Follow the 2-3-4 rule

Epithelial Ingrowth protocol guides intervention, therapy

Nice, France—Although the incidence of epithelial ingrowth as a complication of LASIK is declining, considerable uncertainty remains over when to intervene, according to Arun C. Gulani, MD.

In response, Dr. Gulani has devised a grading system to help surgeons answer that question by placing values on the density of the epithelial ingrowth.

Dr. Gulani explained his new system during the XX meeting of the European Society for Cataract and Refractive Surgeons here. He is chief, cornea and external disease, director of refractive surgery, and assistant professor in the department of ophthalmology, University of Florida, Jacksonville.

“If people use this system, there should be no more confusion on what is important about epithelial ingrowth, when they should intervene, or how they should treat,” Dr. Gulani said. “If I see epithelial ingrowth, I see what grade it is, what surface is involved, is it clinically significant, and then I decide how to manage it.” Using this system during LASIK helps prevent the spread of epithelial ingrowth, according to Dr. Gulani.

If a surgeon intervenes unnecessarily, the risk of recurrence increases, so a protocol for intervention and treatment will reduce such situations.

“Once epithelial ingrowth occurs, it is difficult to eradicate,” Dr. Gulani continued. “Therefore, prevention is still the best management. Surgeons must be aware of predisposing factors such as unstable epithelium, epithelial defects, dry eye, epithelial basement membrane disease, and previous incisional surgery.”

“Surgeons also should apply minimal flap handling principles and minimal fluidics and use special instruments that reduce the amount of flap handling,” he said.

Using retroillumination and a slit lamp to get a clear view of the cornea, Dr. Gulani begins the protocol for epithelial ingrowth by evaluating the density.

“When I see the epithelium as an island in a localized form, usually in the periphery, it is grade I,” he said. “This does not block the red reflex.”

If the epithelium is seen in a diffuse form with a faint extension line in front of it, which tends to distort the red reflex, the density warrants a grade II designation.

Grade III density encompasses all of the features of grade II plus blockage of the red reflex.

Figure 1

Central epithelial ingrowth of insignificant clinical significance.

Figure 2

Central epithelial ingrowth of significant clinical significance.

Figure 3

Peripheral epithelial ingrowth of insignificant clinical significance.

Figure 4

Peripheral epithelial ingrowth of significant clinical significance.
Ingrowth CONT...

### Table 1: Criteria for Clinical Significance

<table>
<thead>
<tr>
<th>Visual</th>
<th>Tectonic</th>
<th>Progression</th>
</tr>
</thead>
<tbody>
<tr>
<td>Direct (In visual axis)</td>
<td>Indirect (Away from visual axis)</td>
<td>Rate (Between consecutive visits)</td>
</tr>
<tr>
<td>Melting</td>
<td>Bulking</td>
<td>Direction (Centripetal)</td>
</tr>
<tr>
<td>- induced astigmatism</td>
<td>- surface/tear film abnormal</td>
<td></td>
</tr>
</tbody>
</table>

Source: Arun C. Gulani, MD

---

**The 2-3-4 rule**

After the density has been determined, the physician should follow what Dr. Gulani calls the “2-3-4 rule.” He explained that epithelial ingrowth involves two kinds of tissue: the epithelium and scar tissue. It also requires three factors: a source, a surface deficit such as an abrasion or an ulcer, and space to grow into.

Having space for the epithelium to grow into is especially important in patients who have previously had RK or incisional surgeries, since the incisions can act like gutters or pathways of least resistance, Dr. Gulani said.

The final part of the rule refers to four surfaces: the stromal bed, the underside of the corneal flap, the flap edge, and the flap hinge. “When you’re going after the epithelium, you have to clean all four surfaces,” Dr. Gulani said. “If you leave any of them behind, you’ve left epithelium behind.”

Dr. Gulani also developed a set of guidelines for clinical significance. They include visual criteria, tectonic criteria, and criteria for visual progression (Table 1). Direct visual criteria involve epithelial ingrowth in the visual axis, meaning that it directly affects vision.

Indirect criteria are those in which the epithelial ingrowth is away from the axis and affects vision by inducing astigmatism or inducing abnormality in the surface tear film.

The tectonic category encompasses melting and bulking. The corneal flap can melt when epithelial ingrowth spreads, while at other times the presence of epithelial ingrowth generates bulk, Dr. Gulani said. Progression includes rate, direction, and density. The rate refers to the rate of epithelial growth between consecutive visits; direction refers to centripetal growth, or growth toward the visual axis; and density refers to Dr. Gulani’s three-tiered density classification.

**Management of ingrowth**

The next step in Dr. Gulani’s protocol is the management cascade for central and peripheral ingrowth.

With this flowchart, the physician assesses whether the problem is stable and clinically insignificant or increasing in intensity or size with visual or anatomic decompensation. If the ingrowth is increasing, there are treatment guidelines for either central or peripheral cases. With central cases, the protocol choices are to lift the flap and debride the entire epithelium or, in some cases, use the Nd:YAG laser. In peripheral cases, there are three treatment options: lift the flap and debride, use surface cryotherapy, or apply chemical modulators with chemical debridement. Surface cryotherapy is typically used with preexisting incisions, such as those from RK, or with cut-down drainage incisions.

Dr. Gulani is working on a fourth treatment option, genetically engineered immunotherapy in the form of special drops that might be able to control epithelial ingrowth.

“If you have minimal growth, you won’t need to lift the flap. Lifting the flap itself increases the risk of the next ingrowth,” Dr. Gulani said. “If these drops work and work well, maybe the physician could just put a topical drop in and watch the ingrowth disappear.”