Artigo de Revisão

Guidelines for excimer laser refractive surgery on cornea

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RESUMO

A cirurgia refractiva tem tido um crescimento fulgurante nas últimas décadas, tanto na sua evolução técnica como na sua popularidade junto dos doentes. O objectivo deste trabalho é apresentar diversos conceitos actuais sobre cirurgia refractiva corneana com laser Excimer. Os autores, baseados numa revisão da literatura existente e na sua própria experiência, apresentam aspectos práticos relativos à selecção e avaliação de doentes, escolha de procedimento, aspectos técnicos da cirurgia e seguimento pós-operatório dos doentes. São analisados os dois procedimentos refractivos com laser Excimer mais frequentes - LASIK e PRK. São sugeridas as práticas adequadas na avaliação pré-operatória do doente, no sentido de pesquisar as contra indicações à realização deste tipo de cirurgia e estabelecer com rigor o seu estado de saúde ocular. As contra indicações absolutas e relativas para ambos os procedimentos são discutidas, assim como as mais valias de cada técnica nos diversos doentes. São propostos limites de ametropia óptimos para correcção com as plataformas de tratamento disponíveis actualmente. Reconhece-se a importância da avaliação do risco de ectasia iatrogénica e os novos avanços teóricos e técnicos na identificação de candidatos de risco. Seguimento a longo prazo dos doentes é essencial para o aperfeiçoamento dos resultados: orientações práticas são apresentadas e resultados de longo prazo disponíveis na literatura científica são analisados.

Palavras-chave
Córnea, laser Excimer, cirurgia refractiva, miopia, hipermetropia .

ABSTRACT

Refractive surgery has undergone an extraordinary growth in recent decades, both in technical sophistication and in its popularity among patients. The goal of this work is to present current concepts on corneal Excimer laser refractive surgery. The authors, based on a comprehensive review of the literature and on their own experience, discuss practical topics regarding patient selection and evaluation, procedure choice, different aspects of surgical technique, and post-operative follow-up recommendations. The discussion is focused on the two most popular Excimer procedures: LASIK and PRK. Clinical good conduct regarding patient evaluation is reviewed, focusing on appropriate patient selection and on rigorous assessment of the patient's pre-operative status. Contra-indications, absolute and relative, as well as specific advantages of both procedures are discussed. Optimal maximum attempted correction values are proposed.

The importance of rigorous screening for post-operative ectasia at-risk patients is acknowledged. New advances in screening devices and concepts are discussed. Long-term follow-up of patients is essential for outcome analysis and improvement: practical guidance is suggested and long--term results available are reviewed.

Key-words
Cornea, Excimer laser, refractive surgery, myopia, hyperopia.

INTRODUCTION

Ophthalmology has witnessed an explosion in the demand for surgical refractive correction in recent decades. Since the cornea accounts for almost 70% of the refractive power of the eye, shaping its refractive properties has long been a method to restore the focus plane of parallel light on the retina. Their safety, efficacy and predictability mean that laser corneal treatments have long been in the forefront of advances in refractive correction. The procedures traditionally known as "surface ablation techniques" were among the first laser refractive correction procedures in ophthalmology, and retain their status as the optimal techniques for some important indications.[1] Laser in situ keratomileusis (LASIK) emerged as an alternative technique for refractive correction in which ablation is performed within the stroma instead, after a stromal flap has been created. LASIK appears to have multiple advantages[2] and its increasing popularity has made it the most commonly performed laser corneal refractive surgery today.[3] Procedures continue to evolve as new techniques (femto-LASIK, Flex, SMILE), excimer lasers, accurate topographic analysis software and advanced tracking systems emerge.

Arguably, the biggest advance in terms of outcome improvement was not related to technology but to conceptual framework. Earlier procedures were often performed with little regard for patient selection and poor analysis of the long-term outcome. A classic manifestation of those shortcomings was the rise of post-LASIK ectasias. We now live in a sophisticated age of corneal excimer laser refractive surgery, where the mindset should be much more one of tailored and customized treatments. We now have diagnostic equipment that provides us with a vast amount of information on the cornea about to be operated upon. All of these innovations represent a unique opportunity to offer our patients a better quality of vision that can translate into a better quality of life. With this high level of expectations in mind we set out to compile and propose a group of clinical pearls concerning patient selection, procedure choice and post-operative evaluation. Our main goal was to provide valuable practical information. Of the myriad of new and ever-changing techniques available, the two most common remain PRK and LASIK.[4] As such, we decided to limit this discussion to those two techniques and made a conscious effort to produce concise, high-value, clinical guidance. It is not our intention to provide an exhaustive review of the literature but to share our own experience and expertise. We hope this paper can serve as a valuable tool for residents and referring ophthalmologists in their daily clinical practice.

PATIENT SELECTION

General Considerations

We follow the recommendations of the Royal College of Ophthalmology and limit excimer refractive surgery to patients older than 21 years.[5] A stable refraction is required, defined as prescription change of less than 0.5 diopters (D) in the last year. Despite the lack of a compelling explanatory link, there seems to be a clear trend of association between advanced tiers of education and a higher myopic refraction.[6,7] With that in mind, a more cautious approach - observing a longer follow-up period before surgery- is recommended in young patients presenting with mild myopia that are yet to finish their university studies. Conventional subjective refraction is expected to have intra-examiner and inter-examiner reproducibility within the 0.25 to 0.5 D range for spherical equivalent, sphere power and cylinder power.[8] Any higher variation should be viewed with caution. When in doubt, a scrupulous approach is advisable and the patient should be rescheduled within a year for a new refraction test.

Known absolute and relative contra-indications are displayed on Table 1. Some patients are considered to be completely unfit for surgery while others may be rescheduled to allow for a new appreciation. In the case of pregnancy and breastfeeding, it remains as an absolute contra-indication but the 1st and 2nd trimesters are more problematic, with refractive instability[9,10] and increased ectasia risk.[11,12]

Ideally, treatment should be delayed for 12 weeks after breast-feeding has ended. Patients with dry eye syndrome must be adequately treated beforehand and in patients with HSV or VZV we must consider prophylactic treatment before surgery and in the post-operative period. Diabetes mellitus is known to cause refractive instability and impaired healing response, therefore strict metabolic control must be achieved before surgery. Auto-immune disorders are treated preferentially with LASIK[13,14] rather than PRK[15], and so are patients with propensity to keloid formation.[16] In the case of epithelial basement membrane dystrophy LASIK is not recommended but PRK can actually help reduce the rate of erosions.[17]

Table 1 | Absolute and relative contra-indications for Excimer surgery.

Absolute	Relative
Unstable refraction	Dry eye syndrome
Ectatic abnormalities (e.g. keratoconus, pellucid marginal ectasia, other types of ectasia)	HSV or VZV
Significant external disease (e.g. blepharitis, severe allergy)	Diabetes Mellitus
Exposure keratopathy	Immunosuppressed state
Uncontrolled ocular conditions (glaucoma, uveitis)	Known auto-immune disorders
Pregnancy and breastfeeding	Propensity to keloid scar formation
Single functional eye	Epithelial basement membrane dystrophy

Ophthalmological Examination

Establishing the refractive status of the patient does not obviate the need for a comprehensive medical eye examination. Careful history taking is mandatory and should include a detailed discussion of the reasons for refractive surgery and both present and future visual needs.

Chronic contact lens (CL) use is known to cause corneal warping.[18,19] Contact lens users are advised to discontinue their use before the preoperative evaluation. A gradual approach is used to calculate the discontinuation time needed: 1 week for every 5 years of use of soft contact lenses (e.g. if using soft CL for 10 years they should be removed 2 weeks prior to the consultation) and 2 weeks for every 5 years with rigid contact lenses.[19] Special care should be taken in the case of rigid CL to ensure refractive stability and full regression of corneal warpage.

The best corrected distance visual acuity should be assessed in a properly lit room. A distance of 6 meters is typically used. If the patient is cooperative, subjective refraction is preferred. Under very specific circumstances, objective determination using retinoscopy can be an acceptable option, particularly in young patients with hyperopia or mixed astigmatism. Accommodation should be fully relaxed during distance refraction evaluation, although cycloplegic refraction is not required for every patient. If manifest refraction is used, special care must be taken to ensure full relaxation of accommodation to prevent over-correction for myopia and under-correction for hyperopia. Uncontrolled accommodation can be minimized where necessary by means of plus lenses to create a "fogging" effect.

In patients with hyperopia, hyperopic compound astigmatism or mixed astigmatism, especially in younger patients, some degree of latent hyperopia is common and can be masked when using manifest refraction. In these patients, the full measure of latent hyperopia can only be uncovered through cycloplegic refraction. Cyclopentolate 1% (2 drops, with an interval of 5 minutes, onset of action after 45 minutes) provides effective cycloplegia and a shorter, better tolerated, duration of action.[20] In some patients, the difference between the manifest and cycloplegic refraction exceeds 1 D, indicating the presence of excess accommodative tone or accommodation spasm. In these cases it is advisable to repeat the refraction and try to approximate the subjective refraction to the best tolerated full cycloplegic refraction *(pushing plus)*.

