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First clinical results with a new 200 kHz femtosecond laser system

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ABSTRACT
Background The aim of this study was to perform the first femtosecond laser cuts with a new prototype femtosecond laser, in vivo and to evaluate its safety, stability and efficacy.
Methods A LASIK cut was performed with a prototype 200 kHz femtosecond laser in both eyes of nine patients and one eye of two patients (20 individual eyes in total). A complete ophthalmic examination was performed preoperatively and postoperatively at 1, 3, 6 and 12 months after the procedure.
Results In the pilot series of 20 eyes, flap creation was possible in each case. The mean preoperative manifest refractive spherical equivalent was À−4.22 D (SD±61.22 D). The postoperative spherical equivalent refraction was À−0.1 D (SD±60.26 D) at 1 month, À−0.22 D (SD±60.24 D) at 3 months and À−0.15 D (SD±60.16 D) 12 months after surgery.
Conclusions Femto-LASIK with this new laser system showed high levels of safety, stability and efficacy without any enhancement.
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Since the introduction of excimer lasers for refractive surgery, several million people have been successfully treated to decrease or eliminate their dependency on glasses or contact lenses to correct their vision. Most surgeons prefer the LASIK technique over surface ablation techniques because patients' visual acuity recovers faster and patients have less pain.[1 2] One of the critical steps in LASIK is the creation of the corneal flap. Such complications as 'free flaps', 'buttonholes', epithelial defects, or incomplete cuts have been reported.[3] Although mechanical microkeratomes have been continuously improved over the past few years, the microkeratome cut is still the weak point of the procedure.[3] Solomon et al[4] investigated the thickness predictability of different mechanical microkeratomes, and showed that some microkeratomes had standard deviations of up to 30 μm.

In 1989, Stern et al[5] used a femtosecond laser to create cuts in the cornea. In 1999, the first successful cuts on human patients were performed.[6] Femtosecond lasers utilise ultra-short laser pulses in a femtosecond (10^{-15} s) duration range. The combination of a highly focused laser beam, ultra-short laser pulses and adequate energy causes the induction of plasma. The plasma expands to form a cavitation bubble.[7] Each laser pulse induces a cavitation bubble that is approximately 1−3 μm in size, which can expand to several μm depending on the laser's pulse energy. Overlapping these cavitation bubbles creates the dissection plane for the femtosecond laser flap. The specific characteristics of each femtosecond laser system vary depending on the duration of the laser pulse, the laser pulse energy and the focus.[8−10] New femtosecond laser systems with higher repetition frequencies have been developed to make flap creation more convenient for patients and to reduce the energy of each laser pulse. The first commercially available femtosecond laser system was the IntraLase femtosecond laser, which had a frequency of 10 kHz. Meanwhile, IntraLase has continued to improve their laser systems, while other companies have launched their own femtosecond laser systems. Currently, the Femtec (Technolas Perfect Vision, Munich, Germany),[11] the Ziemer LDV (Port, Switzerland),[12] and the Zeiss Visumax (Carl Zeiss, Jena Germany)[13] have been made available alongside the IntraLase system (Abbott Medical Optics, Santa Ana, California, USA).[14]

The aim of this study was to perform the first femtosecond laser cuts with a new prototype, ie, a 200 kHz femtosecond laser, in vivo and to evaluate its safety, stability and efficacy.

MATERIALS AND METHODS
Patients
This prospective, non-randomised clinical study included 20 consecutive eyes from 11 patients (table 1). This study was carried out after approval from and under the supervision of the local ethics committee. The mean age of the patients was 34 years (SD±8.7, range 21−54 years), and the intended correction ranged from −2.0 to −7.125 dioptres (D) (mean −4.22D, SD±1.22 D, table 2) manifest refractive spherical equivalent (MRSE). The patients were followed postoperatively for 12 months.

