenous sheathotomy in branch retinal vein occlusion. *Retina*. 2007;27:49–54.
 13. Noma H, Funatsu H, Yamasaki M, et al. Pathogenesis of macular edema with branch retinal vein occlusion and intraocular levels of vascular endothelial growth factor and interleukin-6. *Am J Ophthalmol*. 2005;140:256–261.
 14. Sato C, Nakano T, Nakagawa A, et al. Experimental application of pulsed laser-induced water jet for endoscopic submucosal dissection: mechanical investigation and preliminary experiment in swine. *Dig Endosc*. 2013;25:255–263.
 15. Ogawa Y, Nakagawa A, Washio T, Arafune T, Tominaga T. Tissue dissection before direct manipulation to the pathology with pulsed laser-induced liquid jet system in skull base surgery—preservation of fine vessels and maintained optic nerve function. *Acta Neurochir (Wien)*. 2013;155:1879–1886.
 16. Sato Y, Nakagawa A, Hirano T, et al. Pulsed laser-induced liquid jet microcatheter system for rapid and reliable fibrinolysis in acute cerebral embolisms: experiments on safety and preliminary application in porcine cranial vessels. *Minim Invasive Neurosurg*. 2007;50:212–218.
 17. Ohki T, Nakagawa A, Hirano T, et al. Experimental application of pulsed Ho:YAG laser-induced liquid jet as a novel rigid neuroendoscopic dissection device. *Lasers Surg Med*. 2004; 34:227–234.
 18. Nakagawa A, Hirano T, Jokura H, et al. Pulsed holmium:yttrium-aluminum-garnet laser-induced liquid jet as a novel dissection device in neuroendoscopic surgery. *J Neurosurg*. 2004;101:145–150.