Overview Myopia and myopic astigmatism effects an estimated 1.6 billion people worldwide (1). The prevalence of myopia ranges from 4% to 51% among regions, with increasing prevalence observed in recent years. Refractive surgery is one option to correct refractive errors and optimize visual performance. One common refractive surgery technique used since 1989 is LASIK.

The clinical refraction utilized as a globally accepted rule in laser vision correction applied to the cornea either as LASIK, PRK and even Smile has been the subjective refraction established by the dry manifest and or in consideration of the cycloplegic manifest as well.

Current treatment planning for LASIK with WaveLight technology consists of various treatment profiles such as wavefront optimized (WFO), wavefront guided (WFG), and topography guided. These profiles are based on simplified formulas derived from paraxial optics, without considering the multiple lens structure of the eye (2). The objective of wavefront-guided LASIK is to perform an ideal postoperative wavefront for a given eye. In this option, the ablation pattern is determined by the topographic parameters of each patient and allows the surgeon to establish a target asphericity in each case.

The goal of refractive surgery is to provide the patient with the best possible visual performance post-surgically. To achieve this, accurate methods of calculation during treatment planning are required. The new Wavelight plus treatment algorithm for calculating ablation profiles has been developed in order to improve clinical outcomes following LASIK treatment. The Wavelight plus Sightmap captures all diagnostic measurements needed for the Wavelight plus algorithm to generate a patient-specific ablation profile.

We were part of the AIT on Wavelight plus and achieved excellent outcomes in many patients (3). This AIT could show that Wavelight plus is a safe, predictable, and effective treatment option. However, the trial could not prove superiority or non-inferiority in comparison with Q-value customized ablation (CQ) LASIK.

In addition to that for the Wavelight plus AIT the guidance was to perform all preop measurements 4 times but the new recommendation based on simulations is to perform 1 measurement for biometry, 2 for tomography and 4 for wavefront but here are no prospective clinical data available supporting this approach. Germany is the first country that will launch the Wavelight plus algorithm. Therefore, data are needed to support that Wavelight plus is at least non inferior to WFO and to gather data on the current best practice to perform the preop measurements.

Scientific Rationale:

The purpose of this intraindividual study is to show that the WaveLight EX500 excimer laser system for LASIK correction using Wavelight plus in conjunction with the Wavelight Sightmap is at least non inferior to Wavefront optimized (WFO) LASIK.

*Hypothesis

H1: Refractive surgery with Wavelight plus is non-inferior to CQ based on % of eyes with absolute MRSE within ±0.50 D at 3 months after refractive surgery (no more than 20% difference)

H2 Refractive surgery with Wavelight plus is superior to CQ based on % of eyes with absolute MRSE within ±0.25 D at 3 months after refractive surgery

*Objectives

To compare clinical outcomes of Wavelight plus LASIK to CQ LASIK 1 and 3 months postoperatively

Endpoints

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*Statistical Considerations

Sample Size Justification (Hypothesis 1):

Sample Size for Comparing Paired Proportions, Non-inferiority study design:

- One-sided significance level: 2.5%.
- Power: 80%.
- Assumed positive rate within +-0.5 D for Wavelight Plus: 92% (Data Extracted from AIT).
- Assumed positive rate within +-0.5 D for Custom Q: 52% (Data from Reference 12).
- Non-inferiority margin: -20% (based on clinical judgement)

The study would require a sample size is 16 subjects, adding a 20% dropout rate, it results in a total sample size of **20 subjects** (40 eyes, 20 eyes per group).

Sample Size Justification (Hypothesis 2):

Sample Size for Comparing Paired Proportions using Marginal Proportions*:

Significance level: 5%.

Power: 80%.

Wavelight Plus positive rate: 74% (Extracted from the Wavelight AIT)

Custom Q positive rate: 38% (Extracted from Reference 12).

Correlation between Wavelight Plus and Custom Q data = 0.4 (assumed a 'moderate' correlation')

The study would require a sample size of 24 pairs to achieve a power of 80% and a two sided significance of 5% for detecting a difference of -37% between marginal proportions. If we add a 20% dropout rate, **the final sample size is 30 subjects** (60 eyes, 30 eyes per group).

*Note that there is no prior information on Discordant probabilities in the literature. That is why we have considered the Marginal probabilities published in prior studies and assumed a moderate correlation between Wavelight Plus and Custom Q of 0.4.

Analysis

For primary and first secondary endpoint (at 3 months) the differences between the two treatment methods will be assessed using McNemar test. No inferential test for all other secondary endpoints. Descriptive statistics for secondary endpoints.

