Intraocular Pressure Course During the Femtosecond Laser-Assisted Cataract Surgery in Porcine Cadaver Eyes

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PURPOSE. Femtosecond laser-assisted cataract surgery (FLACS) is an increasingly common procedure. Most laser systems require corneal applanation and thereby increase intraocular pressure (IOP). The purpose of the present study was to evaluate the IOP changes that occur during the FLACS procedure performed using the Catalys femtosecond laser system.

METHODS. IOP was measured by direct cannulation of the vitreous body of porcine cadaver eyes (N = 20). By inserting a second cannula connected to a water column, all the eyes were set to a baseline IOP of 20 mm Hg. The eyes were lifted by custom-made stands to achieve the appropriate height and position under the Catalys system. The standard FLACS procedure was performed using varying fragmentation times to assess the influence of tissue fragmentation times on IOP peaks.

RESULTS. We identified significant IOP elevations from baseline IOP levels during all steps of the FLACS procedure (baseline: 20.28 ± 1.32 mm Hg; vacuum: 34.48 ± 4.21 mm Hg; capture: 47.90 ± 13.02 mm Hg; lock: 48.41 ± 9.04 mm Hg; analysis: 47.15 ± 5.97 mm Hg; capsulotomy: 45.74 ± 6.52 mm Hg; fragmentation: 48.41 ± 6.80 mm Hg; end: 17.81 ± 1.61 mm Hg; all P < 0.001). Furthermore, the tissue fragmentation time had a significant effect on the peak IOP values detected (R = 0.62, P = 0.04, n = 9).

CONCLUSIONS. The present study reveals significant IOP increases during FLACS procedures carried out using the Catalys system.

Keywords: femtosecond laser, cataract surgery, intraocular pressure
diameter to human eyes and the scarcity of human cadaver eyes. As shown in Figure 1, a 27-gauge needle connected to a fluid-filled pressure transducer of an electronic data acquisition system (PowerLab 16/35; ADInstruments, Grand Junction, CO, USA) was inserted into the eyeballs. A second cannula connected to an adjustable water column was inserted to set the IOP to a baseline level of 20 mm Hg. Small amounts of Loctite Super Glue (Henkel Corporation, Westlake, OH, USA) were used at the insertion sites to prevent the eyeballs from leaking.

Following this preparation, the eyeballs were placed on custom-made stands to achieve an appropriate height and position under the Catalys femtosecond laser system. Before laser interfaces were mounted on the eyes, the stopcock of the water column was closed to prevent water from leaking in case the IOP rose during the experiment.

Following the preparation of the porcine eyes, the standard Catalys procedure performed in humans was replicated as closely as possible. It takes three steps to connect the interface to the eye, each of which impacts IOP, as shown graphically in Figure 2 of the Results section. The Catalys system can then perform the four steps of cataract surgery: capsulotomy, lens fragmentation, arcuate incisions to correct corneal astigmatism, and corneal incisions. Only capsulotomy and lens fragmentation were performed in this study. Furthermore, all steps were customized to the anatomic dimensions of the enucleated eyeballs (e.g., anterior chamber depth, pupil diameter). The treatment time in this experimental setup exceeds the typically observed treatment time in humans. This is because the laser system was unable to detect the intraocular structures of the porcine eyes automatically and so manual corrections were needed. We varied the volume of lens fragmentation in a different set of experiments \( (n = 9) \) to evaluate the influence of emerging gas bubbles.

All the parameters were recorded at a 1-kHz sampling rate. Unless stated otherwise, all results are reported as the mean ± the standard error of the mean. A repeated measures ANOVA was used for the statistical analysis. Where appropriate, post hoc tests using the Bonferroni correction were applied. Linear regression analysis was used for the correlation between lens fragmentation time and IOP increase during fragmentation.

