SCUOLA DI INGEGNERIA INDUSTRIALE
E DELL'INFORMAZIONE

Executive Summary of the Thesis

A numerical study on the effects of laser refractive surgery: PRK vs SMILE

Laurea Magistrale in Biomedical Engineering - Ingegneria Biomedica

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1. Introduction

Cornea constitutes the highly transparent outer layer of the anterior portion of the eye and acts both as a structural barrier and as a refractive lens: it provides 2/3 of the total refractive power of the eye. It is itself composed of five layers, among which the stroma, which makes up approximately the 90% of the total thickness of the cornea and is mainly responsible for the biomechanical behaviour of the cornea. Its transparency is, in fact, due to the precise organization of stromal collagen fibers [9]. Thus, the quality of our vision mainly depends on the cornea and, more specifically, on its shape. When corneal curvature is higher or eye's axial length is longer, myopic defect arises, causing far vision to be blurred; when corneal surface is irregular, being characterized by different curvatures on different meridians, astigmatism is present and can coexist with myopia, causing blurred vision at every distance.
Myopia is a complex eyesight-threatening disease and is becoming the major cause of blindness. A review estimated that in 2050, half of the global population would be myopic [4]. Among all the vision correction methods, laser refractive surgeries have become increasingly popular in vision defects treatment for achieving a permanent correction.
Photorefractory Keratectomy (PRK) and Small Incision Lenticule Extraction (SMILE) are two different procedures for correction of refractive defects that employ laser ablation. In refractive surgery, a portion of corneal tissue is removed to decrease the curvature of the anterior surface of the cornea, allowing to move the focal point (where the light rays converge and the image is formed) back onto the retina, which is responsible of transmitting the visual information to the brain. More specifically, PRK acts directly on the anterior surface of the cornea, removing a predefined profile by means of laser ablation, while SMILE procedure consists of creating a lenticule in the corneal thickness and extracting it through a small incision, without the direct ablation of the anterior surface (Figure 1). The main objective of this thesis was to develop and validate a numerical methodology to simulate, by means of the finite element method (FEM), PRK and SMILE refractive surgeries.

2. Materials and Methods

A geometrical model of the cornea was created by means of a conical approximation, in order to

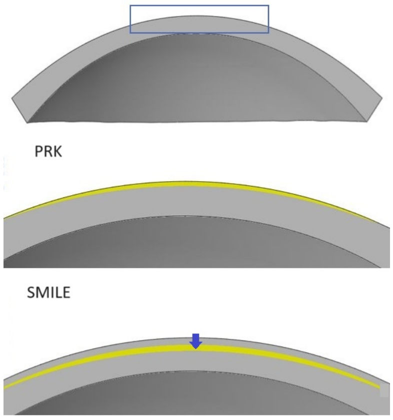


Figure 1: Side view of the ablation portion in our models of PRK and SMILE.

easily analyse the influence of the different parameters that affect the simulation's outcome. Then, the methodology was validated by reproducing both surgeries on a patient, treated with PRK, using, in this case, patient-specific models.

2.1. Corneal and Ablation Geometry

The corneal geometry was reconstructed by using a conic approximation, which constitutes a rotationally symmetric model. The 2D conic is described by the following Eq. 1 [6]:

$$y^2 = 2r_0 z - (1+Q)z^2 \tag{1}$$

where r_0 is the apical radius and Q is the asphericity parameter, whose values were derived from the topography of a patient, by means of a corneal topographer (Pentacam), able to collect corneal surfaces. The 3D model is then obtained by applying a 360° rotation to the 2D model.
The 3D conic geometry was obtained by building the point clouds of the external surfaces in MATLAB 2023a. The ablation volume was built employing a conic profile, as explained by [8], where the apical radius was obtained from Eq. 2, while the ablation asphericity value was obtained applying Eq. 3, where $n = 1.3775$ is the index of refraction and D is the target dioptric correction [5].

$$R_{\text{ablation}} = \left(\frac{D}{(n-1)} \cdot \frac{1}{r_0}\right)^{-1} \tag{2}$$

$$Q_{\text{ablation}} = \frac{R^3_{\text{ablation}}}{r_0^3} \cdot (1+Q) - 1 \tag{3}$$

To validate the current work, PRK and SMILE patient-specific models were then built, starting from pre-surgical Pentacam point clouds of a patient who was treated by PRK. The corneal surfaces were reconstructed by means of a surface fitting algorithm employing Zernike's polynomials [7]. The ablation profile was built using a biconic equation (Eq. 4), that allows to consider astigmatism too, given the possibility to have distinct curvatures on different meridians [10].

