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ORIGINAL RESEARCH

Comparison of Excimer Laser Versus Femtosecond Laser Assisted Trephination in Penetrating Keratoplasty: A Retrospective Study

Gábor Tóth · Nóra Szentmáry · Achim Langenbucher · Elina Akhmedova · Moatasem El-Husseiny · Berthold Seitz

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ABSTRACT

Introduction: To compare the impact of non-mechanical excimer-assisted (EXCIMER) and femtosecond laser-assisted (FEMTO) trephination on outcomes after penetrating keratoplasty (PK).

Methods: In this retrospective study, 68 eyes from 23 females and 45 males (mean age at time of surgery, 53.3 ± 19.8 years) were included. Inclusion criteria were one surgeon (BS), primary central PK, Fuchs' dystrophy (FUCHS) or keratoconus (KC), no previous intraocular surgery, graft oversize 0.1 mm and 16-bite double running suture. Trephination was performed using a manually guided 193-nm Zeiss Meditec MEL70 excimer laser (EXCIMER group: 18 FUCHS, 17 KC) or 60-kHz IntraLase™ femtosecond laser (FEMTO group: 16 FUCHS, 17 KC). Subjective refractometry (trial glasses) and corneal topography analysis (Pentacam HR; Casia SS-1000 AS-OCT; TMS-5) were performed preoperatively, before removal of the first suture (11.4 ± 1.9 months) and after removal of the second suture (22.6 ± 3.8 months).

Results: Before suture removal, mean refractive/AS-OCT topographic astigmatism did not differ significantly between EXCIMER and FEMTO. After suture removal, mean refractive/Pentacam/AS-OCT topographic astigmatism was significantly higher in the FEMTO (6.2 ± 2.9 D/7.1 ± 3.2 D/7.4 ± 3.3 D) than in the EXCIMER patients (4.3 ± 3.0 D/4.4 ± 3.1 D/4.0 ± 2.9 D) ($p \leq 0.005$). Mean corrected distance visual acuity increased from 0.22 and 0.23 preoperatively to 0.55 and 0.53 before or 0.7 and 0.6 after suture removal in the EXCIMER and FEMTO groups, respectively. Differences between EXCIMER and FEMTO were only pronounced in the KC subgroup.

Conclusion: Non-mechanical EXCIMER trephination seems to have advantages regarding postoperative corneal astigmatism and visual acuity compared with FEMTO trephination, especially in KC. A bigger sample size and longer follow-up are needed to evaluate the long-term impact of EXCIMER and FEMTO trephination on postoperative topographic and visual outcomes.

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G. Tóth (✉) · N. Szentmáry · E. Akhmedova · M. El-Husseiny · B. Seitz
Department of Ophthalmology, Saarland University Medical Center, Kirrberger Str. 100, 66424 Homburg/Saar, Germany
e-mail: gabortothgabor@gmail.com

G. Tóth · N. Szentmáry
Department of Ophthalmology, Semmelweis University, Mária utca 39, 1085 Budapest, Hungary

A. Langenbucher
Experimental Ophthalmology, Saarland University, Kirrberger Str. 100, 66424 Homburg/Saar, Germany

Keywords: Astigmatism; Excimer; Femtosecond; Laser; Ophthalmology; Penetrating keratoplasty; Visual acuity

Key Summary Points
Why Carry Out This Study?
Corneal surgeons still work against high and irregular corneal astigmatism after penetrating keratoplasty.
Astigmatism after penetrating keratoplasty may be influenced by the surgeon, technique, wound healing and characteristics of the donor or recipient.
To compare excimer laser and femtosecond laser-assisted penetrating keratoplasty techniques regarding postoperative astigmatism and visual acuity.
What Was Learned from the Study?
Non-mechanical excimer laser trephination seems to have advantages regarding postoperative corneal astigmatism and visual acuity compared with femtosecond laser-assisted trephination, especially in keratokonus.

INTRODUCTION

Penetrating keratoplasty (PK) is the oldest, most successful and frequently performed tissue transplantation worldwide [1]. After achieving a clear corneal graft, corneal surgeons still work against high and irregular corneal astigmatism after PK, as limited visual rehabilitation after surgery remains a challenge [2]. The problem of postoperative astigmatism seems to be unresolved. Astigmatism after PK may be influenced by the surgeon, technique, wound healing and characteristics of the donor or recipient. PK is not only a curative procedure, but also refractive [3].

Regular, circular and central trephination of both the donor and patient with smooth wound edges is crucial to achieve appropriate postoperative visual acuity after PK [4]. New trephination devices have rarely been introduced into corneal surgery. The latest two innovations were excimer laser-assisted (EXCIMER) [5] and femtosecond laser-assisted (FEMTO) [6, 7] PK. These two methods have gained significant interest in ophthalmology because high-precision microsurgical manipulation and incisions became available with their help. EXCIMER trephination has been reported to produce better postoperative visual acuity and less corneal astigmatism than conventional manual trephination. Smooth, perpendicular cutting edges and orientation teeth can help reduce donor button tilt and horizontal torsion [8]. The advantages of the FEMTO compared with conventional manual trephination are the precision of the cut and the different custom-shaped trephinations during PK, such as top hat, zigzag, mushroom and Christmas tree. This allows for patterns and angles that are not achievable with conventional mechanical trephines [9].

