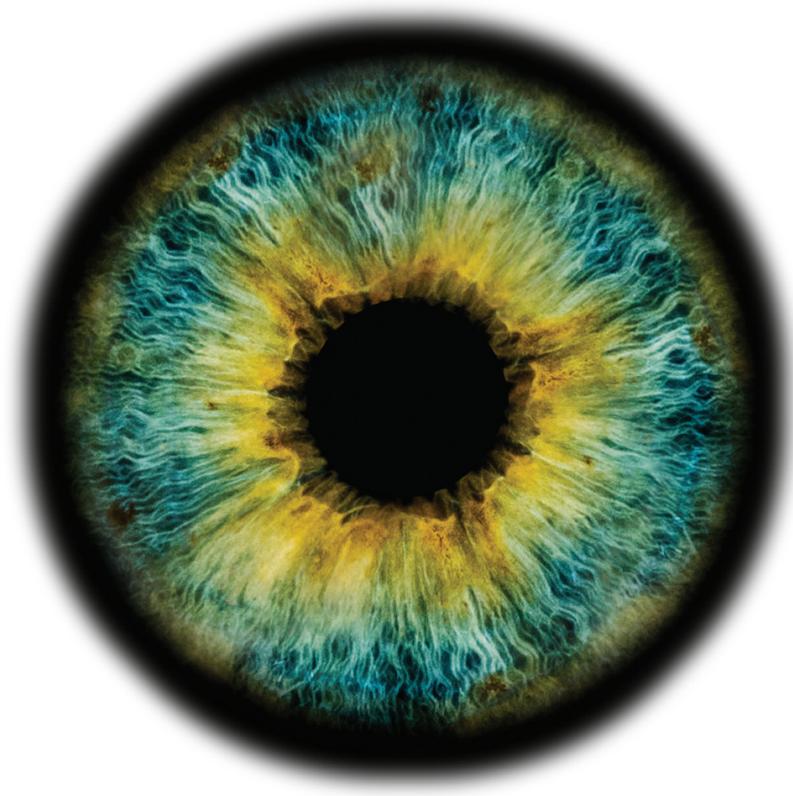
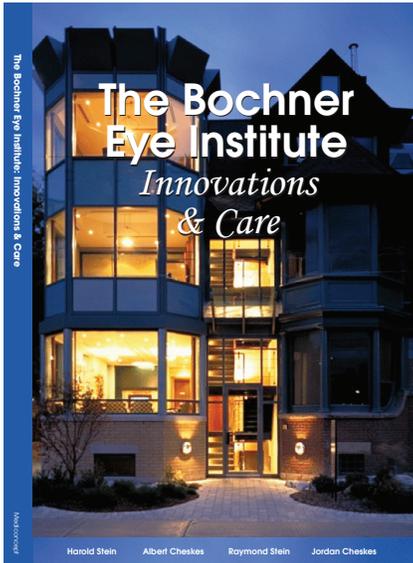


LASIK VS. SMILE



CLINICAL REVIEW AND REPORT FOR EYE CARE PROFESSIONALS

CLINICAL REVIEW AND REPORT FOR EYE CARE PROFESSIONALS



The Bochner Eye Institute has continuously been at the forefront of responsible innovations in eye care, as detailed in this autobiography written in 2015.

As one of the pioneers in refractive surgery in Canada, the Bochner Eye Institute has consistently invested in vision correction technology that has been proven to be safe and offers real clinical benefits over established technology.

Our criteria for consideration and adoption of new technology is as follows:

1. Does the new technology/procedure address a known issue with the current benchmark technique?
2. Does it deliver a better patient experience?
3. Does it deliver better / more consistent outcomes?
4. Is there an improvement in safety?
5. Is there a significant cost savings for the patient?

Over the past 3 years, we have been evaluating the Zeiss SMILE procedure. This is a procedure in which the Zeiss femtosecond laser is utilized to cut a lenticule of tissue within the cornea, which is then extracted through a small incision.

Our due diligence in evaluating this procedure has consisted of critically reviewing published scientific articles, and consulting with well-respected ophthalmologists around the world, some of whom have abandoned the procedure.

