Anterior chamber flare after femtosecond laser–assisted cataract surgery

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PURPOSE: To determine whether postoperative ocular inflammation is less after femtosecond laser–assisted cataract surgery than after conventional phacoemulsification (manual) cataract surgery.

SETTING: Private clinic, Launceston, Tasmania, Australia.

DESIGN: Prospective consecutive investigator-masked nonrandomized parallel cohort study.

METHODS: Consecutive cataract patients who had femtosecond laser–assisted cataract surgery or manual cataract surgery by the same surgeon at a single center were assessed. The primary endpoint was postoperative aqueous flare measured by laser flare photometry at 1 day and 4 weeks. Secondary endpoints included retinal thickness measured by optical coherence tomography and slitlamp examination findings at 4 weeks.

RESULTS: The per-protocol population comprised 176 patients (100 in laser group; 76 in manual group). Postoperative aqueous flare was significantly greater in the manual cataract surgery group at 1 day ($P = .0089$) and at 4 weeks ($P = .003$). There was a significant correlation between effective phacoemulsification time and 1-day postoperative aqueous flare ($r = 0.35$, $P < .0001$). The increase in outer zone thickness measured by optical coherence tomography was less in the laser group ($P = .007$).

CONCLUSION: Anterior segment inflammation was less after femtosecond laser–assisted cataract surgery than after manual cataract surgery, and this appeared to be due to a reduction in phacoemulsification energy.

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Advances in surgical equipment, ophthalmic viscosurgical devices, and phacoemulsification have led to a reduction in surgical trauma.\(^1\) The introduction of femtosecond laser–assisted cataract surgery has led to further reductions in phacoemulsification energy requirements.\(^2–4\) Combined with automated corneal incisions and anterior capsulotomy, femtosecond laser–assisted cataract surgery may further reduce surgical trauma and the resulting inflammation. At present, there is early evidence of a reduction in postoperative swelling at the macula with femtosecond laser–assisted cataract surgery over manual cataract surgery.\(^5,6\)

Postoperative inflammation is associated with a breakdown of the blood–aqueous barrier as a result of surgical trauma–induced prostaglandin production.\(^7\) The inflammation generally manifests as mild iritis, corneal edema, increased cells and protein (flare) in the anterior chamber, and hyperalgesia or pain.\(^8\) Even in its mildest form, postoperative inflammation remains a challenge, and patients have high expectations for rapid visual recovery and minimal associated pain.\(^8,9\) It is not known whether femtosecond laser–assisted cataract surgery lens fragmentation leads to an increase in particulate matter in the anterior chamber, which may exacerbate inflammation.\(^10,11\) This study was performed to compare postoperative inflammation using...
anterior chamber flare between femtosecond laser-assisted cataract surgery and manual cataract surgery.

PATIENTS AND METHODS

Study Design

This was a prospective consecutive investigator-masked nonrandomized parallel cohort study performed at a single center. The study was approved by the Tasmanian Human Research Ethics Committee and was performed in accordance with the Declaration of Helsinki and its subsequent revisions (2004).

Consecutive patients who were older than 18 years and planned to have femtosecond laser-assisted cataract surgery or manual cataract surgery with insertion of a posterior chamber intraocular lens (IOL) were enrolled in the study. All patients were given the option to have femtosecond laser-assisted cataract surgery. Patients who elected to have femtosecond laser-assisted cataract surgery were placed in the laser group, and the remaining patients were placed in the manual group.

Patients were excluded from the study if they had a preoperative flare of more than 15 photons per millisecond (ph/ms) measured with a laser flare photometer without pharmacologic pupil dilation, inflammatory or infectious pathology of the eye, history of postoperative intraocular infection in the fellow eye, glaucoma, posttraumatic cataract, exfoliation syndrome, diabetic retinopathy, history of uveitis, and pathology requiring the use of topical or systemic antiinflammatory or antiinfectious agents. Patients taking medications known to cause fluctuations or alterations in anterior chamber protein composition or effect photometry flare values were excluded. Patients were also excluded from analysis if they had an intraoperative complication of vitreous loss or complicated capsule rupture or had implantation of an anterior chamber IOL.

Patient Assessments

Eligible patients were included in the study after going through an extensive preoperative assessment. Patients also had clinical and fundoscopic examinations using slit-lamp biomicroscopy. Evaluations included optical coherence tomography (OCT) (Zeiss Cirrus HD-OCT 4.0, Carl Zeiss Meditec AG), axial length (AL) and biometry (IOLMaster 4, Carl Zeiss Meditec AG), and laser flare photometry (Kowa FM-600, Kowa Co., Ltd.). The cataract grade was assessed objectively using Scheimpflug imaging (Pentacam (Kowa FM-600)).

