



Bonnie An Henderson, MD

## The true impact of inflammation

by Bonnie An Henderson, MD

**P**ostoperative pain and inflammation is not unusual after cataract surgery, and U.S. surgeons typically expect greater than 1+ cell and flare during the first postop week.<sup>1</sup> In general, about half of U.S. surgeons believe visual recovery and patient comfort/satisfaction are significantly impacted by 1+ cell/flare.

Of course, inflammation is associated with cystoid macular edema, and U.S. surgeons tend to use steroids and nonsteroidals more than non-U.S. surgeons.<sup>1</sup> But how does that translate in the real world settings? Take an example of a hyperope with narrow angles and a short axial length, with a history of laser peripheral iridotomy bilaterally. On postop day 1 after uneventful cataract surgery, the patient was dissatisfied with her outcome. She complained about foreign body sensation (FBS), and uncorrected vision was 20/200. By week 1, vision had improved to 20/80, but she was (understandably) still

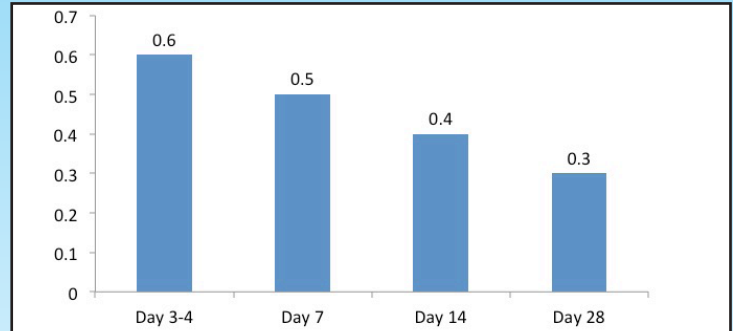


Figure 1. Mean corneal edema scores when no anti-inflammatory therapy has been prescribed

dissatisfied with her vision and still complained about itchy FBS. Eventually her edema resolved, but during those 2 months, I had a very unsatisfied patient.

Most patients with corneal edema do not have pre-existing conditions; the placebo arm of a postop steroid trial noted meaningful corneal edema can be seen throughout the first postop month (dropping from 0.6 at day 3–4 to 0.3 at day 28).<sup>1</sup> See Figure 1. In fact, the incidence

of post-cataract cystoid macular edema (CME) is 1–2%, but there is a higher incidence of angiographic CME.<sup>2</sup> There is a significant impact on both the short- and long-term visual acuity, on cost of care, and on patient satisfaction for a patient who has developed CME postoperatively. See Figure 2 for an example of an eye that developed CME 30 years after extracapsular cataract extraction.

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### Educational Objectives

Ophthalmologists who participate in this course will:

- Distinguish predisposing factors putting patients at higher risk for inflammatory reaction after cataract surgery, including review of key uveitis, retina, and corneal issues;
- Identify the true impact of ocular inflammation levels on outcomes in refractive cataract surgery: (a) variability in visual acuity and quality results, (b) delayed visual recovery that reduces the postoperative “wow” factor, and (c) pain and discomfort that reduce patient satisfaction;
- Acquire strategies to eliminate inflammation and relieve pain by maximizing the penetration of anti-inflammatory agents into target issues;
- Develop key adjustments to perioperative therapeutic strategies for preventing

inflammation specific to those with predisposing factors and in routine cases without predisposing factors; and

- Assess the clinical impact of various levels of ultrasound energy applied during cataract surgery and the amount of reduction in these levels available with laser cataract technology for specific types of patients.

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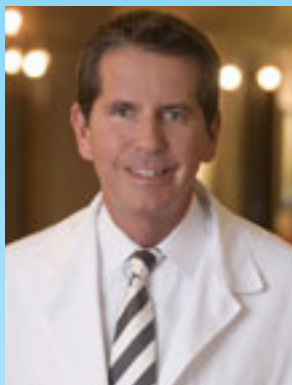
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Stephen V. Scoper, MD