Several studies have compared EXCIMER [5, 8, 10] or FEMTO [9, 11–13] to conventional mechanical trephination techniques. However, no available study has compared corneal astigmatism and visual outcomes of EXCIMER and FEMTO trephination after PK. Thus, the aim of the present study was to assess the impact of EXCIMER and FEMTO trephination techniques on subjective and topographic astigmatism, visual outcome and surface regularity with 'all-sutures-in' and 'all-sutures out'.

METHODS

Patient and Donor Details

In this retrospective study, 68 eyes of 68 patients (23 females and 45 males) with the diagnosis of keratoconus (KC) or Fuchs' endothelial dystrophy (FUCHS) who underwent EXCIMER or FEMTO PK were analyzed (Table 1). Only one eye from each patient was included in the study. The study was approved by the Ethics Committee of Saarland University, Germany (no. 201/11). All procedures performed in our study involving human participants were in accordance with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. Informed

Table 1 Patient and donor characteristics (n = 68)

	Patient age (years)	Organ culture (%)	Post-mortem time (hours)	Preservation time (days)	Donor endothelial cell density (cells/mm^2)
EXCIMER (n = 35)	52.9 ± 20.4	100	16.4 ± 14.5	18.7 ± 6.1	2461 ± 322
FEMTO (n = 33)	53.8 ± 19.6	100	13.0 ± 11.8	17.2 ± 4.1	2453 ± 274

Data are presented as mean ± SD
EXCIMER excimer laser-assisted trephination, *FEMTO* femtosecond laser-assisted trephination

consent for participation and publication of patient data was obtained from all individual participants included in the study.

All surgical procedures were carried out under general anesthesia by one surgeon (BS). The EXCIMER group consisted of 18 eyes with FUCHS and 17 eyes with KC (n = 35 total). The FEMTO group consisted of 16 eyes with FUCHS and 17 eyes with KC (n = 33 total). Exclusion criteria were previous ocular surgery, any type of maculopathy, optic nerve atrophy, amblyopia and simultaneous cataract or other surgery.

Preoperative recipient corneal topographic astigmatism measured by Casia SS-1000 swept-source Fourier domain OCT (Tomey, Erlangen-Tennenlohe, Germany) did not differ significantly between the EXCIMER-KC (5.29 ± 2.89 D) and FEMTO-KC (5.50 ± 3.66 D; p = 0.895) or between the FEMTO-FUCHS (1.88 ± 2.51 D) and EXCIMER-FUCHS groups (1.76 ± 1.67 D; p = 0.865).

Trephination and Suturing Techniques

EXCIMER trephination was performed using a 193-nm MEL70 excimer laser (Carl Zeiss Meditec, Jena, Germany). Mean patient age was 35.6 ± 13.4 years in the EXCIMER-KC subgroup and 69.0 ± 8.9 years in the EXCIMER-FUCHS subgroup. For donor trephination from the epithelial side, a curved circular metal aperture mask (8.1 mm diameter in patients with KC and 7.6 mm diameter in patients with FUCHS), 3.0 mm central opening for centration, 0.5 mm thickness, 0.173 g weight, eight orientation teeth 0.15 × 0.3 mm) was positioned on a corneoscleral button (16 mm diameter) fixed in an artificial anterior chamber under microscopic control. The donor oversize was 0.1 mm in all cases. For recipient trephination, a corresponding circular metal mask was used [14].

FEMTO trephination was performed using a 60-kHz IntraLase^{TM} femtosecond laser [Abbott Medical Optics (AMO), Abbott Park, IL, USA]. The mushroom profile (8.5 mm upper diameter and 7.5 mm lower diameter for the donor cornea) was used in KC patients and the top-hat profile (7.5 mm upper diameter and 8.5 mm lower diameter for the donor cornea) in FUCHS patients [15]. Mean patient age was 39.7 ± 14.0 years in the FEMTO-KC subgroup and 68.8 ± 12.0 years in the FEMTO-FUCHS subgroup. The depth of the lamellar cut of the donor and recipient was two thirds of the mean corneal thickness of the graft and recipient's eye, respectively. All side cut diameters (anterior and posterior side cuts) were performed 0.1 mm larger than the resulting diameter, overlapping each other. Each laser procedure requires a disposable glass interface, which applanates the cornea during the laser procedure [16].

Grafts were fixated with a 16-bite double running diagonal cross-stitch suture (10–0 nylon) according to Hoffmann [17]. No additional surgeries except suture removals were performed in our sample during follow-up.