$$z = z_0 - \frac{\rho^2 A}{\left(1 + \sqrt{1-\rho^2 B}\right)} \tag{4}$$

where

$$A = \frac{\cos^2(\theta - \theta_s)}{R_s} + \frac{\sin^2(\theta - \theta_s)}{R_f} \tag{5}$$

$$\begin{aligned} B = {} & (Q_s + 1)\frac{\cos^2(\theta - \theta_s)}{R_s^2} \\ & +(Q_f + 1)\frac{\sin^2(\theta - \theta_s)}{R_f^2} \end{aligned} \tag{6}$$

R_s and R_f are the radii of curvature of the steepest and the flattest meridians, Q_s and Q_f are the corresponding asphericities and θ_s is the axis of astigmatism. These models were used for the reproduction of both surgeries on the same patient, who was actually treated by PRK. In PRK surgery, the ablation depth was extracted directly from the treatment plan and was 74.09 µm, in order to correct -4 D of myopia and -1.1 D x 170° of astigmatism. In SMILE surgery, according to current clinical setup, the ablation depth was set a 10% higher with respect to PRK and 15 µm of thickness were added to the whole lenticule, to avoid the rupture at the extraction. Consequently, the final lenticule thickness applied to the SMILE model was of 101 µm, to correct -4.4 D of myopia and -1 D x 170° of astigmatism.
All the models used in the current thesis were meshed with quadratic tetrahedrons, using the software ANSA pre-processor by BETA-CAE systems v22.0.1.

2.2. Material model

The collagen fibers composing the corneal stroma are oriented along with nasal-temporal (N-T) and inferior-superior (I-S) directions within the central region of the cornea and they start running circumferentially in the limbus region. Furthermore, in-plane and out-of-plane dispersions were considered. The following strain energy density function has been considered for a hyperelastic nearly-incompressible material: $\psi = \psi(J) + \psi^{\mathrm{m}}(\bar{I}_1) + \sum_{i=4}^{6} \psi^{\mathrm{f}}(\mathbf{C}_{\mathrm{dis}}, \mathbf{H_i})$, where $\psi(J) = \frac{1}{D}(\ln J)^2$ is the volumetric term, $\psi^{\mathrm{matrix}}(I_1)$ represents the isotropic contribution, and $\psi^{\mathrm{fibers}}(\mathbf{C}_{\mathrm{dis}}, \mathbf{H_i})$ accounts for the fibers of the model. A Neo-Hookean model was chosen to describe the behavior of the matrix component of the tissue: $\psi^{\mathrm{m}}(\bar{I}_1) = C_{10}(\bar{I}_1 - 3)$, where C_{10} is a material constant. A Holzapfel-Gasser-Odgen model with dispersion parameters was used to describe the anisotropic behavior of the fibers [9, 11]: $\psi^f = \frac{k_1}{2k_2}\left(e^{k_2(\bar{I}_i^* - 1)^2} - 1\right)$, where k_1 and k_2 are two material constants. The following material parameters were used for the conic models: C_{10}=30 kPa, k_1=20 kPa, k_2=400. The constant C_{10} was then changed for the patient-specific cases (See Chapter 3.5). The material model was implemented through a User Material (UMAT) in Fortran language.

2.3. Surgeries Simulations

2.3.1 Boundary Conditions and Zero-pressure Configuration (ZP)

Two different boundary conditions (BC) were tested: *fixed* BC at the base of the cornea and *sliding* BC, where only radial displacements were allowed, while polar and azimuthal movements were blocked at the base of the cornea.
Furthermore, the initial stress-free configuration (ZP) of the cornea was recovered [1].

2.3.2 PRK and SMILE simulations

All simulations were run using the software ABAQUS 6.13. The ZP configuration was the initial configuration from which the FE simulations were run. The surgery simulation was made of two steps: in the first step, the model is pressurized with a physiological intraocular pressure (IOP = 15 mmHg), applied to the posterior surface of the cornea; in the second step, the laser ablation is performed.

2.4. Performed Analyses

The set up of the models was chosen according to the results obtained from the following analyses:

- Analysis of the influence of the BCs.
- Analysis of the lenticule position in SMILE models.

