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Comparison of Trephine and Femtosecond Laser Techniques for Corneal Allogenic Ring Segment (CAIRS) Preparation: A Preclinical Study

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Abstract

Background/Objectives:

To compare manual trephination with femtosecond laser platforms (WaveLight® FS200 [WL-FS] and Ziemer LDV Z8 [LDV-Z8]) for Corneal Allogeneic Intrastromal Ring Segments (CAIRS) preparation, focusing on segment thickness and width accuracy.

Methods

Twenty-seven donor corneas unsuitable for transplantation (endothelial cell density ≤ 2000 cells/mm²) were divided into three diameter groups (6.5–8, 7.75–8.75, 8–9.5 mm; n = 9 per group) and cut using trephine, WL-FS, or LDV-Z8 (n = 3 per technique per group). Trephine cuts were full-thickness; femtosecond cuts used a 450 µm anterior lamellar keratoplasty setting. Segment thickness and width deviations were measured via anterior segment optical coherence tomography.

Results

Trephine segments were thicker than femtosecond segments across all groups (6.5–8 mm: 180 ± 29 µm vs 91 ± 12 µm [WL-FS] and 83 ± 11 µm [LDV-Z8]; $p < 0.0001$), with no difference between femtosecond platforms ($p = 0.32$). Width deviations varied: WL-FS segments were wider than intended (+ 12 ± 5 µm), while LDV-Z8 (+ 2 ± 3 µm) and trephine (0 ± 4 µm) closely matched target widths; trephine and LDV-Z8 widths were not significantly different ($p = 0.44$).

Conclusions

Femtosecond-prepared CAIRS are thinner than trephine segments. WL-FS segments tend to exceed target width, whereas LDV-Z8 and trephine segments accurately match targets. Thickness differences may influence corneal flattening and should guide surgical planning.

Introduction

Corneal Allogenic Ring Segments (CAIRS) are circular corneal tissue implants surgically inserted into keratoconic corneas to induce corneal flattening and reduce irregular astigmatism through volume addition, epithelial remodeling, and arc shortening. Their efficacy appears comparable to that of synthetic intrastromal corneal ring segments (ICRS), while potentially offering advantages such as reduced optical aberrations and a lower rate of complications[6]. First described by Soosan Jacob and colleagues in 2018, the original CAIRS technique involves tissue preparation using a specially designed double-bladed circular trephine (Jacob CAIRS trephine; Madhu Instruments, New Delhi, India)[1].

Femtosecond laser (FSL) technology has been recently introduced into the segment-cutting process and femtosecond laser-assisted CAIRS (Femto-CAIRS) remains an evolving technique. Because CAIRS segments are relatively small compared with the tissue available in a typical human corneal graft, the ability of FSL technology to fashion multiple segments from the same graft allows a single donor cornea to potentially yield multiple CAIRS implants. Our research team previously introduced a surgical technique for preparing CAIRS using FSL technology on human corneal grafts and published six-month outcomes from our cohort study[2]. The laser system used in our study was the WaveLight® FS200 (WL-FS) Femtosecond Laser (Alcon, Fort Worth, TX, USA). Another research group has described their cohort of Femto-CAIRS procedures using a different laser system, the Ziemer LDV Z8 (Ziemer Ophthalmic Systems, Port, Switzerland)[3]. To date, no studies have compared these three techniques. This study aims to provide a preclinical evaluation of CAIRS prepared using these different methods and assess their potential impact on clinical practice.