## Reducing the intraoperative causes of surgical stress with femtosecond laser surgery

by Stephen V. Scoper, MD

**O**ur primary goal as surgeons is to provide good visual and refractive outcomes, prevent complications such as corneal edema and cystoid macular edema, and limit pain and discomfort. To achieve this, it is essential to lessen inflammation by limiting surgical time and delivering reduced phaco energy to the eye. Femtosecond laser-assisted cataract surgery (FLACS) does just that: It minimizes phaco energy. There are four approved systems on the U.S. market: Catalys, LENSAR, LenSx, and Victus. These lasers perform several key functions during cataract surgery, including creation of the capsulotomy, entry wounds, astigmatic incisions, and lens fragmentation. Refinements, such as delivering ultrasound (US) in smaller pulses of energy, further minimizes tissue trauma. It may be possible to reduce the US time to near zero with these systems.<sup>1</sup> Coupled with smaller incisions and more precise refractive outcomes, fewer complications will result. FLACS and US phaco use cavitation to disrupt tissue, resulting in up to 1,000 times less collateral damage.<sup>2</sup>

### Benefits of reduced phaco time

Studies have shown that FLACS causes less corneal swelling in the early postoperative period<sup>3</sup> and a decreased incidence of macular edema.<sup>4</sup> Takács and colleagues found significantly higher central corneal thickness in patients in the phaco-alone group than in the FLACS group (607  $\pm$  91  $\mu$ m vs. 580  $\pm$  42  $\mu$ m) on day 1, but no significant difference at 1 week and 1 month.<sup>3</sup> In a study involving the Catalys laser system, Conrad-Hengerer et al. found endothelial cell loss was 8.1% with FLACS compared to 13.7% in a traditional phaco group.<sup>5</sup> This study further found less anterior chamber flare compared with manual cataract surgery at

**“Successful refractive cataract surgery requires great visual outcomes and satisfied patients, which can be accomplished by minimizing inflammation with femtosecond laser-assisted cataract surgery”**

day 1 and at 4 weeks, possibly as a result of reduced phaco energy.<sup>6</sup> Several studies concurred that laser pretreatment resulted in significant reductions in effective phaco time with both the Catalys and Victus devices.<sup>2,7,8</sup>

In a preliminary study of the use of the LenSx femtosecond laser in early resident cataract training, there was a trend toward less cumulative dissipated energy, easier wound closure, and fewer complications as a result of reduced phaco time.<sup>9</sup> In addition to phaco time, reductions were observed in operating room time, use of irrigation fluid, and cumulative dissipated energy.

Successful refractive cataract surgery requires great visual outcomes and satisfied patients, which can be accomplished by minimizing inflammation with FLACS. Inflammation can be further minimized medically. Since prostaglandin levels rise immediately after laser treatment,<sup>10</sup> I give patients a nonsteroidal anti-inflammatory the day before surgery and again on the morning of treatment to help maintain mydriasis.

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Figure 2. An example of a pseudophakic eye with cystoid macular edema. Image courtesy of retinagallery.com

There are numerous systemic conditions with which to be concerned, including diabetes and autoimmune disorders (rheumatoid arthritis, lupus, and sarcoidosis). Among ocular comorbidities, diseases such as Fuchs' dystrophy, keratoconus, glaucoma, weakened zonules, or a history of retinal vascular disorders increase a patient's risk of developing CME postoperatively.<sup>2</sup>

Pain is certainly another consideration. Fung et al. analyzed pain levels in 306 patients who underwent cataract surgery and found 37% had mild/moderate postop pain, and 34% required

oral pain medication during the immediate postop period.<sup>3</sup> The higher a patient's perceived pain postoperatively, the lower the patient's satisfaction.

There is also a paradigm shift in who the cataract patient is. Even as recently as a decade ago, the typical patient was retired, drove very little (if at all), did not use a computer, had an expectation of recovery time, and likely needed spectacles postop. Today, however, patients are working well into their senior years, they demand independence, they use cell phones and computers daily, they need good functional vision

as quickly as possible and are unwilling to wait, and they are paying for premium lens technologies, which they believe entitles them to superior visual outcomes immediately after surgery. From the surgeon's perspective, aspects we cannot avoid include the surgical stress we initiate with the wound construction. That stress triggers a cascade of metabolic events that results in increased inflammation. Phaco alone has been shown to increase flare values in the anterior chamber as a sign of an increased permeability of the blood/aqueous barrier. Postop CME is directly related to the amount of ultrasound time, volume of I/A, and cataract density.<sup>2</sup> It is our surgical goal to perform cataract procedures with minimal disruption of other ocular tissue and minimal heat damage.

