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Shaping the refractive laser landscape

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SMILE: A better alternative to LASIK

by Kimiya Shimizu, MD, PhD

Despite being a relatively safe and easy way to correct refractive errors, LASIK is not entirely without complications. Infection, diffuse lamellar keratitis (DLK), epithelial ingrowth, irregular astigmatism, and dry eye can all occur after LASIK. We have observed complications occurring 20 years after the procedure, and the most common—dry eye—can continue for 12 years. Following 55 cases over 5 years, we found that 78% had worse dry eye at 5 years after LASIK than at preop.

These complications were caused by flap-making, an integral part of the LASIK procedure. So I stopped performing LASIK in 2008.

To avoid these complications, I shifted to the flapless and minimally invasive small incision lenticule extraction (SMILE) technique—the 3rd generation of laser vision correction. At the moment, only the VisuMax femtosecond laser system (Carl Zeiss Meditec, Jena, Germany) is able to perform SMILE with its ReLEx SMILE solution. Through photodisruption—rather than ablation—the femtosecond laser creates a refractive intrastromal lenticule that is then removed through a small incision.

In addition to getting away from the flap, my experience showed the operation takes less than half the time it takes to perform LASIK.

We at Kitasato University, Kanagawa, Japan, compared flapless SMILE and with-flap LASIK surgery in a study of 60 eyes in 30 patients. We performed SMILE on one eye and LASIK on the other eye.

The day after surgery, SMILE corneas were beautiful and clear. On the other hand, in the LASIK eyes, we observed corneal microfolds (Figure 1).

Following these patients up to 1 year, we saw no difference in visual outcomes. Safety, efficacy, predictability, and stability were all comparable between SMILE and LASIK.

Instead, the difference was most obvious in two factors we examined: patient comfort and the occurrence of dry eye.

Subjectively rating signs and symptoms from 0 (no symptoms) to 100 (the worst imaginable for the patient) on a visual analog scale (VAS), patients reported significantly less pain, epiphora, and foreign body sensation with SMILE versus LASIK—39.2 vs. 93.1, 34.8 vs. 86.7, and 43.6 vs. 87.1, respectively ($P<0.001$).

Evaluating dry eye, Schirmer's test values did not differ significantly. Schirmer's test decreased immediately in LASIK and at 6 months after surgery with SMILE, leaving just a small difference between the two procedures at 1 year after surgery. However, there was a significant difference in the change in tear breakup time (TBUT): TBUT decreased from 5.1 seconds preop to 2.9 seconds 1 year postop in LASIK, and only from 4.7 seconds preop to 4.4 seconds 1 year postop with SMILE ($P<0.05$).

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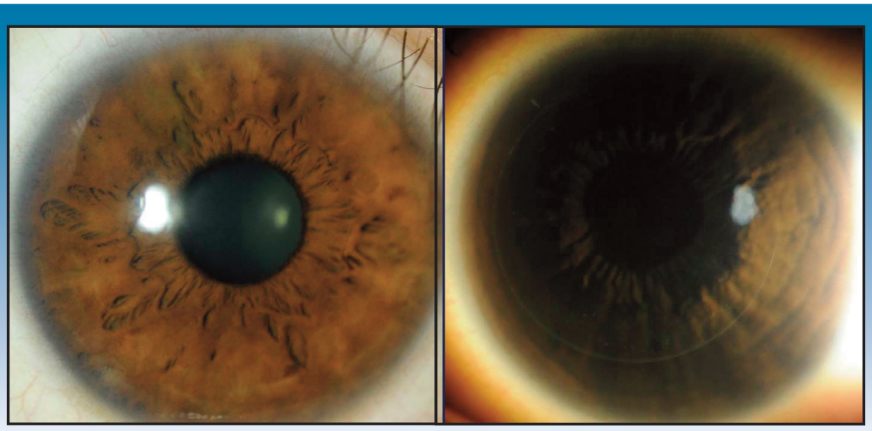

Figure 1. Clear SMILE cornea vs. corneal microfolds in LASIK cornea, 1 day postop