Each eye should be assessed independently and binocular refraction refined afterwards. The duochrome test should be performed, aiming for an equally clear reading of the two halves. In patients over 40 years of age, a "red--preference" can be a desirable result, as a way of achieving slight under-correction of myopia.

The physician should be alert to any significant deviation between the astigmatic error found with subjective refraction and the corneal astigmatism visible on topography. Biomicroscopy evaluation of the tear film, ocular surface and anterior segment should be thorough and comprehensive. Special care should be taken to search for the presence of corneal changes, such as limbic neovascularization or pannus.

Pupillary size is not routinely measured rigorously, but its impact on the quality of vision under scotopic conditions is a matter of debate. It is known that intraocular light scatter and spherical aberrations increase with larger pupil

size, but a large preoperative pupil has not been consistently linked with worse outcomes.[21-24] Moreover, the technical process of pupil measurement is tiresome and its accuracy dubious. Pupil size varies throughout the patient's life and at any given moment it is influenced by a number of confounding factors (medications, emotions, alertness, etc). Ideally it should be measured fixating on a distance target, to achieve a non-accommodated state. There are several devices available (e.g. Rosenbaum cards, Colvard pupillometer, Procyon pupillometer, Neuroptics pupillometer) but there are still issues concerning repeatability and inter-observer agreement.[25,26] Some devices commonly used for the tomographic assessment of candidates, like the Orbscan II® or the Pentacam®, also provide pupil diameter values. We generally rely on the values provided by the Orbscan II® - acquired under mesopic conditions (1-3 cd/m^2) - due to the feasibility of the exam. Regardless of the anedoctal evidence noted before, there is widespread notion that large pupil sizes might be responsible for the visual complaints, such as glare or halo in night vision, reported by some patients.[24] The conceptual reasoning behind such a belief is intuitive: large pupils in scotopic or mesopic conditions may become large enough to allow light passing through the untreated cornea to reach the retinal plane. With a mesopic pupil larger than 4 mm an optical ablation zone of 7 mm is chosen. If the mesopic pupil is under 4 mm we prefer to use an ablation diameter of 6.5 mm, except for patients with mixed astigmatism or hyperopia, who are also treated with a 7.0 mm ablation zone. These values are not immovable and may be tailored as necessary according to the patient's pachimetry. The need for rigorous pupillary measurement should be tailored to the findings of the physical examination and its importance considered when discussing night-vision needs and expectations.

Intraocular pressure should preferably be measured with a Goldman applanation tonometer or similar.[27]

Dilated fundoscopic evaluation is part of the recommended preoperative assessment. Although most candidates are likely to have a best corrected vision of 20/20 or better, the fact remains that perfect visual acuity does not rule out a serious eye condition. In the case of high refractive errors it is common for patients to have sub-optimal best corrected visual acuity, even with perfected refractive correction and in the absence of any structural impairment.

Although their assessment is cumbersome, some reports highlight the importance of psychological factors to refractive surgery outcomes.[28-30] Motivation, expectations and concerns regarding refractive surgery should always be discussed at length with the patient.

INDICATIONS FOR REFRACTIVE ABLATION TECHNIQUES

- Approved indications are specific to the different excimer-laser devices available in the market and the full list of FDA-approved indications for each device is available online.[31]
- Table 2 shows the maximum values of refractive error that our group currently observes for excimer refractive surgery. These values do not reflect the approved maximum indication of the excimer device currently in use in our center and should be used for guidance only.

Table 2 | Current indications considered for PRK and Lasik.

	Myopia	Hyperopia	Astigmatism
PRK	Up to -5.00 D spherical equivalent (32–35)	Up to +2.50 D spherical equivalent (36–38)	Up to 2.50 D cylinder (39,40)
LASIK	Sum of sphere and cylinder should not exceed -7.50 D (34,35,41)	Up to +4.0 D spherical equivalent (35,42,43)	Up to 4.00 D cylinder (40,43,44)

Keratometry Evaluation

The association between keratometry values and outcomes has been extensively studied for both myopic and hyperopic LASIK. Even so, it is not easy to infer firm conclusions from the literature, probably because there is wide variability in the thresholds accepted as steep/flat corneas and in the ametropia levels considered. Nonetheless, keratometric values seem to play a role in visual outcomes and we prefer to maintain postoperative keratometric values within prudent limits.

Conflicting results have been reported for hyperopic LASIK regarding the influence of preoperative and postoperative keratometry. Some series report better results with flatter corneas[45] while other groups found the opposite association, with reduced predictability in greater K powers.[46,47] Moreover, other studies[48-50] found no impact of postoperative keratometry on surgery outcomes. There are also studies that find that successful hyperopic correction is correlated with the magnitude of the corneal change rather than the exact pre- or post-operative value.[49,51] At present, the exact basis for the worse outcomes is not entirely clear and further time and research are needed to clarify some of

the apparent contradictions in the literature. For that reason we share the opinion of other groups[47,52] and suggest caution in performing LASIK in patients with K values that are higher than 48 D. It is important to notice that a steepening of 1.00 D for every diopter of hyperopia treated can be expected, and this effect should be taken into account when predicting a postoperative keratometry value within the intended limit.[17]

For myopic patients, there is a historical trend of results reporting worse outcomes associated with increased flattening.[53,54] However, this is also a controversial issue since some reports showed no impact of keratometric values[55,56] or even better visual outcomes with flatter corneas[57]. Despite the lack of absolute consensus, most surgeons would agree that caution is indicated when causing substantial flattening and we propose a postoperative limit that should not be less than 35 D. Again, a flattening effect of 0.80 D for every diopter of myopia treated can be predicted and should be considered when aiming at a postoperative corneal power over 35 D.[17]

The presentation of extremely steep or flat corneas should also raise some important questions for the surgeon during the procedure. It is important to be aware that excessively flat corneas are at higher risk of developing a free cap.[58,59] Less tissue is likely to enter into the suction head and that should be taken into account when performing the microkeratome cut. Steep corneas, however, are usually associated with thin, irregular or buttonhole flaps.[59-61] The introduction of femtosecond laser flap creation has helped diminish the incidence of these rare complications[62,63], with a more predictable flap thickness[62,64] and the induction of lesser high-order aberrations.[65]

Procedure Choice for Myopia

Despite extensive comparative literature, there is little evidence of one technique being superior to the other. Outcomes like long-term uncorrected visual acuity, refractive accuracy and refractive stability seem to be similar for both techniques.[66-71] There is abundant evidence supporting the widespread notion that visual recovery is faster with LASIK.[72] That is probably why LASIK is the procedure most often performed in refractive centers worldwide.[73-75] Interestingly, a recent study has shown a different trend in more recent years, with a shift in surgeon preference from LASIK back to PRK.[76] That change is thought to result from an increased awareness of ectasia risk and surgeons' desire to avoid such a dreaded complication, even when the estimated risk is slightly more than minimal. Ectasia screening and risk assessment scores are discussed below.

Procedure Choice for Hyperopia

Comparative studies of LASIK and PRK for hyperopia or compound hyperopic astigmatism treatment are fewer and the evidence produced is of poorer quality. Again, no definite superiority was proved for the long-term uncorrected visual acuity achieved, or for the refractive accuracy.[38] As predicted, LASIK involved less post-operative pain and refractive stability was achieved earlier. Moreover, PRK was associated with a high rate of peripheral haze.[77] Earlier reports presented higher rates of regression in patients treated with PRK[37,77] This difference has a tendency to disappear with the passage of time and the long-term efficacy and stability appear to be similar for both procedures.[38]

As for myopia, the differences between the two surgeries should be discussed at length with the patient and the choice tailored by the surgeon according to the patient's needs and the refractive error presented.

Mitomycin-C in PRK Treatments

Mitomycin-C (MMC) inhibits cellular replication and is widely used in ophthalmological surgery, particularly in glaucoma or pterygium surgery, as a way to modulate the local healing response and prevent excessive fibrovascular proliferation. Corneal haze is a known complication of PRK that results from abnormal keratocyte proliferation. It has long been reported that prophylatic healing modulation through the intra-operative use of mitomycin-C could be effective in reducing the incidence of post-PRK haze.[78] Since its description, the use of intra-operative mitomycin-C has gained acceptance and is now widespread among refractive surgeons, with over 90% of ASCRS members reporting using it as an adjunct to PRK.[79] Most studies address the effects on high myopic eyes, for which the use of mitomycin-C appears to be effective, both in preventing haze formation[80-82] and in improving refractive outcomes.[83,84] By regulating the healing process, mitomycin-C can also mitigate the regression that is sometimes seen after treatment.[78,85] This fact should be taken into account when devising the treatment plan because, with long application times, some level of overcorrection is to be expected, requiring nomogram adjustment.[78,85] For shorter periods of MMC exposure no adjustment is needed. Although less evidence is available, the same positive effect on haze prevention, visual outcome and refractive predictability, seems to be expected for hyperopic treatment.[86]

The exact dosing of mitomycin-C remains a matter of controversy. Based on the earliest reports of haze prophylaxis[87], many groups used MMC at 0.02% for 2 minutes. A desire to reduce exposure times and concentration has led to a gradual process of refinement over the years,

and several papers have reported the successful outcomes of different exposure times based on the depth of ablation performed[80] or surgeon's preference.[88] A prospective study comparing the 0.02% MMC with 0.002% found that although the standard dose of 0.02% was more effective for high myopia a reduced concentration was equally effective for low to moderate myopia.[81] Another study found that haze prophylaxis could be achieved with exposure time as short as 12 seconds[88] or 5 seconds.[89] A recent double-masked randomized prospective trial comparing results for different exposure times (60, 30 or 15 seconds) found that with modern ablation profiles MMC might actually not be needed.[90] In our center we performed a study comparing haze formation in myopic-PRK using different concentrations and exposure times or no MMC at all.[91] MMC was able to limit the increase of keratocyte density of the anterior stroma - assessed with confocal microscopy - and reduce haze formation. However no difference was noted when using either 0,02% or 0,01%, applied for 15 or 30 seconds.

