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Tomorrow's vision today: Asia-Pacific Refractive Laser Symposium 2014

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SMILE: The 3rd Generation Laser Vision Correction

Introducing a paradigm shift in the way we perform refractive surgery

In the relatively brief span of 30 years, refractive surgery technology has evolved through 3 whole generations of procedures: PRK, LASIK, and now SMILE.

Each procedure has its own particular set of pros and cons that makes it suited to particular circumstances, conditions, and patient populations. Among these, it is LASIK that has to date dominated the field of refractive surgery. This is especially true following the introduction of the femtosecond laser as a substitute for the mechanical microkeratome. LASIK and this upgraded, completely "bladeless" version called Femto-LASIK have come to provide in the minds of prospective patients the gold standard for refractive surgical correction. However, though LASIK remains—and, for the foreseeable future, probably will remain—the first choice for a particular set of patients, it is not without its limitations. Speaking at the Asia-Pacific Refractive Laser Symposium held in Busan last November, **Kimiya Shimizu, MD**, professor and chairman, Department of Ophthalmology, Kitasato University, School of Medicine, Kanagawa Prefecture, Japan, described his experience with the procedure.

"I started LASIK in 1997," Dr. Shimizu said. "We did a long follow-up study and there were many complications."

Most of these side effects were flap-related, and came in the form of infections, diffuse lamellar keratitis, epithelial ingrowth, irregular astigmatism, and, most commonly, dry eye. There were also other, non-flap-related side effects such as regression and complicated IOL power calculation.

In his follow-up study on 55 LASIK eyes from 1997 to 2008, he found 78% needed eye drops for dry eye about 5 years after surgery, a significant rise from only 18% requiring eye drops preop. Tear breakup time (TBUT) was reduced from a preop average of 9.1 seconds to 4.2 seconds postop.

Dr. Shimizu also found filamentous keratitis in LASIK eyes 2 years after the procedure, and superficial punctate keratitis (SPK) in 1 case 12 years after surgery.

In 2008, these complications led Dr. Shimizu to start looking for other options.

Finally, in September 2011, SMILE arrived. "In order to avoid complications caused by flap-making surgery, I shifted to flapless surgery, SMILE," Dr. Shimizu said.

SMILE experience

Dr. Shimizu was among the first in a growing pool of pioneers who over the brief existence of the procedure have come to see the potential of SMILE surgery—and see that potential realized.

Talking about his own experience with the procedure, **Osama Ibrahim, MD**, professor of ophthalmology, Department of Ophthalmology, Faculty of Medicine, Alexandria University, Egypt, said he and his colleagues have performed SMILE on 4,263 eyes. Because they started using the laser in earlier clinical trials, their data includes a wide range of spherical equivalents, from –1.25 to –14.00 D (MR SEQ –5.92±2.13 D); a wide range of sphere, from –0.25 to –14.00 D (MR sphere –5.28±2.06 D); and cylinder of up to –6.00 D (MR cyl –1.26±1.04 D).

Dr. Ibrahim said he and his colleagues were able to achieve "marvelous" results with SMILE: residual error was less than 0.25 D at 1 week in 84%, and 95% were within ±1.00 D of attempted MR SEQ (Figure 1).

The outcomes remained stable, "showing the same exact pattern" even in cases with more than 1 year of follow up, Dr. Ibrahim said. This stability, he said, is the "striking factor"—the result you get after 1 month "is exactly what you get" even beyond 1 year of follow up.

continued on page 2

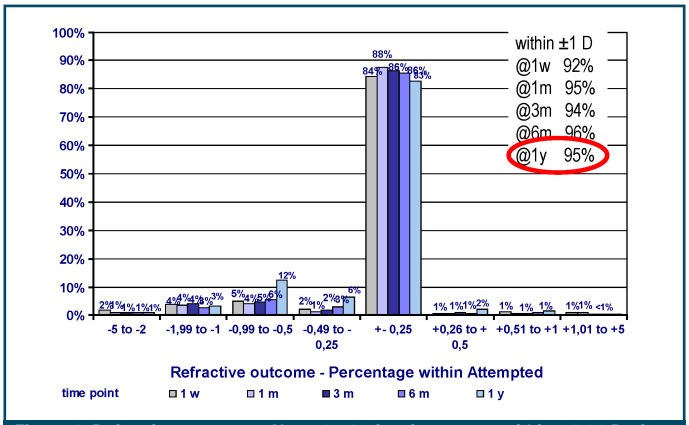

Figure 1. Refractive outcomes: About 95% of patients were within ±1.00 D of attempted MR SEQ (N=2,876).

