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Corneal biomechanical properties after femtosecond laser assisted LASIK with the corneal visualization Scheimpflug technology and ocular response analyzer

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飞秒激光制瓣 LASIK 手术后角膜生物力学变化研究

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摘要

目的:应用可视化角膜生物力学分析仪(Corvis ST)及眼反应分析仪(ORA)评估飞秒激光制瓣准分子激光原位角膜磨镶术(laser *in situ* keratomileusis,LASIK)术后角膜生物力学变化,并分析与其他参数的相关性。

方法:收集63例飞秒制瓣LASIK手术患者,所有收集对象采用右眼数据进行分析。角膜生物力学测量仪器应用可视化角膜生物力学分析仪Corvis ST及眼反应分析仪ORA,手术前及手术后1mo进行生物力学数据采集分析。配对t检验或Mann-Whitney U检验进行手术前后生物力学对比分析。Pearson或Spearman统计学方法进行相关性分析。

结果:与FS-LASIK手术前相比,手术后1st A-time,Vin,2nd A length,Vout以及Radius下降,有统计学差异(P=0.00, P=0.00, P=0.00, P=0.00, P=0.00)。2nd A-time,DA以及PD手术后增加,有统计学差异(P=0.00, P=0.00, P=0.00)。1st A length以及HC time手术后改变不明显,无统计学差异(P=0.96,P=0.08)。与FS-LASIK手术前相比,手术后CH,CRF下降,有统计学差异(P=0.00, P=0.00)。手术后1st A-time, 2nd A-time, DA and Radius变化量与手术前角膜中央厚度有明显相关性(P=0.01, P=0.04, P=0.03, P=0.01)。

结论:飞秒激光LASIK手术后角膜生物力学参数有较明显改变,可通过Corvis ST及ORA生物力学参数计算得出相应变化,手术后生物力学参数变化与角膜厚度相关性明显。

关键词:近视;角膜生物力学;飞秒激光;准分子激光原位角膜磨镶术;可视化角膜生物力学分析仪

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Abstract

• AIM: To investigate the changes of corneal biomechanical properties before and after femtosecond laser assisted LASIK (FS-LASIK) using Corneal Visualisation Scheimpflug Technology (Corvis ST) and Ocular Response Analyzer (ORA), and the correlation with other myopic parameters.

• METHODS: Sixty three patients (63 eyes) who had myopic femtosecond laser assisted LASIK (FS-LASIK) were enrolled in the study. The right eye of each patient was analyzed in this study. The corneal biomechanical parameters pre-operative and 1mo post-operative was measured with the Corvis ST (Oculus, Wetzlar, Germany) and ORA (Reichert, Buffalo, New York, USA). Comparison of the biomechanical property values before and after surgery was peformed using Paired t-test or Mann-Whitney *U*. Pearson or Spearman correlations were used to evaluate the relationship between parameters.

• RESULTS: The postoperative 1st A-time, Vin, 2nd A length, Vout, HC time and Radius demonstrate significant decreases comparing with preoperative values (P=0.00, P=0.00, P=0.00, P=0.00, P=0.00, P=0.00 respectively). The postoperative 2nd A-time, DA and PD significantly increases (P=0.00, P=0.00, P=0.00), however, the 1st A length had no significant difference after surgery. The CH and CRF were significantly lower after FS-LASIK (P=0.00, P=0.00). A statistically significant correlation coefficient was found between preoperative central corneal thickness (CCT) with postoperative-preoperative changes of 1st A-time, 2nd A-time, DA and Radius respectively(P=0.01, P=0.04, P=0.03, P=0.01).

• CONCLUSION: There were significantly changes of corneal biomechanical properties after FS-LASIK surgery. The changes of corneal biomechanical properties after FS-LASIK can be reflected by some parameters of Corvis ST and ORA. The mainly influence of corneal biomechanical alteration was possibly correlation with corneal thickness.