The most mindful approach might be achieved with appropriate patient selection. There is little evidence supporting the use of MMC with very low levels of myopia and therefore MMC might not be needed for every case of surface ablation. We use a stepwise planning process: adjunctive MMC, applied for 12 seconds[88], is used during PRK only when ablation depth exceeds 50 µm.[92]

RISK ASSESSMENT FOR ECTASIA

Progressive keratectasia is one of the most feared complications of refractive ablation surgery. Although the estimated incidence of ectasia appears to be relatively low[93], it has significant consequences for the patient - with potential loss of best corrected visual acuity - and serious medico-legal implications.

Detailed reports have been published on the characteristics of patients who eventually developed ectasia, and those reports have formed the basis of numerous attempts to propose risk factors that could identify at-risk patients. Potentially, all cases could be avoided if at-risk patients were identified and excluded as unsuitable candidates, making this screening a vital point of the preoperative evaluation. Randleman *et al* proposed the Ectasia Risk Score System (ERSS)[94] which stratifies patients into different risks of ectasia according to the number of preoperative parameters present. Large retrospective reviews of long-term results of LASIK in myopic patients seem to validate this strategy.[93]

The stratification model gathers different variables deemed relevant and then assigns different points according to the values observed. The parameters are: (1) topographic pattern, (2) residual stromal bed (RSB) thickness, (3) age, (4) central corneal thickness (CCT), and (5) preoperative refraction. The complete system is presented in Table 3.

Table 3 | Ectasia Risk Factor Score System. ***Adapted from Randleman et al*** **[94].**

	Points				
Parameter	0	1	2	3	4
Topography	Normal	ABT		Inferior steepening/SRA	FFKC
RSB thickness (µm)	>300	280-299	260-279	240-259	<240
Age(years)	>30	26-29	22-25	18-21	
CT (µm)	>510		481-510	451-480	<450
MRSE (D)	< -8	-8 to -10	-10 to -12	-12 to -14	> -14

ABT: asymmetric bowtie; CT: preoperative corneal thickness; D: diopters; FFKC: forme fruste keratoconus; MRSE: preoperative spherical equivalent manifest refraction; RSB: residual stromal bed; ABT: assymmetric bowtie; SRA: skewed radial axis

Patients presenting 2 or fewer points would be at low risk for ectasia, 3 points would foresee a moderate risk, and all patients with 4 or more risk points would be at high risk for ectasia and performing LASIK should be discouraged.

Understandably, ectasia risk should be considered as a continuum and not constrained by arbitrary values. It must always be assessed on a personalized basis. Special care must be taken with cases presenting borderline values but that still fit the criteria.

A thin residual stromal bed is one of the most important factors contributing to biomechanical instability, as the flap left on site has a slight influence on the structural tensile strength of the cornea. The exact thickness of the residual stromal bed can be difficult to calculate accurately because it is affected by multiple factors. First, the depth of

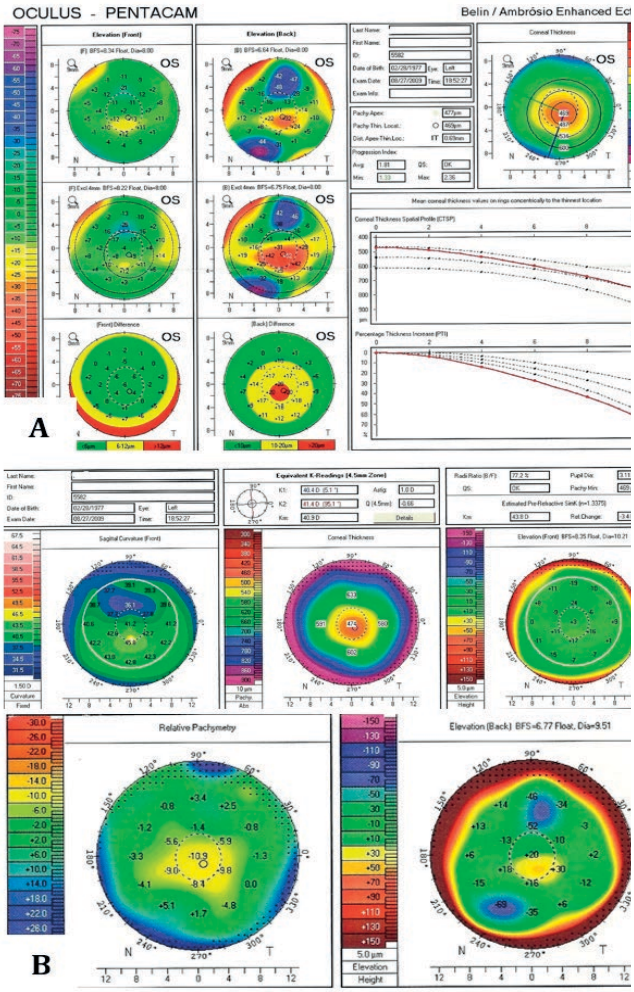

Fig. 1 | Topographic and elevation maps of a post-LASIK ectasia provided by the Pentacam® device. A: Belin/Ambrosio Enhanced Ectasia map; B: Holladay Report maps.

excimer ablation can be altered by the diameter of the optic zone chosen, the corneal profile, variations in the energy delivered[95] and relative dryness of the cornea.[64,96] Nor are devices for measuring corneal thickness without error and some variation has been reported.[97] Lastly, the estimated thickness of the flap intended does not always coincide with the real flap created,[64,98,99] especially handling manual microkeratomes. With all this in mind, we recommend that a minimum residual stromal bed thickness of 300 µm (corresponding to a score of 0 on the ERSS) be respected.

A common finding among patients who developed ectasia was the presence of preoperative topographic abnormalities that went unrecognized. Different imaging modalities are available for topographic screening. Some of the more popular include slit-scanning videokeratography, Scheimpflug camera devices, and wavefront analysis. A high suspicion index is advisable. Important hallmarks for KC screening are the presence of an inferior elevation, steeper inferior curvature, excessive thinning of the steepest zone and a skewed astigmatic axis without the normal bowtie pattern. Patients with PMD will usually present with a thinning area that is 1-2 mm wide, 1-2 mm above the inferior limbus. Unlike KC, the steepest area should be above the thinnest area. A claw shaped pattern is typical but not exclusive to this disease. The normal values of each physician topographic system should also be kept in mind. In the case of Orbscan II, red flags for possible pre-existing ectasia are: 1) posterior float larger than 0.04 mm; 2) anterior float larger than 0.025 mm; 3) irregularity in the 3mm zone > 1.5 D or > 2 D in the 5mm zone. A thinnest point that is 30 µm thinner than the central corneal thickness or more than 2.5 mm from the center of the corneal map is suspicious. Peripheral cornea should always be 20 µm thicker than the central cornea.

