Assessment of the Specificity of Corvis Biomechanical Index-Laser Vision Correction (CBI-LVC) in Stable Corneas After Phototherapeutic Keratectomy

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Abstract

**Purpose:** The CBI-LVC is a biomechanical index to detect ectasia in post-refractive surgery patients (PRK, LASIK, SMILE). This study aims to evaluate the distribution of the CBI-LVC in stable patients who underwent Phototherapeutic Keratectomy (PTK) compared to PRK patients.

**Methods:** Patients who underwent PRK and PTK performed between 2000 and 2018 in Humanitas Research Hospital, Rozzano, Milan, Italy and remained stable for at least four years post-surgery were included. All eyes were examined with the Corvis ST (Oculus, Germany), whose output allows the calculation of the CBI-LVC. The distribution and specificity of the CBI-LVC in the two populations were estimated using a Wilcoxon Mann-Whitney test and compared.

**Results:** 175 eyes of 148 patients were included (85 eyes of 50 PTK patients and 90 eyes of 90 PRK patients). The distribution of CBI-LVC in the two groups showed a minor difference, with a median value in PRK patients of 0.000 (95% CI 0.000; 0.002) and 0.008 (95% CI 0.000; 0.037) in PTK patients (Mann-Whitney U test p = 0.023). The statistical analysis showed that the CBI-LVC provided a specificity of 92.22% in the PRK group, while in the PTK group it was 82.35%. Nevertheless, this difference was not statistically significant (Chi-squared test with Yates, p = 0.080).

**Conclusion:** CBI-LVC provided similar specificity in stable PTK patients compared to those who underwent PRK. These results suggest that the CBI-LVC could be a useful tool to aid corneal surgeons in managing PTK patients.

Introduction

Post-Laser Vision Correction (LVC) ectasia is part of a wider group of pathologies named as “ectatic ocular disorders”, in which the cornea progressively undergoes a process of thinning and steepening. Corneal ectasia strongly impacts vision and, if not timely treated, leads to corneal transplantation. Although rare, this complication is of great concern to refractive surgeons as it can lead to poor visual outcomes. Recent research estimated the percentage of corneal ectasia patients progressing to corneal transplantation at between 8 and 30%. Since its first report in 1998, much effort has been made by the scientific community to understand and prevent its development. Even though any laser refractive surgery procedure, including PRK and SMILE, may lead to ectasia, research over the last 20 years has focused on cases after LASIK, the refractive procedure which seems to have the highest rate of this complication. This research includes a retrospective study, published in 2008, which highlighted that 96% of the ectasia cases analyzed occurred after LASIK, while only 4% took place after PRK.

In theory, three possible contexts are recognized in which iatrogenic keratectasia can arise:

1. When a cornea that is biomechanically fragile and inclined to develop ectasia is further weakened by surgery. This is usually the case of patients who have not yet shown topographically noticeable signs of a corneal disease (e.g. keratoconus) but corneal biomechanics is already altered.
2. When the surgery severely weakens a normal cornea below a safe limit.
3. Intense eye rubbing

Regarding the first context, considerable progress was made in identifying the preoperative risk factors for post-LVC ectasia, which improved patient selection for various refractive procedures, and led to effective prevention of the condition. These risk factors included, most notably, corneal topography, tomography and epithelial maps. Additionally, the assessment of corneal biomechanics is now considered an essential screening tool to identify patients with increased susceptibility to post-LVC iatrogenic ectasia. Recent studies further confirmed the importance of corneal biomechanics in the diagnosis of keratoconus, even in its early stages, as for many it represents the “primum movens” in the development of the disease.

However, while substantial improvements in pre-LVC keratoconus screening and risk factor identification were made over the last 20 years, the same progress was not achieved in the diagnosis and early detection of ectasia post-op. In fact, the main diagnostic method for post-LVC ectasia remains clinical recognition of its signs and symptoms, based on corneal topographic and tomographic alterations. Timely detection of post-LVC ectasia is of foremost importance given the possibility to promptly treat these patients with cross-linking in order to stabilize the cornea.

A recent step forward was the introduction of the CBI-LVC provided by the Corvis ST (Oculus, Germany) – a new biomechanical index that has shown high sensitivity and specificity in separating stable post-LVC eyes from post-LVC eyes with ectasia.

Phototherapeutic keratectomy (PTK) is a surgical procedure that uses the excimer laser to treat corneal pathologies rather than changing the patient’s refraction. Potentially, iatrogenic ectasia can occur after PTK, particularly because PTK patients, on average, present a lower postoperative pachymetry relative to refractive patients, and their corneas are frequently weakened by previous ocular pathologies or surgeries. The aim of this paper is to assess the specificity of the CBI-LVC in eyes that remained stable after PTK when compared to those that underwent PRK.

