

## **Transepithelial Photorefractive Keratectomy versus Conventional Photorefractive Keratectomy in Treatment of Myopia and Compound Myopic Astigmatism (Comparative Study)**

Basma A. Khashaba, Hamdy A. El-Gazzar, Tarek T. Soliman, Walid Abdelghaffar,  
Mohamed A. Al-sayed

### **Abstract:**

**Background:** Lasik is one of the commonest refractive procedures. The occurrence of flap related complications; corneal ectasia and dry eye have increased the popularity of flapless laser vision correction and surface ablation techniques as (SMILE) and (PRK). Aim and objectives: To compare 3-month refractive results, predictability, safety, and efficacy of (TPRK) with (PRK) when used to correct myopia and compound myopic astigmatism.

**Subjects and methods:** This prospective comparative interventional study was conducted at private centers under Benha University medical college staff supervision. From September 2018 to January 2022, forty patients (40 eyes) with contralateral eye control (40 eyes, total of 80 treatments) participated in this research. Stratified into two equal groups. Group 1: patients who underwent PRK with alcohol assisted epithelial debridement. Group 2: patients who underwent TPRK.

**Results:** There was an increase of CET in both groups over the periods, but the most increase is in the PRK group after 1months. Increase mean value of CET in TPRK group after 3 months. The TPRK and PRK Groups were comparison in Pre CET with Post 1month and Post 3 months, there was a highly significant higher mean of post 1months and Post 3 months compared to Pre. There was an increase in the mean difference and change in PRK group compared to TPRK group according to change% of CET, while CET Pre-3m and CET 1m-3m insignificant difference between two groups. **Conclusion:** TPRK and PRK performed on regular corneas produce very similar results 3 months post procedure.

**Keywords:** Photorefractive Keratectomy; Myopia; Astigmatism; Transepithelial Photorefractive Keratectomy.

Ophthalmology Department,  
Faculty of Medicine Benha  
University, Egypt.

Corresponding to:  
Dr. Basma A. Khashaba.  
Ophthalmology Department,  
Faculty of Medicine Benha  
University, Egypt.  
Email:  
basma.khashaba@gmail.com

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## Introduction

Surface ablation may be safer than Laser in situ keratomileusis (LASIK) to avoid flap complications, corneal weakening, and a higher risk of iatrogenic keratectasia, and thus, the era of surface ablation emerged as an alternative to LASIK <sup>(1)</sup>.

Photorefractive keratectomy (PRK) is one of the surface ablation procedures and performed after corneal epithelial debridement accompanied by postoperative pain, discomfort, and high grade of corneal haze, all of which limit its popularity <sup>(2)</sup>.

The original method to remove the epithelium before the excimer laser ablation was manual mechanical scraping, which was later enhanced by using an alcohol solution or brush <sup>(3)</sup>.

Epithelial laser in situ keratomileusis (Epi-LASIK) is another method that uses an epithelial flap, but is performed with a microkeratome with a blunt oscillating blade called epikeratome <sup>(4)</sup>.

Newer generation of faster lasers and improved ablation algorithms and nomograms have over the years, allowed development of a new (tPRK) variant of transepithelial PRK.

Single-step transepithelial PRK allows removing the epithelium and stroma in a single step with one ablation profile. This profile is calculated taking into account data from the literature estimating the central epithelial thickness of a normal cornea to be 55 and 65  $\mu\text{m}$  at 4mm from the center, superimposed on the corneal wavefront guided aspheric ablation profiles <sup>(5)</sup>.

Single step tPRK is a relatively new procedure and a limited number of publications are currently available. Meanwhile, the procedure has undergone several minor modifications and nomogram adjustment <sup>(6)</sup>.

Therefore, the purpose of this study is to compare 3-month refractive results, predictability, safety, and efficacy of transepithelial PRK (tPRK) with conventional PRK (PRK) when used to

correct myopia and compound myopic astigmatism.

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## Patients and Methods

**Study population:** From September 2018 to January 2022, forty subjects (40 eyes) with contralateral eye control (40 eyes, total of 80 treatments) participated in this prospective interventional research at private centers under Benha University medical college staff supervision.

Subjects were enrolled after the Research Ethical Committee at Benha Faculty of Medicine. Written informed consent was obtained from each subject enrolled in the study {M.S.9.8.2019} .

Participants were stratified into two equal groups for the research.