Descriptive statistics (i.e., mean, standard deviation, etc.) will be provided for all continuous variables using SPSS software for all categorical variables collected in this study.

Safety Analyses

The type, severity, duration and frequency of reported adverse events will be tabulated. Adverse events will also be summarized for events that were considered treatment-related.

*Study Design Interventional, single surgeon, prospective, single-center, randomized eye, double-masked (patient and optometrist), contralateral clinical trial

This project will be conducted employing 30 consecutive myopic patients; in which one eye (Group-A, 30 eyes) will be treated with Custom Q (FCAT) LASIK, while the contralateral eye (Group B -30 eyes) with WL plus customization

Data will be consisting of all the parameters outlines above

*Treatment and Comparator Bilateral myopic LASIK treatment

*Inclusion/Exclusion Inclusion Criteria

Patients suitable for LASIK procedure

. Subjects between the ages of 18-45 years of age.

Both eyes successfully able to be measured by SightMap and have a treatment plan created for Wavelight plus and Custom Q procedures.

Preoperative myopia up to -8 D and up to -3 D of astigmatism.

Preoperative CCT at least 500 µm.

Best corrected photopic distance visual acuity > or equal 20/20

Stable refraction (within ± 0.50 D) as determined by manifest refraction spherical equivalent for a minimum of 12 months prior to surgery, verified by consecutive subjective refractions or medical records or prescription history

Exclusion Criteria

Any previous ocular surgery

Cataract

Glaucoma

Flap complications

Clinically significant corneal abnormalities including scar in the visual axis

Basement membrane dystrophy

Significant superficial punctuate keratitis

Keratoconus (even suspect as defined by the Pentacam Amsler-Krumeich criteria)

Any other abnormalities that in the investigator's opinion would negatively affect potential for maximum visual outcomes.

Women of childbearing potential, defined as all women who are physiologically capable of becoming pregnant and who are not postmenopausal for at least 1 year or are less than 6 weeks since sterilization, are excluded from participation if any of the following apply:

they are currently pregnant,

have a positive urine pregnancy test result at Screening,

intend to become pregnant during the study period,

are breast-feeding

Note: Subjects who become pregnant during the study will not be discontinued; however, data will be excluded from the effectiveness analyses because pregnancy can alter refraction and visual acuity results.

The existence of this Study is confidential and should not be discussed with persons outside of the study prior to publication. Results will be submitted for publication and presentation at national and/or international meetings.

Plans for disseminating your results: journal article (JRS or JCRS), presentations at professional meetings; AAO, ASCRS, ESCRS, etc.)

Final manuscript/presentation preparation is expected within 1 month of final data entry and analysis. Data entry and analysis is expected within 2 months of start date. Presentation of results will occur at 3-4 major meetings in addition to publication in 2-3 peer reviewed publications. Any presentation, abstract, or manuscript will be made available for review by Alcon prior to submission.

Throughout the course of the study, all efforts will be made to remain alert to possible adverse events or untoward findings. An adverse event is any pathological or unintended change in the structure, function or chemistry of the body that occurs during the study, irrespective of causality, including any illness, injury, toxicity, sensitivity, loss of any senses (i.e., hearing, sight, etc.) or sudden death. The condition must either not be present prior to the LASIK procedure or must worsen in either intensity or frequency after LASIK. If discovery of an adverse event occurs during retrospective review, appropriate medical intervention will be clearly documented. Any severe, serious or unexpected Adverse Medical Event occurring after the LASIK procedure, regardless if it is related to the LASIK treatment(s) or

not, must be reported to the device manufacturer safety contact within 24 hours of awareness of the event. Initial reports must be made by telephone, followed by the completion of a Serious Adverse Event Report and submission by email or facsimile.

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Appendix 1:

Target congresses for abstracts 2024 and journal for publication:

