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SMILE for Myopic Astigmatism: Early Experience in the USA and International Advances

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Abstract

Purpose of Review In this article, we review the early experience with small incision lenticule extraction (SMILE) in the USA as well as recent international data. We address long-term experience, new techniques, optimization of settings, corneal biomechanics, and comparison with other refractive surgical procedures.

Recent Findings Despite promising early experience, US refractive surgeons have adopted the SMILE procedure slowly, owing in part to limitations on energy settings that have impacted early visual recovery. Outside of the USA, advances in parameters and techniques have driven improved early and long-term outcomes, with the result of increasing adoption. Although there remains debate, there is evidence for parity with FS-LASIK in visual outcomes, as well as advantages to SMILE in post-operative dry eye, spherical aberration induction, and biomechanical stability.

Summary SMILE is a safe and effective procedure with promising advantages over other techniques and increasing usership worldwide. Continued improvements in energy optimization, nomogram development, and surgical technique allow for improved outcomes over early iterations of SMILE.

Keywords SMILE · Small incision lenticule extraction · Femtosecond laser · Myopic astigmatism · Refractive surgery

Introduction

The first report of small incision lenticule extraction (SMILE) in 2008 described a novel refractive surgery procedure using a single femtosecond laser for the treatment of myopia [1].

Since that time, SMILE has become increasingly popular throughout the world, with over 3 million procedures performed as of June 2020 and a current global marketshare of 17% [2]. Factors supporting its growth have been: its minimally-invasive approach, which appeals to refractive surgery patients; a reduced impact on the ocular surface compared with other laser refractive procedures [3]; and its potentially lower corneal biomechanical effects compared with other laser refractive procedures [4].

Factors limiting its growth are: the significant reliance of early post-operative visual acuities on energy setting optimization, which can vary between lasers; a steep initial learning curve; and the capital expenditure required to purchase the VisuMax FS laser (Carl Zeiss Meditec, Jena, Germany), which is currently the only commercially-available laser capable of performing SMILE. In addition, the LASIK procedure, which treats similar patients, is very well established, is widely available, and produces outstanding visual acuity results, even during the immediate post-operative period.

SMILE: US Experience

Although many papers discuss the efficacy of SMILE in international markets [5–8], to date, only 4 studies describe experience with the procedure at centers in the USA. Initial approval for the correction of spherical myopia without astigmatism, with spot spacing limited to 3.0 μm, occurred in October 2016. Treatment for myopic astigmatism, together with a broader range

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of spot spacing up to 4.5 μm, was approved in March 2018. It is, therefore, useful to categorize reported US SMILE experience as before and after myopic astigmatism approval.

Earliest among the US papers is a single-site retrospective study of 41 eyes by Moshirfar et al. comparing 6-month SMILE data from 2017 to 2018 against FDA-reported LASIK outcomes from early generation (1999–2000) and more recent (2013–2016) trials [8]. This study was limited to spherical corrections, with untreated pre-operative cylinder up to 0.75D, and high energy density settings. This study yielded post-operative month (POM) 6 uncorrected distance visual acuity (UDVA) 20/20 or better in 74% of eyes and 20/40 or better in 98%, with a trend toward undercorrection and residual astigmatism in eyes that did not achieve target refraction. Notably, the residual astigmatism was expected, given the degree of pre-operative astigmatism that could not be treated. These eyes were not separated out and, consequently, adversely affected the reported outcomes. Notably, the report included the surgeons' first 100 cases, and found a statistically significant improvement in mean spherical equivalent (MSE) in the last 12 cases by comparison with the earliest 12. The authors noted that these early results, despite their limitations, were superior to those seen with LASIK at the same stage in its technological development, but did not achieve the same post-operative quality of vision as modern LASIK. The authors indicated that the ability to treat astigmatism and to operate at a lower energy density, among other future innovations, were likely to bring the two procedures to parity [9].

