

## Study Protocol

Clinical Investigation of the  
iDesign Advanced WaveScan Studio System with 1Design 1.3-PRESBY  
treatment and STAR S4 IR™ Excimer Laser System

NCT Number: NCT02806726

Document Date: 08 Nov 2016

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**Clinical Investigation of the  
iDesign Advanced WaveScan Studio System with iDesign 1.3-PRESBY treatment  
and STAR S4 IR™ Excimer Laser System**

**PROTOCOL NUMBER: STAR-116-TOPS**

**SPONSOR:** Abbott Medical Optics Inc.  
510 Cottonwood Drive  
Milpitas, CA 95035

**Investigator Agreement**

**As an Investigator, I agree to:**

- Implement and conduct this study diligently and in strict compliance with this agreement; the protocol; Good Clinical Practices; Health Canada Medical Devices Regulations, ISO 14155 and all other applicable Health Canada regulations; conditions of approval imposed by the reviewing Institutional Review Board (IRB), Health Canada or other regulatory authorities; and all other applicable laws and regulations.
- Supervise all testing of the device where human subjects are involved.
- Ensure that the requirements for obtaining informed consent are met.
- Obtain authorization for use/disclosure of health information (e.g., Personal Health Information Protection Act authorization or equivalent).
- Maintain all information supplied by Abbott Medical Optics in confidence and, when this information is submitted to an independent IRB or any other group, it will be submitted with a designation that the material is confidential.

**INVESTIGATOR'S AGREEMENT IN ACCORDANCE WITH  
SUBSECTION 81(k) OF THE *MEDICAL DEVICES REGULATIONS***

Device Name/Nom de l'instrument: \_\_\_\_\_

Protocol Number/N° du Protocole: \_\_\_\_\_

I, \_\_\_\_\_,  
undertake, as outlined in Subsection 81(k) of the  
*Medical Devices Regulations*, to:

(i) conduct the investigational testing in accordance  
with the protocol:

\_\_\_\_\_  
\_\_\_\_\_  
\_\_\_\_\_

(ii) inform a patient who is to be diagnosed or treated  
with the device of the risks and benefits associated  
with its use and obtain the written consent of the  
patient,

(iii) not use the device or permit it to be used for any  
purpose other than the investigational testing  
specified in the protocol,

(iv) not permit the device to be used by any person  
other than myself, except under my direction,

(v) in the event of an incident that is related to a  
failure of the device or a deterioration in its  
effectiveness, or any inadequacy in its labelling or in  
its directions for use and has lead to the death or a  
serious deterioration in the state of health of a patient,  
user or other person, or could do so were it to recur,  
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Je, \_\_\_\_\_,  
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décrits ci-bas, à:

(i) effectuer l'essai expérimental conformément au  
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obtiendra son consentement écrit,

(iii) ne pas utiliser l'instrument ni n'en permettre  
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(iv) ne pas permettra que l'instrument soit utilisé par  
une personne autre que moi, sauf sous ma direction,

v) advenant un incident qui d'une part, est lié à une  
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efficacité ou un étiquetage ou mode d'emploi  
défectueux; d'autre part a entraîné la mort ou une  
détérioration grave de l'état de santé d'un patient,  
utilisateur ou autre personne, ou serait susceptible de  
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rapportant, au Directeur et au fabricant, ou à  
l'importateur de l'instrument, et ce, en deçà de 72  
heures après la découverte de l'incident.  
(Tel: (613) 957-4587 Fac: (613) 957-7318)

**I have read this protocol in its entirety and I agree to all aspects.**

Investigator Printed Name	Signature	Date
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Sub-investigator Printed Name	Signature	Date
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Acknowledged By:

Signature of Sponsor's Representative	Date
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Printed Name and Title

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## PROTOCOL CHANGE HISTORY

Version	Section(s)	Page(s)	Description of Change(s)	Rationale for Change(s)
1.0	N/A	N/A	Original	N/A
2.0	Personnel and Facilities	6	Updated contact information	Changes reflect a change in personnel and contact information
	Appendix A and C	44 and 47	Removal of Pentacam and Humphreys	Allow use of any type of topographer



## 1. SYNOPSIS

<b>PROTOCOL:</b>	A prospective study to evaluate the feasibility of a new treatment algorithm to increase depth of focus after wavefront-guided LASIK correction of myopic refractive errors with the iDesign Advanced WaveScan Studio™ System and Star S4 IR™ Excimer Laser System.
<b>PROTOCOL NUMBER:</b>	STAR-116-TOPS
<b>STUDY TREATMENTS:</b>	<u>Investigational Product:</u> iDesign 1.3-PRESBY treatment  <u>Control Product:</u> iDesign Advanced WaveScan Studio™ System (software version 1.3)
<b>STUDY OBJECTIVE:</b>	The purpose of this study is to determine whether wavefront-guided LASIK correction of myopic refractive errors with CustomVue combined with iDesign 1.3-PRESBY (presbyT-LASIK) treatments mitigate the effects of presbyopia by increasing the depth of focus compared to iDesign CustomVue treatments.
<b>CLINICAL HYPOTHESIS:</b>	The results of this study will demonstrate that wavefront-guided LASIK correction of myopic refractive errors with presbyT-LASIK treatments provide improved distance corrected intermediate visual acuity (at 67 cm) and improved distance corrected near visual acuity (at 40 cm) compared to iDesign CustomVue treatments thus reducing symptoms of presbyopia. Additionally, best corrected distanced visual acuity will be maintained with presbyT-LASIK treatments.
<b>OVERALL STUDY DESIGN:</b>	
<b>Structure:</b>	Prospective, multi-center, non-randomized, contralateral, open-label, clinical study.
<b>Number of sites:</b>	Up to 4 sites in Canada
<b>Duration:</b>	9 months
<b>Definitions:</b>	PresbyT-LASIK is defined as the iDesign 1.3-PRESBY Treatment Planning Software, test treatment.  iDesign CustomVue is the iDesign Advanced WaveScan Studio™ System (software version 1.3), control treatment.
<b>Administration:</b>	Surgeons will perform wavefront-guided LASIK for the treatment of myopic refractive errors based upon

measurements obtained with the iDesign System using the STAR S4 IR™ laser and PresbyT-LASIK.

**Visit Schedule:** There will be 10 scheduled study visits: preoperative, contact lens dispense, contact lens follow-up, operative, 1-day, 1-week, and 1, 3, 6 and 9 months.

**STUDY POPULATION CHARACTERISTICS:**

**Condition:** Stable myopic refractive error with and without astigmatism and presbyopia.

**Number of Subjects:** Up to 70 subjects will be enrolled to achieve up to 34 treated subjects. Both eyes of subjects will be treated in the study. The control eye will receive the iDesign CustomVue treatment, test eye will receive the PresbyT-LASIK.

Each site should enroll a minimum of 10 subjects.

**Inclusion Criteria (all criteria apply to each eye):**

1. Signed informed consent and Personal Health Information Protection Act authorization.
2. At least 45 years of age at enrollment (date informed consent signed).
3. The refractive error, based on the iDesign displayed refraction selected for treatment ("4.0 Rx calc" at 12.5 mm), must be myopia with or without astigmatism with sphere up to -6.00 D, and cylinder between 0.00 D and -5.00 D with a maximum spherical equivalent (SE) of -8.00 D.
4. Require an add power of +1.00 D or more during near testing at 40 cm.
5. Anticipated stromal bed thickness of at least 250 microns based on preoperative central corneal pachymetry minus the maximum ablation depth (as calculated by the iDesign system) plus the intended flap thickness.
6. Distance Best Spectacle Corrected Visual Acuity (BSCVA) of 20/20 or better.
7. Uncorrected Visual Acuity (UCVA) of 20/40 or worse.
8. Less than or equal to 0.75 D difference between cycloplegic and manifest refraction sphere.
9. A stable refractive error (based on a previous exam, medical records, lensometry, or prescription at least 12 months prior to the preoperative manifest refraction), as defined by a change of  $\leq 1.00$  D in MRSE.
10. Any eye with a history of contact lens wear within the last 4 weeks must demonstrate refractive stability according to the following:
  - Rigid contact lenses (toric or spherical) must be removed for at least 4 weeks and soft contact lenses (toric or spherical) for at least 2 weeks prior to the first refraction used to establish stability.