Group 1: patients who undergo conventional PRK with alcohol assisted epithelial debridement.

Group 2: Patients who undergo tPRK.

Patients were included if they met any of the following criteria:

All patients must undergo OU treatment to fit the design of the study. Adult patients aged minimum 18 years old. Myopia from (-1D) to (-4D) with or without astigmatism not more than (-2D). BCVA 6/6. No clinical or topographic signs of keratoconus or form fruste keratoconus.

All patients received similar bilateral treatment by the same surgeon at the same session. In addition; we did not include younger patients than 18 years, previous severe ocular inflammations, dry eye, trauma, or surgeries, glaucoma, and cataract.

### Methods:

Complete ophthalmic examinations performed to all patients including the following: History: patient information (age, sex, occupation and residence), any chronic disease (e.g., diabetes), visual acuity: The unaided, best corrected visual acuity, slit lamp biomicroscopy of the anterior segment, lid condition, tear film stability, Shirmer test, fundus examination using indirect ophthalmoscope and slit lamp biomicroscopy for assessment of

retinal pathology, optic nerve and macula, sScheimpflug camera tomography and Anterior segment OCT.

#### **Procedure:**

All surgeries performed with (Allegretto Wave Light® EX500 version 10 Stream light software) Excimer Laser Machine with Custom PRK treatments algorithm. Before the surgery, Benoxinate hydrochloride 0.4% instilled 3 times within a 5-min interval. The eyelids opened using a wire lid speculum.

First Group: The conventional (alcohol assisted) PRK group, treatment was with the standard PRK protocol. Epithelial delamination was performed with 20% ethanol, applied using an 8-9 mm well according to the patient's data interpretation by the surgeon & the determined ablation zone accordingly, followed by epithelial removal with a spatula. These steps avoid uneven wetting & the subsequent risk of uneven ablation.

Second Group: The tPRK group, where aspheric aberration-free TransPRK ablation algorithm used, the epithelium was removed during laser ablation only from the area of the total ablation zone.

In both groups, 0.02% mitomycin C (MMC) applied for 2min followed by generous irrigation of the eye with room temperature balanced solution. After the surgery, a bandage contact lens applied.

#### **Postoperative Examinations:**

##### **Statistical analysis:**

Statistical testing was executed with SPSS, versions 2023 (SPSS Inc., Chicago, Illinois, USA). Mean and standard deviation or median and range were used to describe numerical data. The qualitative information was shown as a frequency and percentage distribution. Data were explored for normality using Kolmogorov-Smirnov and Shapiro-Wilk Test. Independent t-test was used when comparing between two means and Mann Whitney U test: for two-group comparisons in non-parametric data. Paired sample t-test of significance was used when comparing between related

Postoperative assessment and follow ups were performed on 1 day, 1 week, 1 month, and 3 months. Examinations at one day, one week, and one month included UCVA, BCVA, manifest refraction, tonometry, and slit lamp biomicroscopy. Clinical healing duration assessment is done by measuring duration till full epithelization and contact lens removal. This was tested by Slit lamp examination. (Corneal haze evaluated as following : (0=no haze; 0.5=trace haze on oblique illumination; 1=corneal cloudiness not interfering with the visibility of fine iris details; 2=mild effacement of fine iris details; 3 and 4=details of the lens and iris not discernible). Anterior segment OCT were performed after one month of the surgery and at the last visit by (Optovue AS-OCT). Pain level evaluated immediately after the surgery and one week after by a 10-category verbal rating scale (VRS) 1—no pain and 10—the worst possible pain). Three months after the surgery patients were asked about overall satisfaction with the surgery and (high, moderate, low, not satisfied), and whether they would decide to have a surgery again (yes, no). Data acquisition by the corneal densitometry was performed using the rotating Scheimpflug anterior segment analyzer.. All parameters were automatically calculated by the Pentacam software (Version 1.21r65).

samples. The Comparison between groups with qualitative data was done by using Chi-square test and Fisher's exact test was used when the expected count in any cell less than 5. Significant results were defined as having a p-value of less than 0.05.

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#### **Results:**

The results of the present study are demonstrated in the following tables. We aimed by our study to compare 3-month refractive results, predictability, safety, and efficacy of transepithelial PRK (tPRK) with conventional PRK (PRK) when used to correct myopia and compound myopic

astigmatism and we applied our study on 40 patients will be divided into two equal groups: Group 1: patients who will undergo conventional PRK with alcohol assisted epithelial debridement including 40 eyes, with the same inclusion and exclusion criteria, Group 2: patients who will undergo tPRK including 40 eyes .

