Assumption Constraints of Fluorophotometry in Human Eyes

We read with great interest the article entitled “Fluorophotometric Study of the Effect of the Glaukos Trabecular Microbypass Stent on Aqueous Humor Dynamics” by Fernández-Barrientos et al.1 The authors examined aqueous humor dynamics before and after surgery in eyes undergoing cataract surgery and the implantation of the bypass stent (group 1) and in eyes undergoing cataract surgery alone (group 2). They reported a significant increase in outflow facility in both groups, with the combined procedure group having the highest values. Outflow facility was calculated with aqueous flow assessed by fluorophotometry, a standard value of 10 mm Hg for episcleral venous pressure, and negligible uveoscleral outflow in the Goldmann equation. Fluorophotometry is a useful technique for assessment of aqueous humor dynamics, but it does have several assumptions that must be met for the technique to be valid. The anterior chamber fluorescein disappearance technique of Jones and Maurice2 requires the presence of an intact iridolenticular diaphragm,3 which is compromised in eyes undergoing cataract surgery with a lens implant. Most investigators familiar with the technique exclude from study any subject with prior ocular surgeries. In pseudophakic eyes, one can no longer assume that there is minimal loss of fluorescein into the vitreous cavity. Such a loss would manifest itself on fluorophotometry as an apparent increase in aqueous inflow. This can be seen from the results of Fernández-Barrientos et al.1 where aqueous flow values as high as 4.05 ± 1.8 μL/min (compared to a baseline of 1.78 ± 0.44 μL/min) were reported in group 1 at 6 months after the surgical procedure. The apparent increase in aqueous flow was found to be statistically significant in both groups at all but one measurement time in the postoperative period. There is no reason to believe that cataract surgery or the bypass stent itself would increase aqueous flow several months after the procedure is performed. Hence, it is likely that the higher values of aqueous flow obtained by the authors after surgery are the result of a systematic error introduced by the pseudophakic state of the eyes undergoing the measurement. This apparent increase in aqueous flow does seem to resolve spontaneously with time, as seen in their Table 4. At 1 year after surgery, the apparent increase in aqueous flow in group 2 was reduced to a level that differed by a statistically insignificant amount from baseline. Hence, it may be possible to obtain valid aqueous flow measurements in pseudophakic eyes with intact capsules a year or more after the cataract surgery.

Fernández-Barrientos et al.1 also made the assumption that the pressure-independent outflow (uveoscleral outflow) is a negligible component in aqueous humor dynamics. More recent work4 has shown uveoscleral outflow to be a more significant contributor than the <10% cited in 1971 by Bill and Phillips.5 Since the purpose of Fernández-Barrientos et al.1 was to evaluate the effects on pressure-dependent outflow alone, it can be argued that uveoscleral outflow, even though a significant contributor to aqueous outflow, could have been ignored, because it was not expected to change with time and with any of the procedures performed in the study. However, this assumption may not be valid, as any surgical procedure on the anterior chamber angle has a very high probability of disturbing the supraciliary space and altering uveoscleral outflow. Making multiple attempts at proper device placement or implanting multiple devices would make inadvertent communication with the supraciliary space even more likely. An increase in uveoscleral outflow would be expected to lower the intraocular pressure (IOP). However, if the uveoscleral outflow is assumed to be negligible and unchanged, this decrease in IOP could be erroneously attributed to an improvement in the outflow facility.

Further, the artifact in aqueous inflow measurements introduces a systematic error in the calculation of outflow facility that makes the improvement in outflow facility look better than it may have been. As can be seen from the formula used to calculate the outflow facility, \[ \frac{C_T}{IOP - P_{es}} \], any errors in measurement of aqueous flow (F) would directly influence the calculated outflow facility (C_T). We feel that the only valid aqueous flow measurement that satisfies the prerequisite of a fluorophotometric assessment is the one obtained before surgery. Since cataract surgery with or without the microbypass stent should not be expected to change the aqueous humor production rate at the time of the measurement, these values may be used for the calculation of outflow facility after the procedure. The effects of an erroneous F in the outflow facility calculation can be seen in Table 1. The IOP data (after washout of ocular medications) at the time of fluorophotometry is not provided in the article; however, the mean IOP gradient can be calculated readily by using the reported means of F and C_T as IOP gradient = F/C_T.

As can be seen from the table, at 1 year, the mean C_T of 0.27 μL/min/mm Hg in group 1 versus 0.16 μL/min/mm Hg in group 2 is more likely to be representative of outflow facility at these times. These values also are more consistent with the values obtained by Bahler et al.,6 who reported an 84% increase in outflow facility after placement of the bypass stent in cultured human anterior segments.

### Table 1. Effect of Using Preoperative Aqueous Flow Measurements on the Calculation of Outflow Facility

<table>
<thead>
<tr>
<th>Postoperative Time</th>
<th>Reported ( C_T ) (μL/min/mm Hg)</th>
<th>Measured ( F ) (μL/min)</th>
<th>IOP Gradient (mm Hg)</th>
<th>Corrected ( C_T^* ) (μL/min/mm Hg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1: Cataract Surgery with Bypass Stent (mean preoperative ( F = 1.78 ) μL/min)</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>1 mo</td>
<td>0.88</td>
<td>4.30</td>
<td>4.89</td>
<td>0.36</td>
</tr>
<tr>
<td>6 mo</td>
<td>0.88</td>
<td>4.05</td>
<td>4.60</td>
<td>0.39</td>
</tr>
<tr>
<td>12 mo</td>
<td>0.45</td>
<td>2.94</td>
<td>6.55</td>
<td>0.27</td>
</tr>
<tr>
<td>Group 2: Cataract Surgery Alone (mean preoperative ( F = 1.74 ) μL/min)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 mo</td>
<td>0.41</td>
<td>3.9</td>
<td>9.51</td>
<td>0.18</td>
</tr>
<tr>
<td>6 mo</td>
<td>0.38</td>
<td>2.9</td>
<td>7.63</td>
<td>0.23</td>
</tr>
<tr>
<td>12 mo</td>
<td>0.19</td>
<td>2.12</td>
<td>11.16</td>
<td>0.16</td>
</tr>
</tbody>
</table>

*Calculated using preoperative values for aqueous flow.

References:
1. Fernández-Barrientos et al.
2. Jones and Maurice
3. Iridolenticular diaphragm
4. Recent work
5. Bill and Phillips
6. Bahler et al.
In summary, the results obtained by Fernández-Barrientos et al.\(^1\) support that the microbypass stent lowers IOP for months. However, because of design limitations, adequate conclusions cannot be drawn as to the mechanism of the IOP reduction. The stent may improve the outflow facility (0.38 vs. 0.23 μL/min/mm Hg at 6 months), although not to the magnitude concluded by the authors (0.88 vs. 0.38 μL/min/mm Hg at 6 months). Because of technical limitations, aqueous flow measurements in pseudophakic eyes are artificially elevated, which can lead to erroneously high calculations of outflow facility. Potential changes in uveoscleral outflow as a consequence of the procedure itself will further reduce the true magnitude of the difference in outflow facility between the two study groups. Reanalysis of the data with the suggested modifications to the outflow facility calculations will determine whether the increase observed in outflow facility is statistically significant.

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References


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