At this stage in the development of the SMILE procedure, we see no clinical advantages to offering it. In fact, we see some limitations.

1. SMILE does not provide better visual and refractive outcomes than LASIK. There are no clear differences between LASIK and SMILE in terms of predictability and efficacy. However, the safety profile is of concern. The reported loss of 2 lines of best corrected acuity in 1.5 to 2.5% is very high when compared to current LASIK outcomes.
2. There appears to be no significant difference in the incidence of dry eye between LASIK and SMILE.
3. We had hoped that as a flapless procedure, SMILE would offer faster recovery. The results so far indicate that the opposite is true. There is a faster visual recovery in the initial postoperative period with LASIK.
4. Other limitations of SMILE are indicated: inability to utilize Wavefront-guided and Topography-guided ablations, inability to treat hyperopia and mixed astigmatism, a higher risk of decentered ablations, and the need to use PRK if an enhancement is required.
5. When the SMILE procedure was developed it was thought that higher degrees of myopia could be treated. Theoretically, preserving some anterior corneal lamellae could enhance the tensile strength of the cornea and decrease the risk of ectasia. This appears to be false. The depth of treatment for a given refractive error is greater for SMILE than LASIK because the initial anterior cut is deeper. Surgeons performing SMILE must respect the limitations of high myopic ablations.

Based on our research, learning and firsthand experience to date, the perceived advantages of the SMILE procedure are simply not proven.

We hope that in the future our understanding of the true risks of ectasia with SMILE will be better understood, and that refinements can be made to improve the accuracy of centration, the return of visual acuity, and the ability to perform custom ablations.

We will continue to evaluate the development and evolution of this new procedure. Once its limitations have been addressed, and its advantages proven, we will then be in a position to recommend it to our colleagues and make it part of the Bochner Eye Institute's comprehensive eye care offering.

If you have questions, would like more information or like to discuss the SMILE procedure further, please contact us.



Catalys® Laser purchased by the Bochner Eye Institute in 2012, the first to be used in Canada for laser cataract surgery.

ADDENDUM:

Below please find our detailed research notes and clinical information that we have been able to compile.

Our evaluation has focused in the following areas:

- Rate of Return of Vision
- Predictability
- Dry Eye
- Customized Ablations
- Risk of Decentered Ablations
- Enhancement Procedures
- Ability to Treat Hyperopia

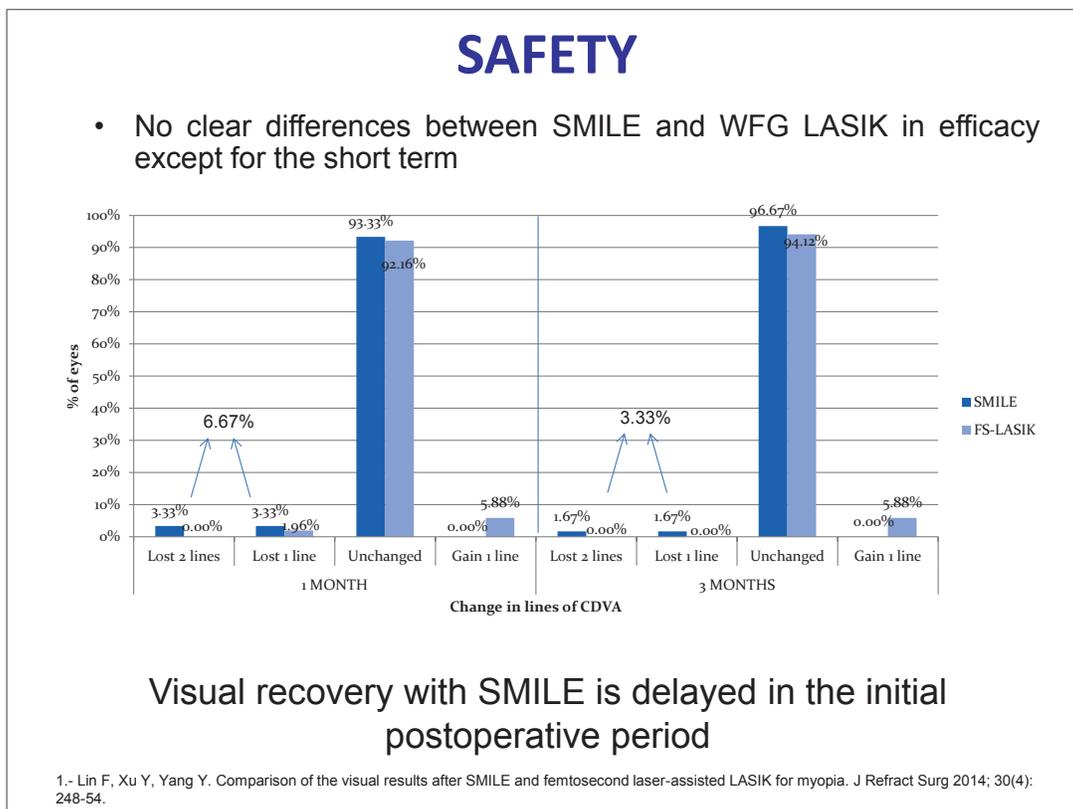
Rate Of Return of Visual Recovery & Predictability