Diagnostic Methods and Main Outcome Measures

Subjective refractometry using trial glasses in a trial frame, corneal topographic astigmatism analysis via two devices (Pentacam HR Scheimpflug tomography, Wetzlar, Germany;

Casia SS-1000 swept-source Fourier domain OCT, Tomey, Erlangen-Tennenlohe, Germany) and corneal topography analysis using TMS-5 (Tomey, Erlangen-Tennenlohe, Germany) were performed by a masked observer before surgery, before removal of the first suture (11.4 ± 1.9 months) and at least 6 weeks after removal of the second suture (22.6 ± 3.8 months) but before any additional surgeries, such as cataract extraction or arcuate keratotomies. Time of first (11.1 ± 2.5 months vs. 11.9 ± 1.4 months; $p = 0.435$) and second follow-up (22.8 ± 4.4 months vs. 22.4 ± 3.4 months; $p = 0.139$) after PK did not differ significantly between the EXCIMER and FEMTO groups.

Main outcome measures included the topographic net astigmatism [difference between the steep and flat meridian in diopters (D)], refractive cylinder in D, spherical equivalent (SEQ), uncorrected distance visual acuity (UDVA), corrected distance visual acuity (CDVA), surface asymmetry index (SAI) and surface regularity index (SRI) of the topographer. Astigmatism was defined as "stable" if the change after suture removal was ± 1.0 D from the 'all-sutures-in' value.

Statistical Analysis

Statistical analyses were performed using IBM SPSS Statistics for Windows, version 19.0 (IBM Corp., Armonk, NY, USA). Two-sided Kolmogorov-Smirnov tests were used to test all variables in all groups for normality. To compare the two treatment groups or subgroups, we used the Student *t*-test in case of normal distribution and the non-parametric Mann-Whitney *U*-test for non-normally distributed variables. To compare before and after suture removal, we used the non-parametric Wilcoxon test. $p < 0.05$ was considered statistically significant.

RESULTS

Astigmatism

Before suture removal, mean refractive (2.9 ± 1.8 D vs. 3.4 ± 2.1 D) and topographic astigmatism with AS-OCT (5.5 ± 2.8 D vs. 5.2 ± 2.9 D) did not differ significantly between the EXCIMER and FEMTO groups (Table 2). After suture removal, topographic astigmatism with Pentacam decreased in 33% and 25% of eyes (2.4 ± 1.1 D and 2.6 ± 1.0 D) in the EXCIMER and FEMTO groups, respectively, and remained stable in 31% and 25% and increased in 36% and 50% (4.0 ± 2.1 D and 4.7 ± 2.6 D), respectively. Refractive astigmatism increased significantly ($p \leq 0.027$) between 'all-sutures-in' and 'all-sutures-out' time points in both groups. Topographic astigmatism measured by AS-OCT was significantly lower ($p = 0.010$) in EXCIMER and significantly higher ($p = 0.002$) in FEMTO after suture removal than before suture removal. After suture removal, mean refractive/topographic astigmatism (Pentacam and AS-OCT) values were significantly lower in the EXCIMER group (4.3 ± 3.0 D/4.4 ± 3.1 D/4.0 ± 2.9 D) than in the FEMTO group (6.2 ± 2.9 D/7.1 ± 3.2 D/7.4 ± 3.3 D; $p \leq 0.005$). Before suture removal, mean topographic astigmatism was significantly higher than refractive astigmatism in the EXCIMER and FEMTO groups ($p < 0.001$).

Before suture removal, mean refractive (3.2 ± 2.0 D vs. 4.4 ± 2.0 D) and topographic (AS-OCT; 4.5 ± 2.0 D vs. 4.8 ± 2.2 D) astigmatism did not differ significantly between the EXCIMER-KC and FEMTO-KC subgroups (Table 2). After suture removal, topographic astigmatism with Pentacam decreased in 50% and 15% of eyes (2.3 ± 1.2 D and 2.6 ± 0.8 D) in the EXCIMER-KC and FEMTO-KC subgroups, respectively, and remained stable in 11% and 8% and increased in 39% and 77% (3.2 ± 1.9 D and 4.7 ± 2.3 D), respectively. Refractive and topographic astigmatism was significantly higher ($p < 0.001$) in FEMTO-KC patients with 'all-sutures-out' than in those with 'all-sutures-in'.

After suture removal, mean refractive/topographic (Pentacam and AS-OCT) astigmatism values were significantly lower in the EXCIMER-KC subgroup (3.0 ± 2.5 D/3.2 ± 2.7 D/3.5 ± 2.9 D) than in the FEMTO-KC subgroup [7.3 ± 2.8 D/8.1 ± 3.0 D/8.3 ± 3.7 D; ($p \leq 0.006$)].