- Two consecutive refractions and keratometric readings must be conducted at least 7 days apart.
  - Refractive stability is defined as a change of not more than 0.50 D in manifest refraction sphere and cylinder as well as mean keratometry between measurements.
  - If the subject/eye meets the refractive stability criteria, contact lens wear is not permitted prior to surgery.
11. Agreement between manifest refraction (adjusted for optical infinity) and iDesign System refraction selected for treatment, as follows:
- Spherical Equivalent: Magnitude of the difference is less than 0.625 D.
  - Cylinder: Magnitude of the difference is less than or equal to 0.5 D.
  - Cylinder Axis Tolerance: If either the manifest cylinder entered into the iDesign System or the iDesign cylinder selected for treatment is less than 0.5 D, there is no requirement for axis tolerance. When both cylinders have a magnitude of at least 0.5 D, the axis tolerance as determined by the iDesign system is linearly reduced from 15° (0.5 D) to 7.5° (7.0 D) based on the average magnitude of both cylinders. Note: If the axis tolerance is not in the calculated range, the iDesign system will produce a warning and this exam may not be used for treatment planning.
12. Willing and capable of complying with follow-up examinations for the duration of the study.

**Exclusion Criteria (all criteria apply to each eye):**

1. Women who are pregnant, breast-feeding, intend to become pregnant, or are not using an adequate method of birth control [examples are any form of barrier contraception (such as condom or diaphragm with contraceptive cream/jelly), birth control pills, hormonal implant, IUD, abstinence or surgical sterilization (tubal ligation, hysterectomy or vasectomy)]. Note: Women who were pregnant or nursing may not be enrolled until 6 months after either delivery or have stopped nursing and there is documented refractive stability.
2. Concurrent use of systemic (including inhaled) medications that may impair healing, including but not limited to: antimetabolites, isotretinoin (Accutane®) within 6 months of treatment, and amiodarone hydrochloride (Cordarone®) within 12 months of treatment.

**NOTE: The use of inhaled or systemic corticosteroids, whether chronic or acute, is deemed to adversely affect healing and subjects using such medications are specifically excluded from eligibility.**

3. History of any of the following medical conditions, or any other condition that could affect wound healing: collagen vascular disease, autoimmune disease, immunodeficiency diseases, ocular herpes zoster or herpes simplex, endocrine disorders (including, but not limited to unstable thyroid disorders and diabetes), lupus, and rheumatoid arthritis.

**NOTE: The presence of diabetes (either type 1 or 2), regardless of disease duration, severity, or control, will specifically exclude subjects from eligibility.**

4. Subjects with a cardiac pacemaker, implanted defibrillator or other implanted electronic device.
5. History of prior intraocular or corneal surgery (including cataract extraction), active ophthalmic disease or abnormality (including, but not limited to, symptomatic blepharitis, recurrent corneal erosion, dry eye syndrome, neovascularization > 1 mm from limbus), retinal detachment/repair, clinically significant lens opacity, clinical evidence of trauma, corneal opacity within the central 9 mm and visible on topography, at risk for developing strabismus, or with evidence of glaucoma or propensity for narrow angle glaucoma.

**NOTE: Subjects with open angle glaucoma, regardless of medication regimen or control, or an IOP greater than 21 mmHg at screening, are specifically excluded from eligibility.**

6. Evidence of keratoconus, corneal dystrophy or irregularity, or abnormal topography.
7. Known sensitivity or inappropriate responsiveness to any of the medications used in the postoperative course.
8. Desire to have monovision.
9. Intolerance to multifocal correction based on questionnaire responses to contact lens trial.
10. Participation in any other clinical study.

#### **EVALUATION CRITERIA:**

The purpose of this clinical study is to evaluate the feasibility of a new treatment algorithm to increase depth of focus combined with wavefront guided LASIK correction of myopic refractive errors using the iDesign Advanced Wavescan Studio™ System (software version 1.2) with iDesign 1.3-PRESBY TPS and Star S4 IR™ Excimer Laser System (Abbott Medical Optics, CA). The primary endpoint is mean monocular distance corrected intermediate visual acuity under photopic conditions at 67 cm. Secondary endpoint is mean monocular distance corrected near visual acuity under photopic conditions at 40 cm. Safety endpoints include mean monocular best spectacle corrected distance visual acuity under photopic conditions, induced manifest refractive astigmatism, and serious and device related adverse events.

#### **DATA ANALYSIS:**

The PresbyT-LASIK treatments will be compared to iDesign CustomVue treatments. All endpoints will be evaluated at 6 months. The safety population will be the primary analysis population for all endpoints and includes all eyes that receive study treatment.

#### **STUDY VISITS AND PROCEDURES:**

Inclusion and exclusion qualifications will be assessed at the preoperative visit according to the inclusion/exclusion criteria. The Informed Consent Document and Personal Health Information Protection Act Authorization must be signed by patients who agree to participate in the study prior to undergoing any study-specific procedures. After

determination that all inclusion/exclusion criteria have been met and the informed consent has been signed, subjects will be enrolled in the study. Subjects and study personnel performing the vision testing and refractions will be un-masked for the duration of the study.

The STAR S4 IR™ Excimer Laser System and the iDesign Advanced WaveScan Studio™ System will be used to perform wavefront-guided LASIK treatments. Both eyes of subjects will be treated in the study. Surgery will be performed with iDesign CustomVue treatments on the dominant eye and PresbyT-LASIK treatments on the non-dominant eye. The Dolman test will be utilized for eye dominance determination as described in **Appendix R**.

Key preoperative and postoperative data include iDesign measurements, visual acuities, manifest refraction, keratometry (iDesign and auto/manual), pachymetry, biomicroscopic slit-lamp findings, intraocular pressure, adverse events, ocular visual symptoms and patient reported outcomes (PRO) assessments of visual functioning and visual symptoms (using the PRVSQ for PRK/LASIK instrument). Ocular health and history are also assessed preoperatively. A chart summary of procedures required at each study visit is provided in **Appendix A**.

## **2. BACKGROUND/INTRODUCTION**

In 2003, VISX, Incorporated (now a subsidiary of Abbott Medical Optics Inc. and herein referred to as AMO) received FDA approval for its first indication of wavefront-guided LASIK treatments. Currently, the STAR S4 IR™ Excimer Laser System with the WaveScan® Wavefront System aberrometer is Health Canada approved in Canada and used internationally for wavefront-guided LASIK treatment of myopia, myopic astigmatism, mixed astigmatism, hyperopia, and hyperopic astigmatism.

AMO has developed a new aberrometry system, the iDesign Advanced WaveScan Studio™ System (referred to herein as the iDesign System). This aberrometer incorporates a higher density Hartmann-Shack sensor than the current AMO aberrometer (WaveScan® Wavefront System). The iDesign System creates treatment tables that are transferred to the STAR S4 IR™ Excimer Laser System for LASIK treatments.

No clinical studies have been conducted with the iDesign 1.3-PRESBY TPS. However, a scleral contact lens study was conducted to evaluate the visual performance of different multifocal optical designs, including the PRESBY-T shape. And a retrospective study was undertaken to collect and analyze the data from presbyopic ablations performed using the PRESBY-T algorithm.

## **3. CLINICAL HYPOTHESIS**

The results of this study will demonstrate that wavefront-guided LASIK correction of myopic refractive errors with PresbyT-LASIK treatments provide improved distance corrected intermediate visual acuity (at 67 cm) and improved distance corrected near visual acuity (at 40 cm) compared to iDesign CustomVue treatments thus reducing symptoms of presbyopia. Additionally, best corrected distanced visual acuity will be maintained with PresbyT-LASIK treatments.

## **4. STUDY DESIGN**

This study is a 9 month, prospective, multicenter, non-randomized, contralateral, open-label clinical study.

The study will be conducted at up to 4 sites in Canada and will include up to 34 test group treated eyes (of up to 34 subjects). Subjects must have both eyes treated in the study. The dominant eye will be treated with the control product; the non-dominant eye will be treated with test product. Analyses will be conducted at 6 months.

## JUSTIFICATION OF STUDY DESIGN

The study is being conducted to evaluate the feasibility of the PresbyT-LASIK to increase depth of focus combined with wavefront-guided LASIK correction of myopic refractive errors.

## **5. ACRONYMS**

The following acronyms are used throughout the document:

- BSCVA: Best Spectacle Corrected Visual Acuity (distance)
- UCIVA: Uncorrected Intermediate Visual Acuity
- UCNVA: Uncorrected Near Visual Acuity
- UCDVA: Uncorrected Distance Visual Acuity
- DCIVA: Distance Corrected Intermediate Visual Acuity
- DCNVA: Distance Corrected Near Visual Acuity
- MR: Manifest refraction
- MRSE: Manifest Refraction Spherical Equivalent
- MRS: Manifest Refractive Sphere
- MRC: Manifest Refractive Cylinder
- D: Diopters

## **6. STUDY OBJECTIVES AND ENDPOINTS**

The purpose of this study is to determine whether wavefront-guided LASIK correction of myopic refractive errors with PresbyT-LASIK treatments mitigate the effects of presbyopia by increasing the depth of focus compared to iDesign CustomVue treatments. All study endpoints will be evaluated at 6 months.

