

No-Alcohol Laser Epithelial Keratomileusis (LASEK) and Photo Refractive Keratectomy (PRK) for the Correction of Low to Medium Myopia: A Review of the Literature

Leopoldo Spadea*, Maria Pia Paroli and Luca Spadea

University "La Sapienza", Department of Sense Organs, Eye Clinic, Rome, Italy

PhotoRefractive Keratectomy (PRK) procedure is commonly used to correct myopia and astigmatism. PRK involves the use of an excimer laser to reshape the anterior corneal surface [1]. The excimer laser alters the refractive state of the eye by removing tissue from the anterior cornea through a process known as photoablative decomposition.

This process uses ultraviolet energy from the excimer laser to disrupt chemical bonds in the cornea without causing any thermal damage to surrounding tissue [2]. Laser Epithelial Keratomileusis (LASEK) is a modified PRK technique introduced by Camellin in 1999 [3] based on the detachment of an epithelial flap after the application of an alcohol solution, and then the repositioning of this flap following laser application.

The popularity of LASEK has been gaining momentum among refractive ophthalmologists after a few clinical series showed that LASEK might have significant clinical advantages over PRK [4]. Autrata et al. compared the clinical results (efficacy, safety, stability, and postoperative pain or discomfort) of LASEK and conventional PRK for the correction of low to moderate myopia and they showed that there were no statistically significant differences in the safety and efficacy indices at 2 years [5]. Lee et al. learned that LASEK-treated eyes had less significant postoperative pain and corneal haze than PRK-treated eyes in the early postoperative period [6].

LASEK consists on the detachment of an epithelial flap after the application of an alcohol solution, and then the repositioning of this flap following laser application. From the viewpoint of the decreased corneal haze after LASEK, although the details of underlying cellular events remain unclear, we speculate that if an epithelial flap is made, it becomes loose and lengthens enough to cover the cut epithelial border. It seals up the bare stroma. That prevents the release of cytokines and growth factors from the stroma and damaged epithelium, which decreases the initial inflammatory damage to the stroma. This may reduce the apoptosis of anterior stromal keratocytes and subsequent replenishment with activated keratocytes, later decreasing the synthesis of collagens [7].

Ethanol was initially used in refractive surgery to assist in the removal of the epithelium before PRK [8,9] and has been shown to enhance corneal flap lifting without significant loss of flap viability. Alcohol acts on the corneal epithelium-basement membrane complex by splitting the epithelial basement membrane without affecting the anchoring of the basement membrane to the underlying Bowman's layer [10].

However, alcohol is known to be cytotoxic; among a multiplicity of toxic effect mechanisms, the predominant mode of action appears to derive from protein coagulation/denaturation [11], which takes

*Corresponding author: Leopoldo Spadea, Head Eye Clinic, Policlinico Umberto I, "Sapienza" University of Rome, Via Benozzo Gozzoli 34, 00142 Rome, Italy, Tel: +39065193220; Fax: +390688657818; E-mail: leopoldo.spadea@uniroma1.it

Received Date: March 10, 2021

Accepted Date: March 22, 2021

Published Date: March 28, 2021

Citation: Spadea L, Paroli MP, Spadea L (2021) No-Alcohol Laser Epithelial Keratomileusis (LASEK) and PhotoRefractive Keratectomy (PRK) for the Correction of Low to Medium Myopia: A Review of the Literature J Ophthal Opto 3: 010.

Copyright: © 2021 Spadea L, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

place at the cell membrane and among the various plasma proteins. Coagulation of enzymatic proteins leads to the loss of cell functions [12].

Hence, caution is required when applying alcohol to the cornea. Removal of the corneal epithelium before PRK with 18% or 20% ethanol left for 20 to 40 seconds is safe to the underlying corneal stroma and is an effective alternative to scraping (ie, mechanical debridement) [13,14]. Even an exposure time of 3 minutes with 25% alcohol appears safe, effective, and predictable without stromal dehydration or toxic effects and is not associated with significant loss of CDVA after PRK [15]. However, higher alcohol concentrations such as 50% [16] and 100% [17] ethanol can lead to substantial damage to the underlying stroma.