• KEYWORDS: myopia; corneal biomechanical property; femtosecond laser; laser *in situ* keratomileusis; corneal visualization Scheimpflug technology

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INTRODUCTION

More and more studies of corneal biomechanical properties are investigated because of the influence of these properties on the predictability and stability of refractive surgery procedures outcomes[1-3]. Previous studies demonstrated that corneal refractive surgery significantly alters the biomechanical properties of the cornea[4-6], which plays an important role in the development of some serious post-operation complications. In some cases, the reduce of corneal biomechanical may contribute to refractive instability and loss of visual acuity, especially keratectasia[7]. Rad *et al*[8] reported that corneal ectasia represents one of the rarest but also one of the most feared complications with an incidence of 0.2% to 0.66% in the literature. Therefore, an effective method of quantifying the biomechanical state of a cornea before and after refractive surgery would be help to reduce the incidence of keratectasia by improving refractive surgery screening. Generally, corneal biomechanics studied by *in vitro* techniques that assess factors such as viscoelasticity, hydration[9] *etc*. Until to 2005, the Ocular Response Analyzer (ORA; Reichert Ophthalmic Instruments, Depew, New York, USA), which is based on a dynamic bidirectional applanation process, has enabled us to measure the biomechanical properties of the cornea in clinical[10], such as the corneal hysteresis (CH) and corneal resistance factor (CRF). This device provides metrics of corneal and/or ocular biomechanics. However, outputs of ORA do not give direct description about the mechanical behavior of cornea.

Recently, The Corvis ST (Corneal Visualisation Scheimpflug Technology, Oculus, Wetzlar, Germany) is a new clinical instrument that allows investigation of the dynamic reaction of the cornea to an air impulse. This novel instrument operates with a Scheimpflug camera taking more than 4 330 images per second along an 8-mm horizontal corneal coverage during corneal deformation under an air puff indentation. The complete visualization of the deformation process can be shown in a video output. Numerous parameters to describe the corneal viscoelastic properties and stiffness are displayed after internal calculation from the captured video image.

It is common knowledge that there have been some studies on the alteration of corneal biomechanical properties after refractive surgery measured by the ORA[11-13], as well as the repeatability and accuracy in measurement of intraocular pressure (IOP) and central corneal thickness (CCT) by the Corvis ST in healthy subjects, patients with ocular hypertension and glaucoma[14-15]. However, as far as we known, there are few published articles on the alteration of corneal biomechanical properties before and after refractive surgery measured concurrently by the Corvis ST and ORA.

Therefore, the purpose of this prospective study was to investigate the biomechanical properties of cornea measured with Corvis ST and ORA before and after laser *in situ* keratomileusis using femtosecond laser flap creation, and examines the relationship between the corneal biomechanical parameters after femtosecond laser assisted LASIK measured using the Corvis ST and ORA device.

SUBJECTS AND METHODS

Patients Sixty three patients (63 eyes) who had myopic femtosecond laser assisted LASIK (FS-LASIK) were enrolled in the study. Only their right eyes were analyzed. All enrolled patients were confirmed to be having a stable refraction and free of ocular and systemic disease. Contact lens wear was discontinued 2wk before the LASIK operation for soft lenses or 4wk before the LASIK operation for hard lenses. Exclusion criteria were corneal disease, glaucoma, retinal disease, previous intraocular surgery, and any other ocular disease, systemic disease could influence the eye. This study was performed in accordance with the tenets of the Declaration of Helsinki and approved by an Institutional Review Board. The written informed consent was obtained from each patient after receiving an explanation of the benefits and the known risks of the procedure.

Measurements Before the surgical procedure, patients had a complete ophthalmologic examination, including manifest and cycloplegic refraction, uncorrected visual acuity (UCVA) and best spectacle-corrected visual acuity (BSCVA), and slit-lamp biomicroscopy, ophthalmoscopy through dilated pupils. Best spectacle-corrected visual acuity was 20/20 or better in all preoperative eyes. The preoperative central corneal thickness (CCT) measured by ultrasound and the corneal biomechanical properties measured by Corvis ST and ORA before and 1mo after surgery were recorded.