Clinical examination
A complete ophthalmological evaluation was performed on all patients before surgery and at 1, 3, 6 and 12 months after surgery. The examination included a detailed history, objective refraction, uncorrected distance visual acuity (UDVA), best-spectacle corrected distance visual acuity (CDVA), slit lamp examination, keratometry, ultrasound pachymetry (Tomey SP-3000; Tomey, Erlangen, Germany), corneal topography (Tomey TMS 4; Tomey), applanation tonometry, scotopic pupil size (Colvard pupillometer; Oasis, Glendora, USA), and

Table 1 Patient data

No of eyes	20
Average age	
34 years	From 21 to 54
Sex	
Female	55%
Male	45%
Eye	
Left	55%
Right	45%

Table 2 Pre and postoperative refraction

	Mean D (SD)	Min/max D
Sphere		
Preoperative	−3.86 (±0.98)	−2.0 to −7.0
Postoperative (12 months)	−0.07 (±0.18)	0.25 to −0.75
Cylinder		
Preoperative	−0.72 (±0.62)	0.00 to −2.25
Postoperative (12 months)	−0.13 (±0.20)	0.00 to −0.5
Spherical equivalent		
Preoperative	−4.22 (±1.22)	−2.0 to −7.125
Postoperative (12 months)	−0.15 (±0.16)	0.25 to −0.875

dilated fundus examination. The patients were also examined 1 day, 3 days and 1 week after surgery, but only objective refraction, UDVA and slit lamp microscopy were performed during these examinations. The inclusion criteria for this study were that participants must be at least 21 years of age with a manifest refraction of less than −8.0 D in SE and 3.0 D or less in cylinder, a central corneal thickness of more than 500 µm (as recommended by the Kommission Refraktive Chirurgie (KRC) in Germany, http://www.augeninfo.de/krc/index_00.php), a residual stromal bed of more than 300 µm, a stable manifest refraction for at least 2 years, and a pupil size of 6.5 mm or less. Before the start of the study, the patients agreed to participate in the study and to submit to the follow-up examinations. Informed consent was obtained from all patients after a thorough explanation of the procedure and its potential risks. Patients with diabetes mellitus, a rheumatic disease, autoimmune conditions, or a dermatological disease that could affect the eyes (eg, rosacea) were excluded from the study. Severe keratoconjunctivitis sicca, corneal diseases (eg, keratoconus), or other pathological eye conditions that could compromise visual acuity (eg, glaucoma or macular degeneration) were further exclusion criteria.

Flap creation

Before every surgery, the ocular surface was anaesthetised with topical oxybuprocaine hydrochloride (Conjucain EDO; Dr Mann Pharma, Berlin, Germany). After sterile draping, the patient was positioned under a prototype of the WaveLight UltraFlap FS200 femtosecond laser (WaveLight AG, Erlangen, Germany). This laser system has a repetition rate of 200 kHz. Then the suction ring was applied to the eye and the suction was turned on. The applanation cone was then inserted. The laser system with the applanation cone was lowered into the suction ring and the eye was flattened until the second vacuum between the suction ring and the applanation cone was applied. This connection creates a stable position of the eye. This procedure can be monitored through the laser microscope or on the monitor. The applanated area was controlled while using the monitor of the laser, and the

laser area was centred on the cornea. The flap parameters and dimensions have been evaluated previously.[15][16] The femtosecond laser cut was carried out with a bed energy of 0.4 µJ and a 5 µm spot and line separation. The side cut energy was 0.5 µJ, and the line separation was 1 µm at an angle of 70°. The time for the femtosecond laser cut was 10 s. As these surgeries were the first cuts made in vivo on human patients using this prototype system, the intended flap thickness was 130 µm and the flap diameter was 8.5 mm with a superior hinge. After the procedure was completed on the first two patients, a relaxation channel was added to the profile because we observed large amounts of opaque bubble layers (OBL) on the first two patients. After application of the femtosecond laser pulses, the vacuum instantly decreased, the suction ring was removed, the patient was moved to the excimer laser, and the flap was lifted with a LASIK spatula. The flap diameter was measured with a manual calliper.

The WaveLight Concept System 1000 was used for the photoablation step. After photoablation, the flap was repositioned, and the interface was rinsed thoroughly with a balanced salt solution (Alcon, Fort Worth, Texas, USA) and dried for 2 min. The postoperative therapy consisted of the administration of dexamethasone eye drops (Monodex; Thea Pharma, Dortmund, Germany) and Levofloxacin eye drops (Oftaquix sine; Santen, Germering, Germany) five times a day for 1 week and the administration of artificial tears (Carbomer, ThiloTears EDO; Alcon) hourly.

All treatments were based on manifest refraction with a target refraction of plano for all treated eyes. No nomogram adjustment has been applied to this study.