Refractive/topographic (Pentacam and AS-OCT) astigmatism did not differ significantly between the EXCIMER-FUCHS and FEMTO-FUCHS subgroups before (2.9 ± 1.4 D/4.3 ± 3.0 D/5.6 ± 2.5 D vs. 3.3 ± 1.9 D/5.2 ± 2.7

Table 2 Postoperative astigmatism (D) before ('all-sutures-in') and after ('all-sutures-out') suture removal (n = 68)

	All-sutures-in			All-sutures-out			p value (comparison of all-sutures-in and all-sutures-out)		
	Refractive	Pentacam	AS-OCT	Refractive	Pentacam	AS-OCT	Refractive	Pentacam	AS-OCT
EXCIMER (n = 35)	2.9 ± 1.8 (0.0–9.8; 1.8)	3.8 ± 2.6 (0.0–12.7; 3.5)	5.5 ± 2.8 (0.8–13.3; 5.4)	4.3 ± 3.0 (0.3–11.5; 3.0)	4.4 ± 3.1 (0.3–9.7; 3.4)	4.0 ± 2.9 (0.3–10.1; 3.6)	**0.027**	0.588	**0.010**
FEMTO (n = 33)	3.4 ± 2.1 (0.0–10.8; 3.0)	5.0 ± 3.3 (0.1–13.0; 4.1)	5.2 ± 2.9 (0.5–17.3; 4.7)	6.2 ± 2.9 (1.3–12.3; 5.5)	7.1 ± 3.2 (0.7–13.7; 6.9)	7.4 ± 3.3 (1.5–15.0; 6.9)	**< 0.001**	**0.002**	**0.002**
Comparison between EXCIMER and FEMTO									
P value	0.110	**0.005**	0.310	**0.005**	**0.001**	**< 0.001**			
EXCIMER-KC (n = 17)	3.2 ± 2.0 (1.0–7.0; 3.0)	3.1 ± 2.0 (0.3–6.8; 2.6)	4.5 ± 2.0 (1.7 ± 7.0; 4.4)	3.0 ± 2.5 (0.3–9.5; 3.0)	3.2 ± 2.7 (0.3–9.7; 3.1)	3.5 ± 2.9 (0.3–9.8; 3.0)	0.441	0.902	**0.047**
FEMTO-KC (n = 17)	4.4 ± 2.0 (1.5–8.0; 4.1)	5.7 ± 2.5 (1.5–9.3; 5.8)	4.8 ± 2.2 (1.3–8.2; 4.8)	7.3 ± 2.8 (3.0–12.0; 7.3)	8.1 ± 3.0 (4.4–13.6; 8.2)	8.3 ± 3.7 (3.5–15.0; 8.2)	**< 0.001**	**0.003**	**< 0.001**
Comparison between EXCIMER-KC and FEMTO-KC									
P value	0.199	**0.005**	0.501	**0.006**	**0.006**	**0.003**			
EXCIMER-FUCHS (n = 18)	2.9 ± 1.4 (1.0–5.5; 2.9)	4.3 ± 3.0 (0.2–10.2; 4.1)	5.6 ± 2.5 (0.8–9.5; 6.0)	4.3 ± 2.5 (2.0–8.5; 3.5)	4.3 ± 2.6 (1.5–9.7; 3.5)	4.6 ± 3.4 (0.8–10.1; 3.4)	**0.022**	0.342	0.112
FEMTO-FUCHS (n = 16)	3.3 ± 1.9 (0.5–6.0; 3.0)	5.2 ± 2.7 (0.5–9.6; 4.5)	6.7 ± 3.3 (1.5–11.6; 7.1)	5.2 ± 2.6 (1.3–11.0; 5.0)	6.1 ± 3.1 (0.7–12.2; 6.1)	6.3 ± 2.9 (1.5–10.1; 5.4)	**0.001**	0.130	0.613
Comparison between EXCIMER-FUCHS and FEMTO-FUCHS									
P value	0.744	0.702	0.376	0.866	0.480	0.171			

Data are presented as mean ± SD (minimum–maximum; median)

EXCIMER excimer laser-assisted trephination, *FEMTO* femtosecond laser-assisted trephination, *EXCIMER-KC* excimer laser-assisted trephination in patients with keratoconus, *FEMTO-KC* femtosecond laser-assisted trephination in patient with keratoconus, *EXCIMER-FUCHS* excimer laser-assisted trephination in patients with Fuchs' endothelial dystrophy, *FEMTO-FUCHS* femtosecond laser-assisted trephination in patients with Fuchs' endothelial dystrophy, *Refractive* refractive astigmatism, *Pentacam* topographic astigmatism with Pentacam HR Scheimpflug topography, Wetzlar, Germany, *AS-OCT* topographic astigmatism with Casia SS-1000 swept-source Fourier domain OCT, Tomey, Erlangen-Tennenlohe, Germany

Significant *p* values are bold

D/6.7 ± 3.3 D) or after (4.3 ± 2.5 D/4.3 ± 2.6 D/4.6 ± 3.4 D vs. 5.2 ± 2.6 D/6.1 ± 3.1 D/6.3 ± 2.9 D) suture removal. Refractive astigmatism was significantly higher after suture removal than before suture removal in both the EXCIMER-FUCHS ($p = 0.022$) and FEMTO-FUCHS subgroups ($p = 0.001$).

