

**Correlation between apical protrusion in the Scheimflug imaging and Corneal Hysteresis and Corneal Resistance factor by Ocular Response Analyzer, among refractive non-keratoconic Egyptian patients**

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**Abstract**

**Introduction:** Apical protrusion in the central 4-mm ring in the Scheimflug imaging (Pentacam), both for the anterior and posterior floats as well as Corneal Hysteresis and Corneal Resistance Factor by Ocular Response Analyzer (ORA), generally are considered important predictors for post-Lasik ectasia. The aim of this work was to find out if there is a statistically significant correlation between these different predictors and their correlation with the central corneal thickness for refractive non-keratoconic Egyptian patients trying to achieve a better decision and avoiding ectasia.

**Methods:** This case-control study involved 142 eyes (of 77 patients with various refractive errors) arriving at the refractive surgery unit in the Research Institute of Ophthalmology in Giza (Egypt) in 2014-2015 seeking excimer laser ablation. The flattest, steepest keratometry readings, central corneal thickness as well as the apical protrusion in the central 4-mm ring, both for the anterior and posterior floats, in microns were measured by Scheimflug imaging. The Corneal Hysteresis and Corneal Resistance Factor were measured by the ocular response analyzer. Statistical analysis was performed by SPSS, using the Pearson correlation test.

**Results:** The spherical refractive error ranged from +7.00 to -13.00 diopters ( $-3.80 \pm 2.89$ ). The central pachymetry ranged from 494 to 634  $\mu\text{m}$  ( $550.35 \pm 32.13$ ). For the central 4-mm ring, the apical protrusion ranged from 0 to +15  $\mu$  ( $6.93 \pm 2.99$ ) for the anterior float and from -3 to +20  $\mu$  ( $9.33 \pm 4.55$ ) for the posterior float. The Corneal Hysteresis (CH) ranged from 7 to 14.8 mmHg ( $10.18 \pm 1.44$ ), while the Corneal Resistance Factor (CRF) ranged from 7.5 to 14.9 mmHg ( $10.58 \pm 1.67$ ). There was a strong positive correlation between the central corneal thickness and both Corneal Hysteresis (CH:  $r = 0.56$ ,  $P \leq 0.01$ ) and Corneal Resistance Factor ( $r = 0.46$ ,  $P \leq 0.01$ ). A significant correlation ( $P < 0.05$ ,  $r = 0.15$ ) existed between apical protrusion in the posterior float and the central corneal thickness. Also, significant negative correlation ( $P < 0.05$ ,  $r = -0.12$ ) existed between apical protrusion in the anterior float by pentacam and the Corneal Resistance Factor by ocular response analyzer.

**Conclusions:** Our finding of a strong positive correlation between both Corneal Hysteresis and Corneal Resistance Factor and the Central corneal thickness being important for biomechanical corneal stability. The findings of this study also support using both machines preoperatively to decrease the risk of post-Lasik ectasia.

**Keywords:** apical protrusion, ocular response analyzer (ORA), Lasik, ectasia

**1. Introduction**

Laser refractive surgery is now one of the most common surgical procedures worldwide, with excellent results and low complication rates (1). However, one of the most devastating complications of laser vision correction (LVC) is progressive ectasia, where the lamellar cut and excimer laser ablation lead to a state of biomechanical failure with an inability to support the continuous stresses caused by intraocular pressure (IOP), extra-ocular muscles action, blinking, eye rubbing, and other forces (2). Refractive surgeons face routinely the challenge to identify cases at higher risk for ectasia aiming at preventing this devastating complication (3). In recent years, different systems have been developed to analyze and characterize the anterior segment of the eye. The correct description of the anterior

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segment, from an optical point of view (4-7) is essential for practicing, planning and later monitoring refractive or cataract surgery. Scheimpflug cameras and slit scanning corneal technology have enabled analysis of both the anterior and posterior corneal curvature and the thickness of the cornea (8). The manual calculation of the best fit sphere (BFS) for 9 mm is usually used to acquire reference values, and a relative scale is 5 microns and 61 colors. Usually, the following criteria are used for anterior elevation maps, i.e., Normal (up to 12 microns), suspected (between 12 and 15 microns), and keratoconus (above 15 microns). Five microns are added to these values for posterior elevation maps (9). Also in recent years, there has been increased interest in corneal biomechanics for use in predicting the response of the cornea to surgical or therapeutic interventions. It is also used for the detection of early keratoconus (10, 11). The Ocular Response Analyzer (ORA) (Reichert Inc., Depew, New York) is generally the commercially available medical device capable of measuring corneal biomechanics in vivo. It measures the Corneal Hysteresis (CH), which reflects corneal viscoelasticity, (corneal damping response), and the Corneal Resistance Factor (CRF), which is thought to primarily reflect corneal elasticity. Both factors were claimed to be useful in predicting the occurrence of post-Lasik ectasia (12). The mean CH and CRF values for normal individuals were  $10.7 \pm 2.0$  mmHg and  $10.3 \pm 2.0$  mmHg, respectively, in one study (13) with almost similar results in another study (14).