### **6.1 PRIMARY ENDPOINT**

#### MONOCULAR DCIVA AT 67 CM

- Success criteria: Statistically significant improvement in mean distance corrected intermediate visual acuity for PresbyT-LASIK treatments (test) compared to iDesign CustomVue treatments (control). Clinical significance will be achieved if the mean logMAR DCIVA for the test group is at least one line better than the mean for the control group.

### **6.2 SECONDARY ENDPOINT**

#### MONOCULAR DCNVA AT 40 CM

- Success criteria: Statistically significant improvement in mean distance corrected near visual acuity for PresbyT-LASIK treatments (test) compared to iDesign CustomVue treatments (control). Clinical significance will be achieved if the mean logMAR DCNVA for the test group is at least 1.5 lines better than the mean for the control group.

## **SAFETY ENDPOINTS**

### **1. MONOCULAR BSCVA**

- Success criteria: Mean postoperative BSCVA will be non-inferior to mean preoperative BSCVA for both PresbyT-LASIK treatments (test) and iDesign CustomVue treatments (control). Clinical significance will be achieved if the mean difference (postoperative – preoperative) in logMAR BSCVA for both the test and control groups is no worse than one line (0.1 logMAR).

### **2. INDUCED MANIFEST REFRACTIVE ASTIGMATISM**

The frequency and proportion of eyes with induced manifest refractive astigmatism will be reported at each periodic study visit. The rate of eyes with induced manifest refractive astigmatism of greater than 2.00 diopters will be summarized.

### **3. SERIOUS AND DEVICE-RELATED ADVERSE EVENTS**

The number and proportion of eyes with serious and device-related adverse events (non-flap related) will be summarized.

## **6.3 OTHER ENDPOINTS**

- UCDVA and BSCVA, monocular and binocular
- UCIVA and UCNVA, monocular and binocular
- DCIVA and DCNVA, binocular
- Low contrast BSCVA (10%), monocular
- Mesopic DCNVA, monocular
- Depth of focus, monocular
- iDesign aberrometry measurements (higher order aberrations)
- Pupil size, photopic and mesopic, distance and near
- Manifest refraction
- Keratometry (auto or manual)
- Anterior segment evaluation (biomicroscopic slit-lamp exam) for determination of medical findings
- Visual symptoms via the patient reported outcomes (PRO) instrument Patient Reported Visual Symptom Questionnaire (PRVSQ) for PRK LASIK
- Ocular/visual symptoms (from non-directed responses obtained from the open-ended question “Are you having any difficulties with your eyes or vision?”).

## **7. STUDY PRODUCTS**

### **7.1 IDESIGN ADVANCED WAVESCAN STUDIO™ SYSTEM**

The iDesign Advanced WaveScan Studio™ System (or iDesign System) incorporates iDesign Measurement System hardware and iDesign Treatment Planning Software. The iDesign Measurement System measures refractive error (lower order aberrations) and



higher-order wavefront aberrations of the human eye using a high density Hartmann-Shack wavefront sensor. In addition, the instrument measures keratometry, pupil diameter, and corneal topography. The Treatment Planning Software uses iDesign measurements to create treatment profiles through a Fourier reconstruction.

In this study, all eyes will be targeted for emmetropia and treatments will be calculated using iDesign 1.3-PRESBY TPS.

The Principal Investigator is responsible for ensuring that the iDesign System with 1.3-PRESBY is only used to treat subjects enrolled in this study.

## **7.2 STAR S4 IR™ EXCIMER LASER SYSTEM**

The STAR S4 IR™ Excimer Laser System is a Class III ophthalmic surgical laser designed to create a superficial lamellar keratectomy on exposed corneal tissue. Corneal tissue is removed by a process known as ablative photodecomposition. Ablative photodecomposition occurs when far-ultraviolet radiation reacts with organic molecules, resulting in the photochemical breakdown of the molecular bonds without a significant thermal effect. The source of the far-ultraviolet photons is a high efficiency, gas-discharge excimer laser that electronically excites a combination of argon and fluorine, producing an ultraviolet wavelength of 193 nm. The STAR S4 IR™ Excimer Laser System combines submicron precision tissue removal by an excimer laser with a sophisticated computer controlled delivery system.

## **7.3 INTRALASE® FEMTOSECOND LASER**

The IntraLase® Femtosecond Laser is an ophthalmic surgical laser indicated for use in patients undergoing refractive surgery or other treatment requiring initial lamellar resection of the cornea. The IntraLase FS Laser delivery system is used in conjunction with a sterile disposable IntraLase Patient Interface, consisting of pre-sterilized suction ring assemblies and pre-sterilized applanation lenses intended for single-use. In this study, the IntraLase laser will be used for all eyes to make the initial lamellar corneal cuts prior to the ablation procedure by the STAR S4 IR Excimer Laser.

## **8. STUDY POPULATION**

All study subjects will be enrolled from the normal myopic patient population at up to 4 sites in Canada. Up to 70 subjects will be enrolled to achieve at least 34 subjects at the 6 month postoperative visit. Each site should treat a minimum of 10 subjects.

This study will include only subjects who will undergo bilateral myopic and myopic astigmatic iDesign CustomVue treatments. The non-dominant eye will receive the PresbyT-LASIK treatment.

All subjects who meet the inclusion/exclusion criteria will be offered enrollment in the study. Eligibility criteria may not be waived by the investigator. Any questions regarding patient eligibility are to be discussed with AMO prior to subject enrollment. Subjects will be enrolled until the recruitment goals are met.

## **8.1 INCLUSION CRITERIA**

Note: All criteria apply to each eye

- 1) Signed informed consent and Personal Health Information Protection Act authorization.
- 2) At least 45 years of age at enrollment (date informed consent signed).
- 3) The refractive error, based on the iDesign displayed refraction selected for treatment ("4.0 Rx calc" at 12.5 mm), must be myopia with or without astigmatism with sphere up to -6.00 D, and cylinder between 0.00 D and -5.00 D with a maximum spherical equivalent (SE) of -8.00 D.
- 4) Require an add power of +1.00 D or more during near testing at 40 cm.
- 5) Anticipated stromal bed thickness of at least 250 microns based on preoperative central corneal pachymetry minus the maximum ablation depth (as calculated by the iDesign system) plus the intended flap thickness.
- 6) Distance Best Spectacle Corrected Visual Acuity (BSCVA) of 20/20 or better.
- 7) Uncorrected Visual Acuity (UCVA) of 20/40 or worse.
- 8) Less than or equal to 0.75 D difference between cycloplegic and manifest refraction sphere.
- 9) A stable refractive error (based on a previous exam, medical records, lensometry, or prescription at least 12 months prior to the preoperative manifest refraction), as defined by a change of  $\leq 1.00$  D in MRSE.
- 10) Any eye with a history of contact lens wear within the last 4 weeks must demonstrate refractive stability according to the following:
  - a. Rigid contact lenses (toric or spherical) must be removed for at least 4 weeks and soft contact lenses (toric or spherical) for at least 2 weeks prior to the first refraction used to establish stability.
  - b. Two consecutive refractions and keratometric readings must be conducted at least 7 days apart.
  - c. Refractive stability is defined as a change of not more than 0.50 D in manifest refraction sphere and cylinder as well as mean keratometry between measurements.
  - d. If the subject/eye meets the refractive stability criteria, contact lens wear is not permitted prior to surgery.
- 11) Agreement between manifest refraction (adjusted for optical infinity) and iDesign System refraction chosen for treatment, as follows:
  - a. Spherical Equivalent: Magnitude of the difference is less than 0.625 D.
  - b. Cylinder: Magnitude of the difference is less than or equal to 0.5 D.

- c. Cylinder Axis Tolerance: If either the manifest cylinder entered into the iDesign System or the iDesign cylinder selected for treatment is less than 0.5 D, there is no requirement for axis tolerance. When both cylinders have a magnitude of at least 0.5 D, the axis tolerance as determined by the iDesign system is linearly reduced from 15° (0.5 D) to 7.5° (7.0 D) based on the average magnitude of both cylinders. Note: If the axis tolerance is not in the calculated range, the iDesign system will produce a warning and this exam may not be used for treatment planning.
- 12) Willing and capable of complying with follow-up examinations for the duration of the study.