The use of Scheimpflug systems - like the Pentacam device (Oculus Optikgerate GmbH) - has also gained wide clinical acceptance, and some papers actually report them to be more sensitive at detecting early forms of KC.[100] The use of posterior elevation values,[100] anterior and posterior elevation differences (maximum - minimum),[101,102] asymmetry of the anterior curvature[101] or reconstructed tomographic elevation data (like the Belin/Ambrósio Enhanced Ectasia Display)[103] have all been reported as important criteria for the screening of subtle corneal changes. Again, important threshold values to identify abnormal corneas have been proposed. A thinnest point (TP) under 500 µm is problematic.[104] A central or paracentral "island" pattern is suspect, usually with elevation values that are 10 µm above the anterior surface or 15 µm below the posterior surface. The thinnest point is usually located within such an "island". A specific parameter is named the "Ambrósio Relational Thinnest" (ART) - calculated as the thinnest pachymetric value divided by the minimal (ART-Min), maximal (ART- Max) and average (ART-Mid) meridians of pachymetric progression. Corneas are deemed abnormal when the ART-Max and ART-Mid are lower than 339µm and 426µm, respectively.[105] The Belin/Ambrosio Enhanced Ectasia Display (BAD) combines front and back elevation values with the pachymetric distribution to obtain a comprehensive insight into the structure of the cornea. The final D (parameter deviation) value was calculated to provide optimal sensitivity and specificity, with a cutoff set at 1.6. The corneal thickness distribution profile is evaluated and the Corneal Thickness Spatial Profile (CTSP) and Percentage Thickness Increase (PTI) curve graphs calculated, providing important information when they escape expected values.[106]

Corneal aberrometric analysis is another effective tool for the detection of subclinical and advanced forms of KC.[107-111] The use of corneal wavefront aberrometry is more discriminating for KC detection than the use of total ocular aberration analysis.[112]

Although it is not included in the ERSS, a positive family history of ectatic disorders, even in the absence of evident corneal abnormalities, makes the patient a "less" desirable candidate.[113]

The development of corneal imaging devices has revealed the potential of corneal epithelial thickness distribution as a biological marker of corneal instability and ectatic or pre-ectatic states. Usually, epithelial maps can be obtained using high-frequency ultrasound[114,115] or OCT.[116,117] Keratoconic eyes seem to display specific patterns of epithelial thickness: significantly thinner over the inferior and temporal corneal area and thicker centrally and superiorly.[115,118] A specific "epithelial doughnut pattern" was described, consisting of a central area of epithelial thinning over the cone area, surrounded by a ring of thick epithelium.[114] This might prove significant when screening refractive surgery candidates that present with subclinical keratoconus and an unremarkable topography.

The epidemiology of keratoconus is highly variable among populations - from 0.3 per 100 000 in a Russian study (0.0003%)[119] to 2 300 per 100 000 individuals in Central India (2.3%).[120] However, even if it is not a particularly common disease in the general population, patients with keratoconus represent a disproportionate percentage of refractive surgery candidates, due to their poor spectacle-corrected quality of vision. These patients, together with others with pellucid marginal degeneration or corneal dystrophies, must be actively screened and identified, given the danger of causing iatrogenic damage to the patient's corneal stability.

Attempts at correcting large refractive errors is another well-known risk factor for ectasia.[121] As shown in Table 1, we are routinely even slightly more conservative relative to what is proposed by the ERSS when it comes to performing LASIK for moderate and high myopia. A recent Cochrane systematic review[122] favours phakic IOLs over excimer laser when treating myopia over -6.0 D. The results were similar in terms of the percentage of patients achieving 20/20 vision or better after 12 months but the safety profile was more favorable in the phakic IOL group, with fewer patients losing best spectacle-corrected visual acuity. Only three randomized controlled trials (RCTs) were considered and summarized[123-125], encompassing largely disparate values of myopia: between - 9.0 to and 19.5 D[123], between -8.0 and -12.0 D[124], and between -6.0 and -20.0D[125]. Further RCTs, with adequately powered sub-group analysis, are needed to discriminate the optimal range of myopia for each method.

A new metric for the assessment of ectasia risk was recently introduced for eyes that present with normal topography.[126,127] Percent Tissue Altered (PTA) is calculated as the percentage of flap thickness combined with ablation depth from the preoperative central thickness. A PTA value over 40 was deemed to be significantly associated with ectasia risk.

Described cases of post-PRK ectasia are fewer than post-LASIK. Although the presence of suspected topographic abnormalities constitutes an absolute contraindication for LASIK, there is little evidence available concerning the outcomes of PRK in corneas with subclinical keratoconus or other abrnormalities.[128] Regardless, most cases reported in the literature with post-PRK ectasia were either diagnosed with KC or had known topographic suspected abnormalities.[129-131] Therefore we recommend that eyes that are candidates for PRK be subjected to the same type of strict risk assessment proposed for LASIK candidates.

LONG TERM FOLLOW-UP

We are now analyzing the long term outcomes of the first generation of excimer laser surgeries performed almost a quarter of a century ago.

A paper reporting on the 20 year follow-up of myopic PRK showed that there was a small degree of myopic regression in the long term: -0.31 D of spherical equivalent after 18 years[132] and -0.54 D of spherical equivalent after 20 years.[133] Female sex and younger age were found to correlate with more regression but the reason for such an association is yet to be elucidated. No vision-threatening complications were reported. Results of 16 year outcomes for myopic PRK from another group[134] found that mean refractive error was -0.58 D. No serious complications were noted. Importantly, all patients said that they would undergo the procedure again today.

Long-term outcomes available for myopic LASIK are not as old, but 10- and 15-year follow-ups have been reported. A group of 40 patients with a minimum of 15 years of follow-up[135] showed some level of myopic regression with 46.15% of the eyes within 1 D of spherical equivalent of the attempted correction and 64.10% within 2 D. Interestingly, very high myopia was corrected in patients who would not be candidates if the surgery took place today. One case of ectasia occurred. Another study[136] reported a shorter follow-up but on a larger cohort of patients (346 eyes). Manifest

spherical equivalent was -0.67 ± 0.92 after 10 years. However, only 52% of patients achieved 20/20 vision. Two eyes had developed corneal ectasia.

POSTOPERATIVE CARE

LASIK

Topical antibiotics are prescribed, customarily a third generation quinolone (e.g. Levofloxacine 5 mg/ml), every 2 hours for the first 2 days and then 4 times a day for the next week. Topical corticosteroids are also prescribed every 2 hours immediately after surgery and then tapered according to clinical response.

Moderate discomfort is expected but oral analgesics or NSAIDs are not routinely prescribed in our clinic.

Patients are then seen again at the first day, third day and 3rd month. Observation in the first few days after surgery is important for the early detection of diffuse lamellar keratitis (DLK).[137,138]

PRK

Bandage contact lens is placed immediately after surgery. Topical antibiotics are prescribed, customarily a third generation quinolone (e.g. Levofloxacine 5 mg/ml), every 2 hours for 1 week.

Postoperative pain is common and oral NSAIDs can be prescribed (our group usually prescribes clonixin 300 mg every 4 to 6 hours).

The patient is re-examined on the 3rd or 4th day postoperative. Bandage contact lens is removed and slit-lamp examination performed to check for corneal reepithelization. Topical corticosteroid is introduced q.i.d. for the first 10 days and then tapered to t.i.d., b.i.d. and i.d. every 10 days. If full reepithelization is not observed, examination should be repeated every 2 or 3 days.

The patient is then re-observed on the 3rd month postoperative.

RETREATMENT

Despite its remarkable efficacy and safety there are still many cases where, because of immediate refractive result, patient expectations or late regression, a retreatment procedure is desirable.

The level of accuracy expected for the intended correction should be discussed with the patient and the possibility of the need for retreatment should be quite explicit on the informed consent signed by the patient.

A stable post-operative refraction should be achieved. In our center, we opt for a waiting period that is never less than 3 months after LASIK and 6 months after PRK. For hyperopic LASIK we prolong the waiting period to 6 months as well. Repeated measurements that strongly document the presence of a stable residual error are important. Considerate reflection on each case should be made on an individual basis, but we usually consider a residual error larger than 0.75 D in a symptomatic patient as a good threshold for retreatment. Before a decision is made, a comprehensive eye examination must be undertaken, including a careful review of all the preoperative elements. The possibility of a new pathologic condition (cataract, retinal changes) or early stage keratectasia altering the refractive stability has to be explicitly excluded, although cases of post-LASIK ectasia have a later time of onset, within 15 months[94,139] on average.

In the case of post-PRK patients it is important to carefully assess for the presence of haze and the potential myopic regression it might induce. The therapeutic efficacy of mitomycin-C irrigation after debridement has been postulated.[87,140]

In the case of post-LASIK patients, post-treatment corneal topography and residual stromal bed thickness should be measured. The use of anterior segment optical coherence tomography is an invaluable option for this assessment. The options most widely accepted for retreatment are lifting the previous flap[141] or performing PRK over LASIK[142-144]. The use of femtosecond laser to create mini-flaps or side-cuts has also been reported recently.[145,146]

CONCLUSION

We have reached a point of sophistication in laser refractive surgery that would have seemed unattainable for ophthalmologists 25 years ago. Numerous studies point to the positive impact that refractive surgery has on people's everyday life, with patients consistently reporting a postoperative improvement in their quality of life.[147,148] Hand in hand with the quasi magical results attributed by the general public to refractive surgery comes an equally inflated level of accountability. The high level of expectation associated with laser refractive surgery is unlikely to be equaled by any other surgical procedure. The ophthalmological community has been able to provide a positive response to that challenge, with new techniques, devices and theoretical approaches emerging every year. And as new areas of progress continue to appear, only further improvement is to be expected. The future of laser refractive surgery seems promising but it will only ever be as bright as the combined input and endeavor

of all its practitioners. Our patients expect great results and only a posture firmly grounded on strong epistemological knowledge and up-to-date practices can achieve that. Advocating, to the greatest extent possible, the harmonization of clinical procedures can only result in an optimized decision--making process. We hope that the clinical coordinates shared in this paper can serve as a frame of reference to both guide everyday medical practice and to foster the scientific debate and cooperation among the refractive community.