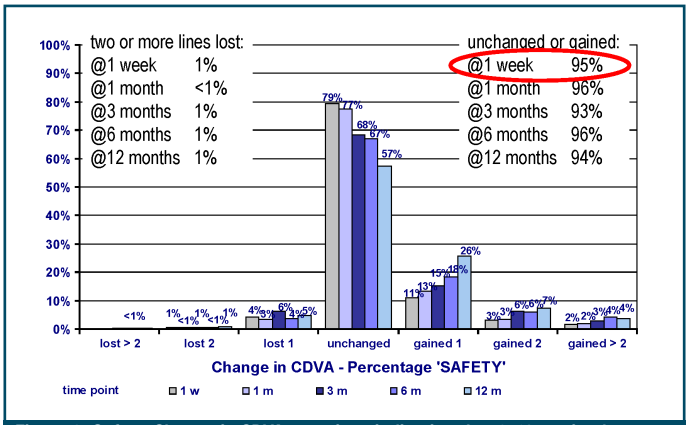

Figure 2. Safety: Change in CDVA over time, indicating that 95% retained or gained their best CDVA (N=2,876).

Source: Osama Ibrahim, MD

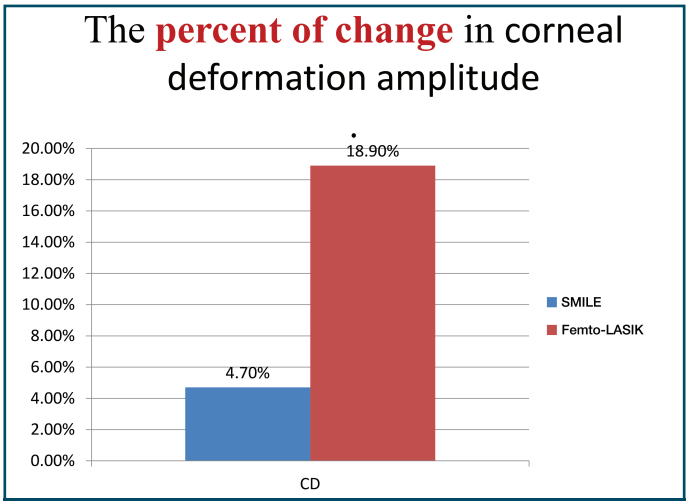

Figure 3. Myopic regression, SMILE vs. LASIK

Source: Kimiya Shimizu, MD

This stability is also seen across the entire range of patients, in both low myopic and high myopic groups. "We don't see what we see in LASIK, the regression in high myopic patients," he said.

In addition to stability, safety—the assurance that the procedure would not lead to reduced or otherwise compromised vision—is of great import. While initially some of Dr. Ibrahim's patients lost 1 or 2 lines of best corrected distance visual acuity (CDVA), he said this was in the beginning, when the procedure was still being refined. Moreover, patients tended to improve over time. "The nice thing is that as time goes by these patients regained their best spectacle-corrected vision," Dr. Ibrahim said. More importantly, 95% retained or gained best CDVA (Figure 2).

Again, the safety pattern is the same in both low myopic and high myopic groups. "You even see more patients gaining lines of best spectacle-corrected vision in the high myopic group," he said.

SMILE vs. LASIK

Going back to Dr. Shimizu's experience, he and his colleagues compared SMILE with LASIK at their institution, compiling data from 30 eyes in 19 patients who underwent SMILE with 30 eyes in 22 who underwent LASIK. Patient characteristics including age, MRSE, mean K, and CCT were comparable across all eyes.

On the very first day, the difference was visually striking—SMILE eyes, Dr. Shimizu said, were "beautiful"; in contrast, microfolds were observed in LASIK eyes, probably resulting from the mechanical folding over of the flap during lift.

The big difference in performance was in terms of stability. "The regression rate of LASIK is about 10%," Dr. Shimizu said. This regression is most evident at 2 years, and his data shows most of the regression occurring after the first year postop in LASIK patients.

In contrast, over the same time period, "SMILE is very stable, no regression" (Figure 3).