Soma et al. evaluated the effect of mechanical epithelial separation with an epikeratome on the histologic ultrastructure of epithelial flaps and stromal beds from human corneas. He showed that on scanning electron microscopy, the cleavage planes of epithelial flaps and stromal beds were relatively smooth; on transmission electron microscopy, epithelial flaps were separated partially within the lamina fibroreticularis and partially within the lamina lucida; immunofluorescence showed positive staining for type VII collagen and discontinuous staining for type IV collagen in stromal beds. Discontinuous linear staining for types IV and VII collagens was observed in epithelial flaps. Staining for integrins alpha 6 and beta 4 was positive in some regions and discontinuous in other regions of epithelial flaps. In stromal beds, integrins alpha 6 and beta 4 had a patchy expression pattern. Staining for laminin 5 was intermittently positive along the basal side of epithelial flaps and stromal beds [18].

In 1995 we examined four human corneas that had undergone PRK and subsequent penetrating keratoplasty by means of light

and electron microscopy in an attempt to detect possible causes for complications after PRK and despite recovery of a continuous epithelial layer as early as 3 days after PRK, abnormalities of both epithelium and superficial stroma could be detected in all specimens, including the one obtained 13 months after the refractive procedure were observed [19]. Cui et al., using immunohistochemical staining and Western Blot analysis, observed and compared the accurate dynamic changes of type I, III, V, VI collagen in the wound healing processes of the rabbit cornea which underwent LASEK or PRK to investigate the possible mechanism of corneal haze and myopic regression.

They showed that after LASEK, the corneal wound healing with type I and III collagen were much faster than PRK, and the wound response was also much weaker. The value of these two types of collagen after PRK were higher than LASEK. Moreover there were significant differences between LASEK and PRK on type V and VI collagens in the time of reacting, reaching an apex and returning to normal. LASEK had slighter intensity of reaction and there was an excessive aggregation of collagens after PRK that it may be the histological foundation of obvious haze and myopic regression in PRK [20].

Zhou et al evaluated short-term corneal endothelial changes after LASEK and they documented that acute endothelial changes occur on specular microscopic examination after LASEK. When taken as a whole, LASEK-treated eyes had a significant increase in post-operative Coefficient of Variation (CV) of cell size and a significant decrease in Endothelial Cell Density (ECD) and cell hexagonality at 15 min post-operatively. These findings indicate that, immediately after LASEK, the number of cells/mm² decreases and the endothelial cells became much more swollen compared with their preoperative size. But these changes were transient; ECD and variations in cell area returned to near baseline (pre-operative) levels by 1 day post-operatively. An increased CV of cell size would be expected if there was a decrease in the percentage of hexagonal cells, as observed by Zhou.

The percentage of hexagonal cells also returned to near the baseline (pre-operative) level by 1 week post-operatively, suggesting that endothelial cell function recovered 1 week after LASEK [21]. Studies that have evaluated the endothelium after PRK have reported little or no endothelial change, with no clinically significant decrease in central ECD [22,23].

The vitality of the epithelial flap is probably a crucial factor in the dampened wound response in LASEK versus PRK. Gabler et al [24]. Investigated the vitality of the corneal epithelium after exposure to 20% ethanol during LASEK and they demonstrated that after 15 and 30 seconds of exposure to 20% ethanol, the epithelium is intact and most corneal epithelial cells are alive. They also recommend 20- to 30-second exposure to 20% alcohol (ethanol) for LASEK. At 30 seconds, they found predominantly vital epithelial cells, whereas after 45 seconds, the fraction of dead cells increased substantially to about 50%. Predominantly dead epithelial cells are seen after 60 and 120 seconds of exposure.