Phaco technology and surgical techniques have benefited from a continuous stream of incremental refinements; the advent of laser-assisted femto cataract surgery has the potential to reduce the amount of energy delivered to the eye. Because this technology delivers energy more efficiently, with less heat and less collateral damage than ultrasound, the cavitation diameter is much smaller, resulting in substantially less collateral damage.<sup>4,5</sup>

In summary, CME has a real impact on visual acuity and visual quality. Although it is uncommon, CME is a serious complication of cataract surgery, but by knowing the risk factors, cataract surgeons can minimize the impact.

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## Discussion

**Dr. Henderson:** Dr. Yeu, have you noticed a difference in inflammation with regard to the amount of phaco energy and time?

**Dr. Yeu:** The lens fragmentation has cut my time in half on the nuclear disassembly component. This is important because that's where the energy is being induced into the cornea and placed into the anterior chamber, resulting in increased inflammation. With regard to reducing inflammation, the greatest benefit comes from lens fragmentation.

**Dr. Henderson:** What impact will laser cataract surgery have on postoperative inflammation rates over conventional cataract surgery?

**Dr. Goldman:** That depends on the cataract. If a patient has a posterior subcapsular cataract, there won't be much initial inflammation. But I have seen marked differences in patients with very dense cataracts.

**Dr. Henderson:** What are some clinical pearls for decreasing the risk of subconjunctival hemorrhage? Does your postop topical drop regimen change?

**Dr. Scoper:** The subconjunctival hemorrhage occurs when the suction is engaged, but I think our current topical steroid and corticosteroids decrease inflammation adequately. I do advise alerting the patient that this is likely to occur, however.

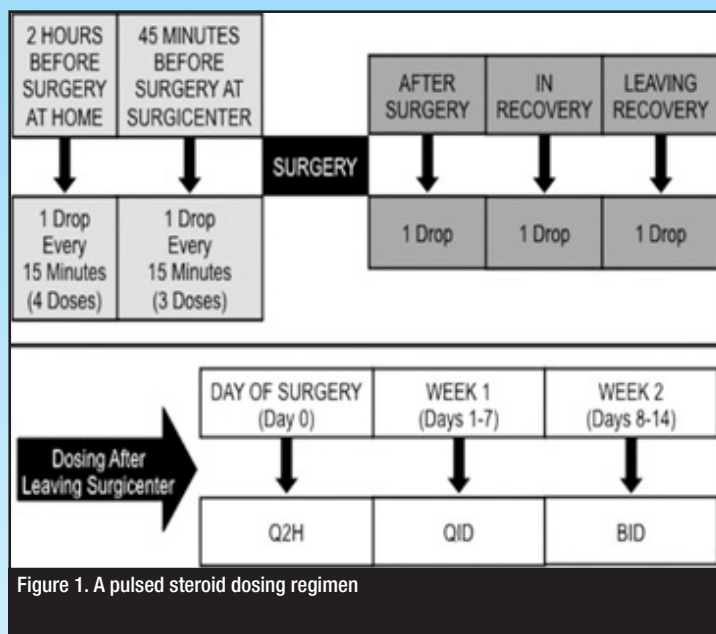
**Dr. Goldman:** I try to get the NSAID in as soon as possible to get it all in the anterior chamber and minimize the effect on the ocular surface, but also we do give a little naphazoline to our patients later when they get to the ASC to minimize that vasoconstriction.



David A. Goldman, MD

## Managing the impact of surgical stress with practical, proactive, pharmaceutical management of inflammation

by David A. Goldman, MD



Some patients have a more robust inflammatory response than others after cataract surgery, and to some extent, we can predict which patients are at increased risk. Common comorbidities, such as uveitis, diabetes, macular disease, having a history of cystoid macular edema (CME), a vitreoretinal interface abnormality, an epiretinal membrane, or a history of retinal surgery predispose patients to postsurgical inflammation.<sup>1-4</sup> Postsurgical inflammation is further exacerbated by medications patients may be taking, such as uroselective alpha blockers, which have been associated with poor dilation and floppy iris, requiring increased manipulation of phaco instruments and further increasing the potential for inflammation.<sup>5</sup> Men being treated for benign prostatic hyperplasia and women being treated for kidney stones might be taking tamsulosin, which increases the risk of inflammation. Several studies have also linked

the use of prostaglandin analogs for glaucoma to CME.<sup>6,7</sup> It is my belief that preventing CME is far better than having to treat it, as patients with long-standing CME never quite regain their former visual acuity.