Visual Acuity and Spherical Equivalent

Mean CDVA increased from 0.22 and 0.23 preoperatively to 0.55 and 0.53 before and to 0.70 and 0.60 after suture removal in the EXCIMER and FEMTO groups, respectively. UDVA was significantly better in the EXCIMER than in the FEMTO group after suture removal ($p = 0.044$). Mean SEQ did not differ significantly between the EXCIMER and FEMTO groups before (0.1 ± 3.5 D vs. − 0.6 ± 3.6 D; $p = 0.054$) or after suture removal (− 0.6 ± 4.1 D vs. − 0.8 ± 3.3 D; $p = 0.666$) (Table 3). CDVA was better in both groups as well as in every subgroup, at 'all-sutures-out' compared with 'all-sutures-in' ($p \leq 0.005$). Moreover, UDVA was significantly better in the EXCIMER-FUCHS subgroup at 'all-sutures-out' compared with 'all-sutures-in' ($p = 0.002$), and SEQ was significantly less myopic before suture removal in the EXCIMER-KC subgroup than in the FEMTO-KC subgroup ($p < 0.001$).

Regularity of Corneal Topography

Mean SRI was significantly lower in the EXCIMER-KC subgroup than in the FEMTO-KC subgroup after suture removal (0.57 ± 0.40 vs. 1.16 ± 0.54; $p = 0.003$) indicating a higher regularity of corneal topography in the EXCIMER-KC subgroup (Table 4). Mean SAI and SRI decreased significantly after suture removal in all groups and subgroups ($p < 0.001$), except the FEMTO-KC subgroup ($p \geq 0.128$), indicating a lower regularity of corneal topography in this subgroup.

DISCUSSION

Our study confirms for the first time that post-PK outcomes after non-mechanical EXCIMER trephination are superior to those of FEMTO trephination, especially in patients with KC. Today, most of the eyes with FUCHS and many eyes with KC can be well treated with posterior and anterior lamellar keratoplasty techniques in experienced hands. Nevertheless, even in the "lamellar age" many indications for PK will persist. The present study was planned about 10 years ago, when Descemet membrane endothelial keratoplasty was just about to be disseminated around the world.

Corneal astigmatism following PK can be a serious problem that can limit postoperative visual performance. Therefore, corneal surgeons attempt to minimize the onset of post-PK astigmatism [3]. Accurate trephination is still a challenge in corneal surgery. Button ovality, eccentric trephination, disturbances in wound healing (wound dehiscence or graft elevation) and wound configuration may be factors in the development of astigmatism. Mechanical distortion induced by radial and tangential forces during trephination can hamper the creation of perpendicular cutting edges and regular-sized buttons (with the same anterior and posterior diameter) because of protrusion of the corneal tissue into the barrel of the trephine [10]. As Olson reported [18], 0.1 mm of tissue disparity in the graft-recipient interface can induce up to 4 D of astigmatism. Graft-recipient mismatches can be enhanced after suturing and cause "vertical tilt" of the corneal button. Furthermore, asymmetric suture placement plays an important role in rotation of the corneal graft and can establish "horizontal torsion" of the button in the recipient bed [19]. Graft-recipient mismatches can be decreased with donor trephination from the epithelial side rather than the endothelial side. Graft and recipient trephination should be performed using the same system in every case of PK [20].

A donor button punched from the endothelial side with mechanical trephination, using the same device as in the recipient, tends to be smaller than the recipient bed because of the protrusion of the corneal tissue inside the trephine. Therefore, the graft button is commonly planned larger than the recipient bed diameter. An oversized donor button compared with the recipient bed diameter results in a lower

Table 3 Spherical equivalent, uncorrected visual acuity (decimals) and best corrected visual acuity (decimals) before ('all-sutures-in') and after ('all-sutures-out') suture removal (n = 68)