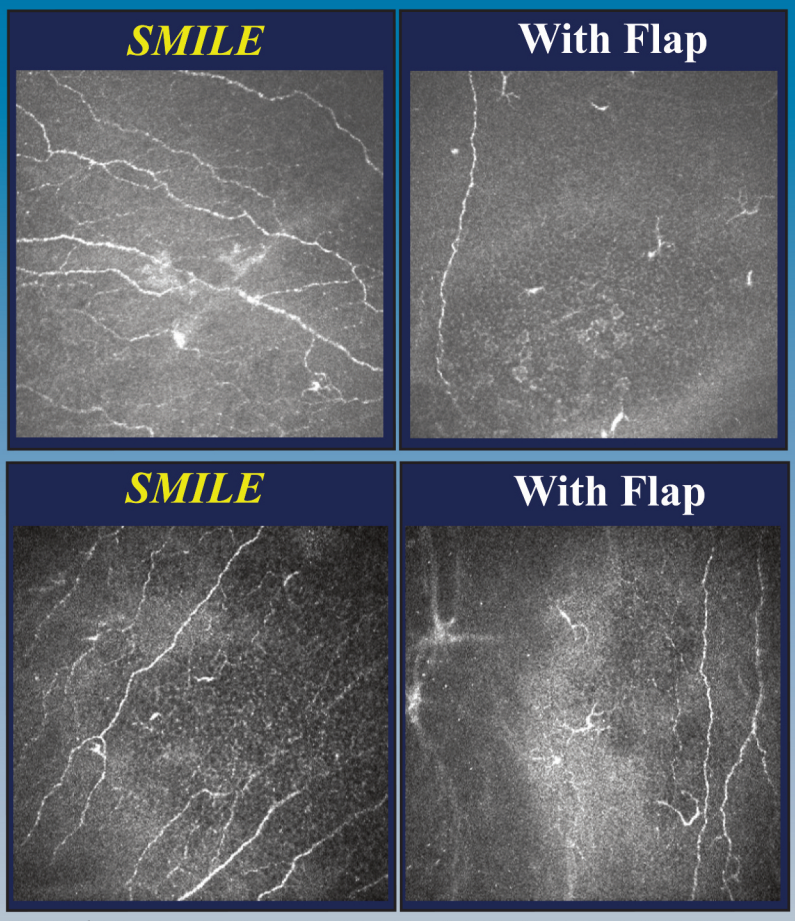

Figure 2. Confocal specular microscopy comparison at 3 months (top) and 1 year (bottom)

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We looked into what caused these differences. Examination of central corneal sensation provided a clue: Central corneal sensation in LASIK was significantly reduced ($P<0.05$) compared with SMILE at 1 month (41.7 mm vs. 59.0 mm), 3 months (50.3 mm vs. 58.3 mm), and 6 months (56.3 mm vs. 59.6 mm).

In addition, confocal specular microscopy at 3 months and 1 year showed a significant difference between LASIK and SMILE (Figure 2).

These findings demonstrate that flap-making damages the sub-basal corneal nerves. At 1 year, the sub-basal corneal nerve density had been reduced by 59.8±27.3% in LASIK but only 22.5±53.4% in SMILE.

Therefore, SMILE is the less invasive surgery. It is an innovative procedure that leaves the cornea strong against trauma and eliminates the problem of dry eye. I no longer have to counsel patients about dry eye.

My personal history with refractive surgery began with PRK in 1990, progressing through mini-RK in 1993 and LASIK, including wavefront-LASIK from 1997 to 2008. I have now stopped performing LASIK for refractive correction completely and have been performing SMILE since 2010.

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Results of ReLEx SMILE in low to moderate myopia

by Sri Ganesh, MD

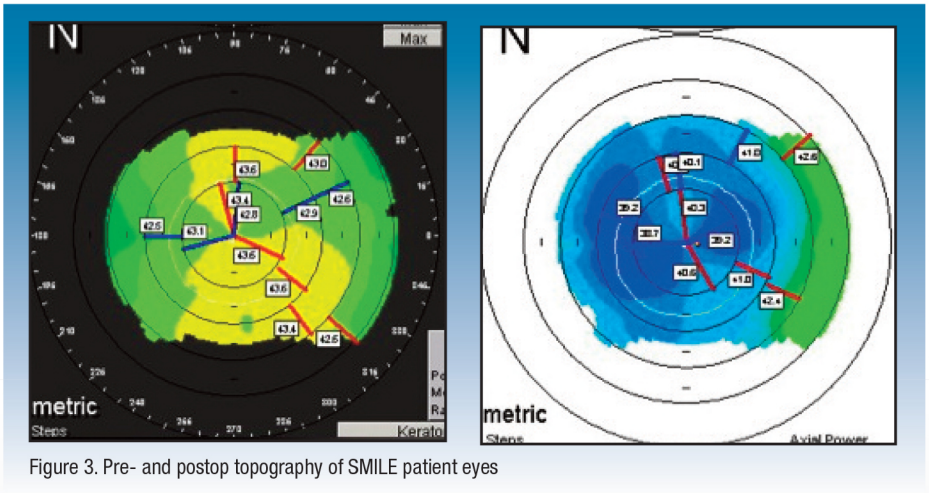

Figure 3. Pre- and postop topography of SMILE patient eyes

ReLEx SMILE combines state-of-the-art femtosecond technology—the VisuMax femtosecond laser system (Carl Zeiss Meditec, Jena, Germany)—with high-precision lenticule extraction, aiming to provide minimally invasive refractive correction in a single system.

