Patient Reported Outcomes on Vision Quality and Dry Eye Following Treatment with Wavelight LASIK

An investigator-initiated clinical trial

1. TITLE PAGE

Protocol Number:	ML-24-01
Amendment Number	Version 1.0
IRB / ERC	Advarra IRB 6940 Columbia Gateway Drive, Suite 110 Columbia, MD 21046
Sponsor Name & Address:	Mark C. Lobanoff, MD OVO Lasik and Lens LLC 6099 Wayzata Boulevard Saint Louis Park, MN 55416 ***(funding only, this is an investigator-initiated study IIT # 92645913)*** Alcon 6201 South Freeway, Fort Worth, TX 76134-2099, USA
Test Articles:	WaveLight® EX500

2 . INVESTIGATOR AGREEMENT

I confirm that I have read and that I understand this protocol and understand the use of the study products. I agree to conduct this study in accordance with the requirements of this protocol and also protect the rights, safety, privacy, and well-being of study subjects in accordance with the following:

- The ethical principles that have their origin in the Declaration of Helsinki.
- All applicable laws and regulations, including, without limitation, data privacy laws and regulations.
- Regulatory requirements for reporting serious adverse events defined in Section 13 of this protocol.

Signature of Investigator (Date)

Investigator Name (print or type)

Investigator's Title

Name of Facility

Location of Facility (City)

3. GENERAL INFORMATION

Objective	To assess patient subjective response regarding satisfaction of vision following Wavelight LASIK. The hypothesis is that a high percentage of subjects will be completely satisfied/very satisfied with vision following Wavelight LASIK.
Test Article(s)	WaveLight® EX500
Control Article(s)	None.
Sample size	300 subjects
Study Population	Subjects 21 to 35 years (at the time of surgery) who underwent Wavefront Optimized or Phorcidies Planned Contoura LASIK for myopia or myopic astigmatism 12 to 15 months prior.
Number of sites	Four
Study Design	Multi-site, single-arm, ambispective, observational study
Masking	None
Variables	Primary: Percentage of subjects satisfied (Completely Satisfied or Very Satisfied) with vision after Wavelight LASIK based on a modified PROWL Questionnaire (Question #1 only). Secondary: • Remaining questions on the modified PROWL Questionnaire • Mean postoperative OSDI and the percentage of patients asymptomatic (< 12). • Percentage of subjects using artificial tears or prescription dry eye medication.
Duration / Follow-up	12+ months postoperative.

The study will be registered with clinicaltrials.gov.

The study will be conducted in compliance with the protocol, GCP and applicable regulatory requirements

4. TABLE OF CONTENTS

5. INTRODUCTION

Early LASIK was associated with dry eye and often glare and halo complaints. This may have been due to microkeratome-cut flaps and the excimer ablation treatment patterns available at the time. Now, modern LASIK combines femtosecond laser-created flaps with more advanced excimer ablation treatment patterns. However, there are limited data on patient reported outcomes for dry eye symptoms and quality of vision for modern LASIK.

The purpose of this study is to assess patient subjective response regarding satisfaction of vision following Wavelight LASIK.

6. OBJECTIVE(S)

To assess patient subjective response regarding satisfaction of vision following Wavelight LASIK.

7. SUBJECTS

7.1. Subject Population

Eligible test subjects will be 21 to 35 years of age (at the time of surgery) and who underwent Wavefront Optimized or Phorcidies Planned Contoura LASIK for myopia or myopic astigmatism 12 to 15 months prior.

A total of 300 subjects at four sites will be enrolled. Subjects must meet the inclusion criteria. Prior to enrollment, subjects will be provided information on the study and asked to sign a patient information and consent form to participate. The patient information and consent form will be approved by an appropriate ethics committee.

7.2. Inclusion Criteria

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

Note: Ocular criteria must be met in both eyes.

- Wavefront Optimized or Phorcidies Planned Contoura LASIK for myopia or myopic astigmatism 12 to 15 months ago
- Age: 21 to 35 years of age at the time of surgery.
- Preoperative myopic sphere of -1.00 D to -8.00 D
- Preoperative regular astigmatism of 0.00 D to -3.00 D.
- Stable refraction preoperatively defined as < 0.5 D of change over at least 1 year.
- Refractive target of bilateral emmetropia.

7.3. Exclusion Criteria

If any of the following exclusion criteria are applicable to the subject or either eye, the subject should not be enrolled in the study.

- Corneal ectatic disorders.
- Patients with a calculated residual stromal depth of < 300 um.
- Pre-existing retinal or corneal pathology, or irregular astigmatism.
- Pre-existing autoimmune diseases, dry eye, glaucoma, diabetes, etc.
- Previous corneal surgeries prior to LASIK.
- LASIK enhancements.

The principal investigator reserves the right to declare a patient ineligible or non-evaluable based on medical evidence that indicates they are unsuitable for the trial.

8. STUDY DESIGN

8.1. Study Design

This study is a multi-site, single-arm, ambispective, observational study of subject satisfaction, after successful bilateral LASIK surgery. Subjects will be assessed 12+ months post-operatively. Clinical evaluations will include administration of the OSDI, modified PROWL, and dry eye questionnaires.