BIBLIOGRAPHY

1. Ambrósio R, Wilson S. LASIK vs LASEK vs PRK: advantages and indications. Semin Ophthalmol. 2003;18:2–10.
2. Sugar A, Rapuano CJ, Culbertson WW, Huang D, Varley GA, Agapitos PJ, et al. Laser in situ keratomileusis for myopia and astigmatism: Safety and efficacy: A report by the American Academy of Ophthalmology. Ophthalmology. 2002;109:175–87.
3. Sutton GL, Kim P. Laser in situ keratomileusis in 2010 - a review. Clinical and Experimental Ophthalmology. 2010. p. 192–210.
4. Leaming D V. Practice styles and preferences of ASCRS members - 2003 Survey. Journal of Cataract and Refractive Surgery. 2004. p. 892–900.
5. Ophthalmologists TRC of. A Patients ' Guide to Excimer Laser Refractive Surgery [Internet]. 2011. Available from: https://www.rcophth.ac.uk/wp-content/uploads/2015/03/Patient-Guide-to-Excimer-Laser--Refractive-Surgery-2011.pdf
6. Mirshahi A, Ponto K a., Hoehn R, Zwiener I, Zeller T, Lackner K, et al. Myopia and Level of Education. Results from the Gutenberg Health Study. Ophthalmology [Internet]. Elsevier Inc; 2014;121(10):2047–52. Available from: http://dx.doi.org/10.1016/j.ophtha.2014.04.017
7. Williams KM, Bertelsen G, Cumberland P, Wolfram C, Verhoeven VJM, Anastasopoulos E, et al. Increasing Prevalence of Myopia in Europe and the Impact of Education. Ophthalmology [Internet]. Elsevier Inc; 2015;122(7):1489–97. Available from: http://linkinghub.elsevier.com/retrieve/pii/S0161642015002808
8. Goss DA, Grosvenor T. Reliability of refraction--a literature review. J Am Optom Assoc. 1996;67:619–30.
9. Park SB, Lindahl KJ, Temnycky GO, Aquavella J V. The effect of pregnancy on corneal curvature. CLAO J. 1992;18(4):256–9.
10. Spoerl E, Zubaty V, Raiskup-Wolf F, Pillunat LE. Oestrogen-induced changes in biomechanics in the cornea as a possible reason for keratectasia. Br J Ophthalmol. 2007;91(11):1547–50.
11. Hafezi F, Iseli HP. Pregnancy-related exacerbation of iatrogenic keratectasia despite corneal collagen cross-linking. J Cataract Refract Surg. 2008;34(7):1219–21.
12. Padmanabhan P, Radhakrishnan A, Natarajan R. Pregnancy-triggered iatrogenic (post-laser in situ keratomileusis) corneal ectasia--a case report. Cornea. 2010. p. 569–72.
13. Smith RJ, Maloney RK. Laser in situ keratomileusis in patients with autoimmune diseases. J Cataract Refract Surg. 2006;32(8):1292–5.
14. Cobo-Soriano R, Beltrán J, Baviera J. LASIK Outcomes in Patients with Underlying Systemic Contraindications. A Preliminary Study. Ophthalmology. 2006;113(7).
15. Cua I, Pepose J. Late corneal scarring after photorefractive keratectomy concurrent with development of systemic lupus erythematosus. J Refract Surg. 2002;18(6):750–2.
16. Young J, Karnmhel E. Preoperative Evaluation for Refractive Surgery. Ophthalmology. 3rd ed. Mosby, an imprint of Elsevier; 2009. p. 118–21.
17. American Association of Oftalmology. Photoablation: Techniques and Outcomes. Basic and Clinical Science Course - Refractive Surgery. San Francisco; p. 65–91.
18. Liu Z, Pflugfelder SC. The effects of long-term contact lens wear on corneal thickness, curvature, and surface regularity. Ophthalmology. 2000;107:105–11.
19. Nourouzi H, Rajavi J, Okhovatpour MA. Time to Resolution of Corneal Edema After Long-Term Contact Lens Wear. Am J Ophthalmol. 2006;142:671–3.
20. Rosenbaum AL, Bateman JB, Bremer DL, Liu PY. Cycloplegic refraction in esotropic children. Cyclopentolate versus atropine. Ophthalmology. 1981;88:1031–4.
21. Schallhorn SC, Kaupp SE, Tanzer DJ, Tidwell J, Laurent J, Bourque LB. Pupil size and quality of vision after LASIK. Ophthalmology. 2003;110:1606–14.
22. Helgesen A, Hjortdal J, Ehlers N. Pupil size and night vision disturbances after LASIK for myopia. Acta Ophthalmol Scand. 2004;82:454–60.
23. Myung D, Schallhorn S, Manche EE. Pupil size and LASIK: a review. J Refract Surg [Internet]. 2013;29:734–41. Available from: http://www.ncbi.nlm.nih.gov/pubmed/24203804
24. Chan A, Manche EE. Effect of preoperative pupil size on quality of vision after wavefront-guided LASIK. Ophthalmology [Internet]. Elsevier Inc.; 2011;118(4):736–41. Available from: http://dx.doi.org/10.1016/j.ophtha.2010.07.030

25. Ho LY, Harvey TM, Scherer J, Balasubramaniam M, Dhaliwal DK, Mah FS. Comparison of Rosenbaum pupillometry card using red and blue light to Colvard and Iowa pupillometers. J Refract Surg. 2010;26(7):498–504.
26. Schallenberg M, Bangre V, Steuhl K-P, Kremmer S, Selbach JM. Comparison of the Colvard, Procyon, and Neuroptics pupillometers for measuring pupil diameter under low ambient illumination. J Refract Surg. 2010;26(2):134–43.
27. Society EG. Patient Examination. Terminology and Guidelines for Glaucom. 4th ed. Savona: PubliComm; 2014. p. 33–72.
28. De la Jara PL, Erickson D, Erickson P, Stapleton F. Pre-operative Quality of Life and psychological factors that influence patient decision making in LASIK. Eye (Lond). 2010;24:270–5.
29. Gupta N, Naroo SA. Factors influencing patient choice of refractive surgery or contact lenses and choice of centre. Contact Lens Anterior Eye. 2006;29:17–23.
30. Morse JS, Schallhorn SC, Hettinger K, Tanzer D. Role of depressive symptoms in patient satisfaction with visual quality after laser in situ keratomileusis. J Cataract Refract Surg. 2009;35:341–6.
31. FDA. FDA-approved lasers for LASIK, PRK and other refractive surgeries [Internet]. [cited 2015 Mar 3]. Available from: www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/SurgeryandLifeSupport/LASIK/ucm168641.htm,
32. Alió JL, Muftuoglu O, Ortiz D, Artola A, Pérez-Santonja JJ, de Luna GC, et al. Ten-Year Follow-up of Photorefractive Keratectomy for Myopia of Less Than -6 Diopters. Am J Ophthalmol. 2008;145:29–37.
33. Alió JL, Muftuoglu O, Ortiz D, Artola A, Pérez-Santonja JJ, de Luna GC, et al. Ten-Year Follow-up of Photorefractive Keratectomy for Myopia of More Than -6 Diopters. Am J Ophthalmol. 2008;145:37–46.
34. Barsam A, Allan BD. Excimer laser refractive surgery versus phakic intraocular lenses for the correction of moderate to high myopia. Cochrane Database Syst Rev. 2012;(5):CD007679.
35. Murray A, Jones L, Milne A. A systematic review of the safety and efficacy of elective photorefractive surgery for the correction of refractive error. Rev Body Rep… [Internet]. 2005;(April). Available from: http://www.gserve.nice.org.uk/nicemedia/live/11251/31559/31559.pdf
36. ZZ N, RR K, H H-N, A F, A K, E K, et al. Photorefractive keratectomy for hyperopia in 800 eyes with the Meditec MEL 60 laser. J Refract Surg. 2001;17(5):525–33.
37. Spadea L, Sabetti L, D'Alessandri L, Balestrazzi E. Photorefractive keratectomy and LASIK for the correction of hyperopia: 2-year follow-up. J Refract Surg. 2006;22(2):131–6.
38. Settas G, Settas C, Minos E, Yeung IYL. Photorefractive keratectomy (PRK) versus laser assisted in situ keratomileusis (LASIK) for hyperopia correction. Cochrane Database Syst Rev. 2012;(6).
39. Shen EP, Yang CN, Hu FR. Corneal astigmatic change after photorefractive keratectomy and photoastigmatic refractive keratectomy. J Cataract Refract Surg. 2002;28(3):491–8.
40. Katz T, Wagenfeld L, Galambos P, Darrelmann BG, Richard G, Linke SJ. LASIK versus photorefractive keratectomy for high myopic (> 3 diopter) astigmatism. J Refract Surg. 2013;29(12):824–31.
41. Dirani M, Couper T, Yau J, Ang EK, Islam FMA, Snibson GR, et al. Long-term refractive outcomes and stability after excimer laser surgery for myopia. J Cataract Refract Surg [Internet]. ASCRS and ESCRS; 2010;36(10):1709–17. Available from: http://dx.doi.org/10.1016/j.jcrs.2010.04.041
42. Jaycock PD, O'Brart DPS, Rajan MS, Marshall J. 5-Year follow-up of LASIK for hyperopia. Ophthalmology. 2005;112(2):191–9.
43. Varley G a., Huang D, Rapuano CJ, Schallhorn S, Boxer Wachler BS, Sugar A. LASIK for hyperopia, hyperopic astigmatism, and mixed astigmatism: A report by the American Academy of Ophthalmology. Ophthalmology. 2004;111(8):1604–17.
44. Salz JJ, Stevens CA. LASIK correction of spherical hyperopia, hyperopic astigmatism, and mixed astigmatism with the LADARVision excimer laser system. Ophthalmology. 2002;109(9):1647–57.
45. Ditzen K, Fiedler J, Pieger S. Laser in situ keratomileusis for hyperopia and hyperopic astigmatism using the Meditec MEL 70 spot scanner. J Refract Surg [Internet]. 2002;18(4):430–4. Available from: http://www.ncbi.nlm.nih.gov/pubmed/12160151
46. Esquenazi S, Mendoza A. Two-year follow-up of laser in situ keratomileusis for hyperopia. J Refract Surg [Internet]. 2013;15(6):648–52. Available from: http://www.ncbi.nlm.nih.gov/pubmed/23375692\nhttp://www.ncbi.nlm.nih.gov/pubmed/10590002
47. Williams LB, Dave SB, Moshirfar M. Correlation of visual outcome and patient satisfaction with preoperative keratometry after hyperopic laser in situ keratomileusis. J Cataract Refract Surg. 2008;34(7):1083–8.
48. Jin GJC, Lyle WA, Merkley KH. Laser in situ keratomileusis for primary hyperopia. J Cataract Refract Surg. 2005;31(4):776–84.