	Preoperative			All-sutures-in			All-sutures-out			p value (comparison of all-sutures-in and all-sutures-out)		
	SEQ (D)	UDVA	CDVA	SEQ (D)	UDVA	CDVA	SEQ (D)	UDVA	CDVA	SEQ	UDVA	CDVA
EXCIMER (n = 35)	− 4.5 ± 6.8 (− 20.9–3.4; 1.3)	0.15 ± 0.13 (0.01–0.40; 0.10)	0.22 ± 0.16 (0.001–0.50; 0.20)	0.1 ± 3.5 (− 4.6–9.3; − 0.5)	0.32 ± 0.18 (0.09–0.80; 0.30)	0.55 ± 0.19 (0.20–0.90; 0.50)	− 0.6 ± 4.1 (− 9.0–9.4; 0.5)	0.32 ± 0.23 (0.02–0.80; 0.28)	0.70 ± 0.23 (0.30–1.0; 0.65)	0.682	0.014	< **0.001**
FEMTO (n = 33)	− 4.9 ± 7.3 (− 22.0–4.8; -1,5)	0.11 ± 0.10 (0.02–0.40; 0.06)	0.23 ± 0.15 (0.03–0.50; 0.20)	− 0.6 ± 3.6 (− 7.8–4.6; − 0.6)	0.23 ± 0.14 (0.05–0.50; 0.20)	0.53 ± 0.22 (0.16–1.0; 0.50)	− 0.8 ± 3.3 (− 6.0–6.3; − 0.8)	0.19 ± 0.14 (0.03–0.50; 0.16)	0.60 ± 0.25 (0.16–1.20; 0.60)	0.696	0.396	< **0.001**
Comparison between EXCIMER and FEMTO												
p value	0.810	0.338	0.766	0.054	0.075	0.951	0.666	**0.044**	0.189			
EXCIMER-KC (n = 17)	− 9.2 ± 8.1 (− 20.9–3.4; − 5.6)	0.07 ± 0.05 (0.01–0.20; 0.05)	0.13 ± 0.09 (0.03–0.40; 0.10)	0.1 ± 3.6 (− 5.6–10.6; 0.00)	0.27 ± 0.19 (0.05–0.90; 0.20)	0.48 ± 0.27 (0.05–1.0; 0.50)	0.7 ± 3.6 (− 4.8–9.4; 0.4)	0.32 ± 0.26 (0.02–0.80; 0.23)	0.75 ± 0.21 (0.30–1.0; 1.00)	0.405	0.648	**0.001**
FEMTO-KC (n = 17)	− 9.2 ± 6.6 (− 22.0–0.3; − 6.3)	0.06 ± 0.04 (0.02–0.20; 0.05)	0.17 ± 0.11 (0.03–0.30; 0.20)	− 1.8 ± 2.6 (− 6.3–1.8; − 1.2)	0.21 ± 0.16 (0.04–0.60; 0.16)	0.48 ± 0.25 (0.04–1.0; 0.50)	− 2.1 ± 2.8 (− 6.0–1.5; − 1.0)	0.24 ± 0.16 (0.05–0.50; 0.23)	0.67 ± 0.20 (0.16–1.0; 0.65)	0.252	0.428	**0.005**
Comparison between EXCIMER-KC and FEMTO-KC												
p value	1.000	0.971	0.264	< **0.001**	0.113	0.920	0.509	0.628	0.334			
EXCIMER-FUCHS (n = 18)	− 1.0 ± 2.5 (− 9.1–1.3; − 0.6)	0.24 ± 0.12 (0.02–0.40; 0.28)	0.32 ± 0.16 (0.001–0.50; 0.40)	− 0.3 ± 3.2 (− 6.3–6.3; 3.2)	0.19 ± 0.13 (0.02–0.50; 0.10)	0.35 ± 0.21 (0.02–0.90; 0.30)	− 2.0 ± 4.0 (− 9.0–2.8; − 1.0)	0.36 ± 0.23 (0.10–0.80; 0.30)	0.66 ± 0.26 (0.30–1.0; 0.60)	0.193	**0.002**	< **0.001**
FEMTO-FUCHS (n = 16)	0.2 ± 1.9 (− 3.3–4.8; 0.3)	0.18 ± 0.11 (0.03–0.40; 0.20)	0.29 ± 0.16 (0.05–0.50; 0.27)	0.6 ± 4.1 (− 7.8–4.6; 2.4)	0.17 ± 0.13 (0.02–0.60; 0.1)	0.34 ± 0.22 (0.02–1.0; 0.30)	0.8 ± 3.4 (− 5.5–6.3; − 0.3)	0.19 ± 0.14 (0.03–0.50; 0.13)	0.57 ± 0.27 (0.2–1.2; 0.6)	0.243	0.631	**0.002**
Comparison between EXCIMER-FUCHS and FEMTO-FUCHS												
P value	1.000	0.146	0.635	0.912	0.336	0.733	0.683	**0.024**	0.289			

Data are presented as mean ± SD (minimum–maximum; median)

SEQ spherical equivalent, *UDVA* uncorrected distance visual acuity, *CDVA* corrected distance visual acuity, *EXCIMER* excimer laser-assisted trephination, *FEMTO* femtosecond laser-assisted trephination, *EXCIMER-KC* excimer laser-assisted trephination in patients with keratoconus, *FEMTO-KC* femtosecond laser-assisted trephination in patient with keratoconus, *EXCIMER-FUCHS* excimer laser-assisted trephination in patients with Fuchs' endothelal dystrophy, *FEMTO-FUCHS* femtosecond laser-assisted trephination in patients with Fuchs' ndothelial dystrophy

Significant p values are bold

Table 4 Regularity of postoperative topography (TMS-5) before ('all-sutures-in') and after ('all-sutures-out') suture removal (n = 68)

