

# Optimizing the Ocular Surface to Improve Outcomes With LASIK

Confirming the presence of ocular surface disease before surgery may reduce complications after surgery.

BY TERRENCE P. O'BRIEN, MD

Ocular surface disease (OSD) is a common condition that is frequently underdiagnosed and can range in severity from asymptomatic or episodically symptomatic to a chronic debilitating state. Dysfunctional tear syndrome, or dry eye disease (DED), results from the complex interrelationship between the amount of tears produced and the rate of tear evaporation and can lead to hyperosmolarity and ocular surface inflammation.<sup>1</sup> This activation of the inflammatory cascade results in an unstable, unhealthy ocular surface, leading to OSD. Optimizing the ocular surface during the preoperative management of LASIK and other keratorefractive patients may lead to faster epithelial healing and visual recovery and reduce the impact of DED and other complications postoperatively.

## MATRIX METALLOPROTEINASE-9 ACTIVITY

Matrix metalloproteinase-9 (MMP-9) is a proteolytic enzyme that is produced by stressed epithelial cells. Its link to OSD and refractive surgery are described below.

**OSD.** Elevated MMP-9 levels have been observed in the tear fluid of patients with DED,<sup>2</sup> and they have been shown to destabilize the tear film and alter the corneal barrier function, leading to corneal epithelial irregularity and visual morbidity.<sup>3-9</sup> Higher levels of MMP-9 are present in patients with more severe DED, and concentrations of MMP-9 in the tear film correlate with the severity of clinical examination findings.<sup>3,10,11</sup>

Inconsistency and lack of correlation between the clinical symptoms and signs of DED and OSD make diagnosis and treatment challenging. Chalmers et al<sup>12</sup> reported a low level of agreement between the assessment of

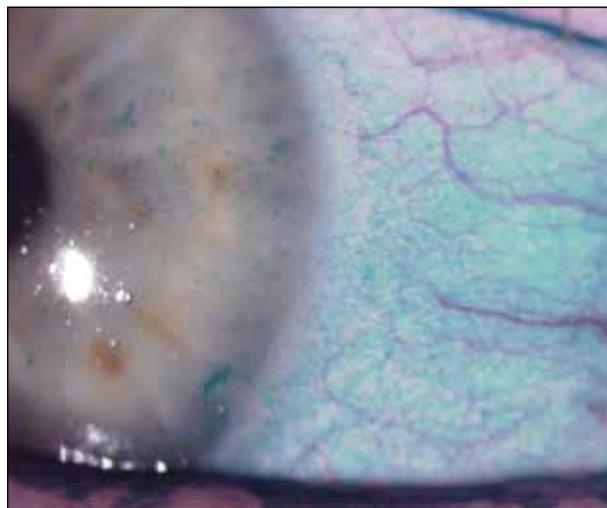


Figure 1. Dissatisfied patient 6 weeks after LASIK, with fluctuating vision, dryness, and sensitivity to light using preserved artificial tears every 2 hours. Vital staining with lissamine green showed significant punctate epithelial erosions of the conjunctiva and cornea with a mucus filament present.

severity of DED between clinicians and their patients, confirming the widely suspected clinical underdiagnosis of DED. This finding is especially true in patients who do not report the symptoms of DED because they may have reduced corneal sensitivity.

**Refractive surgery.** In addition to patients who present with signs and symptoms of DED, studies have shown an important link between elevated levels of MMP-9 and ocular surgery. One of the most common

postoperative complications of ocular surgery such as PRK and LASIK, DED affects approximately 50% of LASIK patients 1 week postoperatively, 40% 1 month postoperatively, and 20% to 40% 6 months postoperatively.<sup>13,14</sup> Other complications such as fluctuating vision, reduced BCVA, and severe discomfort occur in approximately 10% of patients.<sup>15</sup> DED is also a leading source of dissatisfaction among patients after LASIK (Figure 1).<sup>16</sup>

DED diagnosis becomes more challenging after corneal and refractive surgery. Punctate epithelial keratopathy was detected with rose bengal or fluorescein staining in 2% to 6% of eyes that had LASIK,<sup>17-19</sup> but symptoms of ocular dryness and irritation were found in 48% to 59% of these eyes.<sup>20</sup> One to 6 months after LASIK, Wilson found that Schirmer tests with anesthesia detected no significant difference in tear production between eyes that developed symptoms and signs of DED versus asymptomatic eyes.<sup>17</sup>

