

# Effect of Paracentesis on Retinal Function Associated With Changes in Intraocular Pressure Caused by Intravitreal Injections

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**Purpose:** Intravitreal injections of antivasular endothelial growth factor agents are widely performed, and subsequent intraocular pressure increase may cause retinal nerve fiber damage. This study aimed to determine the effects of paracentesis before intravitreal injection of an antivasular endothelial growth factor on electroretinograms.

**Methods:** This was a retrospective observational study in a university hospital. Twenty-five eyes of 25 patients who underwent intravitreal injections of antivasular endothelial growth factor agents were selected for evaluation. Intraocular pressures and electroretinograms were recorded before surgery (baseline), after anterior chamber paracentesis, and after intravitreal injection. The amplitudes and latencies of the a- and b-waves, photopic negative response, and oscillatory potential were measured. Changes in each component of the electroretinograms, intraocular pressure, and relationships between these two factors were investigated. The preoperative and postoperative ocular perfusion pressure was calculated based on blood pressure.

**Results:** The amplitudes of the b-waves were significantly smaller after intravitreal injection than at baseline ( $P = 0.02$ ), while no significant change was found in the other components during surgery. There were no significant changes in the latencies of any component during surgery. The intraocular pressure was significantly lower ( $P < 0.001$ ) after anterior chamber paracentesis ( $6.8 \pm 4.3$  mm Hg) compared to baseline ( $24.1 \pm 8.1$  mm Hg) or after intravitreal injection ( $17.1 \pm 9.6$  mm Hg;  $P < 0.001$ ).

**Conclusions:** Performing anterior chamber paracentesis before an intravitreal injection can prevent the intraocular pressure elevation and thus minimize the electrophysiological retinal dysfunction.

**Translational Relevance:** Anterior chamber paracentesis before an intravitreal injection mitigates the adverse effects on retinal function.

## Introduction

Intravitreal injections of antivasular endothelial growth factor (anti-VEGF) agents are widely used to treat a variety of retinal disorders including age-related macular degeneration, subfoveal choroidal neovascularization, diabetic macular edema, choroidal neovascularization in eyes with pathological myopia, and macular edema associated with retinal vein occlusion. The use of these intravitreal injections is

increasing worldwide, and significant complications can arise, including endophthalmitis, increased intraocular pressure (IOP), traumatic cataract, and vitreous hemorrhage.<sup>1,2</sup> Among these, an increase in the IOP occurs in approximately 4% of cases after intravitreal injection.

There are individual differences in the extent and duration of the increase in the IOP after intravitreal injections.<sup>3</sup> Although the IOP usually returns to preinjection levels within 30 to 60 minutes, it reportedly takes much longer in glaucomatous eyes.<sup>4</sup> A sudden increase

in the IOP by  $\geq 50$  mm Hg after intravitreal injection of an anti-VEGF agent can depress the retinal function rapidly, and the retinal ganglion cells (RGCs) can be permanently damaged.<sup>5</sup> However, if the elevation of the IOP is more gradual, e.g., over one hour, the alterations in retinal function are not as severe.

It is well known that anterior chamber paracentesis can reduce the high IOP associated with acute glaucoma attacks.<sup>6</sup> In the same way, anterior chamber paracentesis can also block the elevation of the IOP caused by intravitreal injection of a therapeutic agent and thus prevent retinal dysfunction and damage to the RGCs.

Miyake et al.<sup>7</sup> showed that it is possible to monitor retinal function during ophthalmic surgery by recording electroretinograms (ERGs). They also reported that a transient increase in the IOP to reduce vitreous hemorrhage during vitreous surgery reduced the flicker responses of the ERGs.<sup>8</sup>

As demonstrated by Soheilian et al.,<sup>9</sup> another way to assess the effects of an elevated IOP on the retina is to examine the circumpapillary retinal nerve fibre thickness (cpRNFLT thinning) by optical coherence tomography. They reported that performing anterior chamber paracentesis before an intravitreal injection could suppress the increase in the IOP immediately after the intravitreal injection and significantly reduce the decrease in cpRNFLT thinning at three months after the injection compared to when paracentesis was not performed.

We have also previously evaluated the changes in retinal function associated with a sudden increase in the IOP after an intravitreal injection in real time by intraoperative ERGs.<sup>10</sup> Our results showed a temporary decrease in the ERGs that occurred after the intravitreal injection, and the ERGs recovered after the IOP recovered. Therefore, some surgeons perform anterior chamber paracentesis immediately before an intravitreal injection to avoid this increase in the IOP. However, to the best of our knowledge, the in situ effect of an intravitreal injection of medication on retinal function has not been investigated.

Thus the purpose of this study was to investigate the effects of an anterior chamber paracentesis before an intravitreal injection on retinal function. To accomplish this, we recorded intraoperative ERGs before any procedures, after paracentesis, and after the intravitreal injection of an anti-VEGF agent.