"This refractive stability is one of the big advantages of SMILE," he said.

One year later, the SMILE eyes continued to look clearer than LASIK eyes, visibly indicating the health of the ocular surface.

This, he said, is the other advantage of SMILE, having to do with the ocular surface up to and including the tear film, with a big difference in TBUT.

TBUT, he said, "did not decrease in SMILE," but dropped from a mean of 5.1 seconds to 2.9 seconds at 1 year in the LASIK group. The change in TBUT was significantly different between the 2 groups beginning at 1 month after surgery ($P<0.05$).

What causes these differences? To begin with, when comparing SMILE with LASIK, it's important to remember that "we are comparing apples and oranges," Dr. Ibrahim said. "They are 2 completely different concepts."

The difference in underlying concept between the 2 procedures manifests in structurally different corneas postop, and provides SMILE with the advantages already identified by Dr. Shimizu. The reduced incidence of dry eye, for instance, is the result of reduced nerve damage: With SMILE, surgeons cut fewer nerves in the superficial part of the cornea, Dr. Ibrahim said.

Looking for evidence of this difference, Dr. Shimizu and his colleagues studied the sub-basal corneal nerve plexuses of postop eyes by confocal specular microscopy.

Flap-making in LASIK, Dr. Shimizu said, resulted in a 70% decrease in nerve fiber density; in contrast, SMILE eyes lost only 30%.

Therefore, he said, "SMILE is the less invasive procedure."

Corneal biomechanics

Dr. Ibrahim and his colleagues further compared the effects of SMILE with the effects of Femto-LASIK on corneal biomechanics. Using a Corvis ST non-contact tonometer (Oculus, Wetzlar, Germany), they found a significant increase in corneal deformation amplitude following Femto-LASIK—18.9±3% against 4.7±2% in SMILE.

The cornea is simply biomechanically stronger with SMILE, according to **Rohit Shetty, MD**, senior consultant and vice chairman, Narayana Nethralaya, Bangalore, India. Most of the cornea's structural integrity is contained in the anterior third—the portion of the cornea left wholly intact by SMILE, but not by flap-making LASIK.

Dr. Shetty also cited mathematical algorithmic analysis published in the *Journal of Refractive Surgery* that showed "considerably higher" postop tensile strength with SMILE than with either LASIK or PRK. The authors concluded that this means SMILE should be able to correct higher levels of myopia.[1]

Tear film optics

Looking past the corneal tissue—or immediately above it—Dr. Shetty analyzed the tear film itself—from quantifying the lipid layer, studying microimplants, to trying to see how much tears affect quality of vision—to see if he could find an answer to whether, how, and why SMILE causes less dry eye.

First, looking at refractive surgery and dry eye in general, Dr. Shetty looked at the meibomian glands. Meibography is still not part of the routine examination. And yet, through this procedure, he found that 20–22% of chronic contact lens wearers have altered glands.

"These are the patients, if you do a flap or a PRK, who are going to come back to us with repeated dry eye we didn't see at presentation, where the drops used can go up for more than 5 years," Dr. Shetty said.

continued on page 3

continued from page 2

Another factor not typically assessed is blinking—30–32% of patients don't blink properly; these patients also have issues with dry eye.

Considering these factors, just how much does the effect of surgery on tears contribute to quality of vision, particularly after SMILE? Using an HD analyzer, Dr. Shetty looked at the quality of vision after every blink, as tear film breakup takes place. What he found in post-SMILE patients is that, throughout the whole process, the tear film does not show change.

"This is one thing that answered my question, does it really cause less dry eye, and if it's causing less dry eye, is it giving [patients] the quality of vision that is important," he said. "The same patients, when I come back and look at the other eye, quality of vision is brilliant because [with] femtosecond lasers, especially in a learning surgeon, when you're not manipulating much, your tear film is more or less the same."

As previously demonstrated by Dr. Shimizu, neurotropic factors also play a role, creating in addition to dry eye unusual symptoms such as neuralgia. Aberrant regions can occur when nerve fibers do not regenerate properly after flap cutting with LASIK. "Changes occur when a lot of nerve fibers are regenerating, and one of the things that happens is nerve fibers behave differently when they regenerate," Dr. Shetty said. For patients, these changes translate into unusual symptoms such as incapacitating eye pain.