The aim of this work was to determine the correlation between the apical protrusion in the Scheimpflug imaging both for anterior and posterior floats and Corneal Hysteresis and Corneal Resistance Factor detected by Ocular Response Analyzer (ORA). The correlation of the central corneal thickness with these items also was studied. The aim is to achieve a better decision and to avoid ectasia.

## 2. Material and Methods

In this case-control study 142 eyes (of 77 patients) arriving at the refractive surgery unit in the Research Institute of Ophthalmology, Giza, Egypt, between 2014 and 2015 seeking excimer laser ablation for various refractive errors were randomly included. There was 98 eyes of female patients and 44 eyes of male patients. The age ranged from 15-53 ( $28.10 \pm 7.94$ ). The spherical refractive error ranged from +7.00 to -13.00 diopters ( $-3.80 \pm 2.89$ ). The cylindrical refractive error (Cyl.) ranged from +1.5 to -3.25 Diopters ( $-1.28 \pm 0.89$ ). The Spherical equivalent ranged from +5.63 to -13.75 Diopters ( $-4.28 \pm 2.91$ ). The refractive error was measured using an autorefractometer (Topcon RM 8800) and confirmed by trial. The flattest, steepest keratometry readings in the central 3-mm ring were measured in diopters, central corneal thickness as well as the apical protrusion in the central 4-mm ring both for the anterior and posterior floats in microns were measured by Scheimpflug imaging (ALLEGRO Oculyzer Version 1074; Allergo, Germany). Only reliable examinations (i.e., with Quality specification (QS) denoting OK) were included in the study. The Corneal Hysteresis and Corneal Resistance Factor in mmHg were measured by the ocular response analyzer (Reichert Ophthalmic Instruments, Inc., Buffalo, NY, USA). Only reliable examinations (i.e., with waveform score (WS) above 7) were included in the study. In the statistical analysis, for each studied item, the mean and standard deviation and the minimum and maximum values were reported. Pearson product-moment correlation test was performed between the apical protrusion in the central 4-mm ring in the Scheimpflug imaging (Pentacam), both for anterior and posterior floats and Corneal Hysteresis and Corneal Resistance factor detected by Ocular Response Analyzer (ORA). Similarly, Pearson correlation test was performed between the central corneal thickness and the main four studied items, i.e., apical protrusion for the anterior and posterior floats, Corneal Hysteresis and Corneal Resistance Factor. Exclusion criteria included patients with previous laser refractive or other ocular surgery, evidence of keratoconus on topography, systemic collagen diseases (such as rheumatoid arthritis), history of corneal injury, and incomplete data that precluded analysis.

## 3. Results

The Spherical refractive error ranged from +7.00 to -13.00 Diopters ( $-3.80 \pm 2.89$ ). The flattest keratometric readings (K1) ranged from 39.4 to 46.8 Diopters ( $42.83 \pm 1.43$ ). The steepest keratometric readings (K2) ranged from 40.2 to 48.8 Diopters ( $44.25 \pm 1.59$ ). The average keratometric readings (Km) ranged from 40.15 to 47.7 Diopters ( $43.54 \pm 1.44$ ). The central pachymetry ranged from 494 to 634  $\mu\text{m}$  ( $550.35 \pm 32.13$ ). The apical protrusion in the central 4-mm ring anterior float ranged from 0 to +15  $\mu$  ( $6.93 \pm 2.99$ ). The apical protrusion in the central 4-mm ring posterior float ranged from -3 to +20  $\mu$  ( $9.33 \pm 4.55$ ). The Corneal Hysteresis (CH) ranged from 7 to 14.8 mmHg ( $10.18 \pm 1.44$ ). The Corneal Resistance Factor (CRF) ranged from 7.5 to 14.9 mmHg ( $10.58 \pm 1.67$ ). There was a strong positive correlation between both Corneal Hysteresis and Corneal Resistance Factor and the central corneal thickness (CH:  $r = 0.56$ ,  $p \leq 0.01$  and CRF:  $r = 0.46$ ,  $P \leq 0.01$ ). A non-significant correlation ( $p > 0.05$ ,  $r = 0.07$ ) existed between apical protrusion in the central 4-mm ring in the anterior float and the central corneal thickness by pentacam. A statistically significant correlation ( $p < 0.05$ ,  $r = 0.15$ ) existed between apical protrusion in