More recently, Sia et al. published a retrospective study comparing outcomes of SMILE, LASIK, and PRK for 563 eyes within a military population. As with Moshirfar et al., results reported were for sphere-only corrections with high energy density, with untreated astigmatism up to 0.5 D, as the updated parameters were not yet available. The group found that SMILE outcomes were superior in efficacy to PRK at POM1, although a higher proportion of PRK eyes achieved 20/20 at 3 months. Meanwhile, SMILE and LASIK achieved similar rates of UDVA 20/20 throughout the study period, but SMILE demonstrated greater predictability at 6 months, with 96.3% of SMILE and 83.8% of LASIK eyes achieving MSE within ±0.50 D of target ($p = 0.02$). The study authors also observed that, for the purposes of the military, healing time was equivalent for SMILE and LASIK, as LASIK patients are typically mandated 1 month leave to recover. SMILE recovery was, by comparison, more rapid than with PRK, whose mandated recovery time is 3 months [10].

Papers discussing the US experience with SMILE for myopic astigmatism have focused primarily on data from the second FDA trial. This trial resulted in the approval of cylinder correction up to 3.0 D, a smaller surface incision (reduced from 90° to 60°), and spot spacing up to 4.5 μm. However, while the second FDA study did examine a minority of eyes over a wider range of energy settings, the majority of eyes were treated using energy densities that are higher than what is currently utilized clinically throughout the world. In addition, it is important to note that no nomogram adjustments were allowed during either of the FDA studies.

Dishler et al. published a report of data from the pre-market FDA trial demonstrating excellent efficacy and refractive stability from 3 months through 12 months, with 89% of eyes achieving 20/20 or better, 95.3% of eyes within ± 0.5D of emmetropia, and 91.7% of eyes within ± 0.5 D of target cylinder. While astigmatism outcomes were excellent overall, there was a trend toward undercorrection in high astigmatism [11].

A 2019 article by Schallhorn et al. compared the same FDA SMILE data for myopic astigmatism against the equivalent studies for topography-guided (TPG) LASIK and wavefront-guided (WFG) LASIK, concluding outcomes were comparable between the 3 procedures. SMILE demonstrated delayed recovery—with 65.8% reaching 20/20 at 1 month, 82.2% at 3 months and 89% at 1 year—which the study authors attribute to interface irregularity from high energy deposition, observing that newer innovations in energy density may reduce this effect. Notably, at 6 months there was no statistically-significant difference between the rate of eyes achieving UDVA of 20/20 or better among the 3 groups. Moreover, there was no statistically-significant difference in efficacy or stability of astigmatic correction or in the rate of patients within ± 0.50 D of emmetropia between the SMILE and TPG-LASIK, whereas WFG-LASIK underperformed both SMILE and TPG-LASIK with regard to predictability, residual astigmatism, and refractive stability [12].

A manuscript submitted for publication by DRH and colleagues is the first to compare early post-operative SMILE results in eyes treated after the approval of myopic astigmatism correction and expanded energy settings with those treated prior to the approval (i.e., higher energy) and with results from wavefront-optimized (WO) LASIK [13•]. Of note, even with the wider spot settings, the lowest spot energy approved in the USA remains 125 nJ, which is higher than what is currently used clinically outside the USA (i.e., 110–115 nJ).

The study is comprised of eyes from a single site in the USA treated by a single surgeon (DRH) using SMILE and WO LASIK. DRH found that SMILE patients whose surgeries were performed with low energy density (LE) had significantly better POD1 vision (20/19.86) compared with high energy density (HE) patients (20/27.67) ($p < 0.001$). Moreover, the mean UDVA on POD1 for the LE-SMILE group was equivalent to that of the WO LASIK group (20/19.50) ($p = 0.498$). Importantly, the percent of patients with UDVA 20/20 or better on POD1 was equivalent when comparing the LE-SMILE group to the WO LASIK group (Fig. 1). Furthermore, induced higher-order aberrations (HOAs) were equivalent between LE-SMILE and WO LASIK at post-operative month 1 (POM1), with the exception of induced