Comparing the nerve fibers at the Bowman's and subepithelial nerve plexuses as well as at ablation depth between a LASIK eye and a SMILE eye shows a significant difference, with the corneal nerves in the SMILE eye remaining intact.

Cumulative evidence

Today, Drs. Shimizu, Ibrahim, and Shetty are joined by more than 400 surgeons in more than 230 centers in 38 countries trained to perform SMILE surgery. The cumulative evidence demonstrates comparable efficacy, great accuracy and predictability, but with greater stability and fewer complications than LASIK.

SMILE has now been performed on more than 125,000 eyes worldwide, and according to internal company sources, will soon have been performed in more than 200,000 eyes.[2] A U.S. FDA clinical trial is ongoing, and there are currently more than 110 peer-reviewed papers published on the procedure. As data accumulates and surgeons gain and continue to build on experience with the procedure around the world, SMILE surgery is proving to be a worthy successor to LASIK, thus gaining traction as the 3rd generation of laser vision correction.

References

1. Reinstein DZ, Archer TJ, Randleman JB. Mathematical model to compare the relative tensile strength of the cornea after PRK, LASIK, and small incision lenticule extraction. *J Refract Surg*. 2013;29(7):454–460.
2. Data on file.

'Serious business': SMILE in practice

On positioning SMILE as USP, premium procedure

Having stated the theoretical and clinical advantages of SMILE, incorporating the procedure into a practice, said **Mahipal Sachdev, MD**, chairman and medical director, Centre for Sight, New Delhi, should be considered "serious business."

"I think SMILE is a revolution that one should be a part of if we are really considering laser vision correction," Dr. Sachdev said. "If you look at laser vision correction or buying this SMILE technology as just a hobby, then I think you are at the wrong place. It has to be taken as serious business, and you have to look at the return on capital as to how do we break even and make profits."

Speaking at the Asia-Pacific Refractive Laser Symposium, Dr. Sachdev discussed practice management, introducing SMILE and making it work in a refractive surgery practice today. He addressed concerns—particularly a reluctance to adopt new technology and procedures—refractive surgeons may have developed over the last decade.

While early on Baby Boomers rushed to have LASIK surgery, numerous factors over the last decade—including various reports on adverse events that were further sensationalized on the Internet, the economic downturn, and a price war that trivialized refractive surgery in general—resulted in a dip in the number of patients seeking LASIK.

However, Dr. Sachdev believes this dip was not a question of low penetration indicating patients were dissatisfied. Instead, he believes the dip was the result of contemporary economic issues and was not indicative of long-term market saturation.

More indicative of the state of refractive surgery is the consumer confidence index (CCI), which he said correlates well with the number of patients going for refractive procedures. The CCI now appears to be on the rise, particularly in economies such as India. "That is where the discretionary expenses like refractive surgery would tend to start to grow," Dr. Sachdev said.

"Now are you today poised and ready to lead? Because there is a crowd and you need to stand out," he said. "You need to be different from the others, and you need to offer the most advanced technology to differentiate yourself. That would be your USP [unique selling proposition]."

A decade ago, refractive surgeons began pushing "bladeless" surgery with femtosecond LASIK. With SMILE, Dr. Sachdev said, surgeons can now offer not only "bladeless" but also "flapless" technology.

As such, it is important for surgeons to offer SMILE as a premium product. "You should not be ashamed about talking about the price and that it is a premium procedure from a premium company, and it comes at a cost," Dr. Sachdev said.

MEL 90: Gold standard excimer laser

Key hardware and software features

LASIK continues to have an important role in refractive surgery clinics. For this procedure, the MEL 90 (Carl Zeiss Meditec, Jena, Germany) is, "far and away, the gold standard of the excimer lasers that are available to us as surgeons in the world today," said **Glenn Carp, MD**, refractive surgeon, London Vision Clinic, London. Compared to other excimer lasers on the market, "it's the usability of these machines that I think makes the biggest difference," he said.

Dr. Carp discussed the MEL 90's key features at the Asia-Pacific Refractive Laser Symposium held in Busan last November.

The first key feature of the MEL 90 is it keeps 90% of the beam as it passes through the laser in vacuum. This minimizes the attenuation of the beam, while also providing servicing advantages as most of the MEL 90's mirrors are also kept in vacuum.