### Lowering prostaglandin levels

During surgery, trauma causes the release of phospholipids from the cell membrane. Studies have shown that postsurgical prostaglandin levels become elevated following femtosecond laser treatment.<sup>8</sup> These elevations have been attributed to inflammation and intraoperative miosis. Thus, when using the femtosecond laser, it is important to employ pharmaceutical strategies that minimize the release of prostaglandins. Pretreatment with a nonsteroidal anti-inflammatory drug (NSAID) will block the synthesis of prostaglandin, minimize intraoperative miosis, and increase patients' postoperative comfort. Postoperatively, I

recommend using an NSAID plus a steroid for the synergistic effect. The choice of NSAID is usually driven by patients' comorbidities. When it comes to inflammation, I prefer starting with a strong regimen to resolve it as rapidly as possible.

Donnenfeld and colleagues investigated the idea of pulsing steroids just before and after surgery, driven by the assumption that cataract surgery should be treated as you would spinal trauma: dose the patient hard at the beginning.<sup>9</sup> The first eye randomly received difluprednate 0.05% or prednisolone acetate 1%; the other eye received the alternative. Seven doses were administered over 2 hours before surgery; 3 more doses were given after surgery (Figure 1). Corticosteroids were administered every 2 hours for the remainder of the day, then 4 times daily for 1 week and twice daily during the second week. Approximately 62% of patients who received difluprednate were free of corneal edema on postoperative day 1 compared with 38% of patients who received prednisolone acetate. Difluprednate also resulted in less retinal edema at day 15, less endothelial cell loss, and better visual acuity.<sup>9</sup>

I avoid antibiotics or steroids before surgery and usually begin NSAIDs the day before surgery and again on the day of surgery to ensure high levels of drug in the anterior chamber and to block the synthesis of prostaglandin. I give patients 1 drop of difluprednate immediately after surgery and 1 drop in recovery, and use epi-Shugarcaine to minimize intraoperative miosis, particularly in patients undergoing femtosecond laser surgery. I also provide a pulsing dose, as demonstrated by Donnenfeld et al,<sup>9</sup> but because difluprednate is so potent, I do not provide it as frequently. Postoperatively, I prescribe difluprednate once in the morning and

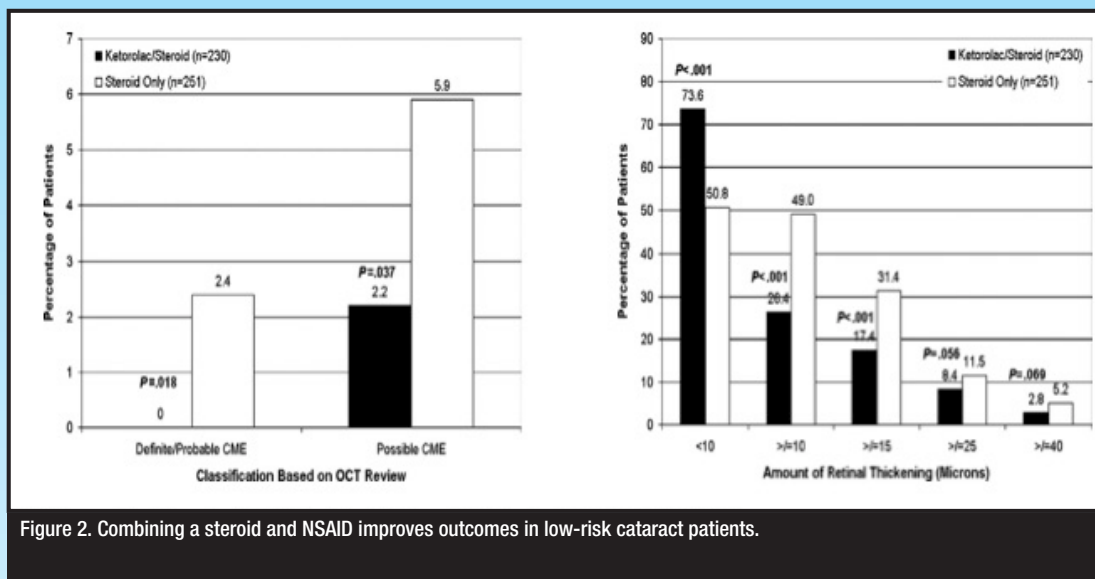


Figure 2. Combining a steroid and NSAID improves outcomes in low-risk cataract patients.

