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TITLE:	Comparative Study of the DMM and Conventional Toric Marker
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1. Executive Summary

NEED

There is currently a paucity of data comparing ARGOS combined with the Digital Marker Microscope and other Conventional Marking Modalities for Toric IOL alignment during cataract surgery.

STUDY OBJECTIVE

To evaluate the postoperative refractive accuracy of the common toric Intraoperative marking method of Toric CAM and Mendez marking when compared to ARGOS combined with the Digital Marker Microscope (DMM)/Vision Suite.

STUDY HYPOTHESIS

The DMM linked to Argos preoperative measurements with limbal registration determines the angle for toric IOL alignment intraoperatively more accurately than the manual Mendez marker.

SUPPORTS CLINICAL MESSAGE

The use of ARGOS with intraoperative image guidance improves the toric alignment error significantly and allows for more % of eyes within 0.5D residual CYL (20% more eyes) as compared to manual marking.

STUDY DESIGN

Sample size	35 eyes	
Endpoints	Primary:	Difference in intraoperative axis marks with Mendez marker, in degrees and direction, when compared to the DMM as viewed in the intraoperative heads-up display
	Secondary:	% of eyes less than 0.25, 0.5, 0.75, 1.00 and 1.25 D of residual refractive cylinder (CYL) in each group at 1 month postoperatively
Design:	Single-site, head to head, prospective, interventional (all eyes will be planned/implanted using ARGOS with image guidance axis; and the manual marker results will be back calculated utilizing IOL position and post-operative refraction)	

DURATION/FOLLOW-UP: Preoperative to 1 month postoperative

This study will be registered with clinicaltrials.gov. The study will be conducted in compliance with the protocol, GCP, and applicable regulatory requirements.

2. Study Background

Toric IOLs offer patients with corneal astigmatism, increased spectacle independence after cataract surgery. Toric marking aims at improving the accuracy of incision location and IOL alignment. Conventional markers rely on a reference mark tied to gravitational alignment and the accuracy in manual marking methods is affected by head position, errors on marking and smearing of ink. Digital marking methods aim to reduce intraoperative IOL misalignment using images captured in the sitting position which are used as overlay for IOL alignment intraoperatively[1]. The DMM linked to ARGOS preoperative measurements with limbal registration determines the exact angle for toric IOL alignment intraoperatively.

The purpose of this study is to compare the outcome of toric IOL implantation guided by manual or digital marking techniques. The intrinsic difference in the toric axis alignment may lead to a significant difference in the marked alignment axis intraoperatively resulting in superior refractive outcomes and less residual astigmatism using intraoperative alignment from the ARGOS Vision planner and DMM.

3. Study Design

- A single site, interventional study comparing the ARGOS/ DMM axis to the Mendez toric marker paired with the toriCAM smart phone app.
- There will be 35 eyes total that meet the inclusion criteria. Patient's refraction will be evaluated 4 weeks after cataract surgery with a monofocal toric IOL (Clareon Toric).
- Intraoperative difference in toric marks will be recorded in degrees and direction of marking difference (clockwise and counterclockwise).
- Post operative refraction will be obtained at 4 weeks after surgery using standard Snellen acuity chart and phoropter. IOL position will be verified with slit lamp photography aligned with preoperative Argos toric imaging to ensure that IOL position is NOT a source of refractive error.
- We will perform back calculation of theoretical refraction, as if the IOL was positioned at Mendez marking axis rather than the Argos axis. This will be calculated using the IOL position and post operative refraction with Astigmatismfix.com calculator or equivalent calculator

4. Study Inclusion and Exclusion Criteria

4.1 Inclusion Criteria

Subjects are eligible for the study if they meet the following criteria:

- Subjects willing and able to participate in this study.
- Subjects that have signed a consent to participate in the study.
- Subjects that are 50-80 years of age that have had uncomplicated femto-second assisted cataract surgery
- Subjects will have been implanted with the toric Alcon Clareon Toric monofocal IOL
- Subjects with IOLs implanted based on digital marking performed using ARGOS DMM
- Subjects will have BCDVA of LogMar 0.20 (20/32) or better in both eyes
- Subjects able to perform a post-op refraction.