Optical coherence tomography measurements were performed preoperatively within 2 weeks of the surgery and postoperatively at 4 weeks. The same trained individual obtained each scan and was masked to the patient’s treatment group. The repeatability and reproducibility of time-domain OCT thickness measurements have been established. Macular measurements were taken after pupil dilation. Scans were performed using a default AL (24.46 mm) and refractive error to allow consistency with usual practice. Scans were accepted if they were free of artifact. The instrument software automatically determined retinal thickness as the distance between the internal limiting membrane and retinal pigment epithelium (RPE). Measurements were provided for a central area as well as for 2 concentric regions. The central area (foveal region) had a radius of 0.5 mm (central macular thickness [CMT]). The inner and outer concentric regions were split into 4 zones each as follows: superior, temporal, inferior, and nasal. The mean of the 4 values in each ring comprised the inner OCT measurement and outer OCT measurement, respectively. The inner ring and outer ring had a radius of 1.5 mm and 3.0 mm, respectively.

Anterior chamber aqueous flare was measured objectively using laser flare photometry (Kowa FM-600). This instrument and its operation have been described in detail. Anterior chamber flare was measured by a masked investigator who was unaware of the patient’s treatment group. Measurements were taken within 1 week preoperatively as well as 1 day and 4 weeks postoperatively. Seven measurements were taken under scotopic conditions without pharmacologic pupil dilation. The 2 extreme values were excluded from the mean value, according to the manufacturer’s guidelines. Measurement conditions were kept consistent for all patients. The 5 measurements were averaged to a single score in photons per millisecond.

Postoperatively, patients were seen at 1 day and 4 weeks. Study assessment at the postoperative visits included slit-lamp examination, fluorescein staining for corneal epithelial erosions, and intraocular pressure (IOP) measurement using Goldmann applanation tonometry. Dilated fundoscopy was performed at 4 weeks. Concomitant medications used to treat inflammation related to cataract surgery were recorded at the preoperative and at the postoperative visits.

Surgical Technique

All patients instilled topical ketorolac and chloramphenicol for 2 days before the procedure. On the day of surgery, patients received topical anesthesia and pupil dilation with a gel formulation consisting of phenylephrine 2.5%, cyclopentolate 1.0%, tropicamide 1.0%, lidocaine hydrochloride jelly 2.0% (Xylocaine), and diclofenac 0.1%. The femtosecond laser procedure has been described. After the laser procedure, the patient was transferred to the operating room for regional anesthesia via sub-Tenon injection. Patients in the manual group also had regional anesthesia. The interval between the completion of the laser treatment and the initiation of operative cataract surgery was recorded for all patients in the laser group.

Intraoperatively, corneal incisions were made manually using a 2.75 mm keratome and a 1.20 mm side-port blade. Patients having the laser procedure had the cut anterior capsule removed using a capsulorhexis forceps, after which hydrodissection was performed. Lens segmentation was completed with the standard phacoemulsification procedure (Megatron S4, Geuder AG). The effective phacoemulsification time (EPT) was recorded for all patients. Patients who had manual cataract surgery had a continuous curvilinear capsulorhexis, hydrodissection, and phacoemulsification. After successful removal of lens cortex, both cohorts had IOL placement in the capsular bag. All surgical characteristics except those related to the laser procedure were kept consistent between groups.

Postoperatively, all patients were prescribed topical chloramphenicol, dexamethasone, and ketorolac 4 times a day for 4 weeks.

Outcome Measures

The primary endpoint was aqueous flare measured with laser flare photometry 1 day and 4 weeks after cataract surgery. Secondary endpoints included EPT, fortified balanced
salt solution (BSS Plus) fluid volume used during surgery, interval between the laser procedure and initiation of manual surgery steps, postoperative IOP, and the change in retinal thickness from baseline measured by OCT. Retinal thickness measured by OCT included central thickness and the mean of the 4 inner pericentral and 4 outer quadrants separately, as described above, at 4 weeks. An ophthalmologist assessed patients at 1 day and 4 weeks using slitlamp biomicroscopy (anterior segment and fundus).

### Statistical Analysis

All data were imported into Stata 12 (Stata Corp LP) for analysis and examined with descriptive and frequency analyses. Categorical data were analyzed using the chi-square test. Nonparametric continuous data were transformed to approximate a normal distribution, and t tests were used to detect differences in means. Correlations between EPT and 1-day postoperative aqueous flare and between 1-day aqueous flare and 4-week aqueous flare were assessed using the Pearson correlation coefficient (r). Regression models with post-estimation diagnostics were run to evaluate the relationship between EPT, balanced salt solution used, and aqueous flare at 1 day and 4 weeks. All tests were 2 sided, and a P value less than 0.05 was considered significant.