RESULTS

All the measurements were performed starting at a baseline IOP of approximately 20 mm Hg. The first IOP elevation was observed when the optic interface was mounted on the eyeball and the suction vacuum applied. The weight of the laser lens when connected to the patient interface caused another increase in IOP. Moreover, a significant IOP elevation was observed during lens fragmentation. After treatment, the IOP decreased to near the baseline level. Figure 2 provides a graphical overview of the IOP values during each step. Figure 3 gives a summary of all the experiments, and Table 1 lists the mean values and the range of IOP values obtained, as well as significant differences compared to the baseline.

Figure 4 shows the influence of the fragmentation time on the IOP increases during lens fragmentation. The IOP changes correlate well \( (r = 0.62, \log(\text{IOP}) = -0.17 + \text{time} \times 0.016) \) with the lens fragmentation time, which in turn correlates with the volume of tissue being fragmented (the fragmentation time is provided, as the Catalys does not report the actual volume).

DISCUSSION

The effect of eye fixation on IOP during the FLACS procedure is a concern as shown by previous studies. Table 2 provides
a summary of published studies regarding IOP during FLACS procedures. Talamo et al.\textsuperscript{6} conducted invasive IOP measurements in cadaver eyes by comparing an applanating corneal interface to the LOI, which was also the approach used in the present study. The measurements by Talamo et al.\textsuperscript{6} were performed only during the first step of the Catalys docking procedure (vacuum). IOP elevation at this point was reported as 16.6 mm Hg $\pm$ 1.8 SD. These results are similar to our findings during the initial stage of the femtosecond laser docking procedure. It should, however, be noted that Talamo et al. did not set the cadaver eyes to a constant starting IOP. Furthermore, they did not fully connect the cadaver eyes to the laser system and no laser treatment was performed.

Ibarz et al.\textsuperscript{10} started their experiments at very low IOP levels (5.67 mm Hg $\pm$ 2.39). As the ocular pressure–volume relationship is an exponential function, this makes a direct comparison of the results difficult; that is, if different eyes are measured with different baseline IOP levels, the same volume displacement will yield very different pressure values.

Schultz et al.\textsuperscript{8} and Kerr et al.\textsuperscript{9} evaluated IOP elevations in patients undergoing a Catalys femtosecond laser procedure performed using noninvasive applanating methods. Schultz et al.\textsuperscript{8} reported a mean IOP elevation to 27.7 mm Hg $\pm$ 5.5 SD after a femtosecond laser procedure conducted using a customized Schiotz Tonometer. Using an iCarePRO Tonometer (Tiotat, Oy, Finland), Kerr et al.\textsuperscript{9} also observed IOP elevations to 36.0 $\pm$ 4.4 mm Hg after femtosecond laser treatment. Both groups were able to record IOP elevations with the LOI connected to the eye, but not during the complete femtosecond laser treatment. Furthermore, changes in the corneal surface tension caused by the LOI when the vacuum is applied may influence the values obtained from an indentation/rebound measurement method.

Using a Tono-Pen Avia (Reichert Technologies, Depew, NY, USA), Baig et al.\textsuperscript{11} utilized a different femtosecond cataract laser platform with a multipiece curved interface to also perform IOP measurements on humans. Mean IOP was reported to rise to 42.1 $\pm$ 10.8 mm Hg after the femtosecond procedure. These discrepancies across studies suggest that IOP elevations in IOP vary with different femtosecond cataract laser systems. Interestingly, all the in vivo studies reported IOP elevations after femtosecond laser treatment, whereas we did not find any such elevations in the experimental setup of the present study after the eye was fully disconnected from the LOI.\textsuperscript{6,8,9,11}