Materials And Methods

Two groups of patients were included in this single-center retrospective study. The first group included patients who underwent PTK and demonstrated topographical and tomographical stability for at least three years after surgery. Conversely, the second group included patients who remained stable for at least 3 years after PRK.

Stability was defined as follows:

- No increase in posterior elevation of more than 10 µm in differential map
- No increase in anterior curvature in sagittal map of more than 1 D in differential map
- No decrease in pachymetry of more than 20 µm in differential map
- No change in refraction of more than 1.0 D in spherical equivalent (sph. Eq)
- Stability was also confirmed by one masked cornea expert (R.V., P.V. and/or R.A.) who evaluated postoperative maps

All surgeries were performed between 2000 and 2018 by a single surgeon (PV) at Humanitas Clinical Research Centre, Rozzano, Milan, Italy.

The exclusion criteria included previous ocular surgeries that may have impacted the biomechanics of the cornea (CXL, corneal transplants, intraocular retinal interventions, surgical cerclage for retinal detachment). The exclusion criteria also included ocular diseases, which may have damaged corneal biomechanics (ocular traumas, perforating wounds, glaucoma, or previous hypotonic therapies).

Institutional Review Board (IRB) ruled that approval was not required for this record review study (‘exempt’ category). The research was conducted according to the ethical standards set out in the 1964 Declaration of Helsinki, revised in 2013. Subjects provided written informed consent before using their data in the study. All patients had a thorough ophthalmic examination, including Corvis ST and Pentacam HR or Pentacam HR/AXL (OCULUS Optikgeräte GmbH; Wetzlar, Germany) examinations.

Corvis ST Measurements

Only Corvis ST and Pentacam examinations with quality scores (QS) that allowed calculation of all deformation and tomographic parameters were included in the analysis. All measurements with the Corvis ST were acquired by experienced technicians and captured by automatic air pressure.

Dynamic Corneal Response Parameters

The Corvis ST provides a set of Dynamic Corneal Response parameters (DCRs software version 6.08r22) based on analysis of the dynamic corneal response to air pressure.\(^{19,23,24}\) Some of the DCRs were used in the development of the CBI-LVC including the Applanation 1 velocity (A1vel), Integrated Inverse Radius (1/R), Applanation 1 Deflection Amplitude (A1DeflAmplitude), Highest Concavity and Applanation 1 Arclength (HCArclength and A1Arclength) and Deformation Amplitude Ratio (DA ratio).\(^{19}\)

**Statistical analysis**

The statistical analysis was performed with SPSS version 26 (IBM Corp., Armonk, NY, USA). The nonparametric Mann-Whitney U test was used to compare the mean of the two distributions of CBI-LVC values obtained from the two populations (post-PTK and post-PRK samples). Chi-squared test with Yates’ correction was utilised to assess whether the proportions of false-positive (stable postoperative patients with CBI-LVC >0.5) over the total number of patients in the post-PTK group was significantly different from the rate of false positives in the post-PRK group.
## Results

A sample of 85 stable post-PTK eyes of 50 patients and 90 stable eyes of 90 post-PRK patients was analyzed. The mean age of patients in the PTK and PRK groups was 43.7±13.1 years and 30.9 ± 9.1, respectively (p < 0.001). Mean Kmax and the minimal thickness were respectively 45.14±2.51 D and 433.0±66.1 µm in the PTK group and 43.06±1.64 D and 429.7±42.9 µm in the PRK group (Kmax p < 0.001, minimal thickness p = 0.6955).

The indications for PTK treatment were as follows: previous corneal ulcer leading to irregularity 19 (22.3%), corneal dystrophy 27 (32.0%), LASIK irregularities 1 (1.2%), PRK complications (such as haze and decentered/small optical zone) 33 (38.8%), radial keratotomy 4 (4.7%) and band keratopathy 1 (1.2%).

The distribution of CBI-LVC values in post-PTK and post-PRK patients is represented in Figures 1 and 2. There were significant differences between the CBI-LVC values in the two patient groups (Mann-Whitney U test; p = 0.023), although the median values were similar; 0.008 (95% CI 0.000; 0.037) in the PTK group and 0.000 (95% CI 0.000; 0.002) in the PRK group.

The statistical analysis showed that the CBI-LVC provided a specificity of 82.35% in the PTK group, while in the PRK group, it was 92.22%. Table 1 provides details of false positives of CBI-LVC in the post-PTK and post-PRK groups. The indication for surgery for false-positive patients after PTK (15) were: previous corneal ulcer leading to irregularity 7 (46.7%), corneal dystrophy 4 (26.7%), and PRK complications 4 (26.7%).