	All-sutures-in		All-sutures-out		*p* value (comparison of all-sutures-in and all-sutures-out)	
	SAI	SRI	SAI	SRI	SAI	SRI
EXCIMER (n = 35)	1.85 ± 1.21 (0.20–7.24; 1.55)	1.25 ± 0.57 (0.12–2.79; 1.20)	0.97 ± 0.58 (0.38–2.46; 0.86)	0.78 ± 0.48 (0.02–1.96; 0.70)	**< 0.001**	**< 0.001**
FEMTO (n = 33)	1.90 ± 1.32 (0.46–8.29; 1.61)	1.34 ± 0.58 (0.15–2.74; 1.28)	1.17 ± 1.04 (0.33–5.74; 0.98)	1.00 ± 0.43 (0.39–2.28; 0.92)	**< 0.001**	**0.002**
Comparison between EXCIMER and FEMTO						
p value	0.834	0.233	0.475	0.401		
EXCIMER-KC (n = 17)	1.15 ± 0.66 (0.39–2.76; 0.94)	0.82 ± 0.39 (0.35–1.58; 0.85)	0.75 ± 0.38 (0.38–1.76; 0.72	0.57 ± 0.40 (0.03–1.44; 0.54	**< 0.001**	**0.002**
FEMTO-KC (n = 17)	1.33 ± 1.14 (0.46–4.53; 0.98)	0.98 ± 0.39 (0.37–1.83; 0.91)	1.35 ± 1.45 (0.38–5.74; 0.91)	1.16 ± 0.54 (0.58–2.28; 0.95)	0.128	0.886
Comparison between EXCIMER-KC and FEMTO-KC						
p value	0.913	0.513	0.102	**0.003**		
EXCIMER-FUCHS (n = 18)	1.60 ± 0.91 (0.54–3.70; 1.25)	1.03 ± 0.35 (0.55–1.84; 0.98)	1.09 ± 0.65 (0.47–2.46; 0.96)	0.89 ± 0.49 (0.02–1.96; 0.77)	**0.001**	**< 0.001**
FEMTO-FUCHS (n = 16)	1.65 ± 0.89 (0.70–3.98; 1.40)	1.20 ± 0.40 (0.73–2.04; 1.13)	1.11 ± 0.63 (0.33–2.77; 1.02)	0.96 ± 0.38 (0.39–1.86; 0.89)	**< 0.001**	**< 0.001**
Comparison between EXCIMER-FUCHS and FEMTO-FUCHS						
p value	0.642	0.320	0.552	0.851		

Data are presented as mean ± SD (minimum–maximum; median)
SAI surface asymmetry index, *SRI* surface regularity index, *EXCIMER* excimer laser-assisted trephination, *FEMTO* femtosecond laser-assisted trephination, *EXCIMER-KC* excimer laser-assisted trephination in patients with keratoconus, *FEMTO-KC* femtosecond laser-assisted trephination in patient with keratoconus, *EXCIMER-FUCHS* excimer laser-assisted trephination in patients with Fuchs' endothelial dystrophy, *FEMTO-FUCHS* femtosecond laser-assisted trephination in patients with Fuchs' endothelial dystrophy. TMS-5 = TMS-5 Topography, Tomey, Erlangen-Tennenlohe, Germany
Significant *P* values are bold

incidence of wound leakage, improved wound closure and decreased hyperopia [21]. A trephine tilt can facilitate the establishment of an oval opening and can lead to further corneal astigmatism after PK [22]. Ideal openings could be achieved by good centration in the cornea, perpendicular cutting, minimizing tissue protrusion into the trephine and a particularly sharp blade [23].

To fulfill these requirements, non-mechanical trephination with excimer laser was introduced into clinical practice by Naumann in 1989 [5] and femtosecond laser by Price in 2005 [7]. The main advantage of non-mechanical EXCIMER compared with traditional mechanical trephination techniques is the avoidance of mechanical distortion of the corneal tissue, which leads to perpendicular wound edges, round opening and graft, and appropriate congruent donor-graft wound healing. Due to the trephination procedure from the epithelial side, remarkable oversizing of the donor button compared with the recipient bed is not needed. In our study, the donor size was only 0.1 mm larger [22]. A previous study reported the superiority of non-mechanical EXCIMER compared with the mechanical trephination technique [8], with significantly lower corneal astigmatism, better visual acuity, less myopic SEQ and more favorable SRI in the EXCIMER group after suture removal.

Since introduction of the EXCIMER trephination in corneal transplantation in 1989, femtosecond lasers have been the only promising technique for full-thickness corneal transplants [6, 7]. Farid et al. [24] compared FEMTO zig-zag trephination and Hessburg-Barron trephination, finding faster vision recovery and less postoperative astigmatism at 3 months in the FEMTO group with 'all-sutures-in'. Chamberlain et al. [11] reported significantly less astigmatism after zig-zag FEMTO trephination at 4–6 months, and Gaster et al. [12] reported faster visual recovery and lower astigmatism 3 months following FEMTO zig-zag trephination.