<table>
<thead>
<tr>
<th>N = 20</th>
<th>Mean IOP Values, mm Hg $\pm$ SE</th>
<th>Significant Change From Baseline</th>
<th>Range, min–max, mm Hg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>20.29 $\pm$ 1.32</td>
<td></td>
<td>18.85–23.17</td>
</tr>
<tr>
<td>Vacuum</td>
<td>34.48 $\pm$ 4.21</td>
<td>$P &lt; 0.001$</td>
<td>30.41–42.82</td>
</tr>
<tr>
<td>Capture</td>
<td>47.90 $\pm$ 13.02</td>
<td>$P &lt; 0.001$</td>
<td>52.88–67.34</td>
</tr>
<tr>
<td>Lock</td>
<td>48.41 $\pm$ 9.04</td>
<td>$P &lt; 0.001$</td>
<td>38.41–58.82</td>
</tr>
<tr>
<td>Analysis</td>
<td>47.15 $\pm$ 5.97</td>
<td>$P &lt; 0.001$</td>
<td>39.46–60.34</td>
</tr>
<tr>
<td>Capsulotomy</td>
<td>45.74 $\pm$ 6.52</td>
<td>$P &lt; 0.001$</td>
<td>38.28–58.0</td>
</tr>
<tr>
<td>Fragmentation</td>
<td>48.42 $\pm$ 6.80</td>
<td>$P &lt; 0.001$</td>
<td>39.34–61.55</td>
</tr>
<tr>
<td>End</td>
<td>17.82 $\pm$ 1.62</td>
<td>NS</td>
<td>16.61–20.87</td>
</tr>
</tbody>
</table>

Table 1. The Mean IOP (±SE) Values During the FLACS Procedure (Averaged Over the Different Steps of the Process)

applied force. More interestingly, the IOP rises significantly during lens fragmentation, with the most likely cause being the gas formation that occurs at this point, as this correlates with the tissue fragmentation time and, thereby, the volume (Fig. 4).

When using cadaver eyes for IOP measurements, the shortcomings of the experiment must be noted. The influence of the ocular blood volume of the living eye on the pressure–volume relationship cannot be simulated. This interpretation is supported by previous investigations showing differences in ocular rigidity before and after enucleation.\textsuperscript{12,13} Figure 5 shows the course of the IOP in the eye of a living rabbit in response to the continuous infusion of a balanced salt solution into the vitreous cavity. The graph shows the marked differences between the IOP response predicted by the Friedenwald equation and the IOP response in a living eye.

$$IOP_2 = 10^{(k \cdot dV / \log IOP_1)}$$

where $IOP = $ intraocular pressure, $k = $ rigidity factor, $dV = $ volume increment.

The Friedenwald equation describes the pressure-volume relationship in relation to the rigidity of the eye (rigidity factor $k$). The higher this rigidity, the higher the increase in IOP in response to a particular ocular volume change. Given that the pressure-volume relationship is different in perfused and enucleated eyes, pressure–volume relationships from the literature can be used to estimate the in vivo IOP during the femtosecond laser procedure.\textsuperscript{12,14} In our study, we observed peak IOP levels of 54 mm Hg during fragmentation. The Friedenwald equation allows a theoretical calculation of the IOP increases that can be expected in a perfused eye, based on the assumption that the choroidal blood volume acts as a buffer for IOP changes. An IOP of 54 mm Hg equates to a volume increase of 50 $\mu$L. The choroidal blood volume is assumed to be approximately 250 $\mu$L. Therefore, a calculated volume increase of 50 $\mu$L will lead to only a moderate increase in IOP in a living eye, as it can be buffered by the choroidal volume.

In addition, it is possible to estimate the forces on the lens capsule during the femtolaser treatment. We can deduce from the IOP changes between the beginning and end of lens fragmentation that an IOP elevation of 5 mm Hg occurs during this process. Following the Friedenwald equation, this IOP elevation is caused by a volume increase of 2.5 $\mu$L. This
increase occurs from the gas formation during lens fragmentation. According to the literature, an elevation of 2.5 μL leads to a intracapsular pressure elevation of less than 10 mm Hg.\textsuperscript{15} This elevation of intracapsular pressure is of special interest, because it might lead to tears or even ruptures of the lens capsule during femtosecond laser treatment. The porcine lens volume is approximately 400 μL.\textsuperscript{16} This means that the lens capsule has to resist an intracapsular volume increase of 0.625%. Biomechanical studies on porcine lens capsules show a much higher resistance to strain and stress until the capsule fails compared to human lens capsules.\textsuperscript{17} Assuming that a similar intracapsular pressure elevation is created during femtosecond laser treatment of a human lens, and applying the findings of Fischer\textsuperscript{15} in terms of the strength of the human lens capsule, the gas volumes generated in our experiments do not pose a threat to human lens capsule integrity during femtosecond laser cataract treatment. Additionally, it should be noted that lens fragmentation is followed by capsulotomy, and so the produced gas has space to escape the intracapsular compartment.