RESULTS

The femtosecond laser cuts were performed without any complications in all 20 eyes. A pronounced OBL was visible in the first two patients starting at the hinge area and spreading centrally (figure 1A). In these two patients, the flap was

Figure 1 Opaque bubble layers without (A) and with (B) relaxation tunnel.
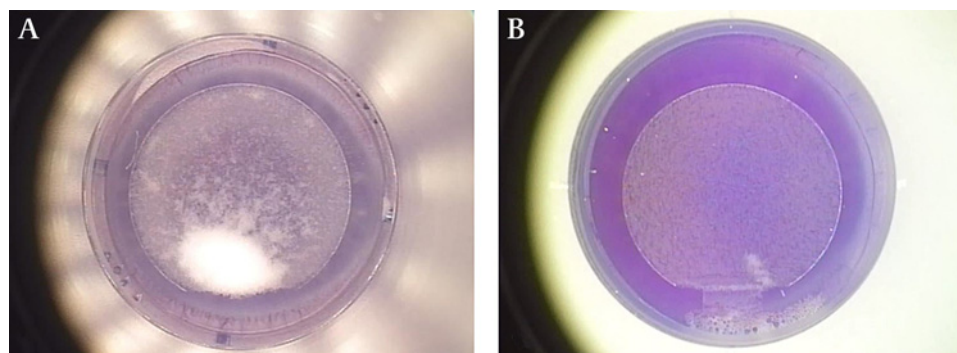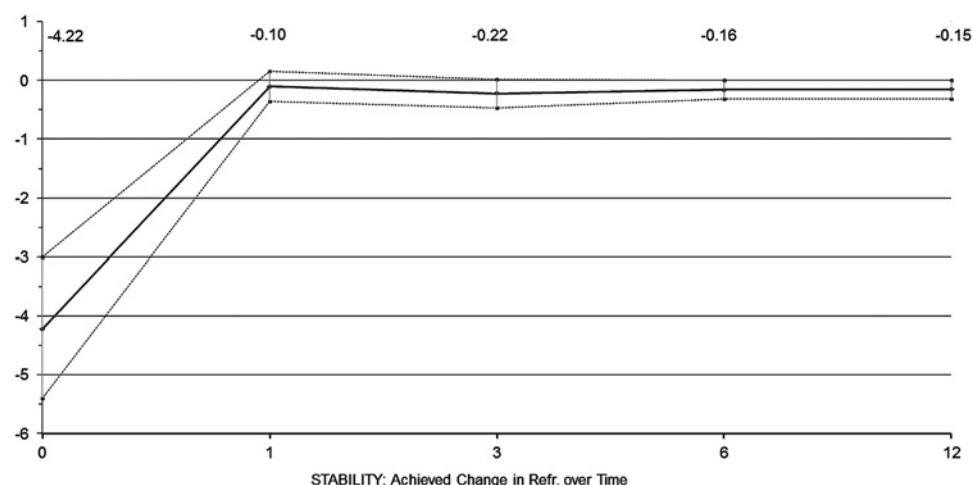
Figure 2 Stability of refraction. Mean spherical equivalent refraction during the first 12 months of follow-up.

adherent but lifting was still possible. In both eyes of the second patient, photoablation with the excimer laser had to be delayed for 5 min because the OBL was interfering with the eye tracker of the excimer laser. Therefore, a relaxation tunnel (like a pocket) was added to the femtosecond laser profile after the second patient in order to allow the gas bubbles to dissolve through this channel, thereby minimising the risk of the formation of OBL. After this channel was added, only a minimal OBL appeared in the hinge area; thus flap lifting was very easy and no further excimer laser ablation had to be delayed (figure 1B). Flap lifting with a LASIK spatula was possible in all eyes. The side cuts were very smooth and easy to open with the LASIK spatula; the stromal bed adhered a little bit more to the flap in the area of the OBL, but the separation could be performed very easily with the LASIK spatula. No holes in the LASIK flaps or incomplete cuts were observed. The mean flap diameter was 8.8 mm (SD±0.3 mm). No epithelial sloughing, oedema or defects occurred in the treated eyes during the entire postoperative period. During the postoperative course, no infections or signs of diffuse lamellar keratitis or similar interface appearances were visible in any patient.