Table (1): This table shows that there is increase in the two groups over the periods, but the most increase is in the PRK group after 1months, while there was increase mean value of CET in TPRK group after 3 months; as there is no statistically significant difference between groups according to CET, with p-value (p>0.05).

Table (2): The TPRK Group were comparison in Pre CET with Post 1month

and Post 3 months, there was a highly statistically significant higher mean of post 1months and Post 3 months compared to Pre, with p-value <0.001.

Table (3): The PRK Group were comparison in Pre CET with Post 1month and Post 3 months, there was a highly statistically significant higher mean of post 1months and Post 3 months compared to Pre, with p-value <0.001.

Table (4): This table shows that the increase mean difference and change in PRK group compared to TPRK group according to change% of CET, with p-value (p<0.05); while CET Pre-3m and CET 1m-3m insignificant difference between two groups, with p-value (p>0.05)

**Table (1):** Comparison between TPRK group and PRK group according to Corneal epithelial thickness (µm).

Corneal epithelial thickness (µm)	TPRK Group (n=40)	PRK Group (n=40)	T-Test	p-value
<b>Pre</b>				
<b>Mean±SD</b>	51.95±2.59	51.35±1.82	1.198	0.234
<b>Range</b>	48-57	48-55		
<b>Post 1 month</b>				
<b>Mean±SD</b>	56.95±3.01	57.13±2.31	-0.291	0.771
<b>Range</b>	51-62	52-62		
<b>Post 3 months</b>				
<b>Mean±SD</b>	58.38±3.13	57.95±2.29	0.694	0.490
<b>Range</b>	53-65	53-62		

Using: t-Independent Sample t-test; p-value >0.05 NS

**Table (2):** Comparison between Pre of CET and other measurements “Post 1month and Post 3 months” in TPRK Group.

Corneal epithelial thickness (µm)	TPRK Group (n=40)	Paired Sample t-test		
		MD±SE	t-test	p-value
<b>Pre</b>	51.95±2.59			
<b>Post 1 month</b>	56.95±3.01	5.00±0.28	-18.180	<0.001**
<b>Post 3 months</b>	58.38±3.13	6.43±0.34	-18.719	<0.001**

Using: t-Paired Sample t-test; MD: Mean Difference, \*\*p-value <0.001 is highly significant

**Table (3):** Comparison between Pre of CET and other measurements “Post 1 month and Post 3 months” in PRK Group.

Corneal epithelial thickness ( $\mu\text{m}$ )	PRK Group (n=40)	Paired Sample t-test		
		MD $\pm$ SE	t-test	p-value
Pre	51.35 $\pm$ 1.82			
Post 1 month	57.13 $\pm$ 2.31	5.78 $\pm$ 0.22	-26.701	<0.001**
Post 3 months	57.95 $\pm$ 2.29	6.60 $\pm$ 0.21	-31.705	<0.001**

Using: t-Paired Sample t-test; MD: Mean Difference, \*\*p-value <0.001 is highly significant

**Table (4):** Comparison between TPRK group and PRK group according to mean difference and change% of CET.

Mean difference		TPRK Group (n=40)	PRK Group (n=40)	Test value	p-value
CET Pre-1m	Mean $\pm$ SE	5.00 $\pm$ 0.28	5.78 $\pm$ 0.22	U:-2.201	0.028*
	Change%	9.66 $\pm$ 0.54	11.25 $\pm$ 0.43	U:-2.330	0.020*
CET Pre-3m	Mean $\pm$ SE	6.43 $\pm$ 0.34	6.60 $\pm$ 0.21	U:-1.090	0.276
	Change%	12.42 $\pm$ 0.68	12.87 $\pm$ 0.41	U:-1.179	0.238
CET 1m-3m	Mean $\pm$ SE	1.43 $\pm$ 0.25	0.83 $\pm$ 0.09	U:-1.945	0.052
	Change%	2.53 $\pm$ 0.45	1.46 $\pm$ 0.15	U:-1.684	0.092

Using: U: Mann-Whitney U-test, p-value >0.05 is insignificant; \*p-value <0.05 is significant

## Discussion

Photorefractive keratectomy (PRK) has commonly been used as an effective, safe, and reasonable method for treatment of patients with low to moderate myopia since 1983. Moreover, PRK is appropriate for patients with refractive errors who are not eligible candidates for laser in-situ keratomileusis (LASIK) owing to thin corneas, subtle topographic irregularities, and epithelial basement membrane disease (7).