A refractive lenticule is created in an intact cornea and removed via a small incision, so there's no ablation, no flap. We thus have a flapless, all-femto, single-step solution using the VisuMax femtosecond laser system.

The laser itself has several key characteristics. It uses a curved contact glass interface so there is not much pressure on the cornea. It uses low suction so it is very comfortable for the patient. It is a very fast femtosecond laser in a system that includes an excellent microscope and slit lamp that allow close-up views of the lenticule extraction.

My colleagues and I at the Nethradhama Super Specialty Eye Hospital, Bangalore, India, looked at data from 600 eyes of 300 patients from 23 to 27 years of age who underwent ReLEx SMILE at our institution. We analyzed low and moderate myopia, with 153 eyes with spherical equivalent up to –3 D (group 1) and 262 eyes between –3 D and –6 D (group 2). We compared the postoperative results between the two groups.

In both groups, we used a 2-mm superior incision, an optical zone of 6 to 6.5 mm, a cap thickness of 100 µm, and a residual bed of 280 µm.

On the first day postop, 89.3% of group 1 and 85.3% of group 2 had an uncorrected visual acuity (UCVA) of 6/6; meanwhile, 7.7% of group 1 and 8.1% of group 2 achieved a UCVA of 6/5.

On the 15th day postop, UCVA improved: 64.3% of group 1 and 62.9% of group 2 were now at 6/5, with 34.5% of group 1 and 36.4% of group 2 at 6/6.

Only 4.9% of group 1 and 6.8% of group 2 had residual error greater than 0.5 D, all between 0.51 and 0.75 D.

Contrast sensitivity decreased in both groups, with a greater, statistically significant drop in group 1, but still within normal range and with improvement by 3 months.

Evaluating dry eye preop and at 1 month postop, there was not much of a change in Schirmer's score in group 1 (33.3 mm vs. 33.29 mm, respectively). There was some reduction in the Schirmer's score in group 2 from preop to 1 month postop (33.7 mm to 32.2 mm, respectively), but the change was not very significant.

Meanwhile, there was a similar, non-statistically significant drop in tear breakup time from preop to 1 month postop in both groups: from 12.22 to 10.02 seconds in group 1 and from 12.35 to 10.16 seconds in group 2.

Higher order aberrations increased from preop to 1 month postop in both groups, from 0.25 to 0.3 µm in the low myopia group 1 and from 0.24 to 0.33 µ in the moderate myopia group 2.

Finally, we looked at topography. The topography of SMILE patient eyes has a nice, large optical zone (Figure 3). If you program a 6- or 6.5-mm optical zone, you get a 6- or 6.5-mm optical zone, unlike with excimer laser ablation, which typically results in a smaller optical zone than you desired.

Patients did not complain of pain intra- or postop. It's a very comfortable, painless procedure, with no significant glare or haze and less postop dryness. Comparing the procedure with LASIK, SMILE provided the highest patient comfort and very clear eyes postop, with no subconjunctival hemorrhage resulting from the suction.

We did encounter some intraop complications: 2 eyes had suction loss, one of which was redocked and treated with ReLEx SMILE, the other required conversion to a flap procedure with excimer correction; 1 eye had extension of incision or a cap tear; 2 eyes had lenticular tear—tearing of the lenticules as they were being extracted. Lenticular tears can be identified by placing the lenticule on the cornea and inspecting it after extraction. If the edge is not pristine, then the surgeon should go back into the pocket and dissect to find the torn piece. This should be done particularly when there is some difficulty during extraction and is more of a risk in low levels of correction since the lenticule tends to be very thin.

Importantly, none of these eyes had a loss of BCVA.

In summary, the flapless ReLEx SMILE procedure makes minimally invasive refractive correction possible for the first time, and our results show that the technique eliminates flap complications, avoids inducing or worsening dry eye, and achieves excellent visual results even in low degrees of myopia up to –3 D of sphere.

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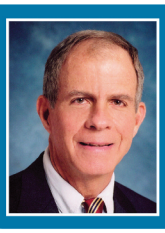
The SMILE procedure: Small incision lenticule extraction



by William W. Culbertson, MD

SMILE is a fantastic procedure that we surgeons in the U.S. have been waiting for since we first heard about it 5 years ago. Intrastromal keratomileusis is a very compelling possibility. A number of technologies have tried to address this, but the VisuMax femtosecond laser system (Carl Zeiss Meditec, Jena, Germany) in particular was made with this procedure in mind.