The preoperative MRSE was −4.22 D (SD±1.22 D, range −2.0 to −7.125 D, table 2). Moreover, the MRSE was −0.15 D (SD±0.16 D, range 0.25 to −0.875 D, figure 2) at 12 months after surgery. The highest preoperative cylinder was −2.25 D (mean −0.72 D, SD±0.62 D). The cylinder was reduced to −0.19 D (SD±0.24 D) 1 month, to −0.13 D (SD±0.20 D) 3 months, to −0.11 D (SD±0.22 D) 6 months and to −0.13D (SD±0.20 D) 12 months after surgery.

Twelve months after the Femto-LASIK procedure, 18 of the 20 treated eyes were within ±0.5 D, and all eyes were within ±1.0 D of the intended correction (figures 3 and 4). No re-treatment was administered.

A quick visual recovery was observed after the Femto-LASIK procedure. On day 1, the average UDVA was 0.08logMAR (SD±0.13) (figure 5). On day 3, the UDVA improved to 0.0logMAR (SD±0.13) with all patients seeing 0.3logMAR or better. One month after surgery, the average UDVA was −0.04logMAR (SD±0.09). Twelve months after surgery, the UDVA was on average −0.01logMAR (SD±0.09). One eye showed 0.2logMAR, two eyes 0.1logMAR, and eight eyes demonstrated 0.0logMAR. The remaining nine eyes showed −0.1logMAR or better (figure 4). Ten eyes had the same pre and postoperative best CDVA; yet, eight eyes gained one line of Snellen distance visual acuity, and two eyes gained two Snellen lines (figure 6).
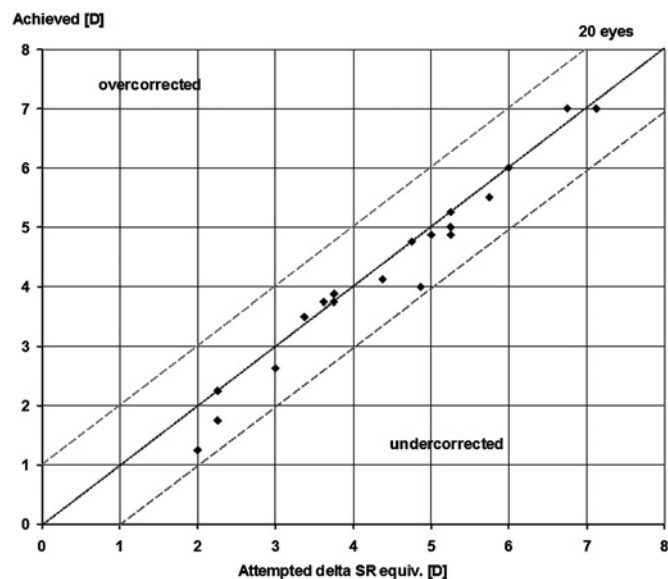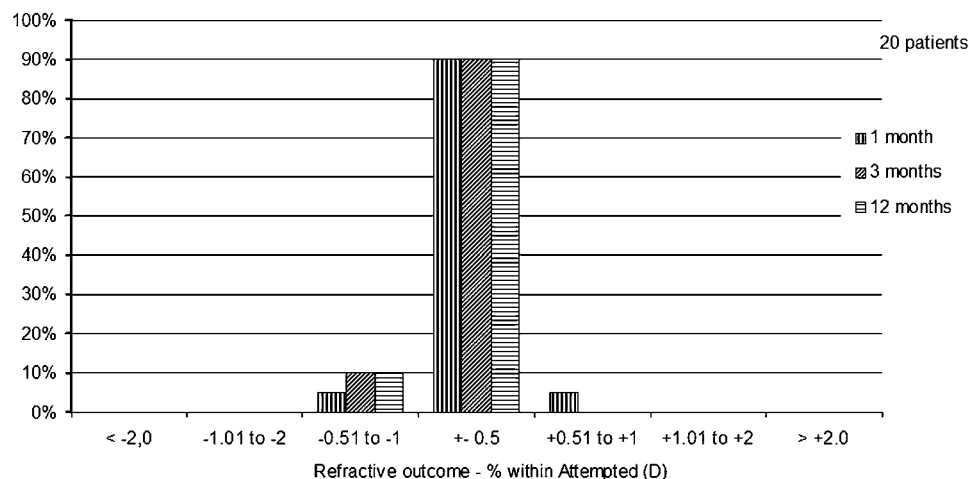
DISCUSSION

To the best of our knowledge, this paper presents the first clinical results for this new prototype femtosecond laser system. However, this laser has proved its feasibility previously via in-vitro experiments.[15–17] The results of the previous study were the basis for using this laser system as a serial femtosecond laser system.