Primary: Percentage of subjects satisfied (Completely Satisfied or Very Satisfied) with vision after Wavelight LASIK based on a modified PROWL Questionnaire (Question #1 only).

Secondary outcome measures are as follows:

- Remaining questions on the modified PROWL Questionnaire
- Mean postoperative OSDI and the percentage of patients asymptomatic (< 12).
- Percentage of subjects using artificial tears or prescription dry eye medication.

8.2. Methods Used to Minimize Bias

As a single-arm study there is no expected bias. Patient selection will be based on the patient's interest and the surgeon's opinion as to whether they are a suitable candidate for inclusion.

Questionnaire instructions will be provided to all patients in a similar manner.

All data collection will be completed through provided Case Report Forms (CRFs) or computer files. All site personnel involved in the study will be trained in regard to conducting study-specific procedures.

9. STUDY PROCEDURE

9.1. Informed Consent / Subject enrollment

No subject will be enrolled into the study who does not meet the inclusion/exclusion criteria and does not sign the current approved informed consent document. Informed consent will be obtained prior to collecting any data for the study. The original signed documents will be maintained by the investigator as a permanent part of the subject's medical records. A signed copy will be provided to the subject.

9.2. Visits and Examinations

Subjects will participate in 1 study visit, at least 12 months postoperative. Details of each study visit, including testing to be conducted, are provided below.

9.2.1. Screening and Questionnaires

After subjects are consented, they will be qualified for the study (compared with inclusion/exclusion criteria) and assigned a study ID/subject number. Subject numbers will be assigned sequentially at each site in the order of enrollment.

Exams will include the tests described below:

- OSDI questionnaire,
- PROWL questionnaire,
- Dry eye questionnaire

Measurements should be made as described in section 9.3 below.

9.3. Study Methods and Measurements

9.3.1. Questionnaire

The PROWL, ODSI, and dry eye questionnaires will be administered to subjects through a mobile app.

The mobile app asks patients questions from the The PROWL, ODSI, and dry eye questionnaires, and patients choose an answer from 4-5 choices. The app records the patient's answer, which are subjective opinions about how the patient feels about their vision. There are no measurements. Accuracy of recording the answers is 100%.

9.4. Unscheduled Visits

Unscheduled exams may be conducted at the discretion of the Investigator with all relevant information from the exam recorded in the source documents and on the Unscheduled Visit pages within the CRF booklet.

9.5. Discontinued Subjects

Discontinued subjects are those who do not have an exit visit or who come into the office to be exited prior to the scheduled final study visit. Subjects may be discontinued from the study at any time if, in the opinion of the investigator, their continued participation in the study poses a risk to their health. Subjects can deactivate the app at any time, and investigators can suspend the app/survey at any time.

10. ANALYSIS PLAN

10.1. Analysis Data Sets

All subjects who are enrolled in the study will be evaluated for safety. Efficacy analyses will be performed based on data from those eyes that completed the study.

10.2. Statistical Methodology

A summary of the data will be prepared for all measurement time points.

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 subjects in each category. These summaries will be provided for all eyes completing the study.

10.3. General Statistical Considerations

The statistical analyses will be performed using R, version 4.4.0 or higher. Any statistical tests of hypotheses will employ a level of significance of alpha=0.05.

11. SAMPLE SIZE JUSTIFICATION

We estimate that the study would require a sample size of 300 subjects to characterize patient subjective responses regarding vision, satisfaction of perceived outcomes, and dry eye symptoms following Wavelight LASIK surgery.

12. CONFIDENTIALITY/PUBLICATION OF THE STUDY

The existence of this Study is confidential and should not be discussed with persons outside of the Study. Results will be submitted for publication and presentation at national and/or international meetings. A manuscript will be submitted to peer-review journals for publication but there is no guarantee of acceptance.

All study data will be collected on appropriate Case Report Forms (CRFs). No protected health information will be included on the forms. CRFs will be retained in the patient's file for a minimum period of 3 years. Collected information will only be used for purposes of this study and no information will be sold to third parties. The following people will have access to your study records:

- Study Doctor and staff involved with the study
- Study Monitor or Auditor
- Sponsor Company or Research Institution
- Review boards or accrediting agencies
- Other State or Federal Regulatory Agencies

The de-identified data may be shared with other researchers for future analysis.

13. QUALITY COMPLAINTS AND ADVERSE EVENTS

Study contact information is provided below.

Table 13.3.-1:
Contact Information for Study

Project Manager	Business Phone	e-mail
Mark C. Lobanoff	952-204-9711	mark.lobanoff@ovoeye.com

14. GCP, ICH and ETHICAL CONSIDERATIONS

This study will be conducted in compliance with Good Clinical Practices (GCPs), including International Harmonization (ICH) Guidelines, and in general, consistent with the 1996 version of the Declaration of Helsinki. In addition, all applicable local, state and federal requirements will be adhered to.

This study is to be conducted in accordance with Institutional Review Board regulations. The investigator will obtain appropriate IRB/ethics committee approval prior to initiating the study.