The beam itself has a Gaussian beam cross-section that is created through a patented beam shaper. "What this translates to is that the laser that's presented to the surface of the stroma is flat in its orientation, which ensures that most of the energy is transmitted to the surface of the cornea and not lost," Dr. Carp said.

The MEL 90 also allows surgeons to toggle between 250-Hz and 500-Hz speeds. "The 250-Hz mode is still of use and that's why ZEISS elected to keep it," Dr. Carp said. "It's very good for your surface procedures—LASEK, PRK, PTKs—as the corneal stroma acts as a heat sink, and in this way using a low frequency you get less heat build up in those types of procedures where we know heat is not always desirable."

Meanwhile, in the 500-Hz mode, the MEL 90 delivers a continuous (as opposed to oscillating, as used on other "superfast" laser platforms) 500-Hz speed that, combined with the ZEISS laser's precise flying spot pattern, allows high-speed performance while minimizing heat induction by allowing the stroma to act as a heat sink.

Finally, on the hardware side, the MEL 90 features plume homogenization. Whereas most other lasers rely on extracting the little plumes of particles from each laser pulse as a direct consequence of their production, the MEL 90 homogenizes the plume and counteracts it with an energy differential, leading to more consistent energy transmission to the stromal bed.

On the software side, the MEL 90 provides an update on the MEL 80's tissue sparing ablation (TSA) and aspheric ablation (ASA) profiles.

The advanced ablation algorithm (Triple-A) profile, Dr. Carp said, is a wavefront-optimized profile that has the advantages of shallower ablation depth and enhanced peripheral biomechanical compensation.

Dr. Carp and his colleagues found that these features allowed the MEL 90 to achieve a statistically significant improvement in terms of attempted versus achieved spherical equivalent refraction and contrast sensitivity in comparison with previous nomograms.

The MEL 90 otherwise compared favorably in terms of accuracy, efficacy and safety.

Taking a closer look at the (Triple-A) profile, **Patrick Versace, MD**, partner and medical director, Vision Eye Institute, Bondi Junction, Australia, examined the effect of excimer laser refractive surgery on spherical aberration.

"When we did our first laser treatments, we were increasing spherical aberration significantly," Dr. Versace said. "We were multiplying it by a factor of four … that explained a lot of the poor quality vision particularly in low light."

The Triple-A profile, he said, now standard on the MEL 90 laser, is designed for linear compensation of spherical aberration. "Regardless of the refractive error that we're treating, the compensation for spherical aberration in theory is appropriate as compared with the earlier profiles."

Echoing Dr. Carp's comments, Dr. Versace said the first thing he looks for in a profile—the nomogram for a laser—is ease of use. He also looks for reduced ablation depth, refractive predictability, astigmatic predictability, control of spherical aberration, and universality.

Using the Triple-A profile, the MEL 90 removes less tissue; refractive outcomes are stable over time; predictability is very good across a wide range of refractive error, including hyperopia; and the profile provides tighter control of astigmatism outcomes than the older ASA profile.

Comparing the Triple-A profile with the ASA profile in terms of spherical aberration control in a matched control study, Dr. Versace found a statistically significant improvement in the control of spherical aberration in low myopes (p=0.03).

For high myopes, there was an unexpected statistically significant improvement in the control of coma, although the improvement in the control of spherical aberration in this group did not reach statistical significance.

In addition, the Triple-A profile is universal, providing one profile across a range of refractive errors, obviating the need to select the TSA or ASA profiles.

The Triple-A profile, however, only describes one approach to spherical aberration. The MEL 90 allows another: controlled induction of spherical aberration.

This, believes Dr. Carp, is what sets ZEISS's MEL 80 and MEL 90 apart from other lasers: the ability to create blended vision using the PRESBYOND Laser Blended Vision profile with ZEISS's CRS-Master planning station. With PRESBYOND, controlled induction of spherical aberration is combined with a small amount of monovision to treat presbyopia by increasing depth of focus.

PRESBYOND completes ZEISS's refractive laser correction repertoire, providing an effective means for restoring range of vision to presbyopes.

This is the first of 3 *EyeWorld Asia-Pacific* supplements focusing on the latest laser refractive surgery technologies from ZEISS, as presented at ZEISS's Asia-Pacific Refractive Laser Symposium held in Busan from 28 to 30 November 2014. Learn more about SMILE, PRESBYOND, and practice management in the next issue.

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