A post hoc power analysis found that the study had statistical power greater than the 0.80 level at α 0.05 to detect a difference in mean aqueous flare between the laser group and manual group given the sample size in each group.

### RESULTS

The study analyzed 100 eyes in the laser group and 76 eyes in the manual group. All eyes completed the study. There were 53 (53%) men in the laser group and 33 (56%) in the manual group. The mean age was 72.5 years ± 10.5 (SD) (range 41 to 94 years). There was no significant difference in age, refractive error, AL, anterior chamber depth, smoking status, preoperative IOP, nonocular medical history, or ocular comorbidities between the groups.

The mean preoperative aqueous flare was 5.3 ± 3.1 ph/ms in the laser group and 5.3 ± 3.4 ph/ms in the manual group; the difference was not statistically significant (P = .96). The mean cataract grade was 2.8 ± 0.8 and 2.9 ± 0.8, respectively; the difference was not statistically significant (P = .77).

There was a significant difference in mean EPT between groups (P < .0001). The laser group had a lower mean EPT (0.94 ± 3.47 seconds) than the manual group (6.5 ± 4.3 seconds). Similarly, the laser group required less balanced salt solution volume during the manual steps of surgery than the manual group (175.2 ± 71.8 mL versus 195.1 ± 76.5 mL), although the difference was not statistically significant (P = .08). There were no intraoperative complications in either group.

At 1 day, the mean aqueous flare was 16.6 ± 8.9 ph/ms in the laser group and 21.8 ± 12.0 ph/ms in the manual group (P = .0089) (Figure 1). At 4 weeks, the mean aqueous flare was 11.1 ± 8.1 ph/ms and 14.6 ± 10.7 ph/ms, respectively (P = .003) (Figure 1). There was no difference in IOP between groups at 1 day. There was a significant correlation between the 1-day and 4-week aqueous flare score (r = 0.51, P < .0001). There was also a significant correlation between EPT and 1-day postoperative aqueous flare (r = 0.35, P < .0001).

The multiple regression of EPT and balanced salt solution use as predictors of aqueous flare at 1 day was significant (F3,101 = 8.6, P < .05). For each 1-unit (1-second) increase in EPT, a 0.63 increase in aqueous flare at 1 day would be expected. For each 1-unit (1 mL) increase in balanced salt solution, a 0.05 increase in aqueous flare at 1 day would be expected. The regression of EPT and balanced salt solution as predictors of aqueous flare at 1 month was also significant (F3,83 = 3.1, P < .05).

The mean interval from completion of laser lens fragmentation to initiation of manual cataract surgery in the laser group was 35 ± 16 minutes. There was a trend toward increased aqueous flare at 1 day with greater intervals between laser treatment and cataract surgery; however, it was not significant.

At 4 weeks, the mean increase in OCT measurements (CMT, inner zone, and outer zone) from baseline were greater in the manual group (Table 1). There was a significantly larger increase in the outer zone internal limiting membrane and RPE thickness in the manual group (P = .007) (Table 1).

No statistically significant differences were found in the slitlamp examination and fundoscopy results between the treatment groups at 1 day and 4 weeks. Furthermore, none of the study participants in either group had raised IOP postoperatively or required concomitant medication to treat postsurgical inflammation. There were no adverse effects related to the use of topical medications in either group.

![Figure 1. Mean aqueous flare in the laser group and manual group 1 day and 4 weeks after cataract surgery (ph/ms = photons per millisecond).](image)
DISCUSSION

Several studies have established the safety and efficacy of femtosecond laser–assisted cataract surgery; however, little is known about the postoperative inflammation caused by surgical trauma and fragmented lens matter. The objective of our study was to compare postoperative inflammation after uneventful femtosecond laser–assisted cataract surgery with that after uneventful manual cataract surgery to assess the degree of surgical trauma. Laser flare meter measurements showed that femtosecond laser–assisted cataract surgery resulted in less aqueous flare than manual cataract surgery at 1 day and 4 weeks. The laser flare meter was used as an objective assessment of flare; its use for this purpose has been validated in terms of quantification, sensitivity, reproducibility, and reliability. Slitlamp examination or other scoring methods may be less sensitive, more prone to observer bias or error, and lack reproducibility.