The visual recovery following SMILE is slower than LASIK. Today, LASIK patients are typically 20/15 to 20/20 on the first day postoperatively. SMILE patients are usually 20/25 to 20/30 on the first day and gradually improve. A small percentage of SMILE patients can have a prolonged recovery. Patients usually demand a quick visual recovery. Studies with SMILE have shown that on average only 77% of eyes are within +0.50 to -0.50 diopters at 3 months. Although uncorrected vision improves between 3 and 6 months this is considered delayed healing.

The slower recovery may be secondary to the fact that cutting by a femtosecond laser in the SMILE procedure, especially in the deeper tissues, is much rougher than what can be achieved with the excimer laser in LASIK. Significant microdistortions in Bowmans layer have been reported in SMILE, which may account for delayed recovery. Loss of best-corrected acuity in the SMILE procedure is higher than LASIK at 1 month and 3 months.

Yao P, Zhao J, Li M, Shen Y, Dong Z, Zhou X. Microdistortions in Bowman's Layer Following Femtosecond Laser Small Incision Lenticule Extraction Observed by Fourier-Domain OCT. J Refract Surg 2013; 29(10): 668-674

Lin F, Xu Y, Yang Y. Comparison of the visual results after SMILE and femtosecond laser-assisted LASIK for myopia. J Refract Surg 2014; 30(4): 248-54.

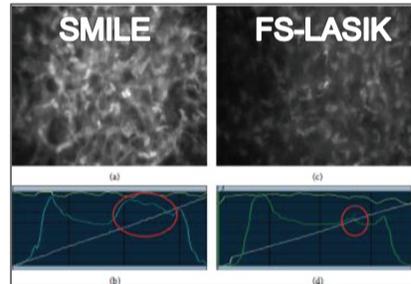


PREDICTABILITY

| AUTHOR (YEAR) | PREOP REFRACTIVE ERROR | WFG-LASIK (SE±0.50 D) | SMILE (SE±0.50 D) | FOLLOW-UP |
|--|------------------------------|-----------------------|-----------------------|-----------|
| Kim et al (2015) BMC Ophthalmol | <-6.00 D ≥-6.00 D | --- | 87.9% 88.0% | 12 months |
| Yao et al (2015) J Refract Surg | -6.63±1.48 D | --- | 67.6% | 3 months |
| Reinstein et al (2014) J Refract Surg | SE ≤3.50 D | --- | 84.0% | 12 months |
| Lin et al (2014) J Refract Surg | -4.85±1.68 D | --- | 98.33% (SE±1.00 D) | 3 months |
| Schallhorn et al (2014) J Refract Surg | -3.28±1.79 D | 93.0% | --- | 1 month |
| Yu & Manche (2015) CataractRefract Surg | -4.62±2.32 D -4.66±2.30 D | 95.1% | --- | 12 month |
| He et al (2014) Am J Ophthalmol | -4.75±2.22 D | 91.0% | --- | 12 months |
| Shaheen et al (2013) J Refract Surg | -3.36±1.71 D | 97.3% | --- | 4 years |