An article by Soong and Malta[10] provided an update and review of femtosecond lasers in clinical ophthalmology. The authors noted, 'Femtosecond LASIK complications are rare but include unique problems, such as interference of surgery by cavitation gas bubbles during treatment.'[10] The first commercially available femtosecond laser systems had a frequency of 10 kHz. These systems used high energy levels per pulse, thereby resulting in large cavitation bubbles. Photodisruption induced by each laser pulse causes a gas bubble that must disappear. Some of these bubbles find the path of least resistance, which can include the interlamellar spaces of the cornea, thereby resulting in an OBL in the subepithelial space[18] and even the anterior

Figure 3 Scattergram intended versus attempted correction (12 months postoperative).

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Figure 4 Spherical equivalent (mean spherical equivalent refraction) refractive outcome bar graph.

chamber.[19][20] The higher laser repetition rates and improved optics of the newer femtosecond laser systems have led to a reduction in the energy requirements. Consequently, the cavitation bubble size is reduced, less tissue inflammation is observed, the time for flap creation is decreased, and the lifting of the flap becomes easier.[10] Faster repetition rates also allow the leading edge of treatment to stay ahead of the spreading OBL.[10] The femtosecond laser that was used in this study has a frequency of 200 kHz, which is even faster than the newest IntraLase system, which has a frequency of 150 kHz. Therefore, the energy level of each laser spot could be reduced. In this study, we used a bed energy of 0.4 μJ with a 5 μm spot separation. Previous histological examinations on porcine and human cadaver eyes had shown the ability to produce a nice side cut, a smooth stromal bed and almost no OBL.[16] To our surprise, we noticed more OBL in our present study than in the previous in-vitro study. The ablation with the excimer laser had to be delayed for a few minutes in two eyes. Therefore, a relaxation channel was added to the laser profile of the prototype femtosecond laser in order to allow the gas bubbles to dissolve through this channel. Because lifting the flap was easy, the bed energy

could possibly be lowered, thus achieving a further reduction of the OBL. Our patients all experienced a quick visual recovery time. One day after surgery, the average UDVA was 0.08logMAR with 68% of all eyes having 0.0logMAR or better. Visual acuity even improved after 3 days with 75% of the eyes seeing 0.0logMAR or better. These results are comparable with previously published results with different femtosecond laser platforms.[21][22]

Higher raster (laser) energies have been associated with more tunnel-positive cells,[23] and therefore with this newer 200 kHz system we suspect the lower laser energy would be associated with even less inflammation. Previously, our study group evaluated the UltraFlap FS 200 femtosecond laser in a laboratory setting on 20 porcine and three human cadaver eyes.[16] The surface of the cornea and the structure and ultrastructure of the corneal cells and stroma were evaluated using light microscopy, transmission electron microscopy and scanning electron microscopy. The structural and ultrastructural evaluation using light microscopy and transmission electron microscopy revealed no side effects of the laser application. The area around the flap cut was only minimally affected. The keratocytes and collagen