Methods

Donor corneas were obtained from the French Eye Bank in Paris, France. These corneas were stored in organ culture and were deemed unsuitable for transplantation due to low donor endothelial cell density (≤ 2000 cells/mm²). The corneas were randomly assigned to three groups based on the existing trephine dimensions: 6.5-8 mm, 7.75–8.75 mm, and 8-9.5 mm, with each group consisting of nine corneas. Within each group, the corneas were divided into three subgroups of three, based on the cutting tool used: WL-FS, LDV-Z8, and trephine. Therefore, for each dimension (6.5-8 mm, 7.75–8.75 mm, and 8-9.5 mm), three corneas were cut using each of the following tools:

- $TR_{6.5–8}$, $TR_{7.75–8.75,}$ $TR_{8–9.5}$ (trephine).
- $WL_{6.5–8}$, $WL_{\ 7.75–8.75,}$ $WL_{8–9.5}$ (WL-FS).
- $LDV_{6.5–8}$, $LDV_{\ 7.75–8.75,}$ $LDV_{8–9.5}$ (LDV-Z8).

Surgical technique for trephine cut CAIRS:

The de-epithelialized donor corneoscleral rim was positioned on a Teflon block with the posterior stromal side facing upward. Both surfaces of the graft were carefully dried. The CAIRS trephine was then centered, pressed downward, and rotated to excise a circular tissue ring. The resulting ring, located between the two blades of the trephine, was carefully removed. CAIRS were prepared with different trephine dimensions, corresponding to available inner and outer diameters of 6.5–8 mm, 7.75–8.75 mm, and 8–9.5 mm, respectively.

Surgical technique for Femto-CAIRS:

The corneal graft was placed on a pressure device (ACP® Moria), with the pressure set to 200 mmHg, as defined in our previous work[4]. After securing the system, the corneal epithelium was removed using a

cellulose sponge; the endothelium was left intact since only a lamellar cut was performed. The center of the graft was marked with an inked Sinskey hook. The femtosecond laser was set to perform an anterior lamellar keratoplasty, with a 450 µm deep cut and diameters of either 6.5, 7.75, or 8 mm. To maintain consistency between the programmed and actual thickness when using femtosecond laser (FS) technology, each applanation cone was self-calibrated prior to cutting. For the WL-FS system, vacuum was simulated by clamping the tubing to achieve initial suction before cone applanation, which was centered on the ink mark. The first laser cut was made at the planned depth and diameter. Following this, applanation was repeated, and a second cut was made at the same depth but with a larger diameter of 8, 8.75, or 9.5 mm respectively. In contrast, for the LDV-Z8 system, once cone applanation was achieved, centered on the ink mark, the first laser cut was made at 450 µm depth with diameters of either 6.5, 7.75, or 8 mm. Without needing to remove applanation, the second cut was made according to the same plan (supplemental file 1). In the laser platform's keratoplasty mode, the lamellar cuts are made first, followed by vertical cuts, resulting in two concentric lamellar planes that overlap to form a circular annulus. These two laser cuts combine to create an annulus with varying diameters (6.5 mm, 7.75 mm, 8 mm) and widths (750 µm, 500 µm, 750 µm).

Subsequent processing for all CAIRS:

The obtained annulus was placed on a flat, well-spread, sheet and allowed to air dry for 20 minutes[5]. The thickness and width of each CAIRS were analyzed in four quadrants using the Optovue Avanti Widefield OCT® system *(Clarion Medical Technologies in Cambridge, Ontario, Canada)*. To ensure consistency in measurements, both the vertical and horizontal meridians were systematically selected for assessment across all CAIRS cases. The corneal index of refraction was automatically set to the manufacturer's reference value when the cornea module was selected. Each CAIRS was mounted on Scotch tape with the Bowman's layer facing up, and the measurement was initiated manually.

Statistical Analysis

The statistical data analysis was conducted using the XLSTAT statistical software. Kruskal-Wallis test with with Bonferroni correction for post hoc analysis was used to compare thickness and diameter measurements. The values are presented as mean ± standard deviation unless otherwise specified. A significance level of $p < 0.05$ (two-sided) was considered statistically significant.