## Methods

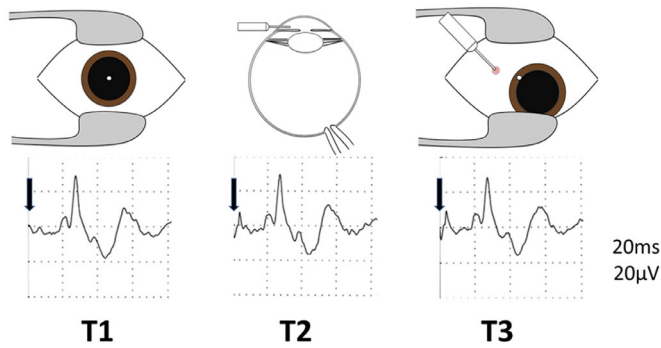
Twenty-five eyes of 25 patients who underwent intravitreal injections of an anti-VEGF agent for

various retinal disorders at the Teikyo University Hospital were studied. The exclusion criteria were severe myopia with a refractive error (spherical equivalent) of  $-6.0$  diopters (D) or greater or an axial length of  $\geq 26$  mm or the presence of glaucoma. This study was conducted in accordance with the tenets of the World Medical Association Declaration of Helsinki and the Ethical Guidelines for Medical and Health Research Involving Human Subjects. The procedures were approved by the Teikyo University Ethics Review Committee (Teirin 11-033-5, 14-122-3). After providing an explanation of the study and possible complications, informed consent was obtained from all patients before beginning the study.

The intravitreal injections were performed according to an approved guideline.<sup>11</sup> The surgical field was disinfected and draped. Next, 4% topical lidocaine was applied for local anesthesia. Before the intravitreal injection, a 30-gauge needle on a 1-mL syringe was inserted into the anterior chamber of the eye, and approximately 0.05 mL of aqueous humor was withdrawn. The intravitreal injection was then performed with either ranibizumab (0.5 mg/0.05 mL) or aflibercept (2.0 mg/0.05 mL) through a 30-gauge needle that was inserted into the sclera 3.5 mm from the corneal limbus. During the injection, the room temperature was set at 25.0°C, and the drugs used during surgery were stored at room temperature.

Intraoperative ERGs were recorded as described by Miyake et al.<sup>7</sup> A contact lens ERG electrode (LS-100, Mayo Co, Aichi, Japan) with a built-in light-emitting diode was sterilized and placed on the cornea. The intraoperative ERG settings were as follow: stimulus intensity 1000 cd/m<sup>2</sup>, 300 ms measurement times, 2 Hz frequency, 25.1 cd/m<sup>2</sup> background luminance, 100 Hz low-pass filter, and 500 Hz high-pass filter 20 responses were averaged. The preinjection ERGs were recorded after a five-minute adaptation to the room lights. Subsequently, ERGs were recorded immediately after the anterior segment paracentesis and then after the intravitreal injection of an anti-VEGF agent.

The amplitudes and latencies of the a- and b-waves, photopic negative response (PhNR), and oscillatory potential (OP) 1, OP2, and OP3 were measured. The amplitude of the a-wave was measured from the baseline to the trough and that of the b-wave from the trough to the peak. The PhNR was measured from the baseline to the trough of the negative wave occurring immediately after the b-wave. OP1, OP2, and OP3 were measured from the trough of the negative wave to the peak of the following positive wave. The sum of all the OPs was calculated and expressed as the  $\Sigma$ OP. The latencies were measured from the time of light stimulus onset to the peak of each component.



**Figure 1.** Changes in the electroretinogram at each stage in representative cases. Arrow indicates stimulus onset. The intraocular pressure measurement was 29 mm Hg before surgery (T1), 4 mm Hg after anterior chamber paracentesis (T2), and 21 mm Hg after intravitreal injection (T3).

The ERGs were recorded before the surgery (T1), after the anterior chamber paracentesis (T2), and immediately after the intravitreal injection (T3) (Fig. 1). The IOP was measured immediately before each ERG measurement with an AVIA Tono-pen (Reichert, Depew, NY, USA). IOPs  $\geq 56$  mm Hg and  $< 5$  mm Hg could not be measured with the Tono-pen; therefore IOPs  $\geq 56$  mm Hg were set at 56 mm Hg, and those  $< 5$  mm Hg were set at 4 mm Hg for the statistical analyses.

Blood pressures were measured before the surgery and immediately after the intravitreal injection to calculate the ocular perfusion pressure (OPP) and the mean blood pressure. The OPP in the supine position was calculated as follows:<sup>12</sup>

$$\text{OPP} = (115/130 \times \text{mean blood pressure}) - \text{intraocular pressure}$$

The mean blood pressure was calculated as follows:  
 mean blood pressure = diastolic blood pressure + 1/3  
 (systolic blood pressure – diastolic blood pressure).