Figure 5 Uncorrected distance visual acuity bar graph in logMAR. CDVA, best spectacle distance corrected visual acuity.
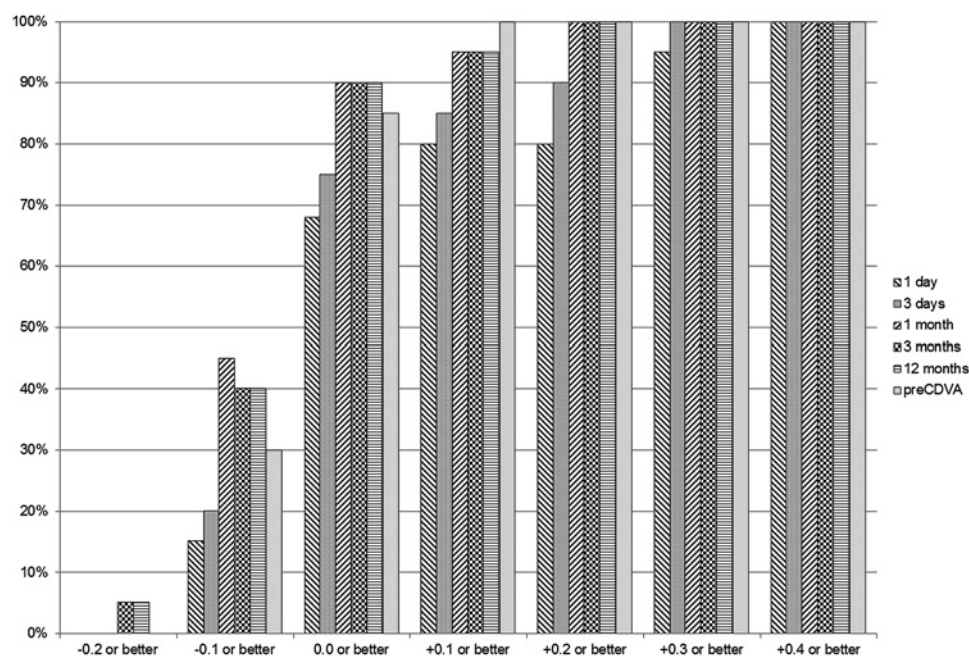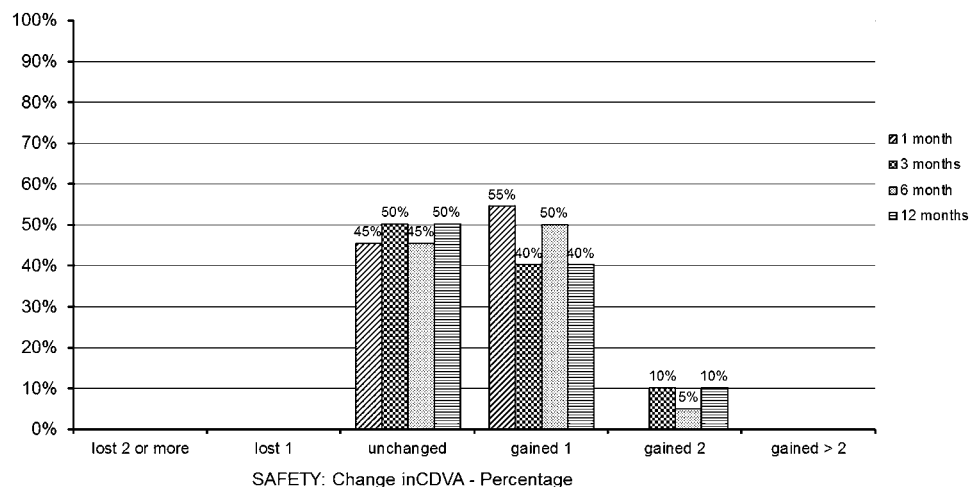
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Figure 6 Safety: change in best spectacle-corrected distance visual acuity (CDVA) bar graph.

fibres showed no to very little alterations due to the laser treatment. Scanning electron microscopy revealed in all cases smooth surfaces and precise side cuts. In the current study, corneal flaps could be created easily with this new femtosecond laser. At the same time, no structural and thermal side effects on corneal epithelium, stroma and endothelium were observed. The in-vitro results of our previous study were confirmed in our present in-vivo study, in which none of the flaps showed any signs of inflammation during the entire follow-up period.

The initial results with the prototype 200 kHz femtosecond laser are very promising. The creation of flaps was possible in all of the eyes, and the visual recovery time was very quick. Nevertheless, further studies with larger patient cohorts and longer follow-up times are necessary. Furthermore, after the first successful use of this femtosecond laser for flap creation, further applications, such as femtosecond laser assisted keratoplasty and tunnel preparation for intracorneal ring segments, should be explored.

Competing interests CWvM, RK, JS, MM and CPL none. CW and CD are employees of WaveLight GmbH, Erlangen, Germany.

Patient consent Obtained.

Ethics approval Ethics approval was obtained from the local ethics board.

Contributors CWvM, conception and design, analysis and interpretation of data; CW, RK, JS, analysis and interpretation of data; MM, CD drafting the article or revising it critically for important intellectual content; CPL, final approval of the version to be published.

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