Subsequently, geometrical, optical and mechanical parameters were investigated:

- Variation of the target dioptric correction (from -4D to -8 D);
- Simulation of 5 SMILE models based on the clinical practice, where a dioptric correction of 10% more with respect to patient's refraction is applied and the lenticule has a minimum thickness of 15 µm;
- Variation of the central corneal thickness (CCT) of the models, from 500 µm to 600 µm;
- Variation of the optical zone (OZ) radius (3, 3.5 and 4 mm) where the ablation is performed;
- Mechanical sensitivity analysis: 2^5 full factorial design, varying C_{10}, k_1 and k_2 of ± 50 % of the values reported in 2.2 and the IOP and CCT in a physiological range (IOP = 10-22 mmHg and IOP = 490/500-600 µm);
- Montecarlo analysis, varying the material parameters in a randomized fashion: 60 different values for C_{10} between 15 and 45 kPa, k_1 between 10 and 30 kPa and k_2 between 200 and 600 kPa.

In patient-specific simulations, sliding BC were used and patient's biomechanically-corrected IOP measured with Corvis Non-Contact Tonometer was applied (bIOP = 19.88 mmHg). Moreover, the material parameters used in all the conic simulations were applied. Then, the constant C_{10} was changed to 60 and 15 kPa, to simulate a stiffer and a softer material (both for PRK and SMILE) and evaluate how the matrix component of the material model affected the opto-mechanical outcome.

2.5. Opto-mechanical Analysis

The dioptric correction was evaluated by looking at the curvature ([D]) of the anterior corneal surface before and after the laser surgery. In order to calculate these values, an ellipsoidal fit [3] was used: the parameter of interest are the mean pre- and post-surgical curvatures (K_m). An OZ radius of 4 mm was considered for the ellipsoidal fit analysis.
Moreover, sagittal and mean curvature maps were computed to have a graphical view of the

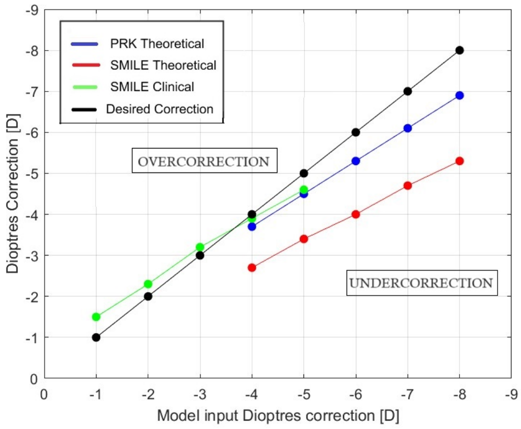


Figure 2: Dioptrical corrections' numerical models results: PRK and SMILE theoretical ablation profiles (blue and red), SMILE based on clinical data ablation profile (green) and desired correction.

pre- and post-surgical anterior surface of the models, as in clinics. Zernike polynomials were used to fit the surfaces and to reduce the error [7], by smoothing the surface point cloud. The mechanical analysis consisted in evaluating the maximal principal stress and maximal principal logarithmic strain distributions on the models, their difference before and after surgery and the apical node displacement.

3. Results

3.1. BC analysis

The analysis of the BC revealed that both models behaved similarly both mechanically and optically in the optical zone of interest.

3.2. Lenticule position analysis

In SMILE simulations, after evaluating the different lenticule positions in the corneal thickness, the chosen one was at 20% of CCT going downwards from the anterior surface, since it allowed to achieve the best dioptric correction and, moreover, is the current setup used in clinics (cap thickness of 110 - 120 µm). In addition, at this depth, the posterior surface of the cornea is subjected to lower stresses, reducing the likelihood of corneal ectasia or keratoconus [2]. By means of this analysis, a threshold has been found at 60% of CCT, where no dioptric correction was reached and beyond which the dioptric defect was worsened.

Dioptric Correction Input [D]	Mean Curvature [D]		
	pre-ablation	post-ablation	achieved correction
- 1	41.7	40.2	-1.5
- 2	41.7	39.4	-2.3
- 3	41.7	38.5	-3.2
- 4	41.7	37.8	-3.9
- 5	41.7	37.1	-4.6

Table 1: Mean curvatures for SMILE models, based on the clinical ablation depths.

3.3. Dioptric corrections analysis

Changing the dioptric target led to the results in Figure 2, where we can see that the target correction is never reached in the models with the ablation profile built following the theoretical approach [8]. For low dioptric targets, PRK got really close to the desired correction, while SMILE had a poor result. As the dioptric target increases, both models lose accuracy in the optical performance. Given the worse optical outcome of SMILE simulations, other 5 SMILE models were built, based on the clinical practice, that is imposing a 10% higher dioptric correction. The results are shown in Table 1, highlighting an improved optical performance of the SMILE simulation, as shown in Figure 2, too.