At Bascom Palmer Eye Institute (BPEI), Miami, Fla., we have all 3 femtosecond and excimer laser platforms currently available on the market, and we're very happy with the results in all of them. However, it is the SMILE procedure made possible by the VisuMax femtosecond laser that I believe is the most exciting and compelling.

We have had 5 years of experience using the VisuMax femtosecond laser system for LASIK and keratoplasty. When the possibility came along of having a U.S. Food and Drug Administration (FDA) trial for approval of the SMILE procedure using the instrument,* we jumped at the possibility of participating.

The SMILE procedure performed with the VisuMax takes 3 steps: first, a lenticule and access cut are created. In step 2, the lenticule is manually separated through the access cut. Finally, the lenticule is extracted through this small incision (Figure 4).

In our study, we create the lenticule under a 120-µm cap. The laser needs to be extremely accurate, and the patient interface is curved to minimize compression of the cornea—it only minimally changes the corneal shape, is very comfortable for the patient who is able to maintain fixation throughout the procedure, and does not induce subconjunctival hemorrhage.

In the U.S., 5 sites are involved in the FDA trial: BPEI; the Dishler Laser Institute, Greenwood Village, Colo.; Discover Vision Center, Leawood, Kan.; Sanford Clinic, Sioux Falls, S.D.; and Dean Health Systems, Madison, Wis. BPEI is at sea level; the Dishler Laser Institute in Colorado is at about 2,000 meters. The machine has also been used successfully in Kathmandu, Nepal at 3,000 meters. Despite this wide range of environments, we are all getting the same results.

For the FDA trial, we performed the SMILE procedure over a wide range of refractive errors, from –1 to –8 D of sphere. However, for purposes of the trial we did not treat cylinder.

We first looked at the postoperative refraction at 1 week, 1 month, 3 months, 6 months, 9 months, and 12 months (Figure 5). Over the course of the follow-up period, the mean residual spherical equivalent tightened from –0.12 D (range of –1.13 to +1.00 D) to –0.01 D (range –0.25 to +0.75 D), maintaining good predictability over the full range of correction, with the same predictability for high myopes as for low myopes. The FDA trial has now been extended to even higher levels of myopia with equally precise, predictable results.

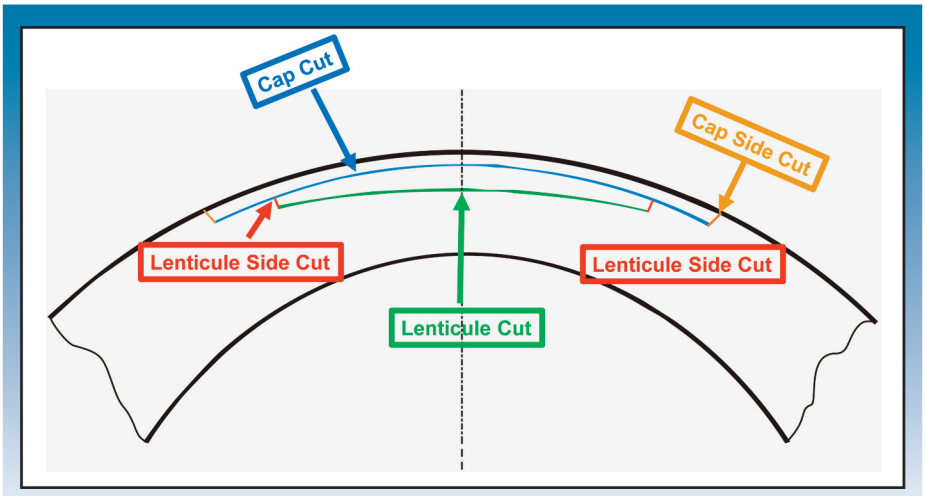


Figure 4. The laser is used to create 2 lamellar and 2 side cuts for SMILE.