Daniel et al. [13] reported shorter visual recovery with the mushroom FEMTO than motor trephine. Shumway et al. [25] reported better visual acuity in the running suture group than in the interrupted or combined running-interrupted suture group after full suture removal following zig-zag FEMTO PK.

The strengths of our work are that only two well-defined diseases were included in the study, corneal buttons were uniformly oversized by 0.1 mm, standardized double running suture was used, and each operation was performed by only one experienced surgeon. In our study, refractive and topographic astigmatism increased significantly following suture removal in the FEMTO group. In contrast, topographic astigmatism measured by Pentacam and AS-OCT decreased or did not change, and only refractive astigmatism increased in the EXCIMER group. Mader et al. [26] reported that removal of single running sutures after conventional mechanical PK caused an average 0.52 D decrease in astigmatism. Seitz et al. [2] showed that, after complete suture removal, astigmatism decreased in 52% vs. 11%, remained stable in 27% vs. 9% and increased in 21% vs. 80% of eyes in the EXCIMER vs. motor trephination groups, respectively. Seitz [8] reported a 0.9 D decrease in topographic astigmatism after EXCIMER PK, which is similar to our 1.5 D decrease in AS-OCT topographic astigmatism but slightly better than our non-significant 0.6 D increase in topographic astigmatism measured by Pentacam in the EXCIMER group.

Chamberlain et al. [11] reported lower topographic astigmatism after zig-zag FEMTO trephination compared with conventional trephination (5.79 D vs. 8.42 D) at 4- to 6-month follow-up, but the difference diminished later. Shumway et al. [25] found an average astigmatism of 4.51 D after removal of running sutures in patients who underwent zig-zag FEMTO trephination.

Refractive cylinder values also approximated the topographic astigmatism measured by Pentacam and AS-OCT in the FEMTO group at "all-sutures-out." Similar to our study, Seitz et al. [8] found increasing refractive and stabile or decreasing topographic astigmatism after suture removal following EXCIMER PK. Only refractive and regular astigmatism can be corrected with spectacles; increasing refractive astigmatism after suture removal after EXCIMER and FEMTO PK may be explained by the proportion of irregular astigmatism decreasing and the regularity of the corneal surface improving following suture removal. The decreasing SAI and SRI values in our study sample strengthen this conception after suture removal in both groups.

Lin [27] and Seitz [8] also reported a remarkable decrease in the SAI value following suture removal after PK; we found almost the same SAI values after suture removal in the EXCIMER group (0.97) as Seitz [8] (0.90) and Lin [27] (0.93). These results also suggest that removal of a double running suture may increase the symmetry of the corneal surface.

With further analysis of subgroups, the difference in postoperative astigmatism was highest between patients with FEMTO-KC and EXCIMER-KC. Patients with KC underwent mushroom-shaped trephination in the FEMTO group with a larger anterior graft diameter. The mean topographic astigmatism values (Pentacam: 8.1 D; AS-OCT: 8.3 D) after mushroom-shaped trephination in patients in the FEMTO-KC subgroup were higher than those reported by Birnbaum [9] (5.6 D) 16.8 months and Daniel [13] (5.9 D) 24 months after PK with all-sutures-out, but we had a smaller donor diameter. We always used an 8.5-mm anterior graft diameter in KC. In contrast, Birnbaum and Daniel et al. [9, 13] most frequently used a graft with an anterior diameter of 9.0–9.4 mm.

FEMTO trephination uses an applanation mechanism during the trephination, which can distort the eye during the procedure. The applanation may even distort an eye with severe preoperative astigmatism, as in KC, and can result in a higher postoperative astigmatism [20]. Disadvantages of FEMTO trephination may be more apparent in mushroom-shaped trephination with larger anterior diameter, and our results can further support the common sense that mushroom-shaped FEMTO trephination should be avoided in people with KC because of the high rate of immune reactions after PK [13]. We suspect that the greatest disadvantage of FEMTO trephination is the applanation and tissue distortion during the procedure resulting in oval or pear-shaped host openings. This is analogous to former mechanical trephination with an obturator to applanate the cone.

Limitations of our study include the following: it was performed in a retrospective fashion and the sample size was relatively small. A prospective randomized study with a larger sample size is needed to confirm the validity of our results.

CONCLUSIONS

Based on our analysis of both 'all-sutures-in' and 'all-sutures-out' long-term data, non-mechanical EXCIMER trephination seems to be superior to the pseudomechanical FEMTO trephination for PK, especially in KC patients. A bigger sample size and longer follow-up are needed to evaluate the long-term impact of EXCIMER and FEMTO trephination on postoperative topographic and visual outcomes.

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amendments or comparable ethical standards. Informed consent for participation and publication of patient data was obtained from all individual participants included in the study.

Data Availability. The data sets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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