4.2 Exclusion Criteria

If any of the following exclusion criteria are applicable to the subject, the subject should not be included in the study:

- History of amblyopia, macular disease, glaucoma, corneal disease, prior corneal surgery, or diabetes
- IOL final position greater than 2 degrees from intended axis.
- Ocular comorbidity that might hamper post operative visual acuity
- Previous ocular or refractive surgery
- Expected post-op VA worse than 20/25 (Snellen)
- Irregular corneal astigmatism and keratoconus
- Difficulties comprehending written or spoken English language
- Patients that are unable to fixate due to physical or intellectual disability (e.g. Down's Syndrome, Parkinson's Disease)
- Severe/uncontrolled Ocular surface disease/Dry Eye Disease
- Intraoperative complications during procedure

5. Study Procedures

5.1 Preoperative

At the preoperative exam, subjects will undergo all routine, usual standard-of-care procedures, including a medical history, demographics, ARGOS biometry, and a slit-lamp and dilated fundus examination. Subjects will then be consented for the study, and a review of inclusion and exclusion criteria will be done prior to the surgery.

5.2 Operative (Day of Surgery)

All subjects will undergo femto-second assisted cataract surgery with implantation of the Clareon monofocal toric IOL.

The toriCAM smartphone app will be used to mark the horizontal axis as a reference preoperatively in a sitting position. The target axis of the IOL, as calculated by the Argos, will be marked intraoperatively with a Mendez marker based on the horizontal reference marker from the Toric Cam.

After phacoemulsification, the Digital Marker Microscope (DMM) will be used to determine the target axis by using an image overlay

The difference in the final marked IOL axis and the DMM axis will be measured using the DMM degree overlay intraoperatively. The difference in degrees and the direction will be recorded.

5.3 Postoperative Visits

Subjects will undergo all routine, usual standard-of-care postoperative procedures and follow up appointments.

In addition, 4 weeks following cataract surgery, the final position of the IOL will be confirmed using a slit lamp photograph compared to the ORIGINAL Argos reference image. The surgeon will confirm that the IOL is within 2 degrees of the final intended axis as calculated by the Alcon Vision Planner.

Then the postoperative subjective refraction shall be measured by Snellen and Phoropter method and the theoretical refraction shall be back calculated using the double vector method to arrive with the refraction that would have been obtained by the Mendez marking

method. This will be calculated using the IOL position and post operative refraction with Astigmatismfix.com calculator or equivalent calculation.

6. Statistical Analysis

A summary of the data will be prepared for all measurements. For variables measured on a continuous scale, these summaries will include the sample size, as well as the mean, standard deviation, median, minimum, and maximum. For variables measured on a categorical scale, summaries will provide the number and percentage of eyes in each category. These summaries will be provided for all eyes completing the study.

The statistical analyses will be performed using R, version 4.2.2 or higher. Any statistical tests of hypotheses will employ a level of significance of alpha=0.05.

The primary endpoint will be compared using the paired t-Test. Secondary endpoints will be compared using McNemar's test. Analysis will follow a step down approach:

- Difference in intraoperative axis marks with Mendez marker, in degrees and direction, when compared to the DMM viewed in the intraoperative HUD
- % of eyes less than 0.5D CYL in each group
- % of eyes less than 0.25D CYL in each group
- % of eyes less than 0.75D CYL in each group
- % of eyes less than 1.0D CYL in each group
- % of eyes less than 1.25D CYL in each group

7. Sample Size Justification

Based on the primary endpoint, the study would require a sample size of 21 pairs (to achieve a power of 80% and a level of significance of 5% (two sided), for detecting a mean of the differences of 4.4 between pairs, assuming the standard deviation of the differences to be 6.5.[1]

However, in order to achieve a sample size that allows for statistical analysis of the secondary endpoints, we estimate the sample size required for detecting a difference of 0.20 between the percentage of with postoperative residual astigmatism 0.5 D or less (85% compared to 65%), power of 85%, correlation between paired observations 0.80, and a two-sided significance of 5% is 30.[2]

To account for dropout, the sample size will be increased to 35 eyes.

References

1. Lipsky L, et al. Comparison of toric intraocular lens alignment error with different toric markers. J Cataract Refract Surg. 2019; 45:1597–1601.
2. Webers VSC, Bauer NJC, Visser N, Berendschot T, van den Biggelaar F, Nuijts R. Image-guided system versus manual marking for toric intraocular lens alignment in cataract surgery. J Cataract Refract Surg. 2017; 43: 781-788.