There might have been an overestimation of the fraction of dead cells because of the time between the donor's death and the beginning of the study. However, their experiments confirmed that after exposure of the cornea to 20% ethanol for up to 30 seconds, the epithelial flap contained predominantly vital cells, which is probably one of the

crucial factors in the dampened flap contained predominantly vital cells, which is probably one of the crucial factors in the dampened wound response in LASEK compared to that in PRK. The exposure of the human cornea to ethanol reduces the number of vital epithelial cells rapidly [25] and increases cell death in a dose- and time-dependent manner. Chen et al. studied the effect of dilute alcohol on human corneal epithelial cell morphology and viability with electron microscopy and they showed that the conventional concentrations and duration of alcohol treatment (20%, 25 seconds) resulted in varying morphological changes in the basement membrane zone by electron microscopy and varying viability in standard tissue culture conditions.

Their electron microscopic findings showed morphological differences in the plane of cleavage among several patients, in whom the same technique was used for creating the epithelial flap. This may be due to variability between individuals in relation to the adhesion of the epithelium to the basal membrane or to the variability of the effect of alcohol on adhesion of epithelial cells. Electron microscopy showed varying degrees of basement membrane alterations after alcohol application, including disruptions, discontinuities, irregularities and duplication.

Cellular destruction and vacuolization of basal epithelial cells associated with absent basement membrane were also observed. Their studies in vitro suggest a dose- and time-dependent effect of alcohol on epithelial cells. The 25% concentration of ethanol was the inflection point of epithelial survival. Significant increase in cellular death occurred after 35 seconds of ethanol exposure. Forty seconds of exposure further increased apoptosis after 8 hours of incubation. These findings are consistent with the clinical observations of varied epithelial attachment to the stromal bed after LASEK surgery.

Then they demonstrated that alcohol diluted in Keratinocyte Serum-Free Medium (KSFM) had no effect on cellular survival and apoptosis. At this time, it is not clear whether modification of the preparation of dilute alcohol, used during LASEK and PRK, would allow for better cell survival and adhesion in vivo [26]. The dilution of alcohol in Balanced Salt Solution (BSS), physiologic solution, or sterile water, thus obtaining different osmolarities, is an area of active debate but none of the LASEK studies has shown a definite advantage of a specific formulation.

Camellin strongly points out the importance of a hypotonic solution obtained by diluting alcohol in distilled water for facilitating epithelial detachment [4].

Yuksel et al. evaluated clinical and confocal results of alcohol-assisted LASEK for correction of myopia in twenty-two eyes with a mean follow-up duration of 45 months and they showed that LASEK offered safe and effective correction of myopia in the long term [27].

In a retrospective study the stability of visual acuity and refraction, the predictability, corneal keratometry, safety, efficacy, and postoperative complications after 10 years after excimer laser surface ablation performed on thin corneas were evaluated. It was demonstrated that surface ablation seems to be safe and effective to correct myopia in corneas thinner than $\mu\text{m}500$, with stable visual and refractive outcomes [28].

In 2016 Li SM et al. performed a Cochrane study to compare LASEK versus PRK for correction of myopia by evaluating their efficacy and safety in terms of postoperative uncorrected visual acuity, residual refractive error, and associated complications. They concluded that

uncertainty surrounds differences in efficacy, accuracy, safety, and adverse effects between LASEK and PRK for eyes with low to moderate myopia. Future trials comparing LASEK versus PRK should follow reporting standards and follow correct analysis. Trial investigators should expand enrollment criteria to include participants with high myopia and should evaluate visual acuity, refraction, epithelial healing time, pain scores, and adverse events [29].

In 2015 we performed a study evaluating the effectiveness and safety of no-alcohol LASEK after long follow-up of 60 months and comparing the obtained results with no-alcohol standard PRK [30]. Twenty-five eyes were treated with LASEK and twenty-five eyes with standard PRK. Twenty-one eyes and 22 eyes completed follow-up of 60 months in LASEK and PRK group respectively. Manifest refraction at 60 months follow-up was -0.01 and 0.26 in LASEK and PRK group respectively. In the LASEK group mean Uncorrected Distance Visual Acuity (UDVA) and mean Corrected Distance Visual Acuity (CDVA) were 20/22 and 20/20 respectively ($p > 0.01$). In the PRK group mean UDVA and mean CDVA at 60 months follow-up were 20/20 and 20/20 after 60 months ($p > 0.01$). The efficacy indexes were 0.87 and 0.95, and the safety indexes were 1.25 and 1.4 respectively for LASEK group and PRK group. Therefore both standard PRK and no-alcohol LASEK offered safe and effective results in the long term period without any statistically significant difference between the two groups.