## Statistical Analyses

Friedman tests were used to determine significance differences between values before surgery to those after anterior chamber paracentesis, and those after intravitreal injection. The a- and b-wave amplitudes of the different ERG components, implicit times, and IOPs were analyzed. Bonferroni adjustments were made for multiple comparisons. Wilcoxon signed-rank tests were used to determine significant differences between values before surgery and after intravitreal injections for the mean blood pressure and the OPP. A  $P$  value  $< 0.05$  was considered significant.

## Results

The assessments were made on 14 eyes from 14 men and 11 eyes from 11 women with an overall mean age of  $70.8 \pm 12.5$  years. The conditions for which the intravitreal injection was required included age-related macular degeneration in 16 eyes, diabetic macular edema in five eyes, macular edema associated with branch retinal vein occlusion in three eyes, and macular edema due to central retinal vein occlusion in one eye. Ranibizumab was administered to 14 eyes and aflibercept to 11 eyes.

The mean amplitude of the b-waves was significantly smaller after intravitreal injection (T3) than before surgery (baseline) (T1,  $P = 0.02$ ; Fig. 2). The mean amplitude of the b-waves after intravitreal injection (T3) was smaller compared with that after paracentesis (T2,  $P = 0.085$ ; Fig. 2), but this was not significant. There were no significant differences in the amplitude of the a-wave, PhNR, and  $\Sigma$ OP at the three test times (Fig. 2).

There was no significant difference in the latencies for the a-wave, b-wave, PhNR, and  $\Sigma$ OP at the three test times (Fig. 3).

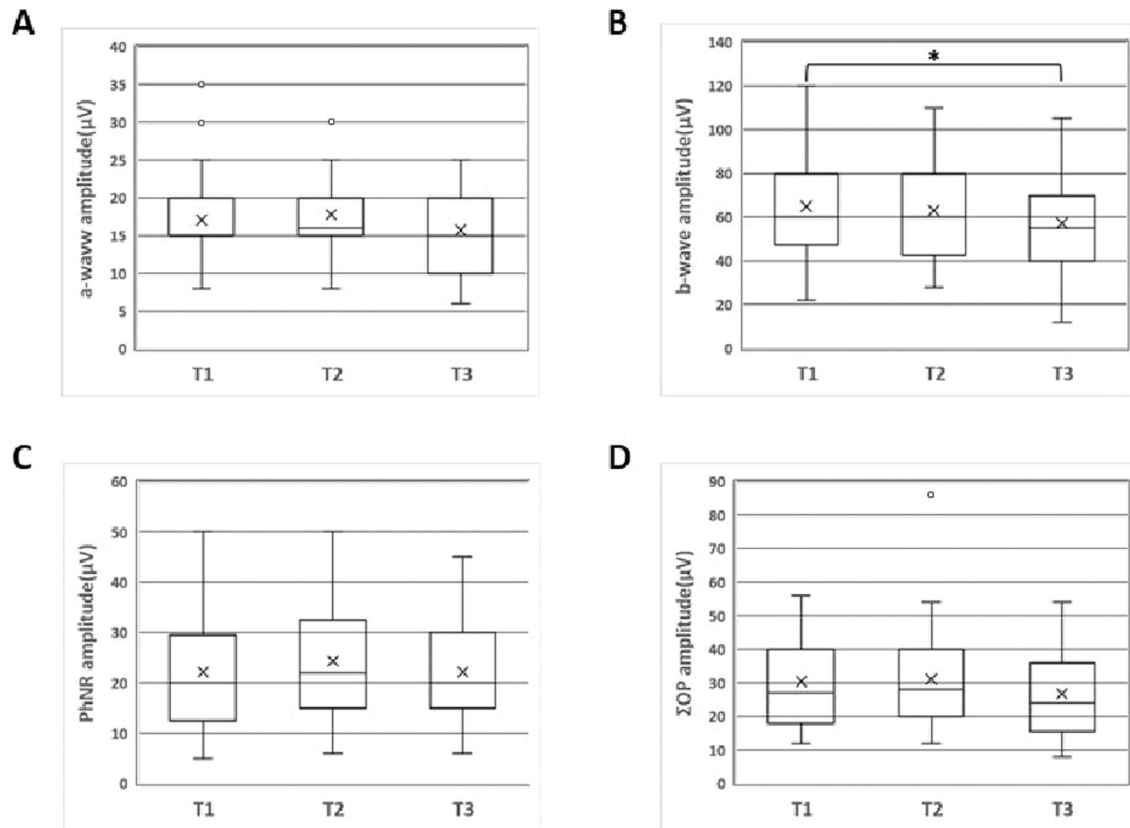
The IOP was measurable in all eyes before surgery (baseline) (T1), and the IOP in 14 eyes was  $< 5.0$  mm Hg after the anterior chamber paracentesis (T2), and in 3 eyes after the intravitreal injection (T3). The mean IOP was significantly lower after the paracentesis (T2,  $6.8 \pm 4.3$  mm Hg) than before surgery (baseline) (T1,  $24.1 \pm 8.1$  mm Hg;  $P < 0.001$ , Fig. 4). It was also significantly lower after the paracentesis (T2) than after the intravitreal injection (T3,  $17.1 \pm 9.6$  mm Hg;  $P < 0.001$ , Fig. 4). There was no significant difference in the IOP before surgery (baseline) (T1) and after the intravitreal injection (T3,  $P > 0.05$ ; Fig. 4).