3.4. Full-Factorial and Montecarlo analysis

The mechanical sensitivity analysis highlighted that the parameter that influenced the most the simultaions was C_{10}. Both the sensitivity and the Montecarlo analysis show that the highest dioptres correction is reached for softer materials (C_{10}=15 kPa and C_{10} = 17.37 kPa respectively). Through a linear regression, a function that relates the effective dioptric correction and the CCT has been traced, using the mean values obtained in each group of simulations with the same CCTs (Figure 3).

	Post-ablation		
	Pentacam data	PRK	SMILE
K1 [D]	40.1	39.8	39.1
K2 [D]	41.0	41.2	40.5
Km [D]	40.5	40.5	39.8
C [D]	0.9	1.3	1.5
α [°]	21.6	179.6	179.8

Table 2: K1, K2, Km, C and α post-ablation values.

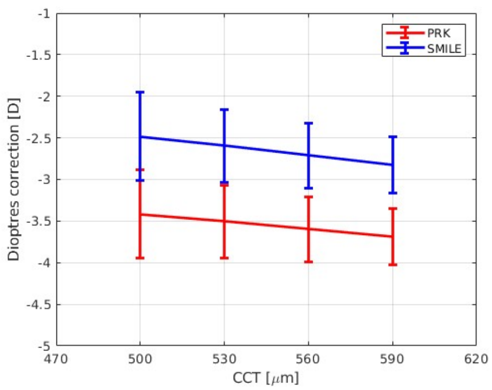


Figure 3: Linear regression lines that relate the CCT to the dioptric correction (for input=-4D).

3.5. Patient-specific models

The optical accuracy of the pre-surgical patient-specific models was validated comparing the patient anterior surface sagittal curvature of the topographer with the one of our models (Figure 4). Moreover, the highest dioptric corrections for both PRK and SMILE were obtained considering $C_{10} = 15$ kPa and are reported in Table 2, where K1 and K2 are the principal curvatures, Km is the mean curvature, C is the cylinder or astigmatism and α is the astigmatism axis, that indicates the orientation of the astigmatic defect.

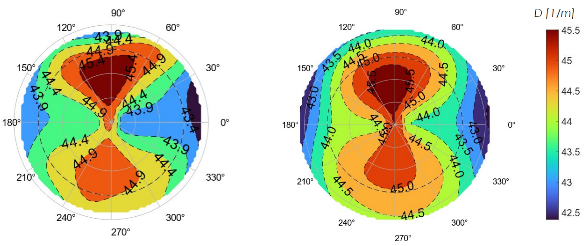


Figure 4: Anterior surface sagittal curvature map (a) Pentacam-derived and (b) patient-specific model.

In Figure 5, the stress-strain plot of the anterior surface only of PRK patient-specific simulation is shown, considering the three cases of interest ($C_{10} = 15, 30, 60$ kPa). The optical performance of the simulation does not vary linearly with the variation of the material constants: in fact, the highest correction was achieved for the softest case ($C_{10} = 15$ kPa), the intermediate correction value for the stiffest case ($C_{10} = 60$ kPa) and the lowest correction for the medium case

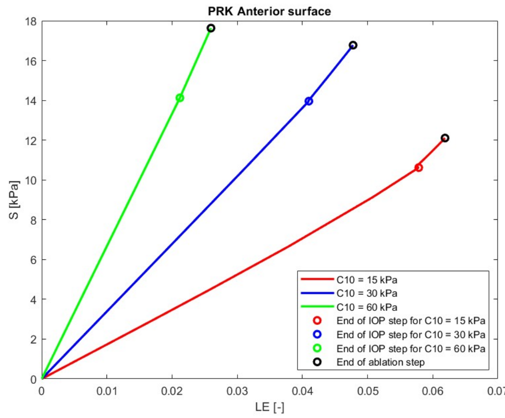


Figure 5: Mechanical behaviour of the anterior surface of the patient-specific PRK model.

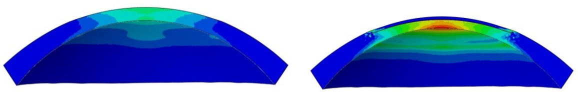
($C_{10} = 30$ kPa). This could be probably due to the highly non-linear behavior of the material. SMILE simulation showed similar results.