nepafenac 0.3% once at night. Combining a steroid with a nonsteroidal, as demonstrated by Wittppenn and colleagues<sup>10</sup> (who used ketorolac 0.4%) not only decreases the frequency of the dose but also minimizes adverse events and simplifies the regimen for patients. See Figure 2.

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Dr. Goldman is the founder of Goldman Eye in Palm Beach Gardens, Fla. He can be contacted at 561-630-7120.

## Discussion

**Dr. Henderson:** Your postoperative regimen is very innovative, and I agree that most patients would probably prefer once-daily dosing. For the remaining participants, what are your thoughts?

**Dr. Scoper:** I use nonsteroidal nepafenac 0.3% once a day for 5 weeks. Do others use a nonsteroidal? I also use difluprednate 0.05% twice a day for 2 weeks and then once a day to complete the 5-week course.

**Dr. Yeu:** My regimen is very similar to Dr. Scoper's. For the most part, in routine cases with no corneal edema, a short phaco time, and patients with light irides, it's probably not necessary. Difluprednate 0.05% is such a strong drop that it's not something that can just be stopped suddenly. You also want to use it to help the cornea recover, so using for that 4–5 weeks is wonderful. But our staff needs to have standard operating procedures and something that will work for more than 95% of the patients, so Dr. Scoper's regimen is very good.



Elizabeth Yeu, MD

## Putting it all together: A comprehensive approach to refractive cataract surgery

by Elizabeth Yeu, MD

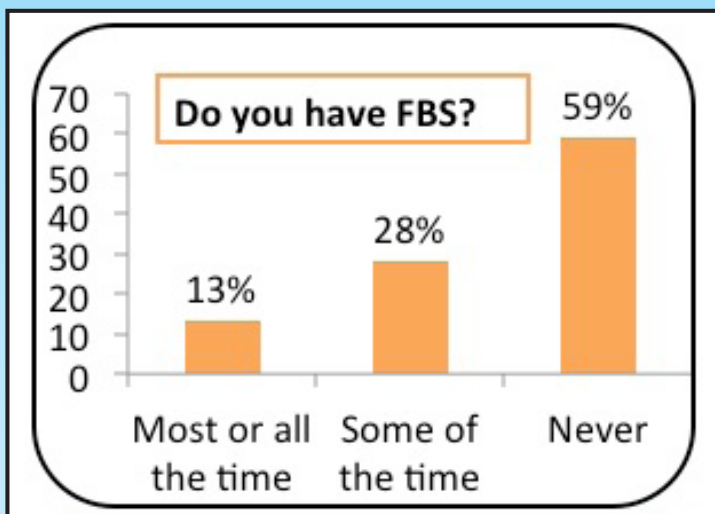


Figure 1. Despite a lack of discomfort, dryness, or foreign body sensation (FBS), >60% of subjects had significant signs of OSD.<sup>4</sup>

Despite our attempts to mitigate inflammation through topical medications and improved technology, satisfying patients is not always easy. Lasers and lenses don't solve everything. Systemic and ocular comorbidities also play a role in outcomes. Postoperative pain, another consequence of inflammation, has been shown to be a significant predictor of dissatisfaction with the surgical experience.<sup>1</sup> It is imperative to optimize the patient's clinical experience, from the preoperative care through the postoperative healing period. According to the 2014 ASCRS Clinical Survey, respondents felt that 38% of patients present at their preoperative cataract refractive surgery consultation with some ocular surface dysfunction that requires treatment beyond artificial tears.<sup>2</sup> Furthermore, almost one-third of respondents expect normal cell and flare levels of 1+ or greater between 3 and 7 days postop.<sup>2</sup> Should we be satisfied with these parameters for our patients?