The mean blood pressure before surgery (baseline) (T1) was  $88.1 \pm 8.2$  mm Hg, and the mean blood pressure after the intravitreal injection (T3) was  $88.8 \pm 8.2$  mm Hg ( $P > 0.05$ ; Fig. 5).

The OPP before surgery (baseline) (T1) was  $53.8 \pm 7.3$  mm Hg, which was significantly lower than that after the intravitreal injection (T3,  $61.4 \pm 11.6$  mm Hg;  $P < 0.05$ , Fig. 6).

## Discussion

A growing number of intravitreal injections are performed worldwide, with many patients requiring repeated injections, raising concerns regarding cumulative adverse effects. The conventional method of intravitreal injection is associated with an acute



**Figure 2.** Changes in the amplitude for each electroretinogram component. The upper end of the whisker is the maximum value, whereas the lower end is the minimum value; the box indicates the interquartile range, the line in the box indicates the median value, the  $\circ$  indicates outliers, and the  $\times$  indicates the mean. (A) a-waves, (B) b-waves, (C) PhNRs, and (D)  $\Sigma$ OP. T1, Before surgery (baseline); T2, after anterior chamber paracentesis; T3, After intravitreal injection. The b-wave amplitude after the intravitreal injection (T3) was significantly smaller than that at baseline (T1). There were no significant differences in the a-waves, PhNR, or  $\Sigma$ OP at the three time points. \* $P < 0.05$ .

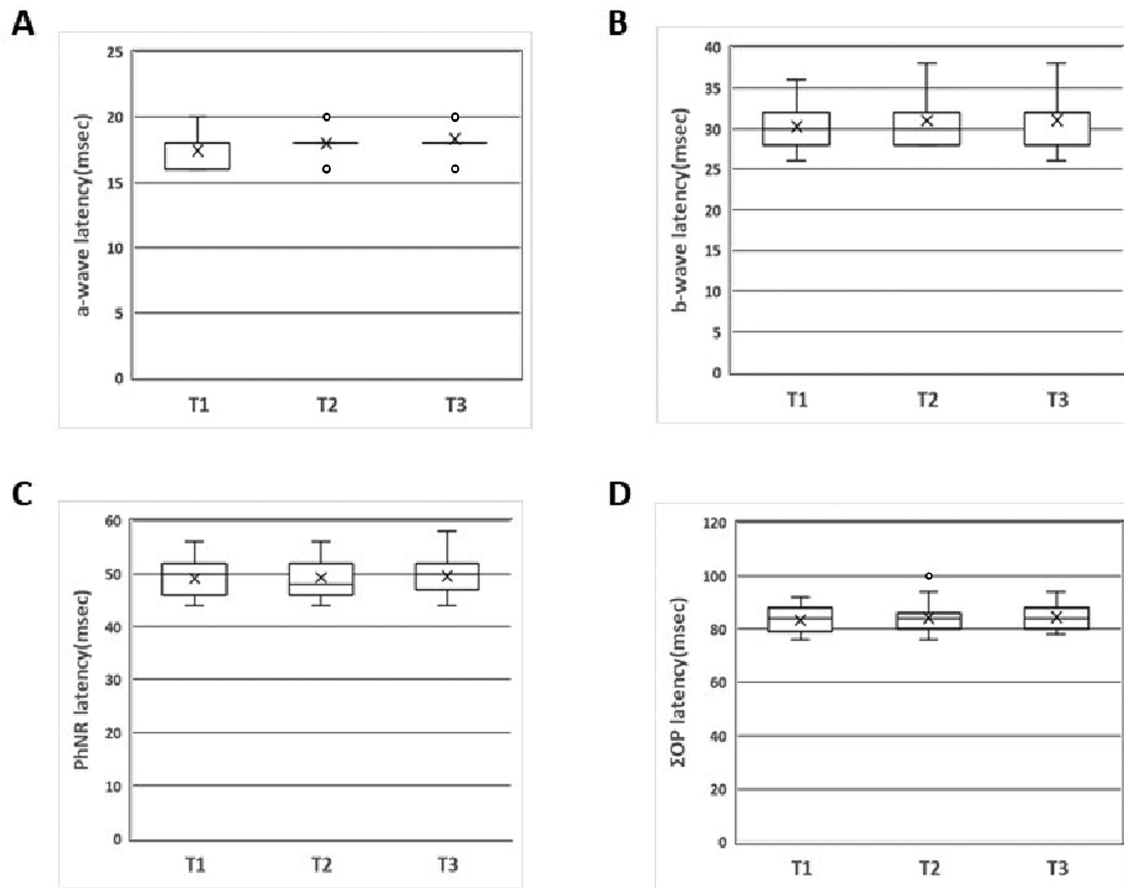
IOP rise, which causes significant cpRNFLT thinning three months after injection.<sup>9</sup> We proposed that this rise in IOP could be prevented by anterior chamber paracentesis.