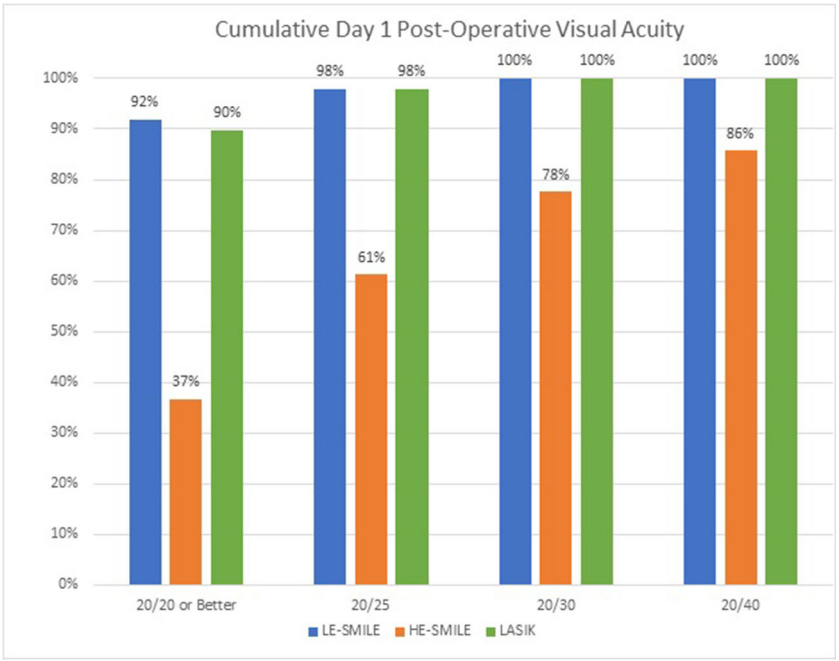

Fig. 1 Cumulative post-operative day 1 acuities (20/X): comparison of low-energy (LE) SMILE, high-energy (HE) SMILE, and WO LASIK

spherical aberration (SA) measured at a 6.0-mm OZ, which was lower in the LE-SMILE group (0.136 μm) compared with WO LASIK (0.186 μm, $p = 0.034$) [13•].

These improved outcomes underscore the importance of energy optimization when performing SMILE, a concept that is new to refractive surgeons, who are used to significant flexibility in femtosecond laser energy levels for LASIK flap formation. The appearance of the bubble pattern that results from laser application during the SMILE procedure can be useful to the surgeon both in anticipating the difficulty of dissection and to guide patient expectations for early post-operative visual acuity recovery (see Fig. 2). By comparison, the bubble pattern appearance following LASIK flap creation using FS laser is much less important with regard to flap dissection and typically has no impact on early post-operative visual acuity recovery [13•].

SMILE: Outside US Experience and Advances

Long-term Safety and Efficacy Data

Just over a decade after Sekundo et al. first published on SMILE [1], long-term data is emerging to evaluate the safety and efficacy of the procedure.

Notable among these recent publications is a study by Blum et al. presenting 10-year SMILE data for 56 eyes treated for myopia and myopic astigmatism. Within this cohort, 64.3% were within ± 0.50 D of target, and 82.1% were within ± 1.00 D at 10 years. UDVA remained stable from 1 month through 10 years, though a statistically-significant regression of 0.30 D was seen in MSE. Among the studied eyes, 29% gained at least 1 line of CDVA, 14% lost 1 line, and no eyes lost 2 or more lines, suggesting a favorable safety profile. No ectasia was observed within this cohort, and no patients

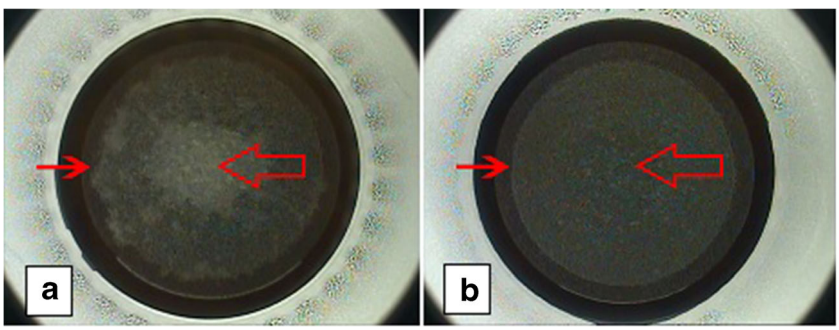

Fig. 2 Comparison of bubble pattern between HE-SMILE (a) and LE-SMILE (b). **a** HE-SMILE bubble pattern, manifesting significant opaque bubble layer (OBL) in the visual axis (open arrow) and fluffy irregularity at the lenticular side cut (small arrow). **b** LE-SMILE bubble pattern without OBL or (open arrow) and with a sharp lenticular border (small arrow), suggestive of easier dissection and better POD1 vision