Corvis ST[16] used a rapid air impulse to deform the cornea, and the corneal deformation was recorded by Scheimpflug technology. The air puff induced 2 corneal applanations (flattening), Appl 1 and Appl 2, of the cornea. The first applanation occurs when an air puff is delivered to the eye, causing the cornea to flatten, whereas the second applanation is the flattened status of the cornea when it rebounds from its

Table 1 Preoperative and postoperative findings in corneal biomechanical parameters

Parameter	Preoperative		Postoperative		t (Z), P
	Mean±SD	Range	Mean±SD	Range	
1st A-time	7.37±0.26	6.87 to 8.14	7.03±0.29	6.57 to 7.98	9.03, 0.00[a]
1st A length	1.79±0.08	1.38 to 1.89	1.75±0.15	1.26 to 1.92	0.01, 0.96
Vin	0.15±0.02	0.07 to 0.18	0.14±0.02	0.03 to 0.18	13.70, 0.00[a]
2nd A-time	21.72±0.30	20.98 to 22.30	21.90±0.44	20.76 to 22.65	-3.07, 0.00[a]
2nd A length	1.56±0.36	0.78 to 2.19	1.36±0.47	0.74 to 2.10	3.12, 0.00[a]
Vout	-0.42±0.07	-0.66 to -0.30	-0.49±0.09	-0.72 to -0.26	6.84, 0.00[a]
HC time	16.72±0.45	15.48 to 17.79	16.59±0.38	15.48 to 17.56	1.77, 0.08
DA	1.06±0.09	0.89 to 1.28	1.13±0.13	0.80 to 1.43	-4.78, 0.00[a]
PD	4.56±1.04	2.37 to 5.45	4.69±1.18	2.23 to 5.94	9.63, 0.00[a]
Radius	7.11±0.83	5.62 to 10.37	5.89±0.71	2.21 to 7.94	10.74, 0.00[a]

1st A-time: Time from start until the first applanation; 1st A length: Cord length of the cornea in the first applanation; Vin: Corneal velocity during the first applanation moment; 2nd A-time: Time from start until the second applanation; 2nd A length: Cord length of the cornea in the second applanation; Vout: Corneal velocity during the second applanation moment; HC time: Time from start until the highest concavity of cornea is reached; DA: Maximum deformation amplitude at the corneal apex; PD: Peak distance. [a]$P<0.05$, corneal biomechanical values post-op were significantly different from pre-op values.

highest concavity[16]. During one measurement process, 1st A-time: time from start until the first applanation; 1st A length: length of the flattened cornea in the first applanation ; Vin: corneal velocity during the first applanation moment; 2nd A-time: time from start until the second applanation; 2nd A length: length of the flattened cornea in the second applanation; Vout: corneal velocity during the second applanation moment; DA: maximum deformation amplitude at the corneal apex; PD: peak distance; Radius can be obtained from the images generated. Furthermore, IOP and corneal pachymetry data are provided in addition to some biomechanical response values[16]. The ORA was used to measure CH and CRF. An experienced ophthalmologist obtained the ORA waveforms, all of which showed symmetric peak heights and similar widths.

Surgical Technique All flaps were created using a femtosecond laser (IntraLase Corporation, Irvine, CA). All LASIK procedures were performed by wavefront-guided ablation. The attempted flap thickness was 90 μm and the flap diameter was 8.4 mm. After a flap was created, excimer laser ablation was performed with the VISX S4 laser system (Visx USA, Inc., Santa Clara, CA). After ablation, the corneal flap and stroma surface were cleaned with a balanced salt solution, and the flap was repositioned. The remaining procedures were the same as for the laser ablation.

Statistical Analysis The statistical software used was SPSS 13.0. All data sets were tested for normality using the Kolmogorov-Smirnov test. Data was expressed as the mean ± standard deviation. Comparison of the preoperative and postoperative biomechanical properties values were performed using Paired t-test or Mann-Whitney U. Pearson or Spearman correlations were used to evaluate the relationship between variables. A P value <0.05 was considered to be statistically significant.