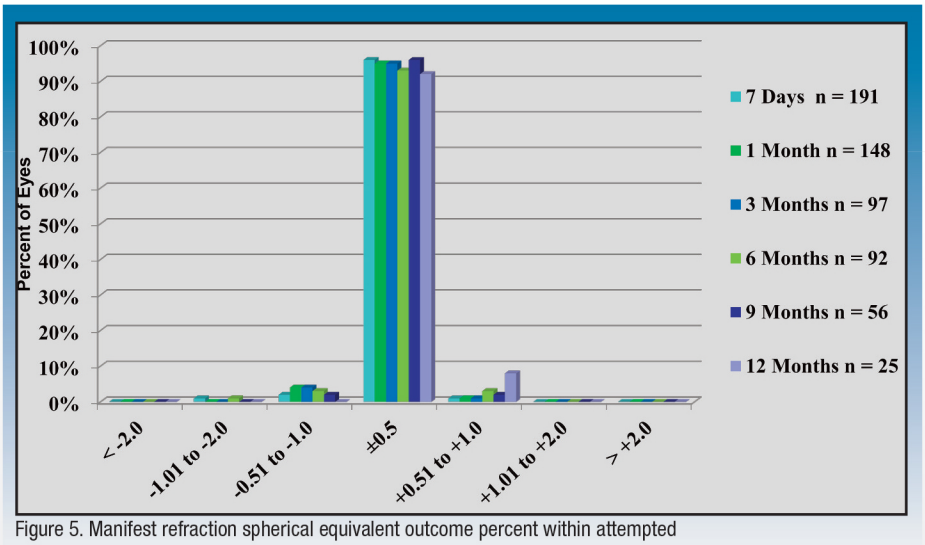


Figure 5. Manifest refraction spherical equivalent outcome percent within attempted

I think that is the beauty of this procedure: We can treat these very high myopes and get the same results that we get with the low myopes.

Looking at efficacy, most of the results at the various time intervals are clustered around ±0.50 D of target, with a few undercorrections and overcorrections. One or 2 patients initially had uncorrected visual acuities (UCVAs) of 20/40, but the results improved over time so that more than 95% were at 20/20 or better and 60% were 20/16 or better by 12 months.

Bearing in mind that none of the surgeons in the U.S. trial had performed this procedure before, these results illustrate our learning curve. Compared with sites elsewhere around the world, where surgeons have performed the surgery in more than 125,000 eyes, we had only treated 238 eyes around the end of last year in the 5 trial sites. We are thus still perfecting our technique, and yet the results are already quite impressive.

In terms of safety, best corrected visual acuity was unchanged in most patients, with a few people gaining 1 or 2 lines. There were a few intraoperative problems: 2 eyes with difficult or incomplete lenticule removal, 3 eyes with suction loss with completed procedure, 2 eyes with suction loss with discontinued procedure, and 1 perforated cap. All of these resolved without sequelae.

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ReLEx SMILE is a unique, flapless procedure performed in a single step with the VisuMax femtosecond laser system. There is 80% less side cut and 30% less lamellar cap cut compared with LASIK, thereby preserving the integrity of the upper corneal layers, the strongest layers of the cornea. We are hopeful that this will decrease the incidence of corneal ectasia.

In addition, fewer corneal nerves are severed, which may decrease the severity of dry eye. No flap means minimal risk of complications such as epithelial ingrowth, infection, and traumatic flap dislocation.

We have never seen a patient with striae. There is a large optic zone corrected from the center to the periphery, as demonstrated by corneal topography.

There are some disadvantages. At the moment, we have used it in myopia with sphere only; however, myopic astigmatism is treated around the world, and work on hyperopic treatments has begun elsewhere. Enhancements are difficult; however, in theory you could make a new side cut to lift the flap or perform a surface ablation for small corrections. There had been some questions as to the smoothness of the interface, but we have examined interface tissue under scanning electron microscopes, demonstrating surfaces that are very smooth compared to LASIK flaps. Centration may also be an issue.

Nonetheless, measuring these disadvantages against the advantages, I believe that with this procedure we certainly have something to smile about.

**FDA Clinical Study (IDE) ongoing*

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A true customized power package: MEL 90 with Triple-A in my clinic

by Bertram Meyer, MD

We have been working with the new MEL 90 excimer laser (Carl Zeiss Meditec, Jena, Germany) since July 2013. This is a very compact, flexible, and reliable excimer laser. It has touchscreen operation and a second workstation for data input and control. The platform allows seamless data transfer to the VisuMax femtosecond laser system, creating an ergonomic, easy workflow.

The MEL 90 features FLEXIQUENCE, a frequency switch option that allows surgeons to choose between two frequency modalities: 250 Hz, which is good for surface ablations, and 500 Hz, for intrastromal ablations. The MEL 90's 500-Hz setting means about 1.3 seconds per diopter intraoperatively, setting a standard in ablation speed.

This new excimer laser also features rapid eye tracking at 1,050 fps.

A third feature of the MEL 90 excimer laser is a new ablation profile: the Triple-A (advanced ablation algorithm) profile—one profile that fits all.