It has been demonstrated that retinal dysfunction after a sudden increase in the IOP begins with a dysfunction of the cells in the inner retinal layer, and the damage extends to the outer retinal layer over time.<sup>5,13,14</sup> In this study, we found no significant changes in the latencies for any of the components of the ERGs after the intravitreal injection. In addition, there were no significant changes in the amplitudes of any component other than the b-waves. These results are consistent with the reports that the effects of a sudden increase in the IOP could be suppressed by an anterior chamber paracentesis.<sup>9,15</sup> This is in keeping with the absence of a thinning of the cpRNFLT thinning by a paracentesis before the injection as previously reported.<sup>9</sup>

Our findings showed that there was no significant difference in the IOPs before (T1) and after

(T3) the intravitreal injection if an anterior chamber paracentesis was performed. It has also been reported that small-diameter needles are more likely to result in an increase in the IOP after surgery because there is less reflux with smaller diameters compared with larger diameters.<sup>4</sup> We used a 30-gauge needle for the intravitreal injection, and the absence of an increase in the IOP postinjection period emphasizes the effectiveness of the anterior chamber paracentesis.

We have reported that intravitreal injection was performed without anterior chamber paracentesis, and the injection caused an increase in the IOP and caused considerable reduction in the b-wave amplitude.<sup>10</sup> In addition, the latencies of the a-waves and OPs were prolonged. We think that paracentesis before injection may be one of the effective choices to minimize the alteration in the electroretinographic function. However, although the magnitude was not much, the b-wave amplitude reduction suggests the possibility that repeated injection may cause adverse effects in the eye, especially with vulnerable retinal ganglion cell



**Figure 3.** Changes in latency for each electroretinogram component. The upper end of the *whisker* is the maximum value whereas the lower end is the minimum value, the *box* indicates the interquartile range, the line in the box indicates the median value, the  $\circ$  indicates outliers, and the  $\times$  indicates the mean. (A) a-waves, (B) b-waves, (C) PhNR, and (D)  $\Sigma$ OP. T1, before surgery (baseline); T2, after anterior chamber paracentesis; T3, after intravitreal injection. There was no significant difference in a-waves, b-waves, PhNR, and  $\Sigma$ OP during surgery.

functions such as retinal vascular occlusive disease and glaucoma. The evaluation of the retinal function and structure of the retinal nerve fiber<sup>9</sup> in eyes that received repeated injection would be helpful for determining the ideal intravitreal injection procedure.

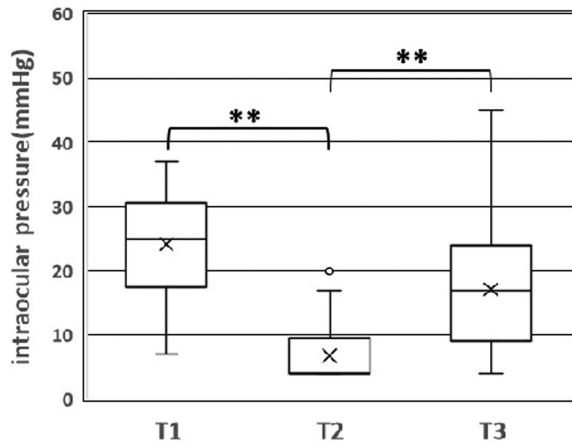
Given that reduction of the b-wave amplitude, signal outputs from the bipolar cells to the third-order neural cells should decrease. We cannot explain why the amplitude of the PhNR and OPs driven by the third-order neurons remained unchanged. The changes of the third-order neurons might be too small to be detected in the current study.