ESCRS and ASCRS

Hellenic Society of Intraocular Implant and Refractive Surgery

Hellenic ophthalmological society

Journals: JRS, JCRS

Appendix 2

Methodology

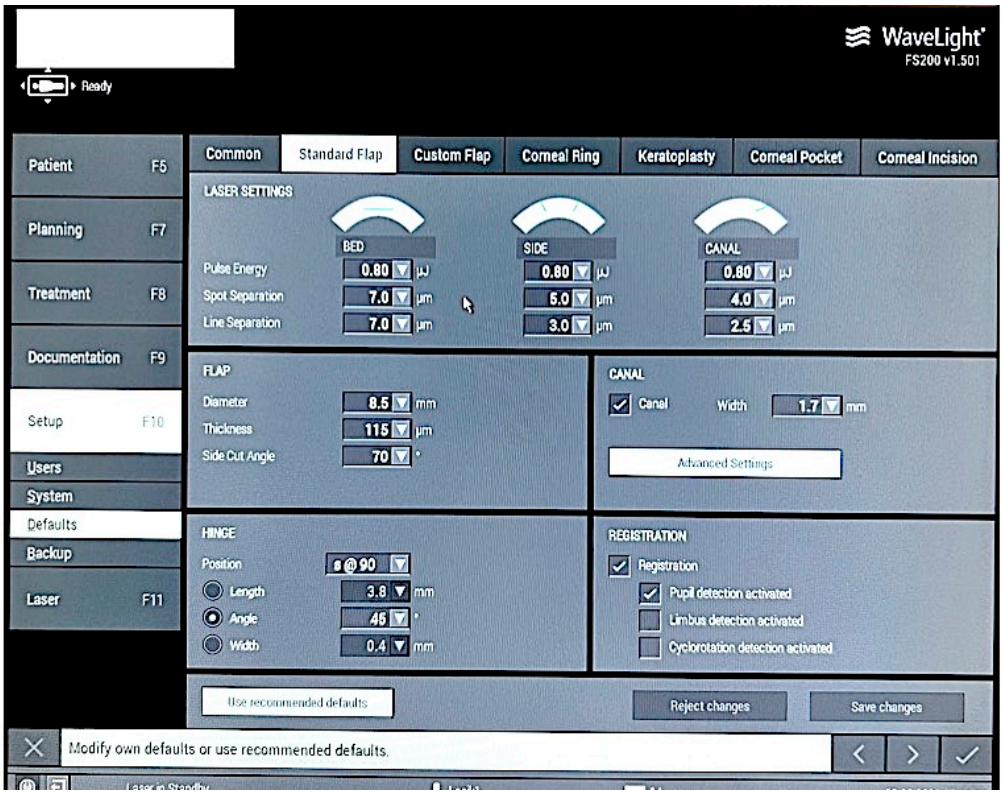
Sightmap measurement is performed on both eyes prior to surgery (1x for biometry, 2x for tomography, 4x for wavefront). Both eyes must be suitable for wavelight plus and CQ treatment. Randomization for the treatment procedure (right or left eye) will be done intraindividually prior to surgery using block randomization. For CQ treatment the pre-op is targeted as defined by the pentacam measurements at 6mm diameter

The measurements for Lasik planning will be done in the following order:

1. Wavelight plus Sightmap
2. Autorefraction
3. Tomography with Pentacam
4. Subjective refraction at 4m
5. Cycloplegic refraction (1 drop of 1% tropicamide)

LASIK surgery will be performed at the same day for both eyes. Eyes will be randomized to either wave light plus or CQ procedures. Subjects will be masked from randomization until the end of the study.

FS200 standard for this study flap parameters



Appendix 3 assessment schedule*We will use the OCT epithelial data for establishing

Assesments	Visit 0 preop	Visit 1 1st day	Visit 2, 2nd day	Visit 3, 3rd day	Visit 4, 4th day	Visit 5 5th day	Visit 6 1 week	Visit 7 1 mnth	Visit 8 3 months
Informed Consent/Demographics	x								
Topolyzer Vario	x								x
OCT (Optovue Avanti)*	x	x	x	x	x	x	x	x	x
Pentacam	x						x		x
Sightmap measurement	x							x	x
Contrast sensitivity by Stereo Optics device	x							x	X
Slit lamp (picture)	x	x					x	x	x
Endothelia cell imaging (Nidek CEM-530 specular microscope)	x								x
Optos wide field fundoscopy	x							x	x
UDVA	x						x	x	x
CDVA	x						x	x	x
Subjective Refraction	x						x	x	x
Cycloplegic Refraction	x							x	x
Autorefraction	x	x	x	x	x	x	x	x	x
Keratometry /(4.5mm total cornea keratometry with Pentacam)	x	x	x	x	x	x	x	x	x
Adverse events		x	x	x	x	x	x	x	x

healing pattern and correlate with refractive data. They have proven crucial to WL plus calculations and their non-difference between the 2 groups studied is needed to validate refractive outcome differences

The total corneal thickness changes will correlate intended tissue removal to actual stromal thickness change from pre-op to post-op

Last the 1 week and 1 month data will establish flap thickness actually achieved