This is a completely new ablation profile, completely different from the ASA profile used by the MEL 80. This profile has very strong aspherical optimization, with

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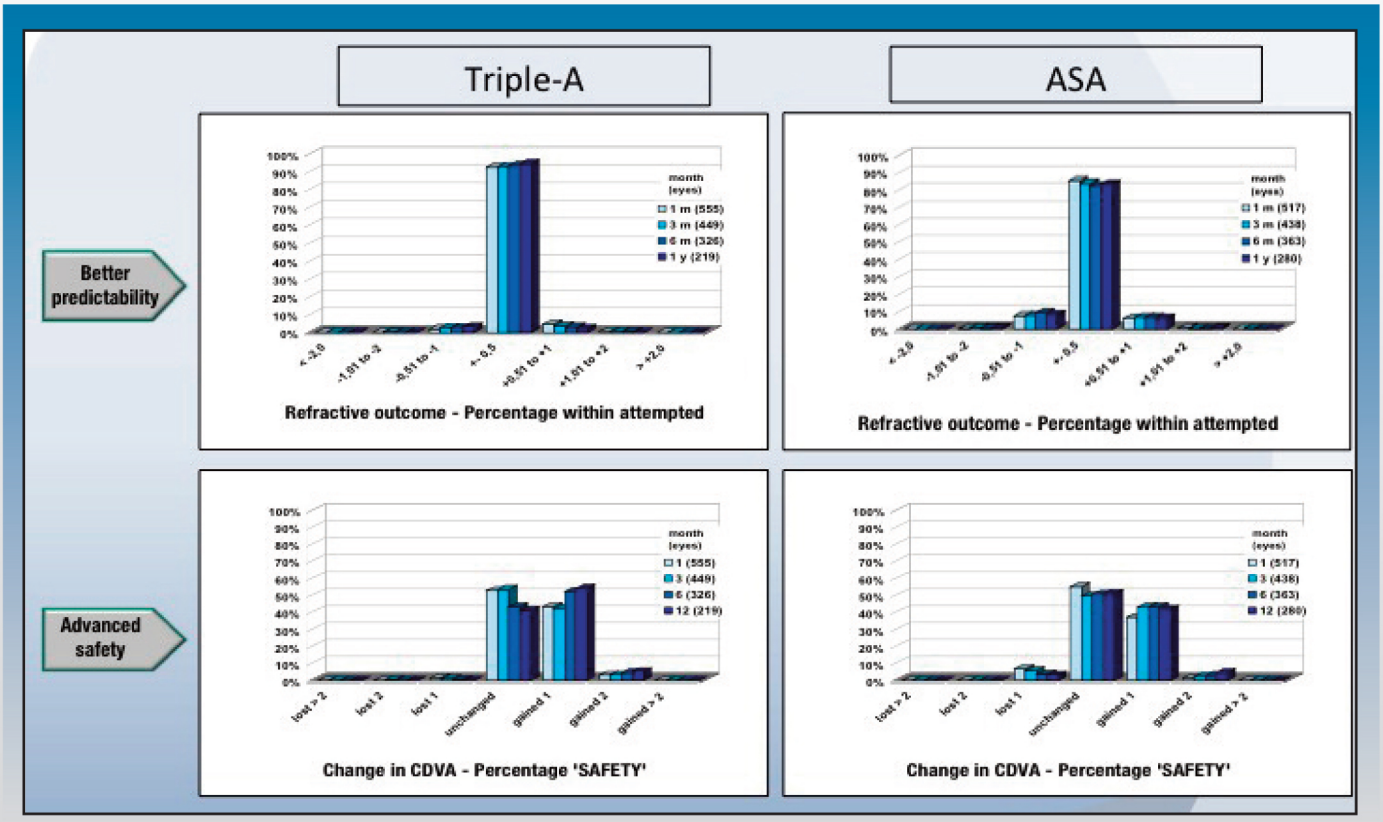

Figure 6. Comparison between the Triple-A and ASA profiles

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aligned asphericity at high diopters much better than the ASA profile and less iatrogenic induction of spherical aberrations.

The Triple-A profile is tissue saving, with a much lower ablation depth, thus ablating less tissue. It has enhanced projection error compensation function, meaning more energy correction to the periphery. This allows the creation of larger optical zones, minimizing disturbances in night vision. Finally, it gives better control of target asphericity.

We have used this profile to perform myopic treatment in 768 eyes. These eyes had a mean sphere of –4.43±2.1 D (range –1.5 D to –10.5 D) and mean cylinder of –1.14±0.88 D (range up to –4.5 D). We set flap parameters to a mean flap diameter of 8.5±0.26 mm (range 7.9 mm to 8.7 mm) and a mean flap thickness of 115±5 µm (range 100 µm to 120 µm). We experienced no technical complications intraoperatively, no significant side effects.

After 4 weeks, more than 92% of eyes were within ±0.5 D of target. Astigmatism was corrected to less than 0.5 D in all ranges, even in very high astigmatic components (Figure 6).

In terms of safety, 50% of eyes had unchanged corrected distance visual acuity (CDVA) after surgery and 50% gained one or more lines (Figure 6). To date, with up to 12 months of follow-up, none of our eyes lost any lines. Visual recovery was very fast, and corrections have been stable up to 4 years.