the central 4-mm ring in the posterior float and the central corneal thickness by pentacam (Table 1). A non-significant correlation ( $p > 0.05$ ,  $r = 0.06$ ) existed between apical protrusion in the central 4-mm ring in the anterior float by pentacam and the Corneal Hysteresis by ocular response analyzer. A statistically significant negative correlation ( $p < 0.05$ ,  $r = -0.12$ ) existed between apical protrusion in the central 4-mm ring in the anterior float by pentacam and the Corneal Resistance Factor by ocular response analyzer. A non-significant correlation ( $p > 0.05$ ,  $r = -0.01$ ) existed between apical protrusion in the central 4-mm ring in the posterior float by pentacam and the Corneal Hysteresis by ocular response analyzer. A non-significant correlation ( $p > 0.05$ ,  $r = 0.02$ ) existed between apical protrusion in the central 4-mm ring in the posterior float by pentacam and the Corneal Resistance Factor by ocular response analyzer (Table 2).

**Table 1.** Correlation between the Central corneal thickness by pentacam and the four main studied items, i.e., apical protrusion in the central 4-mm ring in the Scheimflug imaging (Pentacam) for anterior and posterior floats, Corneal Hysteresis and Corneal Resistance Factor detected by ORA

Item	Correlation coefficient (r)	p value
CH vs. CCT	0.56	<0.01
CRF vs. CCT	0.47	<0.01
Anterior float vs. CCT	0.07	>0.05
Posterior float vs. CCT	0.15	<0.05

**Table 2.** Correlation between the apical protrusion in the central 4-mm ring in the Scheimflug imaging (Pentacam) for both anterior and posterior floats and Corneal Hysteresis and Corneal Resistance Factor detected by ORA

Item	Correlation coefficient (r)	p value
Anterior float vs CH	0.06	>0.05
Anterior float vs CRF	-0.16	<0.05
Posterior float vs CH	-0.01	>0.05
Posterior float vs CRF	0.02	>0.05

#### 4. Discussion

Laser in situ keratomileusis is currently the procedure of choice for correcting moderate to severe myopia and myopic astigmatism (15). However, one of the most serious complications of Lasik is progressive ectasia (16). The Pentacam is currently the standard instrument that scans the anterior and posterior cornea with a rotating Scheimpflug camera with high repeatability and reproducibility of corneal thickness and posterior elevation measurements that provide a good tool for prediction of post-Lasik ectasia (17, 18). For elevation maps, apical protrusion in the central 4-mm ring in anterior elevation was considered: Normal, up to 12 microns; suspected, between 12 and 15 microns; keratoconus, above 15 microns. For posterior elevation, 5 microns are added to these values (9). Similarly, the Ocular Response Analyzer (ORA) capable of measuring corneal biomechanics in vivo has been introduced recently in preoperative assessment in Lasik candidates to aid in predicting the possibility of post-Lasik ectasia. It measured the Corneal Hysteresis (CH), which reflects corneal viscoelasticity (corneal damping response), and the Corneal Resistance Factor (CRF), which is thought to primarily reflect corneal elasticity (12), and they reflect positive measures for the corneal biomechanical properties. Normal values for both Corneal Hysteresis (CH) and Corneal Resistance Factor (CRF) usually differ according to the patient's race, e.g., in one study conducted in 2012, the mean value in mmHg for Corneal Hysteresis (CH) and Corneal Resistance Factor (CRF) was  $10.8 \pm 1.6$  and  $10.7 \pm 1.5$ , respectively, in Caucasians and  $9.2 \pm 1.5$  and  $9.8 \pm 2.0$ , respectively, in Africans (19). Different correlations between values provided by both machines, i.e., Scheimflug imaging and Ocular response analyzer, have been studied by a number of researchers (20-21) aiming at optimizing the pre-operative evaluation of refractive patients. Zhang et al. (20) conducted a study of 480 normal myopic eyes (240 healthy volunteers), with ages ranging from 18 to 44 (mean, std:  $23.84 \pm 5.08$ ) and mean spherical equivalent (MSE) ranging from -14.00 to -1.13 D (Mean:  $-5.68$ , SD: 2.17 D). They found that the values of CH and CRF presented normal distribution and the mean value for CH was  $10.38 \pm 1.36$  mmHg and  $10.70 \pm 1.59$  mmHg for CRF. There was a good correlation between CH, CRF, and CCT (CH:  $r = 0.54$ ,  $p = 0.000$ , CRF:  $r = 0.61$ ,  $p = 0.000$ ), and CH and CRF were negatively correlated with anterior central elevation (CH:  $r = -0.136$ ,  $p = 0.002$ ; CRF:  $r = -0.152$ ,  $p = 0.001$ ) (20).