## 8.2 EXCLUSION CRITERIA

Note: All criteria apply to each eye

- 1) Women who are pregnant, breast-feeding, intend to become pregnant, or are not using an adequate method of birth control [examples are any form of barrier contraception (such as condom or diaphragm with contraceptive cream/jelly), birth control pills, hormonal implant, IUD, abstinence or surgical sterilization (tubal ligation, hysterectomy or vasectomy)]. Note: Women who were pregnant or nursing may not be enrolled until 6 months after either delivery or have stopped nursing and there is documented refractive stability.
- 2) Concurrent use of systemic (including inhaled) medications that may impair healing, including but not limited to: antimetabolites, isotretinoin (Accutane®) within 6 months of treatment, and amiodarone hydrochloride (Cordarone®) within 12 months of treatment.

**NOTE: The use of inhaled or systemic corticosteroids, whether chronic or acute, is deemed to adversely affect healing and subjects using such medications are specifically excluded from eligibility.**

- 3) History of any of the following medical conditions, or any other condition that could affect wound healing: collagen vascular disease, autoimmune disease, immunodeficiency diseases, ocular herpes zoster or herpes simplex, endocrine disorders (including, but not limited to unstable thyroid disorders and diabetes), lupus, and rheumatoid arthritis.

**NOTE: The presence of diabetes (either type 1 or 2), regardless of disease duration, severity, or control, will specifically exclude subjects from eligibility.**

- 4) Subjects with a cardiac pacemaker, implanted defibrillator or other implanted electronic device.
- 5) History of prior intraocular or corneal surgery (including cataract extraction), active ophthalmic disease or abnormality (including, but not limited to, symptomatic blepharitis, recurrent corneal erosion, dry eye syndrome, neovascularization > 1 mm from limbus), retinal detachment/repair, clinically significant lens opacity, clinical evidence of trauma, corneal opacity within the central 9 mm and visible on topography, at risk for developing strabismus, or with evidence of glaucoma or propensity for narrow angle glaucoma.

**NOTE: Subjects with open angle glaucoma, regardless of medication regimen or control, or an IOP greater than 21 mmHg at screening, are specifically excluded from eligibility.**

- 6) Evidence of keratoconus, corneal dystrophy or irregularity, or abnormal topography.
- 7) Known sensitivity or inappropriate responsiveness to any of the medications used in the postoperative course.
- 8) Desire to have monovision.
- 9) Intolerance to multifocal correction based on questionnaire responses to contact lens trial.
- 10) Participation in any other clinical study.

## **9. INVESTIGATOR SELECTION**

### **9.1 INVESTIGATOR QUALIFICATIONS**

AMO will select ophthalmic surgeons who have completed a residency in ophthalmology (or its documented equivalent), are licensed to practice medicine and perform LASIK at his/her investigative site.

Investigators will be selected from surgeons who are experienced in LASIK with the STAR system for CustomVue™ treatments and the IntraLase®. All sites are required to have adequate staff support for reporting and subject follow-up, as well as the necessary instrumentation to conduct study testing. Each site will have one designated principal investigator; some sites may have additional surgical sub-investigators.

### **9.2 INVESTIGATOR OBLIGATIONS**

Investigators are required to fulfill the following obligations:

- Conduct the study in accordance with the relevant and current protocol. Investigator will only make changes to a protocol after notifying and obtaining approval from AMO, Health Canada or other governing agencies, and the Investigational Review Board (IRB), except when necessary to protect the safety, rights or welfare of subjects
- Personally conduct and supervise the study
- Maintain a list of appropriately qualified persons to whom the investigator has delegated significant trial-related duties
- Be responsible for protecting the rights, safety and welfare of subjects under the investigator's care and be responsible for the control and documentation of the devices under investigation
- Inform patients that the device(s) are being used for investigational purposes and that requirements relating to obtaining informed consent and IRB approval are met according to parts 59 to 62 of the Medical Devices Regulations and all other applicable laws and regulations

- Maintain confidentiality as required by Personal Health Information Protection Act or similar laws and regulations
- Shall not obtain written informed consent from any subject to participate or allow any subject to participate before obtaining Health Canada and IRB approval and approval from the regulatory agency of the country in which the study is being conducted by the investigator (e.g., Health Canada)
- Document in each subject's case history that informed consent was obtained prior to participation in the study
- Report to AMO and the reviewing IRB any adverse experiences that occur during the course of the study in accordance with applicable laws and regulations
- Maintain adequate and accurate records in accordance with applicable laws and regulations and make available all study documents and subject medical records for inspection by either AMO, duly authorized regulatory agencies (e.g., Health Canada) and/or the IRB.
- Submit progress reports on the investigation to AMO and the reviewing IRB at regular intervals, but no less often than yearly
- Ensure the IRB that is responsible for initial and continuing review of the study complies with applicable laws and regulations.
- Report all changes in research activity and all unanticipated problems involving risks to patients to the IRB and AMO.
- Supervise and permit investigational device use and disposition in accordance with applicable regulations and protocol requirements. Upon completion of enrollment or termination of the study or the investigator's part of the study, or at AMO's request, return to AMO any remaining supply of the investigational device
- Provide sufficient accurate financial information to AMO to allow AMO to submit complete and accurate certification or disclosure statements as required by 21CFR54. Promptly update this information if any relevant changes occur during the course of the investigation or for up to one year following completion of the study
- Comply with all other obligations of clinical investigators and requirements according to all applicable Health Canada regulations, all other applicable laws and regulations, and all conditions of approval imposed by the reviewing IRB and Health Canada
- Ensure that all associates, colleagues and employees assisting in the conduct of the study are adequately informed about the protocol, the investigational device, their study-related duties and functions and agree to fulfill their obligations in meeting the above commitments.

Investigators shall provide adequate time and resources to conduct and report on the study. The Investigator, or delegate, shall notify AMO of any change in the conduct of the study including changes in study personnel assigned to the study project, location of the investigational device(s), or maintenance of study records, etc.

### **9.3 INVESTIGATOR APPROVAL**

It is the responsibility of the investigator to obtain prospective approval of the study protocol, protocol amendments or changes, informed consent forms and other relevant documents (e.g., advertisements) from the IRB. All correspondence with the IRB should be retained in the Investigator Study Files/Notebook. Copies of IRB submissions and approvals should be forwarded to AMO. Study sites will obtain IRB approvals and fulfill any other site-specific and/or region-specific regulatory requirements. The investigator is required to report to AMO within five working days any withdrawal of approval by the reviewing IRB for his/her participation in the investigation.

Prior to the start of subject enrollment, the following documents must be signed and returned to AMO:

- Confidentiality Agreement
- Clinical Trial Agreement
- Investigator Agreement/Protocol Signature page
- Clinical Investigator Brochure Signature page
- Financial Disclosure form
- Signed and dated copy of investigator's current curriculum vitae
- Copy of the investigator's current medical license (as available per country)
- Hospital/Ambulatory Surgery Center Clinical Study Acknowledgement, if required

By signing the study documents, the investigator agrees to conduct this study according to the obligations above and all other applicable regulatory and legal requirements.

## **10. EXPERIMENTAL PLAN**

### **10.1 OVERVIEW**

This study will be conducted in accordance with Health Canada Medical Devices Regulations, the Declaration of Helsinki, ISO 14155 and all other applicable laws and regulations. The study will not begin until regulatory and IRB approvals have been obtained.

This study will be prospective, multicenter, non-randomized, contralateral, open-label clinical investigation conducted at up to 4 sites. Up to 70 subjects will be enrolled to achieve approximately 34 treated subjects at 6 months. After signing the informed consent, completing the contact lens study, and meeting all inclusion and exclusion criteria in both eyes, the subjects may then be scheduled for surgery. The follow-up visit schedule will be the same for both eyes, as described in Section 10.2, Visit Schedule.

To maintain consistency, it is recommended that a single individual (study technician or coordinator designated by the investigator) conduct all study-related vision testing at each site, although a back-up person should also be designated and trained.

Key data collection for all subjects/eyes includes distance visual acuities, manifest refraction, iDesign measurements, keratometry, corneal topography, visual symptoms, biomicroscopic slit-lamp findings, complications and adverse events. A chart summary of all examination procedures required at each study visit is provided in **Appendix A**. Specific equipment necessary to perform the required procedures will be supplied for the duration of the study as noted in **Appendix B**.

## 10.2 VISIT SCHEDULE

The study visit schedule for all study subjects is outlined in **Table 1**.

All eyes will be examined preoperatively and postoperatively at 1 day and 1 week, and then periodically at 1, 3, 6, and 9 months. Unscheduled visits may be conducted as necessary at the discretion of the investigator for medically-indicated follow-up.