The conventional PRK procedure involves the removal of the corneal epithelium either manually or with alcohol, followed by excimer laser ablation to correct the refractive error. Manual or alcohol-assisted epithelial removal has been associated with drawbacks, including prolonged epithelial healing due to basement membrane injury or potential alcohol toxicity, significant pain, and variable degrees of stromal haze even with the use of Mitomycin C (8).

Transepithelial PRK (TE-PRK, first described by Dr. Donald Johnson of Canada) was initially introduced as a two-step procedure to overcome the drawbacks of conventional PRK through the use of

excimer laser phototherapeutic keratectomy PTK as a first step to remove the epithelium followed by stromal laser ablation as a second step (9).

With the emergence of new generations of faster lasers, improved ablation algorithms, and nomograms, a new "no-touch" all-surface ablation technique has been developed. This technique allows ablation of the corneal epithelium and stroma in a single step with one ablation profile (10).

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With the emergence of new generations of faster lasers, improved ablation algorithms, and nomograms, a new "no-touch" all-surface ablation technique has been developed. This technique allows ablation of the corneal epithelium and stroma in a single step with one ablation profile (10).

After the introduction of transepithelial photorefractive keratectomy (TPRK), epithelial removal is performed by phototherapeutic ablation, followed by refractive ablation of the corneal stroma. Several studies have advocated various techniques for epithelial removal, but the two-step technique has not been widely adopted due to prolonged surgery times with older lasers, corneal dehydration, increased postoperative pain, and lack of adjusted nomograms<sup>(11)</sup>.

Accurate measurement of epithelial thickness using anterior segment optical coherence tomography (AS-OCT) provides a more precise method to ensure complete epithelial removal, thus avoiding inaccurate stromal ablation resulting in under- or overcorrection. In our study, epithelial thickness was measured using Spectralis OCT epithelial mapping in both groups<sup>(12)</sup>.

The aim of this study is to compare 3-month refractive results, predictability, safety, and efficacy of transepithelial PRK (tPRK) with conventional PRK (PRK) in correcting myopia and compound myopic astigmatism.

In this study we found that among 40 eyes of 20 patients in TPRK group, their mean age was  $24.4 \pm 3.03$  years, 6 patients were males (30%) and 14 patients were females (70%). 40 eyes of 20 patients in PRK group with a mean age  $24.45 \pm 2.87$  years, 9 patients were males (45%) and 11 patients were females (55%). There was insignificant difference between both studied groups as regards age and sex.

That was found the mean age in Trans-PRK group was  $26.70 \pm 5.11$  years, with range of 20–36 years, whereas in PRK group, the mean age was  $28.02 \pm 4.90$  years, with range of 20–38 years. There were more females than males in both groups<sup>(13)</sup>.

Also, found that the mean age was  $26 \pm 4$  years in PRK group and  $26 \pm 6$  years in t-PRK group ( $P = 0.998$ ). In PRK group, 23 (47%) were females whereas in t-PRK group 50 (73%) were females<sup>(14)</sup>.

In this study we found that there was no statistically significant difference between groups according to Pain, Haze and satisfaction, with p-value ( $p > 0.05$ ).

A lower incidence of postoperative corneal haze was detected in the Trans-PRK group compared with the AA-PRK group in the study of at all-time tested points 1 week, 1 month, and 3 months with statistically significant differences possibly due to less keratocytes loss and apoptosis, no alcohol-induced toxicity, less epithelial injury (no touch technique), and hence less haze formation in the Trans-PRK group<sup>(15)</sup>.

Contrary to an older study reporting increased keratocyte activation, intense inflammatory response, and myofibroblast transformation in Trans-PRK, our follow-up showed a decrease in corneal haze intensity until no haze was detected at 6 months postoperatively<sup>(16)</sup>.

Haze was not a significant issue in both groups; it never exceeded a score of 2 in the PRK group and regressed to below score 1 by the end of the study. This could be attributed to the routine use of intraoperative Mitomycin-C and the smoother surface created by laser epithelial removal<sup>(17)</sup>. These results are comparable to those with slightly higher haze scores<sup>(18)</sup>.