In the present study, the Corneal Hysteresis (CH) ranged from 7 to 14.8 mmHg ( $10.18 \pm 1.44$ ). The Corneal Resistance Factor (CRF) ranged from 7.5 to 14.9 mmHg ( $10.58 \pm 1.67$ ). There was a strong positive correlation

between both Corneal Hysteresis and Corneal Resistance Factor and the Central corneal thickness (CH:  $r = 0.56$ ,  $p \leq 0.01$  and CRF:  $r = 0.46$ ,  $p \leq 0.01$ ). A non-significant correlation ( $p > 0.05$ ,  $r = 0.07$ ), existed between the central corneal thickness by pentacam and the apical protrusion in the central 4-mm ring in the anterior float. However, a statistically significant correlation ( $p < 0.05$ ,  $r = 0.15$ ) existed between apical protrusion in the central 4-mm ring in the posterior float and the central corneal thickness by pentacam. A non-significant correlation ( $p > 0.05$ ,  $r = 0.06$ ) existed between apical protrusion in the central 4-mm ring in the anterior float by pentacam and the Corneal Hysteresis by ocular response analyzer. However, a statistically significant negative correlation ( $p < 0.05$ ,  $r = -0.12$ ) existed between apical protrusion in the central 4-mm ring in the anterior float by pentacam and the Corneal Resistance Factor by ocular response analyzer. Also, a non-significant correlation existed between the apical protrusion in the central 4-mm ring in the posterior float by pentacam and both the Corneal Hysteresis ( $p > 0.05$ ,  $r = -0.01$ ) and the Corneal Resistance Factor ( $p > 0.05$ ,  $r = 0.02$ ) by ocular response analyzer among patients in the study. Generally, the results of the present study agreed with the results obtained by Zhang et al., except for obtaining a non-significant correlation between apical protrusion in the central 4-mm ring in the anterior float by pentacam and the Corneal Hysteresis by ocular response analyzer in the present study, which was not confined to myopic eyes but included hypermetropic eyes and where the mean spherical equivalent was lower than that included in the study conducted by Zhang et al. (i.e.,  $-4.28 \pm 2.91$  D in the present study versus  $-5.68 \pm 2.17$  D in Zhang et al.). Ostadimoghaddam et al. conducted a study of 36 normal eyes, and they found significant correlation between Corneal Hysteresis (CH) and central corneal thickness (CCT) ( $p = 0.001$ ,  $r = +0.51$ ) and also a strong association between Corneal Resistance Factor (CRF) and CCT ( $p < 0.05$ ,  $r = +0.71$ ). This suggests that thickness of the cornea can be an important factor in determining corneal biomechanical properties. There also was a significant correlation between Corneal Hysteresis and central corneal elevation ( $P = 0.03$ ,  $r = +0.35$ ) (21); however, no correlation was studied between Corneal Resistance Factor and anterior corneal elevation, which were negatively correlated in the present study. Therefore, this study strengthens the concept that for non-keratoconic eyes, a lower risk of post-Lasik ectasia would be expected with higher values for biochemical properties (22), mainly Corneal Resistance Factor, particularly when associated with acceptable numbers for apical protrusion in the elevation maps of Scheimflug imaging.

## 5. Conclusions

A strong positive correlation existed between both Corneal Hysteresis and Corneal Resistance Factor and the Central corneal thickness ( $p \leq 0.01$ ), which is important for biomechanical corneal stability. Also, a statistically significant negative correlation ( $p < 0.05$ ) existed between apical protrusion in the anterior float by pentacam and the Corneal Resistance Factor by ocular response analyzer, which supports using both machines preoperatively to decrease the risk of post-Lasik ectasia.

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## Conflict of Interest:

There is no conflict of interest to be declared.

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