required management of ocular surface disease after POM3. The authors report that, while some consistent undercorrection of astigmatism was noted in this long-term cohort, eyes enrolled in this study were treated early in the development of SMILE, before adjustments to the nomogram could have corrected for these findings. Results overall, therefore, may underrepresent what we may expect from SMILE as it is currently performed [14•].

The past two years have also seen several reports from Turkey and China presenting promising safety and stability data through 5 years [15–17].

In two 5-year Turkish studies of 54 and 24 SMILE eyes, respectively, 93% and 91% of patients remained within ±0.5 D of intended correction, with the majority of refractive error resulting from undercorrection of high myopia. Safety was also evaluated, with Agca et al. reporting 0 of 54 patients and Ayugin et al. reporting 1 eye in 24 (4%) losing a line of CDVA. In neither study did any patient lose 2 or more lines of CDVA [15, 16].

Chinese studies by Han et al. and Li et al. followed SMILE eyes for 3 and 5 years, respectively. Han et al. found 80% to be within ±0.5 D of attempted spherical equivalent at 3 years, whereas Li et al. observed 90% of eyes within ±0.50 D of target at 5 years. These studies found 2% and 9% of SMILE eyes losing 1 line of CDVA, with no eyes losing 2 or more lines [17, 18].

Ectasia Risk

With the smaller surface incision of SMILE compared against the larger flap incision with LASIK, it is thought that the anterior stromal biomechanical strength is relatively preserved, thus reducing the risk of ectasia development in topographically normal eyes. This hypothesis is supported by mathematical modeling [19]. As SMILE matures and longer-term follow-up is available, investigators are examining the clinical incidence of ectasia.

Ong et al. highlight that evaluation for ectasia risk from SMILE likely differs from established LASIK ectasia risk analysis and warrants further study. The paper presents a case series of 12 SMILE eyes for which percent tissue altered (PTA) or the Randleman Ectasia Risk Score System (ERSS) would have predicted a moderate-to-high risk of ectasia. Although PTA specificity data would have suggested that 8 of these eyes were at high risk for ectasia after LASIK, no eyes developed ectasia at 3 years [20].

Further supporting the relatively low risk of ectasia are a number of recent papers presenting SMILE treatment for myopia greater than 10.0 D. Follow-up ranged from 15 months to 3 years, with no ectasia reported in any of these studies [20–24]. A particularly interesting recent report by Elmassry et al. presents 3-year data for a series of 495 eyes of Egyptian patients with pre-operative myopia exceeding 10.0 D in which no eyes developed ectasia over the course of the study, despite the high incidence of keratoconus in the Middle Eastern population [24].

A review of the literature from 2011 to 2017 found 7 cases of ectasia after SMILE in 4 patients after 750,000 cases of SMILE had been performed worldwide. Two of the patients had abnormal topographies in both eyes, whereas only 1 eye of 1 patient with normal topography developed ectasia [25]. Since that time, there has been 1 case report of ectasia after SMILE. Shetty et al. reported this case of unilateral ectasia after myopic correction for 10.0 D. Pre-operative tangential and axial curvature maps were included, but no posterior elevation or epithelial maps were presented [26]. It is very important to understand that even though the ectasia risk appears to be lower with SMILE than LASIK for an equivalent amount of correction on the same cornea, the identification of normal pre-operative tomographic features is still requisite to avoiding the risk of ectasia with SMILE.

Further discussion of ectasia risk with SMILE compared with LASIK appears in the "SMILE vs. LASIK" section.