**TABLE 1: Visit Schedule**

VISIT	EXAM	VISIT WINDOW
1	Preoperative Exam	Within 120 days prior to surgery
2	Contact lens dispense	After preoperative exam
3	Contact lens follow-up	1 week after dispense
4	Operative	28-120 days following preoperative exam
5	1 day	1-2 days postoperative
6	1 week	5-9 days postoperative
7	1 month	21-35 days postoperative
8	3 months	70-98 days postoperative
9	6 months	147-182 days postoperative
10	9 months	245-301 days postoperative

## 10.3 PREOPERATIVE PROCEDURES

All subjects enrolled in the study must sign the current IRB approved informed consent document and meet the inclusion/exclusion criteria. The informed consent must be signed before any study-specific examinations are performed, and this must be documented in the source documents. An Authorization for medical treatment privacy law documentation must also be signed.

All preoperative testing for the study must be completed within 120 days prior to surgery. Following the informed consent process, completion of the preoperative study exam,



completion of the contact lens trial and determination that the subject's eyes meet all of the required entrance criteria, the eyes may be treated in the study.

*As the Informed Consent Form is signed at the beginning of the preoperative study exam, some subjects may not qualify after study-specific testing is performed. Subjects will be considered screen-failures if they do not qualify or if they qualify but decide not to proceed with surgery. These subjects will be exited from the study.*

The following preoperative procedures are to be performed (see also **Appendix A**). General descriptions and requirements of the various tests are provided in the manual of testing procedures (**Appendix C**).

#### PREOPERATIVE PROCEDURES

- Informed consent documentation
- General medical and ocular history
- Ocular and systemic medications
- Contact lens trial
- Inclusion/exclusion criteria
- PRSVQ Questionnaire
- iDesign System Measurement (refraction, aberrometry, topography, keratometry, pupillometry)
- UCDVA
- Manifest Refraction
- BSCVA
- BSCVA – low contrast (10%)
- Minimum add power
- DCIVA
- DCNVA
- Keratometry (auto or manual)
- Corneal topography
- Anterior segment examination (biomicroscopic slit-lam exam)
- Intraocular pressure (applanation tonometry)
- Pachymetry
- Cycloplegic Refraction
- Dilated fundus examination
- iDesign treatment planning
- Adverse events (Ocular/NonOcular)



- Device deficiencies/complaints
- Refractive stability

#### 10.4 CONTACT LENS STUDY

All subjects will be required to undergo a contact lens trial to simulate their intended correction for a minimum of 7 days. This will involve wearing a multifocal contact lens in the non-dominant eye and a single vision distance contact lens in the dominant eye. Subjects will provide responses on a questionnaire to indicate their level of satisfaction with the simulated correction (refer to Appendix P).

Subjects must indicate “**Very Satisfied**”, “**Satisfied**”, or “**Somewhat Satisfied**” with their vision for all of the following in order to successfully complete the contact lens study:

- Driving during daylight
- Driving at night
- Working on the computer
- Overall experience

Upon successful completion of the contact lens study, subjects will be instructed to remove their contact lenses for a minimum of two weeks prior to surgery.

#### 10.5 OPERATIVE PROCEDURES

Both eyes of the subject may be treated at the same visit. However, if an epithelial defect is present on the flap of the first eye, or if a clinically significant complication or adverse event is observed during the treatment of the first eye, the fellow eye will not be treated until resolution of the event in the first eye.

To ensure control of environmental conditions during treatments, including temperature and humidity, all laser suites shall be equipped with air conditioning and/or heating systems, humidifiers, and environmental monitoring devices. It is important to maintain a carefully controlled surgical environment. All treatments shall be performed in surgical environments where the humidity is between 35-45% and the temperature is between 68-72° F.

All eyes will undergo the LASIK procedure using the IntraLase® Femtosecond laser to perform the initial lamellar cuts and the STAR SR IR™ Excimer laser to perform ablation according to the iDesign-derived treatment plan. Iris Registration (IR) should be used for alignment of all treatments. Following treatment, the use of a bandage contact lens will be at the discretion of the investigator. Refer to **Appendix N** for a detailed summary of the surgical procedure.

## 10.6 POSTOPERATIVE PROCEDURES

Postoperatively, each treated eye will be examined according to the schedule in Section 10.2, Visit Schedule.

### IMMEDIATE POSTOPERATIVE CARE

Subjects may experience pain during the first 24 hours following treatment. The immediate postoperative pain control regimen is left to the Investigator's discretion. All postoperative regimen components shall be recorded. Prescribe the following postoperative regimen and instruct the subject to return the next day:

- Eye shield(s) during sleep (1 week)
- Topical ophthalmic antibiotic: QID for at least 4 days
- Topical ophthalmic corticosteroid: QID for at least 4 days (but should not be prescribed QID for more than 7 days unless medically warranted)

### EARLY POSTOPERATIVE EXAMINATION PROCEDURES (1 DAY AND 1 WEEK)

Postoperative examinations will be conducted at 1 day and 1 week after treatment. The following clinical information shall be assessed and recorded for both eyes during each postoperative exam (see also **Appendix A**). General descriptions and requirements of tests are provided in **Appendix C**.

- Ocular and systemic medical history and concomitant medications
- iDesign System Measurement (refraction, aberrometry, topography, keratometry, pupillometry), (not required at 1-day exam)
- UCDVA
- Manifest Refraction (not required at 1-day exam)
- BSCVA (not required at 1-day exam)
- Keratometry (not required at 1-day exam)
- Anterior Segment Examination
- Adverse Events and Complications
- Device Deficiencies/Complaints

### PERIODIC POSTOPERATIVE EXAMINATION PROCEDURES

Periodic examinations will be conducted at 1, 3, 6, and 9 months after treatment. In the event that extended follow-up is not needed, the follow-up period may be reduced.

Note: Subjects are not to wear contact lenses postoperatively until after completion of this study. Wearing contact lenses may potentially cause corneal edema or topography

changes that may influence the visual acuity results. During the study, if correction is required, spectacles should be prescribed.

The following data shall be assessed and recorded for both eyes during the periodic examinations, although not all are required at all periodic visits (see also **Appendix A**). General descriptions and requirements of the various tests are provided in **Appendix C**.

- Ocular and systemic medical history and concomitant medications
- PRVSQ Questionnaire (1, 3, 6, and 9 month visit)
- iDesign System Measurement (refraction, aberrometry, topography, keratometry, pupillometry)
- UCDVA, photopic, monocular
- UCDVA, photopic, binocular
- Manifest Refraction (logMAR)
- BSCVA, photopic, monocular, distance (logMAR)
  - At 3 months or later, if there is a loss of 2 or more lines of BSCVA ( $\geq 10$  letters) compared to the preoperative visit, a rigid contact lens over refraction should be performed to estimate the best possible corrected visual acuity. If a rigid contact lens over refraction is not medically advisable, then a pin-hole acuity should be obtained
- BSCVA, photopic, binocular, distance (logMAR) (3, 6, and 9 month visit)
- BSCVA, photopic, monocular, distance low contrast, 10%, (logMAR) (3, 6, and 9 month visit)
- DCNVA, mesopic, monocular at 40 cm (3, 6, and 9 month visit)
- Pupil size
  - Mesopic, distance and near (3 month visit)
  - Photopic, distance and near (3 month visit)
- DCIVA, photopic, monocular (3, 6, and 9 month visit)
- DCIVA, photopic, binocular (3, 6, and 9 month visit)
- DCNVA, photopic, monocular (3, 6, and 9 month visit)
- DCNVA, photopic, binocular (3, 6, and 9 month visit)
- UCIVA, photopic, monocular (3, 6, and 9 month visit)
- UCIVA, photopic, binocular (3, 6, and 9 month visit)
- UCNVA, photopic, monocular (3, 6, and 9 month visit)
- UCNVA, photopic, binocular (3, 6, and 9 month visit)
- Defocus curve testing (3, 6, and 9 month visit)
- Anterior Segment Examination

- Pachymetry (6 month exam)
- Auto or Manual Keratometry
- Corneal Topography
- Cycloplegic Refraction (6 month exam)
- Dilated fundus exam (6 month exam)
- Adverse Events and Complications
- Device Deficiencies/Complaints

## **10.7 RETREATMENT PROCEDURES**

### **NON-REFRACTIVE RETREATMENTS**

Non-refractive retreatments or procedures without further laser treatment (e.g., flap lifts, adjustments, realignments, replacement, treatment of complications, removal of epithelial ingrowth) may be performed at any time with the advance notification of the Sponsor. All flap adjustment procedures will be noted and reported to the Sponsor.

### **REFRACTIVE RETREATMENTS**

There will be no refractive retreatments in this study.

## **10.8 EXIT OF SUBJECTS**

An Exit Case Report Form will be completed for all subjects, either when they complete the study or if they exit early.