It is reported that local eye manipulation, such as transpupillary thermotherapy, scleral depression, and cryopexy can decrease ERG amplitude in treated eyes and the fellow eye.<sup>16</sup> This may raise the question whether the b-wave amplitude reduction could be found after paracentesis without intravitreal injection. We think the possibility is very low. First, because we recorded ERG after paracentesis, and the ERG did

not show b-wave amplitude reduction; and, second we showed in a previous study that the b-wave amplitude did not show significant change after paracentesis without intravitreal injection.<sup>10</sup>

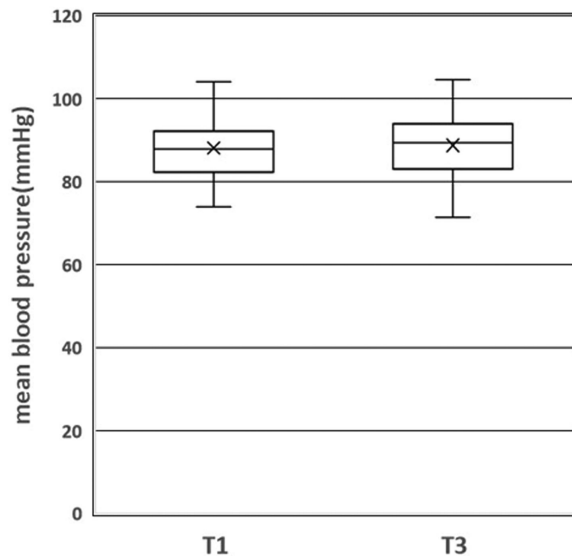
The b-wave amplitude reduction was not accompanied by prolongation of the implicit time. The b-wave implicit time was reported to be delayed in diseases with retinal circulatory disturbance or animal models with experimentally increased IOP.<sup>17</sup> The discrepancy in changes between the amplitude and implicit time in the current study may mean the b-wave amplitude reduction was attributed to a mechanism other than circulatory disturbance, such as changes in temperature and the effect of injected anti-VEGF agents.

One may ask about the duration of the functional change after injection. In this study, we focused on the dynamic change of the retinal function during operation and could not obtain the information of how long the reduction of the b-wave amplitude after the injection lasted. We assumed that it would not last so

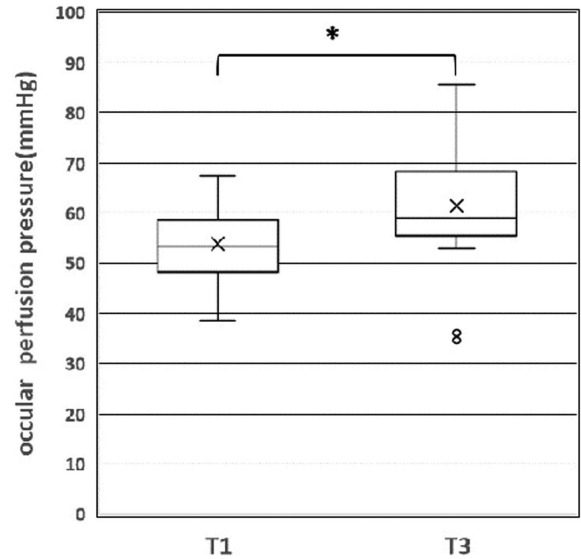


**Figure 4.** Changes in IOP in all subjects. The upper end of the whisker is the maximum value whereas the lower end is the minimum value, the box indicates the interquartile range, the line in the box indicates the median value, the  $\circ$  indicates outliers, and the  $\times$  indicates the mean. T1, before surgery (baseline); T2, after anterior chamber paracentesis; T3, after intravitreal injection. The IOP was significantly lower after the paracentesis (T2) than the baseline (T1), and then after the intravitreal injection (T3). There was also no significant difference in the IOP between the baseline (T1) and after the intravitreal injection (T3).  $**P < 0.001$ .

long because its amplitude was not considerably low before injection. This means that it had been returned to the preinjection level in some eyes that had received the intravitreal anti-VEGF injection before. However,



**Figure 5.** Changes in the mean blood pressure in all subjects. The upper end of the whisker is the maximum value whereas the lower end of the whisker is the minimum value, the box indicates the interquartile range, the line in the box indicates the median value, and the  $\times$  indicates the mean. T1, before surgery (baseline); T3, after intravitreal injection. The baseline mean blood pressure (T1) was not significantly different from that after the intravitreal injection (T3).



**Figure 6.** Changes in the OPP in all subjects. The upper end of the whisker is the maximum value whereas the lower end of the whisker is the minimum value, the box indicates the interquartile range, the line in the box indicates the median value, and the  $\times$  indicates the mean. T1, before surgery (baseline); T3, after intravitreal injection. The OPP after the intravitreal injection (T3) was significantly higher than that at the baseline (T1).  $*P < 0.05$ .

further study is needed to investigate the subtle change in the electroretinographic function, if any, after multiple injections.