Other Adverse Events

Wang et al. recently published a retrospective analysis of adverse events in 6373 SMILE cases through post-operative year 1. The group observed a complication rate of 6.78%, of which nearly half (3.26%) represented punctate epithelial erosions in ocular surface disease, all successfully treated [26].

Diffuse lamellar keratitis (DLK) represented the next most common complication, with a rate of 2.17%, though the majority (91.3%) were stage 1, presenting only at the small incision, and all cases resolved with medical therapy. The remaining complications included interface haze, sterile infiltrates, interface debris, striae, corneal edema, and epithelial ingrowth, each of which was seen in fewer than 0.4% of patients, and all of which demonstrated CDVA of 20/20 or better by 12 months. No infectious keratitis, interface fluid syndrome, or ectasia were observed [27].

Surgical Parameters

Energy Density

Energy density is a proprietary parameter measuring total energy delivered during a SMILE procedure. It is derived from the amount of energy per pulse and the spacing between spots, with higher energy density corresponding to high spot energy and/or close spot spacing. Although each laser must be optimized individually, numerous studies have demonstrated that lower energy densities correlate with more-rapid visual recovery [13, 28–30].

A broad review of SMILE papers published in the past 36 months suggests that POD1 UDVA is improved with lower

vs. higher energy density settings (see Table 1). Surgeons must be cautious, however, not to drop spot energy so low as to cross the plasma threshold for cutting, which can lead to large areas of uncut tissue, subsequent traumatic dissection, and possible false plane creation.

Cap Thickness

Although currently restricted in the USA to 120 μm, the clinical and surgical implications of varying cap thickness have been studied internationally.

Lee et al. performed a multivariable linear regression of 1021 eyes with cap thicknesses ranging from 120 to 140 μm and found a significant relationship between cap thickness and lenticule thickness. Accounting for a 3% overcorrection for every additional 10-μm cap thickness, the group found that 99% of eyes achieved UDVA 20/20 or better and 100% were within ± 0.5 D of target spherical equivalent [36].

Nomogram Adjustment

Alongside adjustments for thicker caps, there has been increasing awareness of a discrepancy between achieved and programmed lenticule thicknesses for higher spherical myopia and astigmatic correction.

Numerous groups have investigated the difference between the estimated (VisuMax-predicted) and measured lenticule thickness. The studies consistently find that the measured lenticule thickness is thinner than the estimated thickness, leading to undercorrection. The average difference in thickness ranges from 11.9 to 15%, though figures as low as 5% have been reported [37•, 38, 39]. One study using AS-OCT demonstrated that this discrepancy is a function of stromal thickness, rather than epithelial remodeling alone [38].

In a linear regression model, Wu et al. observed that the degree of discrepancy can be correlated to the level of preoperative myopia, which is consistent with numerous anecdotal findings of undercorrection increasing with higher corrections. It stands to reason, therefore, that an individualized nomogram based on one's own imaging suite is best suited for correcting this source of error [37•]. As with any nomogram and any modality, it is important for each surgeon to track their refractive outcomes and create a personalized nomogram accordingly. The Wu study employs a 10% adjustment to the spherical attempted correction [37•], whereas DRH utilizes an 8% adjustment.

High astigmatism has also been observed to be consistently undercorrected, even with the FLEx procedure (femtosecond laser extraction: with a flap), which predates SMILE. In a retrospective series of 102 eyes, Pérez-Izquierdo observed that more-aggressive management was required for with-the-rule (WTR) astigmatism greater than 1.50 D, observing a 13% undercorrection of WTR astigmatism [40]. Similarly, DRH nomogram adds 15% to WTR astigmatic corrections and no additional correction for against the rule astigmatism. As with spherical nomograms, it is important for each surgeon to track their refractive outcomes and create a personalized nomogram accordingly.

Surgical Technique

With increased adoption of SMILE, recent literature has focused both on standardizing and refining the surgical technique.