It is the responsibility of the investigator to provide complete follow-up data to AMO for each subject, and every attempt should be made to gather that complete follow-up data for all subjects enrolled as missing data can have a negative effect on the study results. Patients who would be traveling, relocating or otherwise unavailable for postoperative follow-up visits should not be chosen for this clinical study.

Subjects will be discontinued from the study if the subject dies. Subjects will be considered “lost-to-follow-up” from the study only if irretrievably lost for unavoidable reasons such as: subject moved/unable to locate, subject uncooperative/refuses further study participation, subject ill/unable to travel. In the event of subject relocation, efforts must be made by the investigator to secure follow-up information (i.e., slit-lamp findings and general visual acuity, etc.) from the subject’s new physician.

If a subject is exited early from the study, the investigator will complete an Exit Case Report Form indicating the reason for study exit. In the event of a serious adverse event, the subject may be exited from the study; however, efforts must be made by the investigator to follow the subject until resolution of the adverse event.

Additionally, all study subjects are to be instructed to undergo regular eye examinations at least yearly and also to return to their doctor if any eye complications are experienced in the interim.

## **10.9 UNSCHEDULED VISITS**

During the study period, if a non-protocol-required visit is done for the purpose of medically-indicated follow-up for a study eye, data from this visit should be reported using the Unscheduled Visit CRF. The need for unscheduled visits is at the investigator's discretion. Specific examinations to be performed at unscheduled visits are also at the discretion of the investigator (based on the reason for the unscheduled visit) and data are to be recorded in the appropriate section of the case report form.

Data to be collected may include:

- Manifest refraction
- Uncorrected and best corrected distance visual acuity
- Intraocular pressure
- Anterior segment examination
- Dilated fundus exam
- Ocular symptoms
- Adverse events
- Medications

In addition, if a subject is seen at an Unscheduled visit due to an optical/visual symptom complaint, the PRO Visual Symptom Questionnaire will be administered at that visit, as well as prior to any secondary surgical intervention for an optical/visual symptom complaint. If additional unscheduled visits and/or a secondary surgical intervention due to the same optical/visual symptom complaint occur within 2 weeks of each other, it is not necessary to complete the PRO Visual Symptoms Questionnaire a second time.

## **10.10 PROTOCOL DEVIATIONS**

Any departure from the protocol procedures represents a protocol deviation. Protocol deviations may be subject-based (e.g., inclusion/exclusion criteria, informed consent deviation, etc.) or procedural-based (e.g., out-of-interval visits, non-compliance with testing procedures, etc.). All protocol deviations will be documented using protocol deviation case report forms. Any deviation made to protect the life or physical well-being of a subject in an emergency as well as any use of the investigational device without obtaining informed consent must be reported to AMO within 5 working days. Protocol deviations will be monitored by AMO, and if the non-compliance is persistent or egregious, AMO may take action, including but not limited to termination of the investigator's participation in the study. The investigator is also responsible for informing the reviewing IRB of instances of protocol non-compliance in accordance with the IRB requirements.

## **11. ADVERSE EVENTS AND PRODUCT COMPLAINTS**

### **11.1 ADVERSE EVENT DEFINITIONS**

#### **Adverse Event (AE)**

An adverse event is defined (following ISO 14155) as any untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including abnormal laboratory findings) in subjects, users or other persons, whether or not related to the study device.

#### **Serious Adverse Event (SAE)**

An adverse event is considered serious (following ISO 14155) if it is an untoward occurrence which may or may not be related to use of the study device that

- is sight- or life-threatening,
- results in death,
- requires inpatient hospitalization or prolongation of hospitalization (a planned hospitalization for a pre-existing condition is not considered a serious adverse event),
- results in permanent impairment of a body structure or body function,
- necessitates medical or surgical intervention to prevent permanent impairment to a body structure or function, or
- results in fetal distress, fetal death or a congenital abnormality or birth defect

#### **Device-Related Adverse Event**

A device-related adverse event is defined as any adverse even that is believed to be definitely, probably or possibly related to the study device (following the guidelines in Section 11.4, Causal Relationship). A device-related event is considered an adverse device effect (ADE; following ISO 14155 and Canadian Medical Devices Regulations concerning mandatory problem reporting (sections 59 through 61.1(2)) resulting from any untoward or unintended response to the study device.

#### **Study-Specific Anticipated Adverse Events**

The following is a list including, but not limited to, ocular adverse events that are anticipated and must be reported to AMO for this study. Any events that are unlikely but anticipated (i.e., Melting of the flap) will be reported to Health Canada and other appropriate regulatory agencies.

- Diffuse lamellar keratitis (DLK) (Grade 3 or above)
- Corneal infiltrate or ulcer
- Any persistent corneal epithelial defect at 1 month or later
- Corneal edema at 1 month or later
- Epithelium in the interface with loss of 2 or more lines of BSCVA ( $\geq 10$  ETDRS letters)
- Miscreated flap (decentered, lost, incomplete, too thin or other)

- Melting of the flap
- IOP with increase > 10 mmHg above baseline on two consecutive examinations or an IOP greater than 30 mmHg on two consecutive examinations
- Haze beyond 6 months with loss of 2 or more lines of BSCVA ( $\geq 10$  ETDRS letters)
- Decrease in BSCVA of 2 or more lines ( $\geq 10$  ETDRS letters) not due to irregular astigmatism as shown by hard contact lens refraction (or pin hole acuity if hard contact lens refraction is not medically advisable) at 3 months or later
- Retinal detachment
- Retinal vascular accidents
- Any other vision-threatening event
- Ocular penetration
- Severe glare, severe dry eye, or severe halos at 3 months or later
- Transient Light Sensitivity Syndrome

### COMPLICATIONS

The following events are considered refractive surgery complications (not an all-inclusive list) and should also be reported to the sponsor:

- Diffuse lamellar keratitis (DLK) (Grade 2 or less)
- Corneal edema between 1 week and 1 month after the procedure
- Peripheral corneal epithelial defect at 1 month or later (location of the defect to be identified as on, off, or across the flap)
- Epithelium in the interface
- Foreign body sensation at 1 month or later
- Pain at 1 month or later
- Contact lens related adverse events

### **Unanticipated Adverse Device Effect (UADE)/Unanticipated Serious Adverse Device Effect (USADE)**

Any UADE or USADE (ISO 14155) is defined as any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan (i.e., this protocol), application (including a supplementary plan or application), or risk assessment, or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects.

### **11.2 PRODUCT COMPLAINT/DEVICE DEFICIENCY DEFINITION**

A product complaint/device deficiency is defined by Canadian Medical Devices Regulations concerning mandatory problem reporting (sections 59 through 61.1(2)) (and

ISO 14155 as any alleged deficiency related to the identity, quality, durability, reliability, safety, effectiveness, or performance of a device. Product complaints can pertain to any marketed AMO device being used in the study as well as the investigational device. The investigator is to assess whether the deficiency could have led to a serious adverse event without suitable action or intervention or under less fortunate circumstances.

### **11.3 ADVERSE EVENT AND COMPLAINT REPORTING REQUIREMENTS**

All adverse events and any complaint encountered using any AMO product, regardless of severity and whether or not attributed to the study device(s), are to be reported to AMO and recorded on the case report form corresponding to the visit during which awareness of the event occurred. Adverse events are also to be reported to the reviewing IRB as per the IRB's reporting requirements. If required, adverse events will be reported to the appropriate regulatory agencies (e.g., Health Canada) according to all applicable laws and regulations. Specific instructions on notification procedures to AMO are included in **Appendix S**, Adverse Event Reporting.

Reporting of adverse events shall follow the Canadian Medical Devices Regulations concerning mandatory problem reporting (sections 59 through 61.1(2)). For sites located outside the USA, reporting of adverse events shall follow ISO 14155 and country-specific guidelines, of which the shortest/strictest timeline requirement for reporting adverse events will be followed. General guidelines are provided below:

#### **Adverse Event Reporting**

An adverse event that is not serious or device-related is to be reported to AMO in a timely manner. Notification of non-serious and non-device related adverse events will occur by recording events on the CRF when noted. Such adverse events are also to be reported to the reviewing IRB per their reporting requirements.

#### **Complaints/Device Deficiency Reporting**

A general product complaint or device deficiency is to be reported to AMO in a timely manner. Notification of complaints/device deficiencies will occur by either recording complaints on the CRF when the complaint occurred (e.g. operative form) or by a phone call to the Sponsor. Any device deficiency that could have led to a serious adverse event without suitable action or intervention, or under less fortunate circumstances, must be reported to the sponsor immediately (no later than 48 hours after detection). Device deficiencies that could have led to a serious adverse event should also be reported to the investigator's IRB per their reporting requirements.