The intensity of haze was also not significantly different between groups and was at the 0.5 level in all but 2 eyes after tPRK and 1 eye after PRK in which the incidence of haze was evaluated at level 1. During the follow up, corneal haze intensity had a tendency to decrease. There was no significant difference in the incidence of other postoperative. The mean pain scores after the surgery were 4.78 2.65 in the tPRK group and 4.59 2.85 in the PRK group. There were also no differences in pain intensity during first days after the surgery. After tPRK, 86.25% of patients declared high satisfaction with the surgery compared to 88.24% patients after PRK. The ratio for moderate satisfaction was 13.75% for tPRK and 11.76% for PRK, respectively. All patients

would consider having the surgery again<sup>(19)</sup>.

In this study we demonstrated that there was an increase in the two groups over the periods, but the most increase is in the PRK group after 1 month, while there was an increase in the mean value of CET in the TPRK group after 3 months; as there is no significant difference between groups according to CET. The mean CET was significantly larger in the tPRK group compared to the PRK group only on the operation day with no significant difference on the following days<sup>(20)</sup>. In this study we illustrated that TPRK Group were compared in Pre CET with Post 1 month and Post 3 months, there was a highly significant higher mean of post 1 month and Post 3 months compared to Pre. In that there was a significantly lower CCET was observed at 1 week and 1 month compared to baseline CCET. The cornea returned to its preoperative corneal epithelial thickness at 3 months postoperatively<sup>(21)</sup>, which is consistent with previous findings<sup>(22)</sup>. The thickness of the central corneal epithelium in both groups was more than 10  $\mu\text{m}$  thicker than that before surgery in the TPRK group when regression occurred<sup>(23)</sup>. Also, they found that change in central corneal epithelial thickness over time after T-PRK. The epithelium was significantly thicker at 3 and 6 months after surgery compared with preoperative measurements<sup>(24)</sup>.

In this study, it was clearly demonstrated that, in the PRK group, Pre CET showed a significantly higher mean of post 1 month and Post 3 months compared to Pre. In that repeated thickness measures before and after PRK at different follow-up times showed a significant difference in thickness separately in various zones. Afterward, epithelial thickening continued in all zones and reached the preoperative thickness in the midperipheral and peripheral zones 1 month later, whereas the thickness in the central 5-mm zone was significantly thicker than before surgery.

These findings were in accordance with Sedaghat et al, 2019<sup>(25)</sup>.

In addition, El-Sebaey and coworkers, 202, found that there were significant differences between preoperative and postoperative epithelial thickness with more thickening temporally and inferiorly. Temporal thickening was the highest<sup>(26)</sup>. Moreover, our results, in accordance with Chen et al 2015, showed that the epithelial thickness in all of the measured areas continued to increase between 1 and 3 months after the surgery, whereas the refractive stability was achieved by 1 month. No correlation was found between epithelial thickening and postoperative refraction change<sup>(27)</sup>.

Ivarsen et al in 2009, reported that PRK induced an increase in epithelial thickness of ~ 15–20% that persisted after surgery. Preoperative epithelial debridement caused an initial decrease in epithelial thickness, followed by a gradual epithelial thickening over the next 12 months<sup>(28)</sup>.

The corneal epithelium was significantly thicker in eyes treated with PRK and small zone diameters (from 4.1 to 5.0 mm). The most important variables accounting for greater epithelial hyperplasia were small ablation zones, higher attempted corrections, and deeper ablations resulting in large changes in power from the center to the edge of the ablation. This was documented in the work done by Hamberg-Nyström and colleagues<sup>(29)</sup>.

In this study we found that there was a significant difference between PRK groups compared to the TPRK group according to change of CET 1 month postoperatively, while CET measurements showed no significant difference between two groups at 1 month and 3 months. Epithelial healing duration was faster in tPRK compared to PRK (p value < 0.001). These findings were in accordance with Abdel-Radi et al, 2023<sup>(30)</sup>. It was also documented that the epithelial healing rate was faster with the conventional methods compared to tPRK according to Hamberg-Nyström and his coworkers<sup>(20)</sup>.

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## Conclusions

1. Transepithelial PRK and conventional PRK performed on regular corneas produce very similar results 3 months after the surgery.
2. These procedures are predictable, effective, and safe for correction of myopia and compound myopic astigmatism.

## Conflict of interest

None of the contributors declared any conflict of interest

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