49. Cobo-Soriano R, Llovet F, González-López F, Domingo B, Gómez-Sanz F, Baviera J. Factors that influence outcomes of hyperopic laser in situ keratomileusis. J Cataract Refract Surg. 2002;28(9):1530–8.
50. Young JJ, Schallhorn SC, Brown MC, Hettinger KA. Effect of keratometry on visual outcomes 1 month after hyperopic LASIK. J Refract Surg. 2009;25(7 Suppl):S672–6.
51. Tabbara KF, El-Sheikh HF, Islam M. Laser in situ keratomileusis for the correction of hyperopia from+0.50 to+11.50 diopters with the Keracor 117G laser. J Refract Surg. 2001;17(2):123–8.
52. Llovet F, Galal A, Benitez-del-Castillo J-M, Ortega J, Martin C, Baviera J. One-year results of excimer laser in situ keratomileusis for hyperopia. J Cataract Refract Surg [Internet]. ASCRS and ESCRS; 2009;35(7):1156–65. Available from: http://dx.doi.org/10.1016/j.jcrs.2009.03.014
53. Rao SK, Cheng ACK, Fan DSP, Leung ATS, Lam DSC. Effect of preoperative keratometry on refractive outcomes after laser in situ keratomileusis. J Cataract Refract Surg. 2001;27(2):297–302.
54. Perez-Santonja JJ, Bellot J, Claramonte P, Ismail MM, Alio JL. Laser in situ keratomileusis to correct high myopia. J Cataract Refract Surg [Internet]. 1997;23(3):372–85. Available from: http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=9159682
55. Vajpayee RB, Ghate D, Sharma N, Tandon R, Titiyal JS, Pandey RM. Risk factors for postoperative cylindrical prediction error after laser in situ keratomileusis for myopia and myopic astigmatism. Eye (Lond). 2008;22(3):332–9.
56. Hu DJ, Feder RS, Basti S, Fung BB, Rademaker AW, Stewart P, et al. Predictive formula for calculating the probability of LASIK enhancement. J Cataract Refract Surg. 2004;30(2):363–8.
57. Christiansen SM, Neuffer MC, Sikder S, Semnani RT, Moshirfar M. The effect of preoperative keratometry on visual outcomes after moderate myopic LASIK. Clin Ophthalmol. 2012;6(1):459–64.
58. Melki SA, Azar DT. LASIK complications: Etiology, management, and prevention. Survey of Ophthalmology. 2001. p. 95–116.
59. Albelda-vallés JC, Martin-reyes C, Ramos F, Beltran J, Llovet F, Baviera J. Effect of Preoperative Keratometric Power. J Refract Surg. 2007;1–6.
60. Gimbel H V., Anderson Penno EE, Van Westenbrugge JA, Ferensowicz M, Furlong MT. Incidence and management of intraoperative and early postoperative complications in 1000 consecutive laser in situ keratomileusis cases. Ophthalmology. 1998;105(10):1839–48.
61. Leung ATS, Rao SK, Cheng ACK, Yu EWY, Fan DSP, Lam DSC. Pathogenesis and management of laser in situ keratomileusis flap buttonhole. J Cataract Refract Surg. 2000;26(3):358–62.
62. Kezirian GM, Stonecipher KG. Comparison of the IntraLase femtosecond laser and mechanical keratomes for laser in situ keratomileusis. J Cataract Refract Surg. 2004;30(4):804–11.
63. Nordan TL, Slade SG, Baker RN, Suarez C, Juhasz T, Al E. Femtosecond laser versus mechanical microkeratomes for flap creation in laser in situ keratomileusis and effect of postoperative measurement interval on estimated femtosecond flap thickness. J Refract Surg. 2003;19(1):8–14.
64. Rosa AM, Murta JN, Quadrado MJ, Tavares C, Lobo C, Van Velze R, et al. Femtosecond laser versus mechanical microkeratomes for flap creation in laser in situ keratomileusis and effect of postoperative measurement interval on estimated femtosecond flap thickness. J Cataract Refract Surg. 2009;35(5):833–8.
65. Tran DB, Sarayba M a., Bor Z, Garufis C, Duh YJ, Soltes CR, et al. Randomized prospective clinical study comparing induced aberrations with IntraLase and Hansatome flap creation in fellow eyes: Potential impact on wavefront-guided laser in situ keratomileusis. J Cataract Refract Surg. 2005;31(1):97–105.
66. Ivarsen A, Hjortdal J. Seven-year changes in corneal power and aberrations after PRK or LASIK. Investig Ophthalmol Vis Sci. 2012;53(10):6011–6.
67. Lee JB, Kim JS, Choe CM, Seong GJ, Kim EK. Comparison of two procedures: Photorefractive keratectomy versus laser in situ keratomileusis for low to moderate myopia. Jpn J Ophthalmol. 2001;45(5):487–91.
68. Hatch BB, Moshirfar M, Ollerton AJ, Sikder S, Mifflin MD. A prospective, contralateral comparison of photorefractive keratectomy (PRK) versus thin-flap LASIK: Assessment of visual function. Clin Ophthalmol. 2011;5(1):451–7.
69. Wallau AD, Campos M. One-year outcomes of a bilateral randomised prospective clinical trial comparing PRK with mitomycin C and LASIK. Br J Ophthalmol. 2009;93(12):1634–8.
70. El Danasoury MA, el Maghraby A, Klyce SD, Mehrez K. Comparison of photorefractive keratectomy with excimer laser in situ keratomileusis in correcting low myopia (from -2.00 to -5.50 diopters). A randomized study. Ophthalmology. 1999.