RESULTS

The mean age of the 63 patients in this study was 23.63±4.62y (range, 18 to 36 y). Thirty patients (30 eyes) were male and 33 (33 eyes) were female. The mean preoperative spherical equivalent (SE) of refraction was -6.17±1.75 diopters (range, -10.88 to -2.50 diopters), with mean astigmatism of -0.66±0.50 diopters (range, -2.00 to 0 diopters). The preoperative central corneal thickness (CCT) was 531.05±29.03μm (range, 492 to 608μm). The mean ablation depth (AD) was 91.06±12.95μm (range, 52.20 to 109.10μm). The CH was decreased significantly, from 9.67±1.34 to 7.29±1.28 ($t=23.42$, $P=0.00$). The CRF was also decreased significantly, from 9.91±1.52 to 6.46±1.32 ($t=20.18$, $P=0.00$). Table 1 shows the mean values of all measured preoperative and postoperative corneal biomechanical parameters of Corvis ST. Comparing with preoperative values, the postoperative 1st A-time, Vin, 2nd A length and Vout demonstrate significant decreases after treatment respectively ($P=0.00$, $P=0.00$, $P=0.00$, $P=0.00$). The postoperative 2nd A-time significantly increase, however, the 1st A length had no significant difference after surgery. The HC time and Radius had a significant decrease postoperatively ($P=0.00$, $P=0.00$), at the same time, the DA and PD increased significantly ($P=0.00$, $P=0.00$).

After investigating the correlation of postoperative-preoperative corneal biomechanical parameters with ablation depth, diameter of ablation zone, preoperative SE, preoperative CCT respectively, a statistically significant correlation coefficient was found between preoperative CCT with postoperative-preoperative changes of 1st A-time, 2nd A-time, DA and Radius respectively (Table 2). The postoperative-preoperative changes of Vin had a significant correlation with preoperative SE and diameter of ablation zone (Table 2). The postoperative-preoperative changes of Radius had a significant correlation with preoperative SE, ablation

Table 2　The correlation of postoperative–preoperative corneal biomechanical parameters with SE, CCT, ablation depth, diameter of ablation zone

Parameters	SE	CCT	Ablation depth	Ablation zone
1st A–time	0.09, 0.51	–0.33, 0.01[a]	–0.26, 0.04[a]	0.09, 0.51
1st A length	–0.10, 0.47	0.14, 0.29	0.07, 0.62	0.07, 0.61
Vin	0.37, 0.00[a]	0.17, 0.18	–0.04, 0.75	0.31, 0.02[a]
2nd A–time	0.19, 0.17	0.27, 0.04[a]	0.04, 0.75	0.09, 0.50
2nd A length	–0.06, 0.63	–0.07, 0.61	–0.16, 0.23	0.07, 0.59
Vout	–0.11, 0.38	–0.24, 0.07	–0.13, 0.33	–0.01, 0.93
HC time	–0.06, 0.69	0.19, 0.17	0.05, 0.73	0.10, 0.45
DA	0.05, 0.69	0.28, 0.03[a]	0.21, 0.11	0.08, 0.55
PD	0.06, 0.67	0.16, 0.22	0.15, 0.25	0.12, 0.35
Radius	0.37, 0.00[a]	–0.36, 0.01[a]	–0.35, 0.01[a]	0.28, 0.03[a]

1st A–time: Time from start until the first applanation; 1st A length: Cord length of the cornea in the first applanation; Vin: Corneal velocity during the first applanation moment; 2nd A–time: Time from start until the second applanation; 2nd A length: Cord length of the cornea in the second applanation; Vout: Corneal velocity during the second applanation moment; HC time: Time from start until the highest concavity of cornea is reached; DA: Maximum deformation amplitude at the corneal apex; PD: Peak distance. [a]$P<0.05$, corneal biomechanical values post–op were significantly different from pre–op values; SE: Spherical equivalent; CCT: Central corneal thickness. [a]$P<0.05$, changes of corneal biomechanical values post–op were significantly correlated with procedure parameters.

zone and diameter of ablation zone (Table 2).