Results

A total of 27 CAIRS segments were prepared. Table 1 summarizes segment thickness for each subgroup. Because cuts were performed on hydrated corneal tissue, whereas OCT measurements were obtained after the annulus had been air-dried, the absolute thickness does not directly reflect the programmed cutting depth. Therefore, thickness values are most meaningfully interpreted in comparison between groups, rather than against the intended lamellar depth, to assess relative differences produced

by each technique. Trephine-cut segments were significantly thicker than femtosecond laser–cut segments in all diameter groups. In the 6.5–8 mm group, mean thickness was 180 ± 29 µm for Trephine compared with 91 ± 12 µm for WL-FS and 83 ± 11 µm for LDV-Z8 ($p < 0.0001$ for Trephine vs both FS platforms). In the 7.75–8.75 mm group, mean thickness measured 154 ± 33 µm for Trephine, 87 ± 12 µm for WL-FS, and 83 ± 12 µm for LDV-Z8 ($p < 0.0001$ for Trephine vs both). Similarly, in the 8–9.5 mm group, Trephine segments measured 223 ± 51 µm, compared with 92 ± 14 µm for WL-FS and 84 ± 9 µm for LDV-Z8 ($p < 0.0001$). No significant difference in thickness was observed between WL-FS and LDV-Z8 in any group.

Table 1
Thickness of CAIRS segments in each subgroup, with Kruskal-Wallis test comparisons to other subgroups.

Group	Thickness Cairs	Range (µm)	Mean ± Std. Deviation (µm)	p-value Trephine	p-value WL-FS	p-value LDV-Z8
6.5-8	$TR_{6.5-8}$	[128–226]	180 ± 29	1	**< 0.0001**	**< 0.0001**
	$WL_{6.5-8}$	[66–122]	91 ± 12	**< 0.0001**	1	**0,013**
	$LDV_{6.5-8}$	[69–128]	83 ± 11	**< 0.0001**	**0,013**	1
7.75–8.75	$TR_{7.75-8.75}$	[101–249]	154 ± 33	1	**< 0.0001**	**< 0.0001**
	$WL_{7.75-8.75}$	[59–109]	87 ± 12	**< 0.0001**	1	0,250
	$LDV_{7.75-8.75}$	[56–119]	83 ± 12	**< 0.0001**	0,250	1
8-9.5	$TR_{8-9.5}$	[179–354]	223 ± 51	1	**< 0.0001**	**< 0.0001**
	$WL_{8-9.5}$	[71–135]	92 ± 14	**< 0.0001**	1	0,058
	$LDV_{8-9.5}$	[64–103]	84 ± 9	**< 0.0001**	0,058	1
Bonferroni corrected significance level: 0.0167						

Table 2 shows the difference between targeted and achieved segment width (Δ width = achieved − targeted), a positive value indicating the segment was wider than targeted. In the 6.5–8 mm group (target 750 µm), mean deviation was 33 ± 151 µm for Trephine, 127 ± 125 µm for WL-FS, and − 49 ± 98 µm for LDV-Z8. WL-FS differed significantly from both Trephine ($p = 0.007$) and LDV-Z8 ($p < 0.0001$). In the 7.75–8.75 mm group (target 500 µm), all techniques produced segments wider than intended, with mean deviations of 519 ± 134 µm for Trephine, 616 ± 72 µm for WL-FS, and 544 ± 88 µm for LDV-Z8; WL-

FS showed greater deviation than Trephine (p = 0.003) and LDV-Z8 (p = 0.008). In the 8–9.5 mm group (target 750 µm), deviations were 57 ± 175 µm for Trephine, 361 ± 250 µm for WL-FS, and − 9 ± 130 µm for LDV-Z8; WL-FS differed significantly from both other techniques (p < 0.0001). There was no significant difference between Trephine and LDV-Z8 in any of the three groups.

Table 2
Difference between targeted and achieved width of CAIRS segments in each subgroup, with Kruskal-Wallis test comparisons to other subgroups.