71. Costa E, Franqueira N, Rosa AM, Tavares C, Quadrado MJ, Lobo C, et al. Photorefractive keratectomy for myopia and myopic astigmatism correction using the Wavelight Allegretto Wave Eye-Q excimer laser system. Int Ophthalmol. 2014;34(3):477–84.
72. Aj S, Bds A, Jr E. Laser-assisted in-situ keratomileusis (LASIK) versus photorefractive keratectomy (PRK) for myopia (Review) SUMMARY OF FINDINGS FOR THE MAIN COMPARISON. 2013;(1).
73. IC K. Trends in refractive surgery at an academic center: 2007–2009. BMC Ophthalmol. 2011;11(11).
74. Schmack I, Auffarth GU, Epstein D HM. Refractive surgery trends and practice style changes in Germany over a 3-year period. J Refract Surg. 2010;26(3):202–8.
75. Waring GO DD. Emerging trends for procedure selection in contemporary refractive surgery: consecutive review of 200 cases from a single center. J Refract Surg. 2008;24(4):419–23.
76. Moisseiev E, Sela T, Minkev L, Varssano D. Increased preference of surface ablation over laser in situ keratomileusis between 2008-2011 is correlated to risk of ecatasia. Clin Ophthalmol [Internet]. 2013 Jan;7:93–8. Available from: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=3548437&tool=pmcentrez&rendertype=abstract
77. El-Agha MSH, Bowman RW, Cavanagh D, McCulley JP. Comparison of photorefractive keratectomy and laser in situ keratomileusis for the treatment of compound hyperopic astigmatism. J Cataract Refract Surg. 2003;29(5):900–7.
78. Carones F, Vigo L, Scandola E, Vacchini L. Evaluation of the prophylactic use of mitomycin-C to inhibit haze formation after photorefractive keratectomy. J Cataract Refract Surg. 2002;28(12):2088–95.
79. Duffey R LD. US trends in refractive surgery: 2013 ASCRS survey [Internet]. [cited 2015 Apr 7]. Available from: http://www.duffeylaser.com/physicians_resources.php
80. Lee DH, Chung HS, Jeon YC, Boo SD, Yoon YD, Kim JG. Photorefractive keratectomy with intraoperative mitomycin-C application. J Cataract Refract Surg. 2005;31(12):2293–8.
81. Thornton I, Puri A, Xu M, Krueger RR. Low-Dose Mitomycin C as a Prophylaxis for Corneal Haze in Myopic Surface Ablation. Am J Ophthalmol. 2007;144(5):673–82.
82. Sia RK, Ryan DS, Edwards JD, Stutzman RD, Bower KS. The U.S. Army Surface Ablation Study: comparison of PRK, MMC-PRK, and LASEK in moderate to high myopia. J Refract Surg [Internet]. 2014;30(4):256–64. Available from: http://www.ncbi.nlm.nih.gov/pubmed/24702577
83. Bedei A, Marabotti A, Giannecchini I, Ferretti C, Montagnani M, Martinucci C, et al. Photorefractive keratectomy in high myopic defects with or without intraoperative mitomycin C: 1-Year results. Eur J Ophthalmol. 2006;16(2):229–34.
84. Diakonis VF, Kankariya VP, Kymionis GD, Kounis G, Kontadakis G, Gkenos E, et al. Long Term Followup of Photorefractive Keratectomy with Adjuvant Use of Mitomycin C. 2014;2014:10–5.
85. Leccisotti A. Mitomycin C in photorefractive keratectomy: effect on epithelialization and predictability. Cornea. 2008;27(3):288–91.
86. Leccisotti A. Mitomycin-C in hyperopic photorefractive keratectomy. J Cataract Refract Surg [Internet]. ASCRS and ESCRS; 2009;35(4):682–7. Available from: http://dx.doi.org/10.1016/j.jcrs.2008.11.060
87. RAVIV T, MAJMUDAR PA, DENNIS R, EPSTEIN R. Mitomycin-C for Post-PRK Corneal Haze. J Cataract Refract Surg. 2000;26(August):3–4.
88. Virasch V V., Majmudar P a., Epstein RJ, Vaidya NS, Dennis RF. Reduced Application Time for Prophylactic Mitomycin C in Photorefractive Keratectomy. Ophthalmology [Internet]. Elsevier Inc.; 2010;117(5):885–9. Available from: http://dx.doi.org/10.1016/j.ophtha.2009.10.024
89. Shojaei A, Ramezanzadeh M, Soleyman-Jahi S, Almasi-Nasrabadi M, Rezazadeh P, Eslani M. Short-time mitomycin-C application during photorefractive keratectomy in patients with low myopia. J Cataract Refract Surg [Internet]. ASCRS and ESCRS; 2013;39(2):197–203. Available from: http://dx.doi.org/10.1016/j.jcrs.2012.09.016
90. Hofmeister EM, Bishop FM, Kaupp SE, Schallhorn SC. Randomized dose-response analysis of mitomycin-C to prevent haze after photorefractive keratectomy for high myopia. J Cataract Refract Surg [Internet]. ASCRS and ESCRS; 2013;39(9):1358–65. Available from: http://dx.doi.org/10.1016/j.jcrs.2013.03.029
91. D C, R T, MJ Q, JN M. Confocal microscopy evaluation of prophylatic mitomicyn C used to inibit corneal haze after PRK. Stockholm; 2007.
92. Thornton I, Xu M, Krueger RR. Comparison of standard (0.02%) and low dose (0.002%) mitomycin C in the prevention of corneal haze following surface ablation for myopia. J Refract Surg. 2008;24(1):S68–76.
93. Spadea L, Cantera E, Cortes M, Conocchia NE, Stewart CW. Corneal ectasia after myopic laser in situ keratomileusis: a long-term study. Clin Ophthalmol [Internet].

2012 Jan;6:1801–13. Available from: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=3497457&tool=pmcentrez&rendertype=abstract
94. Randleman JB, Woodward M, Lynn MJ, Stulting RD. Risk assessment for ectasia after corneal refractive surgery. Ophthalmology [Internet]. 2008 Jan [cited 2013 Aug 18];115(1):37–50. Available from: http://www.ncbi.nlm.nih.gov/pubmed/17624434
95. Lee DH, Kwon OY KJ. The comparison of corneal ablation amount by MEL-60 excimer laser and Schwind Multiscan excimer laser systems. J Korean Ophthalmol Soc. 2003;44:1048–53.
96. Maldonado MJ, Ruiz-Oblitas L, Munuera JM, Aliseda D, Garcia-Layana A M-MJ. Optical coherence tomography evaluation of the corneal cap and stromal bed features after laser in situ keratomileusis for high myopia and astigmatism. Ophtalmology. 2000;107:81–8.
97. Kanellopoulos AJ, Asimellis G. Comparison of high--resolution scheimpflug and high-frequency ultrasound biomicroscopy to anterior-segment OCT corneal thickness measurements. Clin Ophthalmol. 2013;7:2239–47.
98. Yildirim R, Aras C, Ozdamar A, Bahcecioglu H, Ozkan S. Reproducibility of corneal flap thickness in laser in situ keratomileusis using the Hansatome microkeratome. J Cataract Refract Surg. 2000;26(12):1729–32.
99. Binder PS. One thousand consecutive IntraLase laser in situ keratomileusis flaps. J Cataract Refract Surg. 2006;32(6):962–9.
100. De Sanctis U, Loiacono C, Richiardi L, Turco D, Mutani B, Grignolo FM. Sensitivity and Specificity of Posterior Corneal Elevation Measured by Pentacam in Discriminating Keratoconus/Subclinical Keratoconus. Ophthalmology. 2008;115(9):1534–9.
101. Bae GH, Kim JR, Kim CH, Lim DH, Chung ES, Chung TY. Corneal topographic and tomographic analysis of fellow eyes in unilateral keratoconus patients using pentacam. Am J Ophthalmol [Internet]. Elsevier Inc.; 2014;157(1):103–9.e1. Available from: http://dx.doi.org/10.1016/j.ajo.2013.08.014
102. Nilforoushan MR, Speaker M, Marmor M, Abramson J, Tullo W, Morschauser D, et al. Comparative evaluation of refractive surgery candidates with Placido topography, Orbscan II, Pentacam, and wavefront analysis. J Cataract Refract Surg. 2008;34(4):623–31.
103. Gilani F, Cortese M, Ambrósio RR, Lopes B, Ramos I, Harvey EM, et al. Comprehensive anterior segment normal values generated by rotating Scheimpflug tomography. J Cataract Refract Surg. 2013;39(11):1707–12.
104. R AJ. Simplifying Ectasia Screening with. Highlights Ophthalmol. 2010;38(3).
105. Ambrósio Jr R, Caiado ALC. GFP., Louzada R, Roy AS, Luz A, Dupps WJ., et al. Novel Pachymetric Parameters Based on Corneal Tomography for Diagnosing Keratoconus. J Refract Surg. 2011;27(10):753–8.
106. Ambrósio R, Alonso RS, Luz A, Coca Velarde LG. Corneal-thickness spatial profile and corneal-volume distribution: Tomographic indices to detect keratoconus. J Cataract Refract Surg. 2006;32(11):1851–9.
107. Bühren J, Kühne C, Kohnen T. Defining Subclinical Keratoconus Using Corneal First-Surface Higher-Order Aberrations. Am J Ophthalmol. 2007;143(3).
108. Bühren J, Kook D, Yoon G, Kohnen T. Detection of subclinical keratoconus by using corneal anterior and posterior surface aberrations and thickness spatial profiles. Investig Ophthalmol Vis Sci. 2010;51(7):3424–32.
109. Nakagawa T, Maeda N, Kosaki R, Hori Y, Inoue T, Saika M, et al. Higher-order aberrations due to the posterior corneal surface in patients with keratoconus. Investig Ophthalmol Vis Sci. 2009;50(6):2660–5.
110. Bühren J, Schäffeler T, Kohnen T. Validation of metrics for the detection of subclinical keratoconus in a new patient collective. J Cataract Refract Surg. 2014;40(2):259–68.
111. Bayhan HA, Aslan Bayhan S, Muhafiz E, Can I. Repeatability of aberrometric measurements in normal and keratoconus eyes using a new Scheimpflug--Placido topographer. J Cataract Refract Surg. 2014;40(2):269–75.
112. Piñero DP, Nieto JC, Lopez-Miguel A. Characterization of corneal structure in keratoconus. J Cataract Refract Surg. 2012;38(12):2167–83.
113. Binder PS, Lindstrom RL SR, Al E. Keratoconus and corneal ectasia after LASIK. J Cataract Refract Surg. 2005;31:2035–8.
114. Reinstein DZ, Gobbe M, Archer TJ, Silverman RH, Coleman DJ. Epithelial, stromal, and total corneal thickness in keratoconus: three-dimensional display with artemis very-high frequency digital ultrasound. J Refract Surg. 2010;26(4):259–71.
115. Aslanides IM, Asimellis G. Epithelial Thickness: An Indicator for Early Keratoconus? Investigation with high-frequency UBM detects differences in normal, keratoconic eyes. Cataract Refract Surg TODAY Eur. 2013;(june):50–3.
116. Li Y, Tan O, Brass R, Weiss JL, Huang D. Corneal epithelial thickness mapping by fourier-domain optical coherence tomography in normal and keratoconic eyes. Ophthalmology. 2012;119(12):2425–33.
117. Haque S, Jones L, Simpson T. Thickness mapping of the cornea and epithelium using optical coherence