MICROSTRUCTURAL CHANGES

- Slow visual recovery after SMILE in the initial postoperative period:
 - Microdistortions of Bowman's layer:¹
 - SMILE 88.5% vs. FS-LASIK 42.1%
 - Microdistortions associated with lenticule thickness
- Increased backscattered light intensity in anterior stroma²



a) and c) Activated keratocytes at 150µm depth
b) and d) Anterior back scatter

| Backscattered light intensity 120 µm below the epithelium | | |
|---|------------------|------------------|
| Follow-up | SMILE | FS-LASIK |
| | Mean (SU) ± SD | Mean (SU) ± SD |
| Preoperative | 1062.45 ± 75.51 | 1051.20 ± 88.83 |
| Week 1* | 1728.90 ± 238.50 | 1391.40 ± 238.68 |
| Month 1* | 1491.12 ± 288.36 | 1296.45 ± 199.35 |
| Month 3* | 1340.46 ± 257.49 | 1163.16 ± 191.16 |
| Month 6 | 1212.03 ± 169.92 | 1124.01 ± 148.23 |

1.- Yao P, Zhao J, Li M, Shen Y, Dong Z, Zhou X. Microdistortions in Bowman's Layer Following Femtosecond Laser Small Incision Lenticule Extraction Observed by Fourier-Domain OCT. J Refract Surg 2013; 29(10): 668-674
2.- Agca A, Ozgurhan EB, Yildirim Y, Cankaya KI, Guleryuz NB, Alkin Z, Ozkaya A, Demirok A, Yilmaz OF. Corneal Backscatter Analysis by In Vivo Confocal Microscopy: Fellow Eye Comparison of Small Incision Lenticule Extraction and Femtosecond Laser-Assisted LASIK. J Ophthalmol 2014; ID 265012, 8 pages

Dry Eye

There is debate as to whether there is less dry eye in the SMILE patients versus the LASIK patients. We do know that there is no significant difference in dry eye at 3 months with each procedure. Studies that use questionnaires to evaluate dry symptoms have not demonstrated any differences in symptoms between SMILE and LASIK. Although the anterior corneal lamellae are preserved in SMILE except for the superior incision, the corneal nerves are still transected in the area in which the lenticule is extracted.

Demirok, Ahmet, et al. "Corneal sensation after corneal refractive surgery with small incision lenticule extraction." *Optometry & Vision Science* 90.10 (2013): 1040-1047.

DRY EYE

- Dry eye is a condition difficult to measure due to the lack of correlation between signs and symptoms
- Studies looking at subjective dry eye questionnaires have shown:
 - OSDI worsens after both SMILE and Femto-LASIK procedures, returning to preop values after 1 month postop in both¹
 - By 3 months postoperatively the McMonnies questionnaire scores recovered to their preoperative values in the SMILE and 90- μ m flap LASIK groups²

1. Li M, et al. (2013) Confocal Comparison of Corneal Reinnervation after Small Incision Lenticule Extraction (SMILE) and Femtosecond Laser In Situ Keratomileusis (FS-LASIK). *PLoS ONE* 8(12): e81435
2. Yesheng Xu, MD; Yabo Yang, MD, PhD. Dry Eye After Small Incision Lenticule Extraction and LASIK for Myopia. *J Refract Surg.* 2014;30(3):186-190

Ability To Treat Higher Degrees of Myopia / Risk Of Ectasia

When the SMILE procedure was developed it was thought that higher degrees of myopia could be treated. Theoretically, preserving some anterior corneal lamellae could enhance the tensile strength of the cornea and decrease the risk of ectasia. This appears to be false. The depth of treatment for a given refractive error is greater for SMILE than LASIK because the initial anterior cut is deeper. Typically in LASIK, a 100 to 110 micron flap is utilized. In SMILE, the anterior cut is created 120 to 130 microns below the surface. Today, surgeons performing SMILE must respect the limitations of high myopic ablations. There have been a number of reported cases of corneal ectasia after SMILE. Since there is usually a delay before ectasia develops it is anticipated that additional cases will be seen over time. A study by Ganesh, et al showed changes to the back curvature of the cornea in SMILE patients treated for moderate and high myopia. Posterior curvature changes are thought to be the earliest sign of a weakened cornea or early ectasia. This finding is of significant concern and further follow-up is required to determine the true risk of ectasia with SMILE.