Centration

Without eye registration technology, it is incumbent upon the SMILE surgeon to properly center the treatment on the visual axis. DRH captures a reference image from the tomography system showing the visual axis relative to the pupil. This image is then taken into the laser suite, inverted, and taped next

Table 1 Post-operative visual outcomes after SMILE with variable energy density: organized by decreasing energy density

Study	*N* (eyes)	Spot energy (nJ)	Spot spacing (μm)	UDVA POD1	% POD1 UDVA > 20/20	Follow-up (months)	Final UDVA	% Final UDVA > 20/20
Kind R et al. 2019 [31]	470	120–150	3.8–4.5	20/24.5	NR	3	20/19.1	75.3
Wu D et al. 2020 [32]	100	145	NR	20/20.9	NR	6	20/16.6	96
Ganesh S et al. 2019 [33]	100	140–150	4.5	20/16	100	1	20/14.7	NR
Ji YW et al. 2017 [28]	93	115–140	4.5	20/22.4	NR	3	20/15.2	NR
Wang H et al. 2020 [34]	242	140	NR	20/18.5	NR	1	20/15.9	NR
Chen P et al. 2019 [35]	622	120	NR	20/18.2	81	6	20/17	95
Weng S et al. 2020 [30]	39	105	3	20/15.9	95	3	20/15.2	100
	39	110	4.5	20/17.8	90	3	20/15.2	100
Ji YW et al. 2017 [28]	58	100–110	4.5	20/20	NR	3	20/15.5	NR

NR, not recorded

to the laser oculars. The surgeon reviews the reference image just prior to docking to ensure the position of the fixation target is at the proper location within the pupil.

Several recently-published reports demonstrate reduced HOAs with improved centration on the visual axis [41–43]. Lee et al. observed that an offset greater than 0.335 mm led to increased HOAs, and further observed that the degree of tolerated decentration can be predicted by the programmed OZ: as low as 0.1 mm for a 6.2-mm OZ or as high as 0.6 mm for 7.2mm [43].

Cyclotorsion Correction

There remains controversy as to the necessity and the efficacy of cyclotorsion correction in the management of astigmatism with SMILE.

Overall, observed cyclotorsion appears to be minimal, with average rotation reported to be 2.82–3.52°, and approximately 25.2–28.5% of patients displaying no rotation at all [43–45]. For this reason, some have argued that, with the head position well controlled, cyclotorsion management may be unnecessary [43].

However, with 9.2–22.7% of patients manifesting greater than 5° of cyclotorsion, others have found that confirming appropriate alignment prior to docking significantly reduces residual astigmatism [44, 45]. DRH marks the cornea for astigmatism above 1.25 D. Marking is performed at the slit lamp with an 8-mm slit beam oriented horizontally and the patient looking directly into the light. As the eyepiece reference reticle on the VisuMax will rotate when the oculars are adjusted for pupillary distance, care should be taken to adjust the reticle at the beginning of the surgical day or prior to switching surgeons, to ensure it is oriented with the horizontal exactly at 180°.

Suction Loss

Rates of suction loss among experienced SMILE surgeons are extremely low, with recent publications reporting and incidence of 0.22–0.5% [45, 46].

Management of suction loss varies depending on when the loss occurs during the case. The refractive effect of VisuMax SMILE is achieved at the posterior cut of the lenticule, which we will hereafter refer to as the "refractive cut." The peripheral 10% of the refractive cut does not affect refractive outcome. For this reason, Reinstein et al. recommend that suction loss at any point other than between 10 and 100% of the refractive cut may be may managed by simple redocking and completion of the procedure [47].

Among those patients for whom suction loss occurs during that 10–100% period, a variety of same-day treatments have been proposed, including conversion to LASIK via the CIRCLE procedure (not available in the USA) or to thin-flap LASIK with the flap above the cap cut interface [47].

Gas Bubble Escape Sign

The gas bubble escape (GBE) sign, introduced by Ganesh et al., represents a reassuring sign predictive of superior POD1 outcomes. This sign consists of the visible escape of bubbles upon accessing the lenticule plane, suggestive of a smooth and complete planar separation free of denser adhesions that would inhibit dissection (see online video, courtesy of Sri Ganesh, MD). In a review of 100 consecutive eyes, 68 of 68 eyes displaying the GBE sign presented with UDVA 20/16 or better on POD1 [33].