#### **Serious and/or Device-Related Adverse Event Reporting**

In the event of a serious adverse event (SAE), which may or may not be related to use of the study device, or a device-related adverse event, AMO must be notified



immediately (no later than 48 hours after detection). Any SAE and/or device-related AE is to be reported by phone and by faxing a completed Serious and/or Device-Related Adverse Event CRF. Any SAE or device-related AE should also be reported to the investigator's IRB per their reporting requirements.

#### **Unanticipated Adverse Device Effect (UADE)/Unanticipated Serious Adverse Device Effect (USADE) Reporting**

If during the study, a serious adverse event occurs that may reasonably be regarded as study-device-related and was not previously expected in nature, severity, or degree of incidence, the investigator is to report the UADE/USADE to AMO within 48 hours, and to the investigator's IRB as soon as possible.

### **11.4 CAUSAL RELATIONSHIP**

The investigator should always be alert to adverse events that may be related to the study device and/or the operative procedure. An attempt should be made in every case to determine if the event may be device-related. Additionally, in the case of a serious and/or device-related adverse event, an attempt should be made to determine if the event is also procedure-related.

The following definitions are to be used as guidelines in determining the relationship between the event and the study device and/or procedure.

Definitely related:	There is a definite causal relationship between the adverse event and the device and/or procedure.
Probably related:	There is a reasonable possibility of a causal relationship between the adverse event and the device and/or procedure.
Possibly related:	The adverse event has not been determined to be device- or procedure-related, but no other cause has been definitively identified and the device and/or procedure cannot be ruled out as a possible cause.
Unlikely to be related:	The possibility of a potential causal relationship between adverse event and the device and/or procedure could exist, but the adverse event is most likely explained by causes other than the device and/or procedure.
Not related:	There is no possibility of a causal relationship between the adverse event and the device and/or procedure

If an adverse event is believed to be definitely, probably or possibly related to the study device, the event will be considered device-related.

### **11.5 ADVERSE EVENT FOLLOW-UP**

For every adverse event, appropriate measures should be undertaken to treat and/or monitor the subject until resolution occurs. Obtain and maintain in the subject's files all

pertinent medical data relating to the event including the subject's medical records and medical reports and/or judgments from colleagues or outside specialists who assisted in the treatment and follow-up of the subject. The investigator should keep AMO closely informed as to the outcome of serious and/or device-related adverse events, thereby allowing AMO to comply with the appropriate regulatory reporting requirements. A Serious and/or Device-Related Adverse Event Update CRF should be completed each time the subject returns to the investigator or other specialist(s) for follow-up of serious and/or device-related adverse event until resolution of the event. Any subject who is exited from the study due to a serious and/or device-related adverse event will be followed until the outcome is determined.

## **12. PROTOCOL CHANGES/AMENDMENTS**

If the investigator desires to modify any procedure and/or the design of the study, he or she must contact and obtain consent from AMO regarding the proposed changes prior to implementation. Any modifications (including additional data collection) require approval by Health Canada and all other appropriate regulatory agencies, as well as approval of the governing IRBs prior to implementation.

## **13. ETHICS REVIEW AND PATIENT WELFARE**

### **13.1 INSTITUTIONAL REVIEW BOARD (IRB)**

It is the responsibility of the investigator to obtain prospective approval of the study protocol, protocol amendments or changes, informed consent forms and other relevant documents (e.g., advertisements) from the IRB. All correspondence with the IRB should be retained in the Investigator Notebook. Copies of IRB submissions and approvals should be forwarded to AMO.

The investigator is responsible for notifying the IRB of reportable adverse events as well as any other circumstance in which additional procedures outside the protocol were conducted to eliminate apparent hazards to subjects.

### **13.2 INFORMED CONSENT**

The current version of the IRB approved study informed consent must be signed by each study subject prior to any study-specific examinations being performed. The IRB approved informed consent is to be signed and dated by the subject as well as by the person who conducted the informed consent discussion. The signed informed consent will be maintained by the investigator as a permanent part of the subject's medical records. A copy of the signed and dated form is to be provided to the subject. The investigator will provide AMO written acknowledgement on the preoperative case report form that a signed agreement of informed consent has been obtained and is in the investigator's possession for each subject. The site shall document in the source

documents that informed consent was obtained prior to participation in the study for each subject enrolled.

NOTE: The informed consent process also includes obtaining the subject's signature on an Authorization for Use/Disclosure of Health Information for Research Form or equivalent documentation necessary to comply with applicable privacy laws pertaining to medical treatment in the governing countries.

NOTE: The sponsor will secure appropriate insurance for study subjects prior to study start.

## **14. DOCUMENTATION**

### **14.1 SOURCE DOCUMENTS**

Source documents must be kept for all study subjects. Source documents may include a subject's medical records, hospital charts, clinic charts, the investigator's subject study files, as well as results of any diagnostic tests or procedures such as topographies or laboratory tests with photographs or instrument printouts.

Each site is expected to adhere to the clinic's own standard documentation requirements for medical charts/clinic notes. However, for the purposes of this clinical study, the medical charts/clinic notes must also include, at a minimum, the following data that will be considered source data and will be reviewed by AMO:

- Subject's name and study identification number
- Subject's contact information
- Study protocol number and the Sponsor name (AMO)
- A statement that informed consent was obtained prior to participation in the study (including the date)
- Dates of all subject visits and surgeries throughout the duration of the study
- PRVSQ Questionnaire
- Contact Lens Questionnaire
- Concurrent medications
- Corrected and uncorrected distance visual acuity (NOTE: visual acuity measurement and letter count are considered source documentation and are to be retained by the site in the subject CRF notebooks)
- Manifest refraction
- Occurrence and status of any operative complications, postoperative medical findings and adverse events
- Occurrence and status of any subject complaints, e.g., ocular/visual symptoms
- The date the subject exited the study, and a notation as to whether the subject completed the study or reason for early exit.

## **14.2 SUBJECT CONFIDENTIALITY**

Subjects will be assigned a site/subject number to maintain subject confidentiality. Subject names may possibly be disclosed to the AMO or regulatory agencies during inspection of medical records related to the study, but reasonable precautions will be taken to maintain confidentiality of personal information to the extent permitted by applicable laws and regulations.

## **14.3 CASE REPORT FORM COMPLETION**

This study will use the Electronic Data Capture (EDC) system, Merge, to collect and manage study data.

The investigator is responsible for ensuring that data are properly recorded on each subject's case report forms and related documents. Prior to database lock, the investigator will verify completeness and accuracy of data submitted to AMO.

## **14.4 STUDY SUMMARY**

A final investigator's summary will be provided to AMO and the reviewing IRB within three months after termination or the completion of the study or the investigator's part of the investigation.

## **15. MONITORING**

AMO will perform three types of monitoring to ensure compliance with regulations: data monitoring, administrative monitoring, and safety monitoring.

### **15.1 DATA MONITORING**

In order to ensure a well-controlled clinical trial, AMO will follow specific data monitoring procedures. Following review of EDC data, requests for data clarification will be handled through the EDC data system. To minimize data omissions and inconsistencies on clinical reports and to ensure that data are accurately transcribed to computer data files, AMO will follow internal data processing procedures that include automated and manual quality control checks to identify any data discrepancies. Any such items will be resolved and documented as needed on the case report forms at the investigative site and in the data management system at AMO. Ongoing data review for clinical data monitoring will be conducted and will include evaluation of outliers for visual acuity and refractions as well as review of adverse event listings.

### **Prevention of Missing Data**

Methods used to safeguard against missing data that can have deleterious effects on the study integrity and reliability of its outcomes will include training study staff with centralized and on-site programs. In addition, subjects will be encouraged at the time of

informed consent to avoid missing study visits, as missing data may affect the study reliability and diminish the scientific value of their contribution to the study.

## **15.2 ADMINISTRATIVE MONITORING**

Administrative monitoring procedures will ensure that study devices, subjects, and forms can be traced and will allow monitoring of investigator progress and compliance. Accountability and traceability of study devices will be monitored by AMO.

### **Device Accountability**

Complete accountability will be maintained at the investigative site by maintaining records of all investigational equipment received from and returned to AMO. A site log will be used to track laptops for date of receipt, use and disposition/return to AMO. This site log and any other investigational information will be maintained in the operative room study binder and monitored by AMO personnel. During periodic investigative site monitoring visits, AMO personnel will review investigative site inventory records and logs to ensure equipment accountability compliance and complete investigational device traceability.

### **Site Monitoring Plan**

Prior to performing any study treatments, the requirements of the study and reporting mechanisms will be explained to each investigator either personally at the investigative site or at a formal study investigator meeting. When necessary, a pre-study site qualification visit may be performed to assess the adequacy of the site to perform the study for sites that have not previously worked with AMO or have undergone significant changes, or have not been visited in the past year. A study initiation visit will be conducted for all sites prior to or at the time of the first implant.