The study will be registered with clinicaltrials.gov.

14.1 Confidentiality

The data collected will be data typical for the procedure(s) when performed on eyes outside the study. Any data collected will become part of the patient's clinical record. The data will be subject to the same privacy and confidentiality as other data in the clinical record.

Only the principal investigator, research consultant and clinic staff will have access to the data collected. All data shared outside the practice will be de-identified; patients' protected health information will not be available and will not be reported in any analyses or publications. No data will be sold to third parties. De-identified data may be used for future research.

15. STANDARD EVALUATION PROCEDURES

Table 15.1. Proposed Visits and Study Assessments

(visits are by patient, with both eyes tested)

Activity	Visit 1
Informed Consent	X
PROWL Questionnaire	X
OSDI Questionnaire	X
Dry eye Questionnaire	X
Complete Exit Form[1]	X

[1] Complete Exit Form upon termination of subject participation.

16. CONFIDENTIALITY

No protected health information (PHI), including the patient's name and date of birth, will be collected; to ensure this, no PHI information is permitted to be entered on any of the Case Report Forms (CRFs). Subjects will only be identified by subject IDs and identities will be removed at the initial visit so that there is no further need to protect or destroy the information. Collected information will only be used for purposes of this study and no information will be sold to third parties. The non-PHI information collected may be used for future research, though there is currently no plan to do so.

17. STUDY ENDPOINT CRITERIA

17.1. Patient Completion of Study

If a study patient has completed Visit 1, he/she is considered to have completed the study.

17.2. Patient Discontinuation

Each study patient may voluntarily discontinue the study at any time they choose. Study patients who cannot complete the study for administrative reasons (e.g., non-compliance, failure to meet visit schedule, etc.) will be discontinued from the study.

17.3. Patient Termination

A study patient will be terminated if the study patient develops any severe adverse event that may be related to the study. A study patient will receive appropriate treatment at the discretion of the investigator. Notification of termination will be clearly documented. These study patients are considered to have completed the study and will not be replaced.

17.4. Study Termination

The investigator with appropriate notification may terminate the study. If, after clinical observations, the investigator feels that it may be unwise to continue the study, he may stop the study.

17.5. Study Completion

The study will be complete when all enrolled patients have completed Visit 1 or have been terminated from the study.

18. SUMMARY OF RISKS AND BENEFITS

18.1. Summary of risks

There is no increased risk associated with the proposed study.

18.2. Summary of benefits

Previous studies have shown that the WaveLight® EX500 (Alcon, Fort Worth, Texas, USA) provides good visual outcomes for patients at distance.[2,3]

19. MOBILE APP

The mobile app is hosted on the Azure Cloud, leveraging an Infrastructure as a Service (IaaS) model. This approach allows the system to take full advantage of Azure's scalable virtual machines, storage, and networking capabilities. By utilizing IaaS, the mobile app benefits from high availability, disaster recovery, and dynamic scaling, all without the complexity of managing physical hardware.

With Azure Cloud in an IaaS configuration, the mobile app benefits from enhanced security and control:

- Full Control: We manage all software layers, from the operating system to applications, allowing for customized security configurations.
- Encryption Key Ownership: We maintain full ownership of encryption keys, ensuring complete data protection both at rest and in transit. Azure Key Vault or our own Key Management Service (KMS) can be utilized to secure key management.

For authentication and authorization, the mobile app integrates two key technologies:

- ASP.NET Core Identity: A robust membership system managing user accounts, roles, and security, supporting key features like user registration, password management, role-based access control, and claims-based identity.
- IdentityServer4: A flexible OpenID Connect and OAuth 2.0 framework built on ASP.NET Core, enabling advanced scenarios such as single sign-on (SSO), API access delegation, and token issuance.

In terms of data protection, Azure SQL Database and Azure Managed Disks offer encryption at rest through Transparent Data Encryption (TDE), which automatically encrypts data, backups, and transaction logs using AES-256 encryption.

Additionally, all communication within the mobile app is secured over HTTPS, utilizing SHA-256 encryption for data in transit, ensuring robust protection both while stored and during transmission.

Study staff for each site will be trained on the app/survery technology. They can answer any technical questions. If they encounter a technical issue they don't know the answer to, the software designers of the app will be available to solve technical issues.

REFERENCES

1. Kim T-i, Alió del Barrio JL, Wilkins M, Cochener B, Ang M. Refractive surgery. *The Lancet.* 2019;393(10185):2085-2098.
2. Brunson PB, Mann II PM, Mann PM, Potvin R. Clinical Outcomes After Topography-Guided Refractive Surgery in Eyes with Myopia and Astigmatism – Comparing Results with New Planning Software to Those Obtained Using the Manifest Refraction. *Clinical Ophthalmology.* 2020;14:3975-3982.
3. Stulting RD, Lobanoff M, Mann PM, 2nd, Wexler S, Stonecipher K, Potvin R. Clinical and refractive outcomes after topography-guided refractive surgery planned using Phorcides surgery planning software. *J Cataract Refract Surg.* 2022;48(9):1010-1015.