<table>
<thead>
<tr>
<th></th>
<th>CBI-LVC (PRK)</th>
<th>CBI-LVC (PTK)</th>
<th>Total</th>
</tr>
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<tbody>
<tr>
<td>FP</td>
<td>7</td>
<td>15</td>
<td>22</td>
</tr>
<tr>
<td>TN</td>
<td>83</td>
<td>70</td>
<td>153</td>
</tr>
<tr>
<td>Total</td>
<td>90</td>
<td>85</td>
<td>175</td>
</tr>
</tbody>
</table>

Nevertheless, even as CBI-LVC showed lower specificity in the PTK group when compared to the PRK group, this difference was not statistically significant (Chi-squared test with Yates' correction; p = 0.080, observed power 62.1%).

## Discussion

PTK is an excimer-based procedure that is substantially different from PRK. Even though the surgical procedures are the same, the goal is completely different. While PRK is employed in healthy eyes to eliminate a refractive defect by reshaping the cornea, PTK, as the name suggests, is a therapeutic
procedure, and is therefore utilized in diseased eyes. The aim of the study was to assess whether CBI-LVC performs in stable PTK patients with similar specificity to that observed in patients undergoing PRK.

The statistical analysis showed that the distribution of CBI-LVC values was significantly different in PRK and PTK eyes, even so the difference was not clinically relevant. The CBI-LVC had a specificity of 82.35% – lower than the value obtained in the PRK population (92.22%). However, the statistical difference between the two values of specificity was non-significant by a chi-squared with Yates’ correction. This slightly lower specificity may be caused by a number of factors. First, certain corneal diseases such as radial keratotomies and previous corneal ulcers may alter the tissue’s structure and molecular composition, which in turn can cause changes in corneal biomechanical properties such as viscoelasticity and resistance. Additionally, some eyes may undergo PTK after other corneal interventions because they developed complications. The stress of multiple surgeries and the consequent postoperative healing and repair may also alter the corneas' biochemical and structural properties.

Another difference is the dissimilar inclusion and exclusion criteria of the two patient groups. Some diseases, such as corneal dystrophies and infectious diseases, that represented an exclusion criterion for the post-PRK group were not employed when selecting the post-PTK patients, as they are very common in PTK patients and, in most cases, they are the reason which has led to the PTK intervention. An example is radial keratotomies or previous corneal ulcer.

However, even with these postulations, this study suggest that the CBI-LVC can be suitable and effective for detecting ectasia and estimating ectasia susceptibility post-PTK. The reasonably high specificity also suggests that post-PTK ectasia could be a potential clinical application of the CBI-LVC algorithm, which requires no tomographic measurements, considering that to date, there exists no alternative screening tool.

It should be noted though, that the data gathered and analyzed in this research was for only stable, and therefore negative, patients. No data on positive patients (with post-PTK ectasia) could be included due to the difficulties in locating such patients with statistically sufficient numbers. As a matter of fact, PTK induced ectasia is much rarer compared to the one after LASIK, SMILE and PRK because is performed on a restricted group of ophthalmologic patients. The absence of post-PTK ectasia patients was not an obstacle to evaluating the specificity of the CBI-LVC, but not the sensitivity. Statistically, this is an incomplete way to evaluate the ability of the CBI-LVC to separate stable and ectatic post-PTK eyes. A multi-centre study would help to prevent the problem of enrolling post-PTK ectatic patients for research purposes, which are difficult to find as they need to be examined before any treatment is attempted.

In conclusion, CBI-LVC showed similar specificity in the diagnosis of ectasia in stable patients after PTK compared to patients who remained stable after PRK. The results of this study suggest that the CBI-LVC could be a useful tool to aid management of PTK patients. The results obtained in this retrospective clinical trial justify and encourage future multi-centric research on the CBI-LVC with larger sample to measure its sensitivity.
Declarations

Financial Disclosures:

Riccardo Vinciguerra, Paolo Vinciguerra, Renato Ambrósio Jr., and Ahmed Elsheikh are consultants for OCULUS Optikgeräte GmbH.

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OCULUS Optikgeräte GmbH did not take part in the design, analysis, or interpretation of the results.

Except where noted, none of the remaining authors have financial interests to report.

References


**Figures**

![CBI-LVC values of post-PTK group](image)

**Figure 1**

shows the distribution of the CBI-LVC values of the stable post-PTK group.
Figure 2 shows the distribution of the CBI-LVC values of the stable post-PRK group.