Multiple factors can affect laser flare photometry values. These include mydriatic agents, pupil size, age, cataract, time of day, protein composition, and patient medications. To reduce the probability of laser photometric measurements being influenced by these factors, the factors were kept constant between patients and were taken into account when comparing values between patients and between serial measurements over time. There was no difference in mean age between the groups. Multiple readings were taken to prevent sampling error. Medications that alter flare were assessed preoperatively, and patients were excluded if they were taking any of these medications. All patients were assessed at roughly the same time of day (early morning) and did not have dilating drops before the test, and lighting conditions remained the same (scotopic).

Our original assumption was that residual lens material and particulate matter may be a consequence of femtosecond laser lens fragmentation, resulting in a higher incidence of postoperative inflammation as measured by aqueous flare. The interval between the completion of laser lens fragmentation and the initiation of manual cataract surgery may also have an effect on postoperative inflammation. Residual lens material after cataract surgery or traumatic rupture of the lens capsule is known to provoke intraocular inflammation; however, this does not appear to be the case in our study. The difference in aqueous flare readings between groups was most likely due to the reduction in EPT in the laser group. We also found no significant association between the interval and aqueous flare values, although generally the delay was less than 45 minutes. Therefore, we believe lens particulate matter produced by the femtosecond laser during lens fragmentation has a minimal impact with short intervals. The maximum permitted interval between laser lens fragmentation and manual surgery to limit postoperative inflammation must still be determined.

In terms of secondary endpoints, there was no significant between-group difference in CMT and inner zone change in retinal thickness from baseline measured by OCT. The laser group had a significantly lower increase in the outer zone retinal thickness on OCT than the manual group. This is in agreement with previous studies. An association has been reported between phacoemulsification and the formation of significant clinical cystoid macular edema (CME). Most subclinical postoperative increases in retinal thickness are asymptomatic. Although this may represent the process that in its most advanced stages leads to the formation of CME, it is unlikely to be of clinical relevance unless symptomatic. Based on our results, femtosecond laser–assisted cataract surgery may offer advantages in controlling the physiologic changes contributing to CME. However, the clinical relevance of this is unknown. Randomized controlled trials have shown that clinical CME and perifoveal thickening on OCT are largely prevented by nonsteroidal antiinflammatory drugs (NSAIDs); thus, the additional benefit of the femtosecond laser is unlikely to be of clinical significance. It is difficult to know whether, independently, the femtosecond laser would offer sufficient protection against CME without the need for NSAIDs.

Limitations of this study include the use of topical corticosteroids and NSAIDs during the perioperative period. Many cataract surgeons treat inflammation prophylactically using topical corticosteroid and nonsteroidal antiinflammatory medications. Both medications have been shown to be effective in the

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Table 1. Between-group comparison of the increase in OCT measurements from baseline to 4 weeks.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Laser Group</th>
<th>Manual Group</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline thickness</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CMT</td>
<td>260.87 ± 35.96</td>
<td>262.34 ± 37.51</td>
<td>.792</td>
</tr>
<tr>
<td>Inner zone</td>
<td>312.38 ± 27.78</td>
<td>317.17 ± 30.81</td>
<td>.281</td>
</tr>
<tr>
<td>Outer zone</td>
<td>271.66 ± 21.66</td>
<td>273.63 ± 26.78</td>
<td>.590</td>
</tr>
<tr>
<td>Change from baseline</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CMT</td>
<td>8.37 ± 18.63</td>
<td>9.91 ± 18.43</td>
<td>.586</td>
</tr>
<tr>
<td>Inner zone</td>
<td>5.58 ± 8.72</td>
<td>6.41 ± 10.90</td>
<td>.575</td>
</tr>
<tr>
<td>Outer zone</td>
<td>3.06 ± 7.91</td>
<td>7.11 ± 11.6</td>
<td>.007</td>
</tr>
</tbody>
</table>

CMT = central macular thickness
treatment of postoperative inflammation and pain. However, corticosteroids carry the risk for adverse effects, such as increased IOP and delayed corneal healing. There were no unwanted effects related to the use of these topical medications in either group, and there was no difference in the 1-day IOP between groups. Although both groups were treated with the same drugs with the same frequency and duration, we cannot rule out differences in compliance between groups, which may have produced confounding results.

In conclusion, femtosecond laser pretreatment in cataract surgery significantly reduced the EPT. This appears to result in reduced postoperative ocular inflammation measured by aqueous flare and subsequently a lower risk for macular edema. It is unknown whether this is solely due to the reduction in EPT between groups or is due to other processes.

WHAT WAS KNOWN

- Laser cataract surgery is safe and results in less postoperative macular thickening than manual cataract surgery.

WHAT THIS PAPER ADDS

- There was less postoperative inflammation measured by aqueous flare and macular thickening after femtosecond laser-assisted cataract surgery.

- These results support the view that femtosecond laser-assisted cataract surgery may be less traumatic than conventional phacoemulsification.

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