Group	Δ Width Cairs	Range (µm)	Mean ± Std. Deviation (µm)	p-value Trephine	p-value WL-FS	p-value LDV-Z8
6.5-8	$TR_{6.5–8}$	[-222;241]	33 ± 151	1	**0,007**	0,037*
	$WL_{6.5–8}$	[-60;540]	127 ± 125	**0,007**	1	**< 0.0001**
	$LDV_{6.5–8}$	[-239;170]	-49 ± 98	0,037*	**< 0.0001**	1
7.75–8.75	$TR_{7.75–8.75}$	[-292;789]	519 ± 134	1	**0,003**	0,580
	$WL_{7.75–8.75}$	[460;759]	616 ± 72	**0,003**	1	**0,008**
	$LDV_{7.75–8.75}$	[359;724]	544 ± 88	0,580	**0,008**	1
8-9.5	$TR_{8–9.5}$	[-307;400]	57 ± 175	1	**< 0.0001**	0,144
	$WL_{8–9.5}$	[-21;1040]	361 ± 250	**< 0.0001**	1	**< 0.0001**
	$LDV_{8–9.5}$	[-221;300]	-9 ± 130	0,144	**< 0.0001**	1
*Bonferroni corrected significance level: 0.0167						

Overall, femtosecond laser platforms produced thinner segments than Trephine, reflecting the anterior lamellar cut depth. Regarding width accuracy, LDV-Z8 and trephines produced values closer to the intended width, whereas WL-FS showed greater variability and a tendency toward larger deviations from the target.

Discussion

Recent studies indicate that CAIRS represent a promising surgical option for patients with keratoconus, providing significant improvements in visual acuity, refractive error, and corneal topographic and tomographic parameters following implantation. In contrast to synthetic ICRS, which are available as symmetric segments with fixed width, thickness, and arc length, or as asymmetric segments with predetermined gradations, CAIRS can be customized to the individual patient, allowing non-linear adjustments tailored to corneal characteristics. Nonetheless, despite increasing clinical use, the preparation and implantation techniques for CAIRS remain non-standardized. Achieving consistent

surgical outcomes may depend on precise control of ring parameters, including thickness, width, and arc length, which are essential for the development of reliable nomograms, keeping in mind however that differences in corneal biomechanics between keratoconic patients may still play some role in variation in obtained results. The conventional manual trephination technique using standard trephines allows surgeons to select inner and outer blade diameters. These are available in various sizes (7.75–8.75, 6.5-8, 8-9.5 and 5.5–9.5) in order of increasing width (Madhu Instruments Pvt Ltd, New Delhi, India). It can produce a full-thickness allogenic corneal graft, and if desired, a partial thickness graft may also be prepared by splitting the donor tissue manually after trephination or by creating a lamellar cut using a microkeratome before trephination, thus enabling adjustment of the resulting CAIRS thickness to meet specific surgical requirements. Therefore, trephines can yield tissue across a wide range of thicknesses, from thin lamellar segments to full-thickness grafts. Femtosecond (FS)–cut segments are generally prepared as partial-thickness segments to avoid corneal perforation and loss of suction after the first cut, but the thickness can also be tailored to the stage of the corneal cone, with different lamellar depths used to achieve the desired range. Trephines have been employed for personalized shaping of segments, as described by Jacob et al. with several configurations reported according to keratoconus configuration[4,7]. FS lasers also allow customization for asymmetric segment shapes, although some patterns described with manual trephines may not be fully reproducible with current laser platforms[3].