DISCUSSION

The cornea is a viscoelastic material composited with collagen, proteoglycans, water, and other elements, which can be modeled with quantifiable biomechanical properties[17–18]. Previous studies show that biomechanical properties of the cornea might be changed after myopic femtosecond laser assisted LASIK (FS–LASIK)[19–20]. Dupps and Roberts[21] thought the reason was predominantly due to an immediate near–circumferential severing of corneal lamellae results in a redistribution of stress and unprogrammed biomechanical shape changes during the surgery. In our study, We also found significant reductions in CH and CRF measurement with ORA at 1mo after LASIK using femtosecond laser for flap creation compared with preoperative. These findings are broadly in line with previous findings from Hamilton *et al*[1]. Corvis ST is a noncontact tonometer incorporating Scheimpflug technology to measure corneal deformation from air–puff indentation. During the measurement, the cornea reach the maximum deformation amplitude at the corneal apex under the force of air–puff, and rebound to original stations. 1st A–time, 1st A length, Vin, 2nd A–time, 2nd A length, Vout, HC time, DA, PD and Radius were obtained during this course. In previous study[16], the intraexaminer repeatability and intersession reproducibility of Corvis ST were investigated. Only DA and 1st A–time were found repeatable and reproducible, and the DA, as a reliable corneal parameter, could distinguish abnormal corneas from normal corneas. Hon and Lam reported that the CCT, DA, first applanation time (1st A–time), and IOP were repeatable. In the current study, excepting that the DA was significantly increased after surgical procedures, this was conformed to the result of Hon and Lam[16]. We also demonstrated here that 2nd A–time, Vout and Peak Distance were increased. In addition, we demonstrated that corneal 1st A–time; Vin; 2nd A length and Radius after the surgery captured by Corvis ST were decreased significantly compared with preoperative. Nevertheless, 1st A length and HC time after the surgery were not significant decrease compared with preoperative. For the large variations of some parameters in the measurement might be explained as follows. During the FS–LASIK surgery, the flap creation with femtosecond laser and surgical tissue removal may produce a biochemical parameter related to reduction of corneal stiffness[22–23]. For the DA, the thin cornea after flap creation and tissue ablation could result in decreasing of corneal antagonism to air impulse. The time would be faster from start until the first applanation, at the same time, the deformation amplitude could increase due to the softening of cornea after surgery. Radius could indirectly show the depth of being pressed of cornea. Therefore, the increasing of deformation amplitude could result in reducing of radius. Moreover, the collagen fiber relaxation after a corneal cut may reduce the capacity of the sonic wave to propagate in the corneal surface. The good correlation was demonstrated between biomechanical parameters and CCT in our study. Correlation analysis showed that 1st A–time and radius was negatively correlated with CCT; 2nd A–time and DA was positively correlated with CCT. Many previous studies have shown that corneal thickness could influence on deformation amplitude[24–25]. The changes of 1st A–time, radius and 2nd A–time were primarily result from the changing of deformation amplitude (DA). Therefore, the CCT plays an important part in the alteration of corneal biomechanical.

There was a weakness with this study that we have to acknowledge. Our study just recorded and contrasted the corneal biomechanical of preoperative with 1mo postoperative, and we did not contrasted with 6mo postoperative. We will contrast the forward changing of corneal biomechanical more rigidly in further studies.

In conclusion, there was a significant change in corneal biomechanical following femtosecond laser assisted LASIK (FS-LASIK) procedure. Parameters of Corvis ST and ORA could obviously reflect the changing of corneal biomechanical. CH, CRF, DA and radius had an apparent change in 1mo after surgery. Most of alterations of parameters were correlation with preoperative CCT.

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