In conclusion, this long term study, LASEK with mechanical deepithelialization without the use of alcohol solution demonstrated to be a safe and effective technique to correct low to medium myopia.

References

- Trokel SL, Srinivasan R, Braren B (1983) Excimer laser surgery of the cornea. *Am J Ophthalmol* 96: 710-715.
- Manche EE, Carr JD, Haw WW, Hersh PS (1998) Excimer laser refractive surgery. *West J Med* 169: 30-38.
- Cimberle U, Camellin M (1999) LASEK may offer the advantages of both LASIK and PRK. *Ocular Surg News Int* 10: 14-15.
- Camellin M (2003) Laser epithelial keratomileusis for myopia. *J Refract Surg* 19: 666-670.
- Autrata R, Rehurek J (2003) Laser-assisted subepithelial keratectomy for myopia: Two-year follow-up. *J Cataract Refract Surg* 29: 661-668.
- Lee JB, Choe CM, Seong GJ, Gong HY, Kim EK, et al. (2002) Laser Subepithelial Keratomileusis for low to moderate myopia: 6-month follow-up. *Jpn J Ophthalmol* 46: 299-304.
- Wilson SE (1998) Keratocyte apoptosis in refractive surgery. *CLAO* 24: 181-185.
- Abad JC, Talamo JH, Vidaurri-Leal J, Cantu-Charles C, Helena MC (1996) Dilute ethanol versus mechanical debridement before photorefractive keratectomy. *J Cataract Refract Surg* 22: 1427-33.
- Abad JC, An B, Power WJ, Foster CS, Azar DT, et al. (1997) A prospective evaluation of alcohol-assisted versus mechanical epithelial removal before photorefractive keratectomy. *Ophthalmology* 104: 1566-1574.
- Espana EM, Grueterich M, Mateo A, Romano AC, Yee SB, et al. (2003) Cleavage of corneal basement membrane components by ethanol exposure in laser-assisted subepithelial keratectomy. *J Cataract Refract Surg* 29: 1192-1197.
- Kamm O (1921) The relation between structure and physiological action of the alcohols. *J Am Pharmaceut Assoc* 10: 87-92.
- Sobernheim G (1943) Alkohol als Desinfektionsmittel. *Schweiz Med Wochenschr* 73: 1280-1287.
- Carones F, Fiore T, Brancato R (1999) Mechanical vs alcohol epithelial removal during photorefractive keratectomy. *J Refract Surg* 15: 556-562.
- Shah S, Doyle SJ, Chatterjee A, Williams BE, Ilango B (1998) Comparison of 18% ethanol and mechanical debridement for epithelial removal before photorefractive keratectomy. *J Refract Surg* 14: S212-S214.
- Stein HA, Stein RM, Price C, Salim GA (1997) Alcohol removal of the epithelium for excimer laser ablation: Outcomes analysis. *J Cataract Refract Surg* 23: 1160-1163.
- Helena MC, Filatov V, Johnston WT, Vidaurri-Leal J, Wilson SE, et al. (1997) Effects of 50% ethanol and mechanical epithelial debridement on corneal structure before and after excimer photorefractive keratectomy. *Cornea* 16: 571-579.
- Campos M, Raman S, Lee M, McDonnell PJ (1994) Keratocyte loss after different methods of de-epithelialization. *Ophthalmology* 101: 890-898.
- Soma T, Nishida K, Yamato M, Kosaka S, Yang J, et al. (2009) Histological evaluation of mechanical epithelial separation in epithelial laser in situ keratomileusis. *J Cataract Refract Surg* 35: 1251-1259.
- Balestrazzi E, De Molfetta V, Spadea L, Vinciguerra P, Palmieri G, et al. (1995) Histological, immunohistochemical, and ultrastructural findings in human corneas after photorefractive keratectomy. *J Refr Surg* 11: 181-187.