Although newer anti-inflammatory drugs are potent and require less frequent dosing, there remain mitigating factors that

lead to postop inflammation. For patients with dry eye disease, we must distinguish whether it is the confounding disease or the cataract that is responsible for visual murkiness. Otherwise, patients will blame the surgery and the surgeon for their unsatisfactory visual correction. Cataract surgeons are doing themselves and their patients a disservice if they ignore the ocular surface characteristics before cataract surgery. Bron et al found that 40% of patients with dry eye were asymptomatic.<sup>3</sup> Although the number 1 complaint of cataract surgery patients is fluctuating vision, the majority of patients do not cite foreign body sensation (FBS) and do not complain about dry eye.<sup>4</sup> See Figure 1.

### Assessing the ocular surface

Advanced noncontact imaging technology should be used to assess the ocular surface before surgery. We have numerous modalities ranging from tear film biomarkers to serum biomarkers, to performing a qualitative analysis of the ocular surface, blink response, tear film and meibomian glands. While the

blink response and meibomian gland function can be used to evaluate dry eye, I recommend using one of several available patient questionnaires, such as the Ocular Surface Disease Index or the Dry Eye Questionnaire. The mechanical surface of the eye should then be examined for epithelial disease, such as epithelial basement membrane dystrophy (EBMD) or Salzmann's nodular corneal dystrophy. Asymptomatic EBMD can be clinically significant and result in posterior atypical astigmatism. I recommend using at least 2 devices to assess anterior corneal astigmatism, consider intraoperative aberrometry, and become familiar with at least one nomogram or toric calculator. Figure 2 illustrates what appears to be light irregular astigmatism with inferior skewing, possibly forme fruste keratoconus. But there's a disconnect: If you look at the upper keratoscopic view, this patient has dry eye. Once treated, the image on the right shows a much different astigmatic story than the pre-treated eye.

All surgeons should aim to keep refractive astigmatism at less than 0.5 D; with-the-rule is generally better tolerated than against-the-rule. When we opt to implant a toric IOL, each degree off the target meridian is going to lead to more than a 3% loss of desired effect. I recommend surgeons use at least 2 devices to assess anterior corneal astigmatism and ensure they account for the impact of the posterior cornea in refractive astigmatism. At the minimum, be familiar with nomograms and toric calculators; consider using intraoperative aberrometry to verify your IOL calculations in the aphakic state.

Many cataract patients today are tech savvy. If you tell these patients the procedure is only 10 minutes long and involves no pain, bleeding, or stitches, they will expect excellent uncorrected distance vision. The latest phaco machines, lasers, and IOLs

only provide the platform for a premium experience; it remains the surgeon's responsibility to provide excellent postop vision by preventing inflammation and controlling what inflammation does occur by managing the ocular surface before surgery and by correcting any residual errors.