We achieved excellent visual outcomes in all ranges of myopic correction. To demonstrate this, we subdivided our eyes into three groups: 189 low myopes, with 0 to –2.75 D of correction; 255 moderate myopes, who had –3 to –5.75 D of correction; and 135 high myopes, who had –6 to –10 D of correction.

The results between the three groups were comparable: around 94% of low myopes, more than 92% of moderate myopes, and about 85% of high myopes were within ±0.5 D of target. There were some outliers in the higher ranges, but we had no loss of lines in the long term.

How does the Triple-A compare with the ASA profile from MEL 80? In terms of predictability, the ASA had an accuracy of about 85% within ±0.5 D, compared with the 92% we achieved with the Triple-A. In terms of safety, a few eyes lost 1 line of vision at up to 1 year of follow-up with the ASA profile, while no eyes lost any lines with the Triple-A profile.

We have also used the Triple-A profile to treat 224 eyes with hyperopia and mixed astigmatism. These eyes had a mean sphere of +2.07±1.3 D (range 0.5 to 7.5 D) and a mean cylinder of –2.51±1.88 D (range up to –7.5 D). In these eyes, we set our flap to a mean diameter of 8.7 mm and mean thickness of 115 µm.

In this group of patients, the outcomes are not as perfect as those achieved in the myopic group, but are amazing anyway. About 70% of eyes were within ±0.5 D of target at 1 month, with the number increasing to about 80% at 1 year. Again, we corrected astigmatism down to less than 0.5 D.

In terms of safety, 60% had unchanged CDVA, but at the end of the day, while some eyes lost up to 1 line, more eyes gained 1 to 2 lines of vision. Visual recovery times are as fast as with myopic corrections, but hyperopic corrections are somewhat less stable, with continuous regression that breaks even at about 3 to 6 months, followed by a very low rate of regression.

We looked at the topographies of eyes in both the myopic and hyperopic groups and in each case we found large, very well-centered optical zones.

Finally, we analyzed spherical aberrations, measuring them preoperatively and at 3 months postop. Cumulatively, there was no significant change in spherical aberrations, from –0.41 preop to –0.46 postop, although there was a mild increase in the higher diopter ranges (–0.52 for the 3 to 6 D range, –0.61 for the 6 to 9 D range). In any case, the spherical aberrations were not as advanced as we saw with the ASA profile.

Since we started using the Triple-A profile, I have had no need to return to the ASA profile. The Triple-A profile truly is one profile for the full range of corrections.

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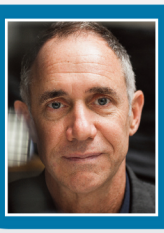
Optimizing vision with aspheric ablations



by Patrick Versace, MD

Our goal as surgeons is to do what we can to make laser surgery as safe and pain-free as possible. In the end, the excimer laser is nothing more than a scalpel that we use to reshape the cornea. The quality of what we achieve is determined by what kind of shape we put onto the cornea, and no matter how we reshape it, we have to achieve good refractive outcomes.

The concept of asphericity or controlling higher order aberrations is much less important than getting good refractive outcomes.

With the MEL 80 excimer laser (Carl Zeiss Meditec, Jena, Germany), the original FDA LASIK data for myopia shows that we are up in the range of 92.7% of patients getting uncorrected visual acuities (UCVAs) of 6/6. In addition, the platform—which is now complemented by the new MEL 90—was very accurate.

Spherical aberration is something that we've worked with in refractive surgery for a long time. And it's worth considering, what should be the target for spherical aberration?

First, we should avoid inducing spherical aberration. This means using an aspheric ablation profile, sometimes called wavefront-optimized.

Second, we should correct preexisting spherical aberration, particularly for patients with higher order aberrations. In these cases, we need to do wavefront-guided or topography-guided procedures.

Third, we may consider controlling the induction of spherical aberration. We may deliberately increase spherical aberration in a very controlled manner to achieve predefined outcomes.

Specifically, this is our approach to compensating for presbyopia, by performing presbyLASIK, using spherical aberrations to increase depth of focus. Here we use an ablation profile such as PRESBYOND Laser Blended Vision (Carl Zeiss Meditec).

Controlled induction of spherical aberration

It is not straightforward whether spherical aberration is good for vision. There are many papers looking at the functional benefit of treating and correcting spherical aberration, but it's very difficult to draw comparisons because studies use different designs and metrics. However, overall, I would conclude from the literature that in patients with less than 0.3 µm of higher order root mean square (HORMS) aberrations—i.e., less than 0.3 HORMS value—wavefront-guided treatments will make the HORMS value worse.[1,2,3]

Thus, if a patient has less than 0.3 HORMS, I would not even consider a wavefront-guided treatment—and that means that almost 100% of my treatments are not wavefront-guided.