Although blood flow was not measured, the changes in the IOP altered the OPP, which should then alter the retinal and choroidal blood flow. It is expected that the a-waves would be more affected by changes in the choroidal blood flow, whereas the b-waves, PhNR, and OPs would be more affected by changes in the retinal blood flow.<sup>18</sup> It has been reported that retinal blood flow decreases after the IOP is increased, but the vascular resistance also decreases, resulting in virtually no change in blood flow.<sup>18</sup> This suggests that there is an autoregulatory function that maintains blood flow at a constant level against these changes in OPP.<sup>19</sup> However, this autoregulatory function is impaired in some diseases.<sup>20–22</sup> In our cohort, the OPP was significantly higher after the intravitreal injection (T3) than before the surgery (T1). It is unclear how this relates to changes in the function of each layer of the retina as assessed by the ERGs. The ERG results showed changes only in the b-waves. The b-wave amplitude seems to be sensitive for detection of retinal function changes after any eye manipulation; for example, after photocoagulation in diabetic retinopathy.<sup>23</sup> Although outside the scope of this study, the ERG responses are sensitive to short-term dynamic changes in the IOP and circulation. We observed an IOP reduction along with

an OPP increase at T3. We anticipate that increased circulation would be related to the b-wave amplitude increase. However, this was not the case. This might be because the influence of the OPP increase was minimal or the influence of other factors such as the acute IOP elevation was greater. We think that the b-wave reduction found at T3 was not related to OPP changes. The retinal circulation may have decreased because of the increase in the IOP in the period from after anterior chamber paracentesis until after intravitreal injection, which may have led to the reduction in the amplitude of b-waves. We have reported that there is a significant decrease in the b-wave amplitude during a rapid increase in the IOP and no changes when the IOP is reduced.<sup>10</sup> The results of this study are consistent with those findings.

Horiguchi et al.<sup>24</sup> reported that the use of an intraocular infusion solution at a room temperature of 25°C during vitreous surgery lowered the temperature of the vitreous cavity, which in turn reduced the flicker ERGs. In this study, the anti-VEGF drug was also stored at room temperature, but the drug volume was only 0.05 mL. Thus it is safe to assume that this small volume would not have altered the retinal temperature and thus had little effect on the ERGs.

ERG changes after intravitreal injections seem to be very small and transient. This does not directly mean the necessity of paracentesis during intravitreal injection. Further investigations to assess long-term effects of intravitreal injection without paracentesis on the retina and optic nerve function should be performed to determine whether there is a real need for paracentesis in intravitreal injections.

This study has several limitations: the small number of cases, the use of different types of intravitreally injected agents, and the study of patients with different types of retinal disorders. It is necessary to increase the sample size and perform the study on one type of retinal disorder treated with the same type of intravitreal injection in the future. Second, no further postoperative changes were confirmed at later postoperative times. Thus it is not known how the decline in the b-wave amplitude observed at the end of surgery changed long term. We focused only on acute changes in the IOP and ERGs during surgery. Third, IOPs >56 mm Hg and <4 mm Hg were not detectable using our measuring device. Another method that allows for a more-precise measurement at the upper and lower bounds of the IOP would be beneficial for future experiments. The fourth limitation is that no information was obtained on the retinochoroidal blood flow or on morphological changes. Intraoperative fundus blood flow monitoring<sup>19</sup> or intraoperative optical coherence tomography<sup>25</sup> should be performed in future experiments, because

this additional information could enable further elucidation of the pathological condition in relation to the retinochoroidal circulatory condition and microstructure. Finally, we excluded myopic eyes with a refraction of  $-6.0$  D or greater or an axial length of  $\geq 26$  mm or longer and excluded eyes affected by glaucoma. However, such cases are commonly encountered in actual clinical practice. The retinal function would be assumed to be worse in those cases than in this study, and it is assumed that the effect of an intravitreal injection-induced increase in IOP on retinal function in such eyes would be greater than that on the eyes in this study.

Our results showed that performing anterior chamber paracentesis before an intravitreal injection prevented the development of high IOP, which then reduced the adverse effects of the elevated IOP on retinal function, although the b-wave amplitude was attenuated. However, performing paracentesis has several drawbacks, and it should be performed with great care. Recording intraoperative ERGs is a useful method for assessing dynamic changes in retinal function.