Wang, Yumeng, et al. "Corneal ectasia 6.5 months after small-incision lenticule extraction." *Journal of Cataract & Refractive Surgery* (2015).

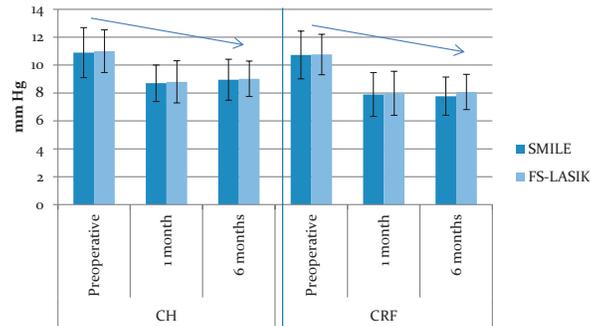
El-Naggar, Mohamed Tarek. "Bilateral ectasia after femtosecond laser-assisted small-incision lenticule extraction." *Journal of Cataract & Refractive Surgery* 41.4 (2015): 884-888.

Ganesh, Sri, Utsav Patel, and Sheetal Brar. "Posterior corneal curvature changes following refractive small incision lenticule extraction." *Clinical ophthalmology (Auckland, NZ)* 9 (2015): 1359.

BIOMECHANICAL CHANGES

- Clinically, no evidence of a better biomechanical behaviour of SMILE vs. FS-LASIK:

- Several clinical studies using the ORA system and CorVis ST^{1,2}
- Pedersen et al (2014): LASIK reached highest concavity faster than SMILE (CorVis ST)³



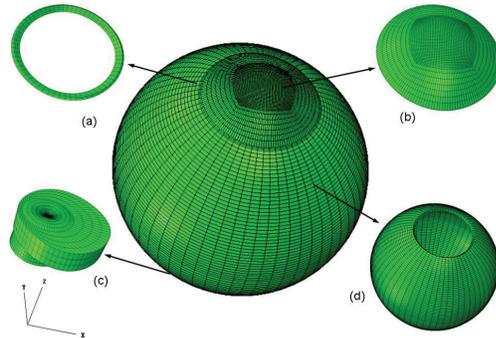
Pre- and postoperative corneal hysteresis (CH) and corneal resistance factor (CRF) values by group¹

1.- Agca A, Ozgurhan EB, Demirok A, Bozkurt E, Celik U, Ozkaya A, Cankaya I, Yilmaz OF. Comparison of corneal hysteresis and corneal resistance factor after small incision lenticule extraction and femtosecond laser-assisted LASIK: A prospective fellow eye study. *Cont Lens Anterior Eye* 2014; 37: 77–80
 2.- Shen Y, Chen Z, Knorz MC, Li M, Zhao J, Zhou X. Comparison of Corneal Deformation Parameters After SMILE, LASEK, and Femtosecond Laser-Assisted LASIK. *J Refract Surg* 2014; 30(5): 310-8
 3.- Pedersen IB, Bak-Nielsen S, Vestergaard AH, Ivarsen A, Hjortdal J. Corneal biomechanical properties after LASIK, ReLEx flex, and ReLEx smile by Scheimpflug-based dynamic tonometry. *Graefes Arch Clin Exp Ophthalmol* 2014; 252: 1329–35

BIOMECHANICAL CHANGES

- Is total stromal tensile strength higher after SMILE compared to LASIK and PRK procedures?:¹

- Estimation based on a mathematical model
- Not validated experimentally
- Assumption: anterior stroma is completely intact



1.- Reinstein DZ, Archer TJ, Bradley Randleman J. 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): 454-60

Customized Ablations

There are specific advantages to performing customized ablations with LASIK or PRK. Unfortunately the techniques of Wavefront-guided and Topography-guided ablations are not possible with the SMILE technique. Customized profiles have significant advantages in patients with abnormal topography, previous refractive surgery, or high angle kappas.