On the other hand, we need to consider that our experiments were performed on clear porcine lenses and so less laser energy was needed for lens fragmentation. In humans, gas formation during laser lens fragmentation could reach higher levels, because more laser energy is needed to treat opaque lenses. This assumption is supported by the higher IOP values after femtosecond laser treatment on humans reported by other groups.\textsuperscript{8,9}

In conclusion, significant IOP elevations occur during the FLACS procedure, as shown by our findings and data from previous studies. The discrepancies of our findings compared to previous literature may be explained by the different study designs.

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References

**TABLE 2.** The Intraocular Pressure Results of Previous Studies

<table>
<thead>
<tr>
<th>Authors</th>
<th>Eyes Used</th>
<th>Preoperative IOP, mm Hg</th>
<th>Before Suction, mm Hg</th>
<th>With Suction, mm Hg</th>
<th>After Femto With Suction, mm Hg</th>
<th>After Femto Without Suction, mm Hg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Schultz et al.,\textsuperscript{8} 2013</td>
<td>Human eyes in vivo</td>
<td>15.6 ± 3.4</td>
<td>15.6 ± 2.5</td>
<td>25.9 ± 5.0</td>
<td>27.7 ± 5.5</td>
<td>19.1 ± 4.4</td>
</tr>
<tr>
<td>Kerr et al.,\textsuperscript{9} 2013</td>
<td>Human eyes in vivo</td>
<td>17.5 ± 2.4</td>
<td>28.9 ± 3.2</td>
<td>36.0 ± 4.4</td>
<td>26.6 ± 4.0</td>
<td></td>
</tr>
<tr>
<td>Baig et al.,\textsuperscript{11} 2014</td>
<td>Human eyes in vivo</td>
<td>17.2 ± 3.2</td>
<td>42.1 ± 10.8</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Talamo et al.,\textsuperscript{12} 2013</td>
<td>Porcine and human cadaver eyes</td>
<td>5.67 ± 2.39</td>
<td>16.6 ± 1.8</td>
<td>20.33 ± 4.18</td>
<td>21.01 ± 6.9</td>
<td>5.44 ± 2.01</td>
</tr>
</tbody>
</table>

**FIGURE 5.** Pressure-volume (P/V) relationship in a rabbit eye. The \textit{dashed line} shows the P/V relationship as calculated by the Friedenwald equation in postmortem eyes using an ocular rigidity coefficient of \( k = 0.02 \). The \textit{solid line} shows the P/V relationship in a living rabbit eye. Two fundamental differences can be observed between the responses. The Friedenwald equation describes an exponential increase in IOP for additional aliquots of volume added to the eye; but the real-world IOP response to a continuous infusion of fluid results in polyphasic behavior of the IOP (\textit{solid line}, infusion rate 120 ml/min). The differences are primarily caused by the fact that, in living eyes, the intraocular vasculature is filled with blood, which is pressed into the eye by the local arterial and venous blood pressure. Increasing IOPs act against the blood pressure, and the volume of the vasculature will be expelled from the eye accordingly (\textit{solid line}). Once the vasculature is empty (at IOP > mean arterial pressure), the P/V relationship follows an exponential function. Since the intraocular vasculature is not filled with blood in porcine donor eyes, no fluid can be expelled by increasing IOP; consequently, the P/V relationship follows an exponential function, as predicted by the Friedenwald equation (\textit{dashed line}).

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