tomography. Optom Vis Sci. 2008;85(10):E963–76.
118. Zhou W, Stojanovic A. Comparison of corneal epithelial and stromal thickness distributions between eyes with keratoconus and healthy eyes with corneal astigmatism ???2.0 D. PLoS One. 2014;9(1).
119. Gorskova EN SE. Epidemiology of keratoconus in the Urals. Vestn Oftalmol. 1998;114(4):38–40.
120. Jonas JB, Nangia V, Matin A, Kulkarni M, Bhojwani K. Prevalence and Associations of Keratoconus in Rural Maharashtra in Central India: The Central India Eye and Medical Study. Am J Ophthalmol. 2009;148:760–5.
121. Condon PI, O'Keefe M BP. Long-term results of laser in situ keratomileusis for high myopia: Risk for ectasia. J Cataract Refract Surg. 2007;33:583–90.
122. Barsam A, Allan BD. Excimer laser refractive surgery versus phakic intraocular lenses for the correction of moderate to high myopia. Cochrane Database Syst Rev. 2010;(5):CD007679.
123. El Danasoury M, El Maghraby A, Gamali T. Comparison of iris-fixed Artisan lens implantation with excimer laser in situ keratomileusis in correcting myopia between -9.00 and -19.50 diopters: a randomized study. Ophtalmology. 2002;109(5):955–64.
124. Malecaze F, Hulin H, Bierer P, Fournie P, Grandjean H, Thalamas C et al. A randomized paired eye comparison of two techniques for treating moderately high myopia: LASIK and artisan phakic lens. Ophthalmology. 2002;109(9):1622–30.
125. Schallhorn S, Tanzer D, Sanders D, Sanders M. Randomized prospective comparison of visian toric implantable collamer lens and conventional photorefractive keratectomy for moderate to high myopic astigmatism. J Cataract Refract Surg. 2007;23(9):853–67.
126. Santhiago MR, Smadja D, Gomes BF, Mello GR, Monteiro MLR, Wilson SE, et al. Association between the percent tissue altered and post-laser in situ keratomileusis ectasia in eyes with normal preoperative topography. Am J Ophthalmol. 2014;158(1).
127. Ambrósio Jr. R, Dawson DG, Belin MW. Association Between the Percent Tissue Altered and Post–Laser In Situ Keratomileusis Ectasia in Eyes With Normal Preoperative Topography. Am J Ophthalmol [Internet]. Elsevier; 2015 Mar 16;158(6):1358–9. Available from: http://www.ajo.com/article/S0002-9394(14)00580-7/abstract
128. Guedj M, Saad A, Audureau E, Gatinel D. Photorefractive keratectomy in patients with suspected keratoconus: Five-year follow-up. J Cataract Refract Surg [Internet]. ASCRS and ESCRS; 2013;39(1):66–73. Available from: http://dx.doi.org/10.1016/j.jcrs.2012.08.058
129. Chiou AGY, Bovet J, de Courten C. Management of corneal ectasia and cataract following photorefractive keratectomy. J Cataract Refract Surg. 2006;32(4):679–80.
130. Reznik J, Salz JJ, Klimava A. Development of unilateral corneal ectasia after PRK with ipsilateral preoperative forme fruste keratoconus. Journal of refractive surgery (Thorofare, N.J. : 1995). 2008. p. 843–7.
131. Malecaze F, Coullet J, Calvas P, Fournié P, Arné JL, Brodaty C. Corneal Ectasia after Photorefractive Keratectomy for Low Myopia. Ophthalmology. 2006;113(5):742–6.
132. Shalchi Z, O'Brart DPS, McDonald RJ, Patel P, Archer TJ, Marshall J. Eighteen-year follow-up of excimer laser photorefractive keratectomy. J Cataract Refract Surg [Internet]. ASCRS and ESCRS; 2015;41(1):23–32. Available from: http://linkinghub.elsevier.com/retrieve/pii/S0886335014015405
133. O'Brart DPS, Shalchi Z, McDonald RJ, Patel P, Archer TJ, Marshall J. Twenty-Year Follow-Up of a Randomized Prospective Clinical Trial of Excimer Laser Photorefractive Keratectomy. Am J Ophthalmol [Internet]. Elsevier Inc.; 2014;158(4):651–63.e1. Available from: http://linkinghub.elsevier.com/retrieve/pii/S0002939414003602
134. Guerin MB, Darcy F, O'Connor J, O'Keeffe M. Excimer laser photorefractive keratectomy for low to moderate myopia using a 5.0 mm treatment zone and no transitional zone: 16-Year follow-up. J Cataract Refract Surg [Internet]. ASCRS and ESCRS; 2012;38(7):1246–50. Available from: http://dx.doi.org/10.1016/j.jcrs.2012.03.027
135. Alió JL, Soria F, Abbouda A, Peña-García P. Laser in situ keratomileusis for −6.00 to −18.00 diopters of myopia and up to −5.00 diopters of astigmatism: 15-year follow-up. J Cataract Refract Surg [Internet]. 2014;33–40. Available from: http://linkinghub.elsevier.com/retrieve/pii/S0886335014015259
136. Ide T, Toda I, Fukumoto T, Watanabe J, Tsubota K. Outcome of a 10-year follow-up of laser in situ laser keratomileusis for myopia and myopic astigmatism. Taiwan J Ophthalmol [Internet]. Elsevier Taiwan LLC; 2014;4(4):156–62. Available from: http://linkinghub.elsevier.com/retrieve/pii/S2211505614000635
137. Johnson JD, Harissi-Dagher M, Pineda R, Yoo S, Azar DT. Diffuse lamellar keratitis: Incidence, associations, outcomes, and a new classification system. J Cataract Refract Surg. 2001;27(10):1560–6.
138. Choe CH, Guss C, Musch DC, Niziol LM, Shtein RM. Incidence of diffuse lamellar keratitis after LASIK with 15 KHz, 30 KHz, and 60 KHz femtosecond laser flap

creation. J Cataract Refract Surg [Internet]. ASCRS and ESCRS; 2010;36(11):1912–8. Available from: http://dx.doi.org/10.1016/j.jcrs.2010.09.003
139. Randleman JB, Russell B, Ward MA, Thompson KP, Stulting RD. Risk factors and prognosis for corneal ectasia after LASIK. Ophthalmology. 2003;110(2):267–75.
140. Vigo L, Scandola E CF. Scraping and mitomycin C to treat haze and regression after photorefractive keratectomy for myopia. J Cataract Refract Surg. 2003;19(4):449–54.
141. Santhiago MR, Smadja D, Zaleski K, Espana EM, Armstrong BK, Wilson SE. Flap Relift for Retreatment After Femtosecond Laser–assisted LASIK. Journal of Refractive Surgery. 2012. p. 482–7.
142. Lee BS, Gupta PK, Davis EA HD. Outcomes of photorefractive keratectomy enhancement after LASIK. J Refract Surg. 2014;30(8):549–56.
143. Neira-Zalentein W, Moilanen JAO, Tuisku IS, Holopainen JM, Tervo TMT. Photorefractive keratectomy retreatment after LASIK. J Refract Surg. 2008;24(7):710–2.
144. Carones F, Vigo L, Carones A V., Brancato R. Evaluation of photorefractive keratectomy retreatments after regressed myopic laser in situ keratomileusis. Ophthalmology. 2001;108(10):1732–7.
145. Vaddavalli PK, Yoo SH, Diakonis VF, Canto AP, Shah N V., Haddock LJ, et al. Femtosecond laser-assisted retreatment for residual refractive errors after laser in situ keratomileusis. J Cataract Refract Surg. 2013;39(8):1241–7.
146. Garcia-Gonzalez M, Teus MA. Creation of a New Femtosecond Laser-Assisted Mini-Flap to Enhance Late Regression After LASIK. J Refract Surg. 2013;29(8):564–9.
147. Chen CY, Keeffe JE, Garoufalis P, Islam FMA, Dirani M, Couper TA, et al. Vision-related quality of life comparison for emmetropes, myopes after refractive surgery, and myopes wearing spectacles or contact lenses. J Refract Surg. 2007;23(8):752–9.
148. Pesudovs K, Garamendi E, Elliott DB. A quality of life comparison of people wearing spectacles or contact lenses or having undergone refractive surgery. J Refract Surg. 2006;22(1):19–27.

Todos os autores declaram não haver nenhum potencial conflito de interesses.

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