ABERROMETRIC OUTCOMES

- Better control of HOAs with WFG-LASIK vs. SMILE
 - Tanzer and colleagues:¹ mean change of $+0.03 \pm 0.10$ and $+0.05 \pm 0.08$ μm in HOA RMS and primary SA after WFG-LASIK in naval aviators
 - Vestergaard et al:² change after SMILE of 0.15 μm , 0.14 μm and 0.33 μm in HOA RMS, SA, and coma RMS
 - Lin et al:³ high levels of HOAs at 3 months after SMILE: 0.503 μm SA, 0.706 μm coma RMS, 0.427 μm HOA RMS
 - Yu and Manche:⁴ no significant levels of HOAs after WFG-LASIK
 - Coma RMS: 0.28 ± 0.14 (150 kHz FS laser), 0.29 ± 0.03 (60 kHz FS laser)
 - SA: 0.22 ± 0.19 (150 kHz FS laser), 0.21 ± 0.17 (60 kHz FS laser)

1.- Tanzer DJ, Brunstetter T, Zeber R, Hofmeister E, Kaupp S, Kelly N, Mirzaoff M, Sray W, Brown M, Schallhorn S. Laser in situ keratomileusis in United States Naval aviators. J Cataract Refract Surg 2013; 39: 1047-58

2.- Vestergaard AH, Grauslund J, Ivarsen AR, Hjortdal JO. Efficacy, safety, predictability, contrast sensitivity and aberrations after femtosecond laser lenticule extraction. J Cataract Refract Surg 2014; 40: 403-11

3.- Lin F, Xu Y, Yang Y. Comparison of the visual results after SMILE and femtosecond laser-assisted LASIK for myopia. J Refract Surg 2014; 30(4): 248-54.

4.- Yu CQ, Manche EE. Comparison of 2 femtosecond lasers for flap creation in myopic laser in situ keratomileusis: one-year results. J Cataract Refract Surg 2015; 41: 740-8.

Risk of Decentered Ablations

The excimer laser tracking systems with LASIK are so advanced that decentered ablations are extremely rare. Unfortunately, with the SMILE procedure when the suction ring is applied for the lenticule extraction no further adjustment in centration can be made. This increases the risk of a decentered ablation, which is very difficult to repair surgically. Centration appears to be less precise with SMILE compared to LASIK. This is one reason why the ophthalmologists at Moorfields Hospital in England have stopped doing the SMILE procedure. This is one reason why the ophthalmologists at Moorfields Eye Hospital in England have stopped doing the SMILE procedure and returned to LASIK and PRK.

Enhancements

Patients often expect an uncorrected visual acuity of 20/20 or better. Unfortunately with the SMILE procedure an enhancement using the lenticule extraction technique cannot be performed. Enhancements are typically performed with PRK, which is associated with a much slower visual recovery.

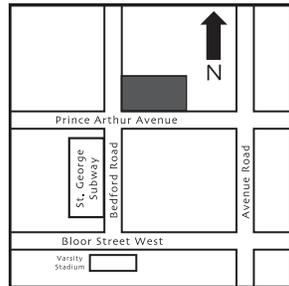
Hyperopia

Current techniques do not allow the treatment of hyperopia or mixed astigmatism with SMILE. It may be possible in the future with further refinements, but unfortunately not available today.

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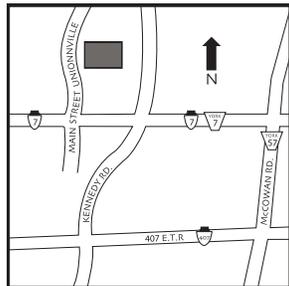
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