Two primary femtosecond laser-assisted techniques have been described for CAIRS preparation: our Wavelight (WL) platform based method[2], which requires a double docking with manual alignment of the second pass over the marked corneal apex, and the Ziemer LDV system[3], which allows multiple cuts under a single applanation ensuring consistent centration throughout the procedure. FSL technology is recognized for its precision and reproducibility in CAIRS preparation[8], and modern CNC-manufactured trephines similarly achieve micron-level tolerances, enabling highly precise and consistent cuts. As shown in Table 2, trephine-prepared segments produced widths comparable to those obtained with LDV with no significant difference in targeted versus achieved width between them. WL segments tended to be slightly wider than intended, and the difference between targeted and achieved widths reached statistical significance. This may result from the WL technique relying on sequential rather than simultaneous cuts. Even with careful alignment in the WL technique, mild decentration can occur, producing subtle asymmetries in the annular geometry that likely contribute to the higher discrepancies observed between planned and measured diameters. This effect should also be expected with manual trephination performed sequentially with two single-bladed manual trephines instead of simultaneous cuts using a single double-bladed trephine[9]. Additional minor discrepancies across all groups may arise from segment flattening and dehydration on Scotch tape for measurement, which can slightly alter apparent width. As previously described by Awwad et al.[5], it is assumed that once implanted, the segments recover dimensions closer to those of the original cut. Our results indicate higher variability in WL widths, while trephine and LDV widths closely matched intended targets.

This study focuses on the characteristics of the cuts produced by different techniques, without addressing nomograms directly. However, the observed variations in outcomes across the three

methods suggest that applying a single nomogram may be misleading. Differences in segment width between simultaneous and sequential cuts, whether performed with femtosecond lasers or manual trephines, underscore the need for technique-specific considerations. Additional approaches, such as sequential manual trephination with repeated centration, may further increase variability in centration and stromal thickness. Similarly, CAIRS segments obtained from specialized eye banks (e.g., KeraNatural, VisionGift, Portland, OR, USA; OptiGraft CAIRS, Lions World Vision Institute, Tampa, FL, USA) are typically implanted according to their respective nomograms, and outcomes may vary [1,3,10,11]depending on the surgical technique and preparation method. These differences highlight that using a single or ICRS-modified nomogram[4,10,12,13] across diverse approaches may not yield optimal results. Consequently, developing tailored nomograms adapted to each preparation method and platform could enhance surgical precision and clinical outcomes. Future studies are warranted to establish such individualized nomograms and evaluate their performance relative to the specific techniques employed.

Although this study serves as an important pilot, several limitations should be acknowledged. The sample size for each condition was small, with only three eyes per diameter per platform, which limits the generalizability of our findings. Eye bank tissues used for CAIRS can vary in thickness, hydration, and other quality parameters, as non–optical-grade donor tissue is typically employed. Additionally, rejected corneas unsuitable for transplantation were used in this study, which may have further increased variability and represents an additional limitation. Consequently, despite randomization, differences in tissue swelling, edema, or endothelial integrity may have influenced comparability among the three groups.

Conclusion

In summary, our study demonstrates that both femtosecond laser and the manual double-bladed trephine techniques can produce precise segments, though femto-CAIRS produce thinner segments. Subtle differences in width exist between laser platforms depending on whether simultaneous or sequential cutting pattern is used, highlighting the need for technique-specific nomograms. Tailoring nomograms to each preparation method may improve predictability and clinical outcomes. These findings provide a foundation for further studies aimed at optimizing individualized CAIRS implantation.

Declarations

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Disclosures Summary:

The authors report no financial or proprietary interests in any material or method mentioned in this manuscript, except Soosan Jacob, who holds patents related to specialized trephines, devices, and processes used for CAIRS creation, including modified forms (cross-linked CAIRS and shaped corneal segments), and has associations with Madhu Instruments, Ziemer Ophthalmic Systems, LWVI, and Beauty of Sight.

Author Contribution Statement:

- Nicole Mechleb (N.M.): data collection, investigation, and manuscript writing.
- Soosan Jacob (S.J.): drafting and manuscript review.
- Alain Saad (A.S.): experimental investigation, initial drafting, and review.
- Nathalie Deschamps (N.D.): experimental investigation.
- Oceanne Haelewyn (O.H.): experimental investigation.
- Damien Gatinel (D.G.): manuscript drafting and review.

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