Interface Irrigation

Interface irrigation has recently been a subject of debate, with some suggesting an advantage to removing debris from the interface and others arguing that the procedure risks implanting foreign material or exacerbating stromal edema. With two recent prospective studies, one a randomized controlled trial, finding no significant difference in outcomes or adverse events between irrigation and non-irrigation, there is no clear indication to irrigate in the absence of a visible interface foreign body [31, 34].

However, loose epithelium originating from the posterior aspect of the small incision can be inadvertently introduced into the interface, later developing into a nest of thickening epithelium. Like epithelial ingrowth in LASIK, this development can cause irregular astigmatism and/or cap melting and may warrant removal. Consequently, an epithelial defect along the posterior edge of the incision without clear identification of the missing epithelium may represent an indication to irrigate the interface.

Retreatment

Though post-operative regression rates remain low (see "Long-term Safety and Efficacy Data"), several recent papers have examined retreatment techniques following SMILE.

Techniques for performing LASIK after SMILE are limited in the USA. While thin-flap LASIK after SMILE can technically be performed, Reinstein et al. advise to leave at least 18 μm between the cap depth and the new attempted flap thickness. Therefore, with the 120-μm cap mandated by the FDA, the LASIK flap should be 100 μm or less. Both the CIRCLE software (not available in the USA), which extends the SMILE cap to a LASIK flap with a larger optical zone, and thin-flap LASIK within the SMILE cap have shown excellent results for safety and efficacy [48, 49].

Surface ablation represents an alternative to a flap-based procedure for retreatment and is the technique that DRH has employed to date. While Siedlecki et al. observed that there remains a risk of post-operative haze following PRK for SMILE retreatment, long-term visual outcomes have been

demonstrated to be safe, effective, and equivalent to flap-based options [50, 51].

SMILE vs. LASIK

Numerous studies over the past 24 months have compared SMILE and LASIK on the basis of efficacy outcomes, with no difference in post-operative uncorrected visual acuity between the techniques [15–17, 20–22, 51, 52]. There are, however, other areas where studies indicate differences between SMILE and LASIK.

Dry Eye

Among the proposed advantages of a cap-based procedure is the relative sparing of the corneal nerve plexus and the resultant reduction in duration and severity of post-operative dry eye. A large meta-analysis of studies comparing SMILE and LASIK in more than 1100 eyes found tear break up time longer in SMILE compared with LASIK eyes at 1 and 6 months. The study also found that central corneal sensitivity was higher in SMILE compared with LASIK eyes at 1 week and 1, 3, and 6 months [53]. Recent studies have reinforced these findings and elucidated the pathophysiology behind the differences.

Speculation about nerve sparing was confirmed by Recchioni et al., who used in vivo confocal microscopy to characterize the health of the corneal nerve plexus 1 month after surgery, including fiber density, branch density, and fiber length following SMILE and LASIK. The group determined that SMILE had less effect on corneal nerve fiber parameters (23% reduction) compared with LASIK (75% reduction) [54]. An analysis of early post-operative protein expression observed that, while neurotrophic growth factors were reduced in both cohorts, SMILE eyes exhibited higher levels of these factors than LASIK eyes [55].

Although SMILE does not entirely eliminate signs and symptoms of dry eye, the effect appears to be limited and transient. Tear film abnormalities following SMILE are less severe than in post-LASIK eyes, with deflection from baseline not achieving significance in some studies and parameters returning to baseline at post-operative month 1 [54, 56, 57]. Similarly, the severity and duration of subjective dry eye symptoms are reduced in SMILE eyes. Whereas dry eye symptoms remain elevated after LASIK through the first post-operative month, several studies found no increase in reported dry eye symptoms among post-SMILE eyes at the same time period [54, 56, 58], and one report by Liu et al. observed relative symptomatic recovery, compared with LASIK, beginning as early as 4 h following surgery [59].