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## References

1. Brown DM, Kaiser PK, Michels M, et al. Ranibizumab versus verteporfin for neovascular age-related macular degeneration. *N Engl J Med*. 2006;355:1432–1444.
2. Rosenfeld PJ, Brown DM, Heier JS, et al. Ranibizumab for neovascular age-related macular degeneration. *N Engl J Med*. 2006;355:1419–1431.
3. Bakri SJ, Pulido JS, McCannel CA, et al. Immediate intraocular pressure changes following intravitreal injections of triamcinolone, pegaptanib, and bevacizumab. *Eye (Lond)*. 2009;23:181–185.
4. Kim JE, Mantravadi AV, Hur EY, Covert DJ. Short-term Intraocular Pressure Changes

- Immediately After Intravitreal Injections of Anti-Vascular Endothelial Growth Factor Agents. *Am J Ophthalmol.* 2008;146:930–934.
5. Resta V, Novelli E, Vozzi G, et al. Acute retinal ganglion cell injury caused by intraocular pressure spikes is mediated by endogenous extracellular ATP. *Eur J Neurosci.* 2007;25:2741–2754.
  6. Arnavielle S, Creuzot-Garcher C, Bron AM. Anterior chamber paracentesis in patients with acute elevation of intraocular pressure. *Graefe's Arch Clin Exp Ophthalmol.* 2007;245:345–350.
  7. Miyake Y, Yagasaki K, Horiguchi M. Electroretinographic Monitoring of Retinal Function During Eye Surgery. *Arch Ophthalmol.* 1991;109:1123–1126.
  8. Miyake Y, Horiguchi M. Electroretinographic alterations during vitrectomy in human eyes. *Graefe's Arch Clin Exp Ophthalmol.* 1998;236:13–17.
  9. Soheilian M, Karimi S, Montahae T, et al. Effects of intravitreal injection of bevacizumab with or without anterior chamber paracentesis on intraocular pressure and peripapillary retinal nerve fiber layer thickness: a prospective study. *Graefe's Arch Clin Exp Ophthalmol.* 2017;255:1705–1712.
  10. Yagura K, Shinoda K, Matsumoto S, et al. Electroretinographic evaluations of retinal function before, just after, and after intravitreal injections. *Sci Rep.* 2016;6:31104.
  11. Aiello LP, Brucker AJ, Chang S, et al. Evolving guidelines for intravitreal injections. *Retina.* 2004;24:S3–S19.
  12. Quaranta L, Katsanos A, Russo A, Riva I. 24-hour Intraocular Pressure and Ocular Perfusion Pressure in Glaucoma. *Surv. Ophthalmol.* 2013;58:26–41.
  13. Hughes WF. Quantitation of ischemic damage in the rat retina. *Exp Eye Res.* 1991;53:573–582.
  14. Chrysostomou V, Crowston JG. The photopic negative response of the mouse electroretinogram: Reduction by acute elevation of intraocular pressure. *Investig Ophthalmol Vis Sci.* 2013;54:4691–4697.
  15. Knip MM, Välimäki J. Effects of pegaptanib injections on intraocular pressure with and without anterior chamber paracentesis: a prospective study. *Acta Ophthalmol.* 2012;90:254–258.
  16. Francis JH, Abramson DH, Marr BP, et al. Ocular Manipulation Reduces Both Ipsilateral and Contralateral Electroretinograms. *Doc Ophthalmol.* 2013;127:113–122.
  17. Bayer AU, Danias J, Brodie S, et al. Electroretinographic Abnormalities in a Rat Glaucoma Model with Chronic Elevated Intraocular Pressure. *Exp Eye Res.* 2001;72:667–677.
  18. Vadalà M, Anastasi M, Lodato G. Transient reduction of the ocular perfusion pressure and the oscillatory potentials of the ERG. *Vision Res.* 2005;45:1341–1348.
  19. Riva CE, Grunwald JE, Petrig BL. Autoregulation of human retinal blood flow. An investigation with laser doppler velocimetry. *Investig Ophthalmol Vis Sci.* 1986;27:1706–1712.
  20. Hashimoto R, Sugiyama T, Masahara H, et al. Impaired Autoregulation of Blood Flow at the Optic Nerve Head During Vitrectomy in Patients With Type 2 Diabetes. *Am J Ophthalmol.* 2017;181:125–133.
  21. Kohner EM, Patel V, Rassam SMB. Role of blood flow and impaired autoregulation in the pathogenesis of diabetic retinopathy. *Diabetes.* 1995;44:603–607.
  22. de Oliveira APC, Kasahara N. Correlation between ocular perfusion pressure fluctuation and glaucoma severity. *Int Ophthalmol.* 2015;35:187–192.
  23. Wepman B, Sokol S, Price J. The effects of photocoagulation on the electroretinogram and dark adaptation in diabetic retinopathy. *Doc Ophthalmol Proc Ser.* 1977;13:139–147.
  24. Horiguchi M, Miyake Y. Effect of temperature on electroretinograph readings during closed vitrectomy in humans. *Arch Ophthalmol.* 1991;109:1127–1129.
  25. Ung C, Miller JB. Intraoperative optical coherence tomography in vitreoretinal surgery. *Semin Ophthalmol.* 2019;34:312–316.