In that case, does spherical aberration really matter? Again, it is difficult to demonstrate the functional benefit of aspheric treatments compared with old-fashioned ablations, in part because it is difficult to distinguish the benefit of using aspheric ablations from simply using modern laser platforms that are much better than what we had before. For instance, we

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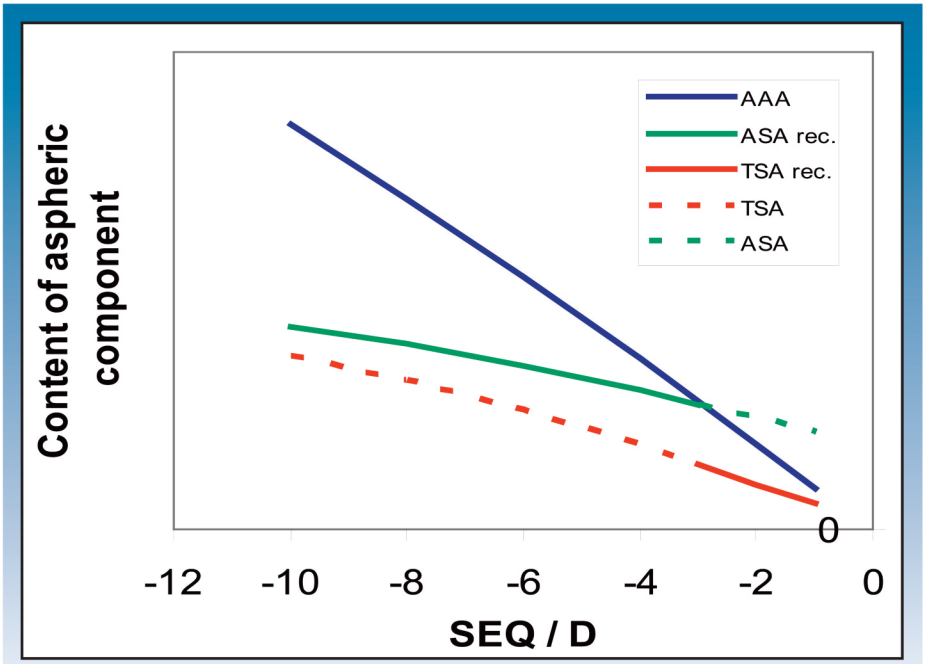

Figure 7. Linear compensation for spherical aberration

have moved to small spot laser profiles with very good tracking and very reliable ablation placement. These are the things that make outcomes better.

In addition, there is the concept that higher order aberrations do not act individually; instead, they interact. Treating third-order aberrations impacts second-order aberrations, and treating fourth-order aberrations impacts some third- and second-order aberrations; thus, if you try and correct some higher order aberrations, you can make it worse because you actually cause other aberrations.

So is there a reason for controlling induction of spherical aberration, using spherical aberrations to increase depth of focus as we do in treatments of presbyopic patients using PRESBYOND Laser Blended Vision?

Published literature has shown that induced negative spherical aberration improves depth of focus[4]; that accommodation amplitude is directly related to increasing negative spherical aberration[5]; and that adaptive optics demonstrates expanded depth of focus with increased spherical aberration.[6]

Using these known aspects of spherical aberration, ZEISS developed the PRESBYOND Laser Blended Vision, which combines a small amount of myopia in one eye with increased depth of focus through spherical aberration in both eyes. This has the added benefit over old-fashioned monovision of better maintaining stereoacuity. Also, modulating spherical aberration results in better distance and near than you would otherwise expect in a patient with –1.25 D of myopia.

Our experience with PRESBYOND is that patients are very satisfied, more so than multifocal implant patients. They do not experience glare and halo, a side effect observed with diffractive multifocal lenses.

Avoiding induction of spherical aberration

LASIK with a conventional LASIK profile increases spherical aberrations by a factor of 4. The amount of preoperative spherical aberration determines the significance of this effect. If you start with a tiny amount, the postoperative spherical aberration may remain insignificant. However, for patients who have a lot of spherical aberration to begin with, it will probably matter at the end of surgery.

The ZEISS Triple-A profile aims to give better control of spherical aberration. With this profile, there is a linear correlation between the compensation for spherical aberration and the refractive error being treated (Figure 7).

It is also an universal profile, which can be used to replace many of the older profiles.

What I like about this profile is that it is easy to use, is kinder in terms of ablation depth, gives good refractive predictability, improves control of astigmatism, provides better control of asphericity, and is universal.

Thus, with my ZEISS refractive laser devices, I now have the benefit not only of using PRESBYOND Laser Blended Vision for my presbyopic ablations, but also performing ablation with the Triple-A profile for the full range of corrections.

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