This finding is important not only for the innate effect of surface disease, but because patient-reported satisfaction with post-operative distance visual acuity negatively correlates with dry eye symptoms. To this end, Pietilä et al. observed that post-SMILE patients had significantly higher patient satisfaction rates, even in the face of worse visual acuity, when compared with LASIK [58]. Early on in DRHs experience, when astigmatism treatment with SMILE was unavailable, several patients were treated with LASIK for myopic astigmatism in one eye while the other eye, with minimal or no astigmatism, was treated with SMILE. Despite high energy levels at that period leading to worse POD1 vision, patients consistently preferred the SMILE to the LASIK eye, because the eye felt more comfortable.

FOZ and HOAs

The biomechanical implication of the SMILE technique also appears to confer an advantage in the size of the post-operative functional optical zone (FOZ) and, by extension, in the reduction of induced spherical aberration (SA) [22, 60, 61]. Hou et al. observed that, although both techniques result in a smaller FOZ than programmed, the decrease was greater in LASIK (32.7%) than in SMILE (17.4%) [61]. Furthermore, several studies reported a larger FOZ in SMILE vs. LASIK eyes, even with smaller programmed optical zones among SMILE eyes [22, 60].

The FOZ reduction was positively correlated with Q value [61], which may explain the consistent observation of decreased induction of SA following SMILE when compared with LASIK [17, 18, 22]. DRHs recent study of SMILE vs. LASIK found a smaller amount of corneal spherical aberration induction (0.136 μm) with SMILE compared with WO LASIK (0.186 μm) measured at 6.0 mm optical zone [13•].

The phenomenon of FOZ preservation was observed to be independent of change in epithelial thickness, and was proposed to stem from a relaxation of lamellar fibers, resulting in remodeling of the corneal stroma [60, 61]. Interestingly, Hou et al. observed that the FOZ was shorter vertically than horizontally in the SMILE cohort which, with all eyes having their surface cut at the 12 o'clock position, may represent a local effect of biomechanical relaxation near the SMILE incision [61].

Biomechanics and Ectasia Risk

Several studies have reviewed the biomechanical impact of SMILE compared with LASIK, with the presumption that greater disruption of the anterior stroma with flap formation would weaken the cornea relative to a small incision.

A clinically-driven biomechanical model by Seven et al. integrating Pentacam data for SMILE and LASIK patients predicts that LASIK causes a 56% reduction in fiber stiffness,

compared against a 7% change estimated for SMILE. Moreover, higher residual bed stresses and displacements are seen with LASIK, suggesting a relatively higher ectasia risk within that group [62].

Similarly, a meta-analysis by Guo et al. determined that ocular response analyzer (ORA) parameters corneal hysteresis (CH) and corneal resistance factor (CRF), which describe viscoelastic and resistance properties, respectively, reflect a relative biomechanical weakening in post-LASIK eyes as compared with SMILE, with this effect increasing beyond the 12-month time point [63].

The question of how these theoretical findings translate to actual risk of corneal ectasia is not a settled point, however. Evaluations of posterior corneal curvature showed no clear difference in the amount of posterior corneal change following SMILE or LASIK, though there was a trend toward increased change in LASIK eyes [64]. Moreover, although ORA data demonstrated a favorable biomechanical profile for SMILE, no difference between the two procedures was observed when comparing data from the Corvis ST [63, 65].

Overall, although some promising studies suggest increased stability following SMILE, no definitive guidelines can yet be established, and further study on relative biomechanical stability and ectasia risk in SMILE and LASIK eyes is warranted.

Conclusion

SMILE represents a promising laser vision correction modality, and, as other ophthalmic surgical device companies develop their versions of the technique and bring new equipment to market, further refinement of the technique is inevitable. With visual outcomes, safety, and predictability already comparable with LASIK, and with potential advantages in post-operative dry eye and biomechanical stability, we expect SMILE to become a standard technique in the armamentarium of the refractive surgeon for the treatment of myopic astigmatism.

Compliance with Ethical Standards

Conflict of Interest Jillian K. Chong declares no potential conflicts of interest.

D. Rex Hamilton received financial support for an Investigator Initiated Trial, the results of which are detailed in this manuscript. Dr. Hamilton is also a consultant for Carl Zeiss Meditec.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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