- Cui X, Bai J, He X, Zhang Y (2005) Western Blot analysis of type I, III, V, VI collagen after laser epithelial keratomileusis and photorefractive keratectomy in cornea of rabbits. *Yan Ke Xue Bao* 21: 141-148.
- Zhou J, Lu S, Dai J, Yu Z, Zhou H, et al. (2010) Short-Term Corneal Endothelial Changes after Laser-Assisted Subepithelial Keratectomy. *J Intern Med Res* 38:1484-1490.
- Stulting RD, Thompson KP, Waring GO, Lynn M (1996) The effect of photorefractive keratectomy on the corneal endothelium. *Ophthalmology* 103: 1357-1365.
- Spadea L, Dragani T, Blasi MA, Mastrofini MC, Balestrazzi E (1996) Specular microscopy of the corneal endothelium after excimer laser photorefractive keratectomy. *J Cataract Refract Surg* 22:188-193.
- Gabler B, Von Mohrenfels CW, Dreiss AK, Marshall J, Lohmann CP (2002) Vitality of epithelial cells after alcohol exposure during laser assisted subepithelial keratectomy flap preparation. *J Cataract Refract Surg* 28: 1841-1846.
- Sandwig KU, Kravik K, Haaskjold E, Blika S (1997) Laser epithelial wound healing of the rat cornea after excimer laser ablation. *Acta Ophthalmol Scand* 75: 115-119.
- Chen C, Chang JH, Lee JB, Javier J, Azar DT (2002) Human corneal epithelial cell viability and morphology after dilute alcohol exposure. *Invest Ophthalmol Vis Sci* 43: 2593-2602.
- Yüksel N, Bilgihan K, Hondur AM, Yildiz B, Yüksel E (2013) Long term results of Epi-LASIK and LASEK for myopia. *Cont Lens Anterior Eye* 37: 132-135.
- De Benito-Llopis L, Alió JL, Ortiz D, Teus MA, Artola A (2009) Ten-year follow-up of excimer laser surface ablation for myopia in thin corneas. *Am J Ophthalmol* 147: 768-773.
- Li SM, Zhan S, Li SY, Peng XX, Hu J, et al. (2016) Laser-assisted subepithelial keratectomy (LASEK) versus photorefractive keratectomy (PRK) for correction of myopia. *Cochrane Database Syst Rev* 2:CD009799
- Spadea L, Verboschi F, De Rosa V, Salomone M, Vingolo EM (2015) Long term results of no-alcohol laser epithelial keratomileusis and photorefractive keratectomy for myopia. *Int J Ophthalmol*. 8: 574-579.



Henry Journal of Acupuncture & Traditional Medicine

Henry Journal of Anesthesia & Perioperative Management

Henry Journal of Aquaculture and Technical Development

Henry Journal of Cardiology & Cardiovascular Medicine

Henry Journal of Case Reports & Imaging

Henry Journal of Cell & Molecular Biology

Henry Journal of Tissue Biology & Cytology

Henry Journal of Clinical, Experimental and Cosmetic Dermatology

Henry Journal of Diabetes & Metabolic Syndrome

Henry Journal of Emergency Medicine, Trauma & Surgical Care

Henry Journal of Haematology & Hemotherapy

Henry Journal of Immunology & Immunotherapy

Henry Journal of Nanoscience, Nanomedicine & Nanobiology

Henry Journal of Nutrition & Food Science

Henry Journal of Obesity & Body Weight

Henry Journal of Cellular & Molecular Oncology

Henry Journal of Ophthalmology & Optometry

Henry Journal of Perinatology & Pediatrics

Submit Your Manuscript: <https://www.henrypublishinggroups.com/submit-manuscript/>