MMP-9 has also been associated with poor epithelial healing, epithelial ingrowth, and corneal ulceration after refractive surgery.<sup>21</sup> Corneal wound healing after LASIK may be prolonged because of an insufficient attachment between the corneal flap and the corneal bed, and the delay is associated with elevated levels of MMP-9.<sup>21,22</sup> MMP-9 is specifically found in the periphery of LASIK wounds, suggesting that its presence may impair flap adherence. The incidence of epithelial ingrowth is about 1% after LASIK, and in 75% of cases involving epithelial ingrowth, MMP-9 was found at the wound site.<sup>23</sup> Also, the dislocation of corneal flaps or ectasia, which consisted of progressive deformation and thinning of the cornea after LASIK, has been shown to be related to corneal wound healing.<sup>22</sup>

## PREOPERATIVE SCREENING AND THERAPY

Patients who have DED before LASIK experience more severe symptoms of tear dysfunction afterward, and their corneal sensitivity takes longer to recover compared with those without preoperative DED.<sup>14,15,24,25</sup> Because preexisting OSD may be exacerbated by LASIK or PRK, its diagnosis and treatment as part of the surgical prescreening process helps to avoid complications.<sup>15</sup> Successful iden-

### TAKE-HOME MESSAGE

- MMP-9, a proteolytic enzyme that is produced by stressed endothelial cells, has been observed in the tear film of patients with DED.
- Screening for MMP-9 will help refractive surgeons identify patients with DED and OSD in advance of surgery.
- MMP-9 has been found in the periphery of LASIK wounds, suggesting that its presence may impair flap adherence.

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tification and treatment of these patients in advance of surgery can also improve the ocular surface and thus allow more accurate presurgical measurements.<sup>15</sup>

Confirmation of the presence of underlying OSD such as DED will drive the initiation of appropriate therapy, especially for the perioperative management of refractive surgery. The treatment of inflammation related to OSD may involve topical cyclosporine,<sup>26,27</sup> topical corticosteroids,<sup>28,29</sup> oral doxycycline,<sup>11,29-31</sup> topical azithromycin 1%,<sup>32</sup> and systemic omega-3 essential fatty acid supplements.<sup>33</sup> Antiinflammatory therapy is reported to improve both the signs and symptoms of OSD and is a targeted and effective therapeutic option for patients with underlying inflammation causing OSD. Topical antiinflammatory therapeutics can normalize the ocular surface and improve the quality of the tear film after LASIK.<sup>34</sup> Additionally, LASIK-induced neurotrophic epitheliopathy often responds to immunomodulation with topical cyclosporine, which treats the underlying inflammation and may facilitate corneal nerve regeneration and the restoration of corneal sensation. Thus, the treatment of DED before refractive surgery may reduce the risk and severity of DED after surgery.<sup>15</sup>

## IN-OFFICE DIAGNOSIS

InflammaDry (Rapid Pathogen Screening, Inc.) is an in-office diagnostic test that is available in Europe. The purpose of the test is to detect abnormally elevated MMP-9 present in the late phase of the inflammatory cycle, which may be more clinically relevant than causal mechanisms or acute symptoms. Although MMP-9 activity is elevated in eyes with symptomatic DED and in a variety of other clinically identifiable ocular surface conditions, the test also reveals asymptomatic OSD and hidden inflammation of DED.

Having a rapid, in-office test for elevated levels of MMP-9 available for patients who present with signs or symptoms of DED should facilitate the ophthalmologist's ability to make an accurate diagnosis. Additionally, administering the InflammaDry test before and after corneal or refractive surgery may uncover subclinical inflammatory conditions, including the hidden inflammation of chronic DED, which could negatively affect postsurgical outcomes. This tool should give physicians an unprecedented capability of optimizing outcomes.

## CONCLUSION

DED and OSD are common conditions that may be present in patients seeking laser vision correction or other keratorefractive procedures. DED is the most common cause for dissatisfaction among patients undergoing LASIK. In-office screening with a rapid, reliable tool to detect markers for DED and OSD with high sensitivity and specificity allows surgeons the opportunity to diagnose and treat in advance

of surgery to improve outcomes, reduce complications, and increase overall patient satisfaction. ■

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