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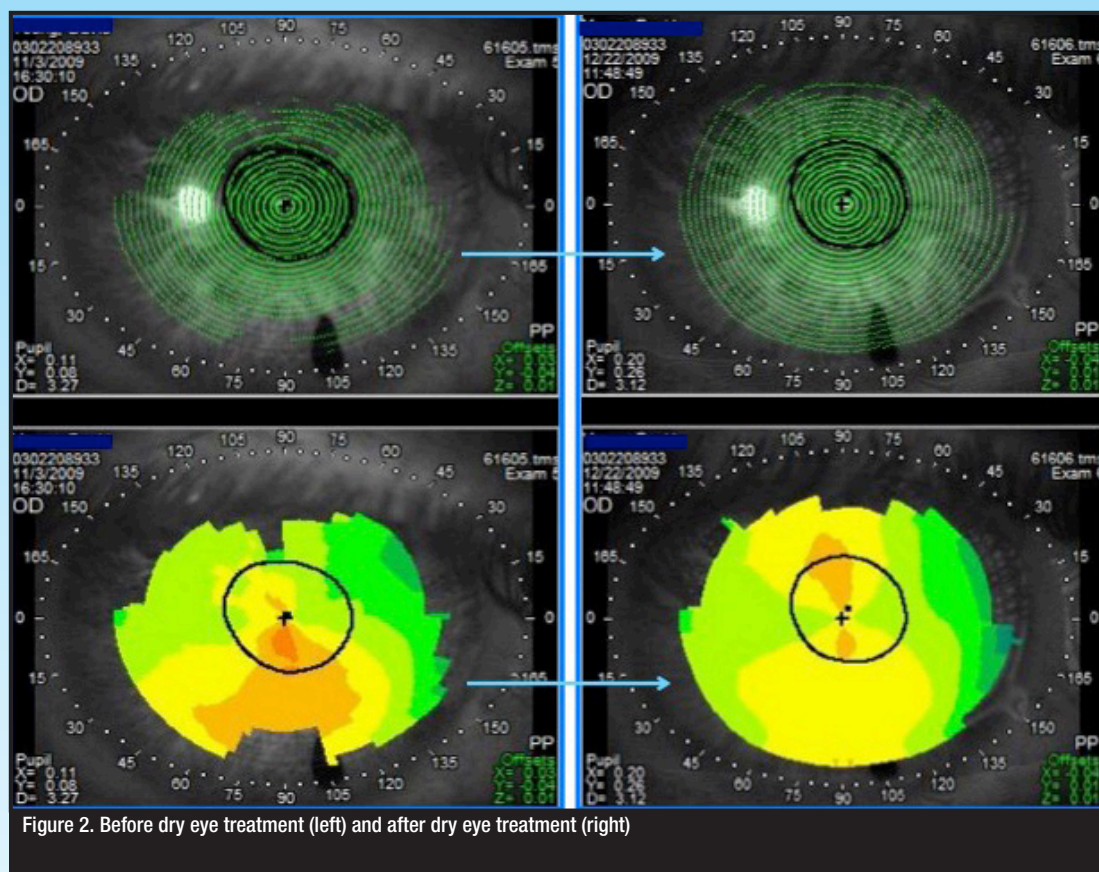


Figure 2. Before dry eye treatment (left) and after dry eye treatment (right)

## Discussion

**Dr. Henderson:** Unfortunately, cataract surgeons tend to ignore dry eye, but I think as surgery becomes increasingly more refractive, we have to pay attention. We now have TearLab, TearScience, and Rapid Pathogen Screening's matrix metalloproteinase-9 (MMP-9) studies. Do any of you incorporate these into your diagnostic tests?

**Dr. Goldman:** I do preoperative topography on just about every patient coming in for cataract surgery. In the clinic, I check for meibomian gland dysfunction. If it is significant, regardless of whether the patient is symptomatic, I treat it aggressively.

**Dr. Scoper:** On nearly every patient coming in for a preoperative cataract evaluation, I use fluorescein to examine the cornea. If there is staining, I use a monofocal or a toric lens. I treat patients' ocular surface disease aggressively and bring them back another day to determine the extent of change on the ocular surface using a LENSTAR LS 900 or IOLMaster. Dr. Yeu, do you consider ocular surface disease an inflammatory disease?

**Dr. Yeu:** Whatever the etiology of the dry eye disease, it eventually leads to inflammation. I perform tear film diagnostics preoperatively on my cataract patients. At the very least, I start any patient who is positive on the InflammDry on cyclosporine 0.05% and topical steroids for a short course, as needed.

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**CME questions (circle the correct answer)**

**1. According to the physicians, what is the lowest level of cell/flare that has a clinically significant impact on visual acuity/quality visual recovery 3–7 days after the initial cataract surgery?**

- a. 0.5+ cell/flare
- b. 1+ cell/flare
- c. 2+ cell/flare
- d. 3+ cell/flare

**2. According to the physicians, which medical regimen will prevent postop inflammation the most after cataract surgery?**

- a. NSAIDs alone
- b. Corticosteroids alone
- c. Combination of NSAIDs and corticosteroids
- d. None of the above

**3. According to the physicians, laser cataract surgery will have a slight-to-significant decrease on postop inflammation when compared to conventional cataract surgery.**

- a. True
- b. False

**4. Which of the following is not a risk factor for postop inflammation after cataract surgery?**

- a. Uveitis
- b. Vitreoretinal interface abnormality
- c. History ocular surgery
- d. History of contact lens use

**5. What percentage of patients generally present with dry eye but is asymptomatic?**

- a. 20%
- b. 40%
- c. 60%
- d. 80%

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