4. Discussion

First, the simulations set up was optimized. The chosen BCs were the fixed BCs, which provide low computational cost and similar opto-mechanical behaviour as sliding BC. In SMILE, the lenticule position was chosen to be set at 20% of CCT in the thickness of the cornea: it couples the highest dioptric correction with with the lowest posterior surface stress loading, which is the major cause of ectatic disease and keratoconus. Moreover, it reflects what is actually performed in clinical practice. Then, the simulation parameters were analysed. The optical desired correction was not fully reached in the conic models with the theoretical ablation profile [8]. In particular, in PRK, it was reached for low dioptric corrections (maximum -4D), while the accuracy was decreasing for higher dioptric corrections due to the stronger mechanical response of the tissue in terms of deformations and due to the higher difference with respect to clinical ablation depths (Table 3). SMILE simulation obtained poor optical results with theoretical ablation profiles. In clinical practice, for PRK surgeries, nomograms data are employed, which provide the most effective ablation depth, while for SMILE a 10% of correction is added and an additional thickness of 15 µm is considered for the lenticule: building a model on these assumptions allowed to achieve improved results. Regarding the validation of the mod-

Correction [D]	Ablation Depth [µm]		
	Theoretical	PRK	SMILE
-1	14	16	33
-2	28	31	51
-3	42	46	69
-4	56	60	85
-5	70	75	101

Table 3: Theoretical and clinical ablation depths in PRK and SMILE models (with an ablation OZ of 6.5 mm).



(a) (b)

Figure 6: Maximum principal stress difference distribution in the section of PRK (a) and SMILE (b) patient-specific models.

els, the patient-specific optical analysis revealed that the models reflected the patient's pre- and post-surgical Pentacam data (as shown in Table 2). SMILE models did not achieve the dioptric correction employing the initial material (Chapter 2.2). For this reason, the coefficient C_{10} was changed and the highest dioptric correction was reached for a softer material, with a $C_{10} = 15$ kPa. This result agrees with the biomechanical sensitivity and the Montecarlo analysis results. This is due to the influence of the stress-free configuration recovery, so that when we pressurize the models, they already reach a high strain state. Moreover, the patient-specific simulations of PRK and SMILE highlighted the different mechanical outputs of the two surgeries: in SMILE, in fact, the highest stresses distribute in a smaller volume than in PRK, just under the lenticule zone, while the anterior portion is unloaded (Figure 6). Nevertheless, in PRK, the stresses distribute through all the corneal thickness, because the ablation is performed on the anterior surface. For this reasons, SMILE causes higher mechanical imbalances, while PRK better preserves the mechanical integrity of the corneal structure.

5. Conclusion and Future Developments

A numerical methodology has been developed to simulate PRK and SMILE surgeries by means of FEM. Theoretical [8] and clinical ablation profiles were tested. The conic models are useful to provide an overall analysis of the parameters that define the surgery, but do not represent the cornea in details with its asymmetries and irregularities. On the other hand, the patient-specific models with clinical ablation profiles ensure a more precise reconstruction of the corneal surfaces and achieve the desired dioptric correction. Moreover, the mechanical parameters analyses shows that a softer material allows to reach a better refractive result. For this reason, as future development, the influence of the material model on patient-specific cases could be investigated more in detail. In addition, the arising of post-surgical complications could be analyzed, to verify if laser surgeries can represent a risk for the development of post-surgical ectasia.

References

[1] Zurita J. Piñero D.P. et al Ariza-Gracia, M.Á. *Ann Biomed Eng.*, 44:1753–1772, 2016.

[2] Khachikian SS. Belin MW. *Clin Exp Ophthalmol.*, 37:14 –29, 2009.

[3] Navarro et al. *J. Opt. Soc. Am. A*, 23(2):219–231, 2006.

[4] Liu JH et al. Hsu WM, Cheng CY. *Ophthalmology*, 111, 2004.

[5] Anera R. G. Del Barco L. J. Jiménez, J. R. *Journal of Refractive Surgery*, 19(1):65–69, 2003.

[6] Smith G. Atchison D. A. Lindsay, R. *Optometry and Vision Science*, 1998.

[7] V. A.D.P. Sicam M. Dubbelman and G. L. Van Der Heijde. *Vision Research*, 46:993–1001, 2006.

[8] Parel JM Culbertson W. Manns F, Ho A. *J Cataract Refract Surg.*, 28(5), 2002.

[9] Holzapfel GA. Pandolfi A. *J Biomech Eng.*, 130, 2008.

[10] Sergio Barbero Susana Marcos, Daniel Cano. *Journal of Refractive Surgery*, 2003.

[11] Hatami-Marbini H. Wang S. *J Biomech Eng.*, 143, 2021.