Throughout the duration of the study, site visits to monitor compliance to this protocol will be made at each investigative site. During a routine site monitoring visit, AMO will review informed consent documents and subject eligibility, and the data on study case report forms will be verified against subject charts and other source documents to ensure complete and accurate reporting. The subject files will also be reviewed to assure that all adverse events and any issues encountered with AMO products have been reported in a timely fashion.

AMO will also review source documents to verify that all required items have been documented in the subject medical charts. Refer to Section 14.1, Source Documents, for a list of items that are required for source documentation. In addition to subject files, study logs will be checked and conformance to lighting levels for visual acuity tests will be verified.

Upon study completion, a final close-out site visit to each site will be made to monitor the last of the subject data records and finalize any outstanding study issues.

A separate Study Monitoring Plan will be established prior to study start that will define the type and frequency of monitoring visits and frequency of record monitoring.

### **15.3 SAFETY MONITORING**

This study will utilize a Medical Monitor for safety monitoring. The Medical Monitor will review and assess any reports of serious and/or device-related adverse events as well as device deficiencies that could have led to a serious adverse event. If necessary, the medical monitor will discuss these events with the reporting investigator(s). The medical monitor will also be available to answer all questions from investigators. The medical monitor, as well as any other qualified personnel designated by AMO, shall also review interim progress reports, as applicable.

The medical monitor will review results throughout the clinical trial as necessary to ensure the continued safety of the equipment and to ensure that no subjects are exposed to unreasonable risk.

## **16. PUBLICATIONS**

Refer to the Clinical Trial Agreement for information regarding AMO publication policies.

## **17. RISK ANALYSIS**

### POTENTIAL RISKS AND RISK MANAGEMENT

#### *RISKS OF THE IDESIGN 1.3-PRESBY TPS*

The potential risks and complications to subjects in the clinical study include the same risks for routine laser refractive surgery with a market-approved procedure, as well as some additional risks specific to the presbyopia treatment.

Typical laser refractive surgery risks include a number of potential complications which may require medical treatment and/or secondary surgical intervention. These risks include vision threatening complications such as flap complications, resulting in a free flap, irregular healing of the flap leading to a distorted cornea and decreased vision, perforation of the cornea, corneal ectasia, partial or total loss of vision, retinal detachment, corneal edema, corneal infection and/or ulcer, corneal epithelial defect, corneal haze, increased intraocular pressure, haze, hemorrhage, venous and arterial blockage, cataract formation, total blindness and even loss of the eye.

Non-vision threatening side-effects of laser refractive surgery may include increased sensitivity to light, glare, ghost images and fluctuations in vision, a “starburst” or “halo” effect around lights at night, pain or foreign body sensation, dry eyes, epithelial ingrowth

of cells under the flap, residual myopic, hyperopic, or astigmatic refractive error requiring the use of vision correction and anisometropia.

The iDesign 1.3-PRESBY TPS may have some additional risks due to the presbyopic ablation and resulting multifocality. Although the procedure was designed to provide an increased depth of focus, there is a possibility this may not be clinically evident. At worst, iDesign 1.3-PRESBY treatment would perform similarly to iDesign CustomVue LASIK. Visual symptoms such as glare, ghost images, starbursts and halos may be worse compared to iDesign CustomVue LASIK because of the higher levels of spherical aberration associated with the presbyopic ablation.

### **Risks of contact lens trial**

This trial is considered to be a non-significant risk based on the International Standards Organization (ISO) guidelines due to the daily wear nature of the study. The contact lenses used in the trial are commercially available and intended for daily wear (NOT extended wear) with usage consistent with typical daily wear.

Complications that may occur during the wearing of contact lenses include discomfort, dryness, aching or itching eyes, excessive tearing, discharge, hyperemia and variable or blurred vision. More serious risks may include photophobia, iritis, corneal edema or eye infection.

### **RISK MANAGEMENT**

Subjects will be closely monitored throughout the trial duration. The occurrence of adverse events and complaints will be assessed at each study visit and reported to AMO according to Section 11.0, Adverse Events and Product Complaints. Additionally, AMO will monitor incoming data following the procedures outlined in Section 15.0, Monitoring. The Medical Monitor will ensure subjects are not exposed to additional risks by monitoring serious adverse events, device-related adverse events, and device-deficiencies that could have led to serious adverse events (Section 15.3, Safety Monitoring).

The clinical investigator shall ensure that no additional software is installed on the AMO laptop.

### **POTENTIAL BENEFITS**

The primary benefits of laser refractive surgery with the investigational iDesign 1.3-PRESBY TPS is the correction of myopic and astigmatic refractive errors which may reduce or eliminate the need for glasses or contact lenses for distance vision, and the potential to mitigate the symptoms of presbyopia. The iDesign 1.3-PRESBY TPS is intended to provide distance vision correction equivalent to iDesign CustomVue LASIK

refractive surgery, and improved intermediate and near vision, and increased spectacle independence compared to iDesign CustomVue LASIK.

## **CONCLUSION**

The hazards/risks associated with iDesign 1.3-PRESBY TPS using the iDesign Advanced WaveScan Studio System in conjunction with the STAR S4 IR Excimer laser are acceptable and expected to be similar to those of LASIK treatment using the iDesign System and STAR S4 IR Excimer laser. The potential clinical benefits of treatment using the iDesign Advanced WaveScan Studio System in conjunction with the STAR S4 IR Excimer laser outweigh the residual risks when the device is used as intended.

## **18. RECORDS RETENTION**

All study-related correspondence, subject records, consent forms, Authorization for Use/Disclosure of Health Information Forms or similar medical treatment privacy law documentation, records of the distribution and use of all study products, and original case report forms should be maintained by the investigator.

The investigator must maintain and have access to the following essential documents until notified by the Sponsor. Note: This may be for a minimum of 15 years after completion of the study unless country-specific requirements are longer. AMO requires notification if the investigator wishes to relinquish ownership of the data so that mutually agreed-upon arrangements can be made for transfer of ownership to a suitably qualified, responsible person.

- All case report forms
- All adverse event information (adverse event forms, follow-up letters, etc.)
- Investigational supply records/inventory
- IRB and regulatory approval documentation
- Study correspondence
- Study agreements
- Site visit documentation
- Protocol(s) and the reason for any deviations from the protocol
- Subject log(s)
- Clinical Investigator's Brochure
- Completed subject informed consent forms and medical privacy forms (e.g., Authorization for Use/Disclosure of Health information or equivalent documentation necessary to comply with applicable privacy laws pertaining to medical treatment in the governing countries)
- Subject medical chart/clinic notes



## **19. TERMINATION OF THE INVESTIGATION**

The clinical investigation will be suspended in the event of high levels of complications and/or adverse events that are unexpected in nature and/or severity and evaluated as to causality relative to the study device. The clinical investigation may be suspended if the Medical Monitor or IRB, upon review and evaluation of the clinical data, finds unacceptable clinical performance or the level of single or total complications and/or adverse events unacceptable for continuation of the investigation.

If causality is shown not to be related to the study device, the study may be resumed in accordance with the IRB and regulations of Health Canada and governing countries. The study will be terminated if causality is shown to be related to the study device.

Additionally, the investigator, or AMO, may stop a subject's participation at any time. AMO may also stop the study at any time for reasons it determines appropriate. However, no suspension of the study would be made to disadvantage the study subjects. Following suspension of the study for any reason, all study subjects who have already received treatment would continue to be followed through completion of the study visit schedule.

## **20. STATISTICAL METHODS**

This section highlights the analyses for the primary and secondary study endpoints as well as the key safety endpoints. The key time point for analyzing study endpoints will be at 6 months.

### **20.1 ANALYSIS POPULATION**

The safety population will be the primary analysis population for all endpoints and includes all eyes that receive study treatment.

### **20.2 PRIMARY AND SECONDARY STUDY ENDPOINTS**

#### **Primary Endpoint**

##### **MONOCULAR DISTANCE CORRECTED INTERMEDIATE VISUAL ACUITY (DCIVA)**

The primary endpoint is mean monocular DCIVA under photopic conditions at 67 cm. Results will be reported by PresbyT-LASIK treatments (test) group versus iDesign CustomVue (control) group and compared using a one-sided, paired t-test with alpha level of 0.025. The null hypothesis is that the mean difference between eyes (control minus test) for LogMAR DCIVA is less than or equal to zero (ie, test acuity is the same as or worse than that of control). The alternative hypothesis is that the mean difference between eyes for DCIVA is greater than zero (ie, test acuity is better than that of control).

$H_0: \mu_{\text{diff}} \leq 0$  (test is worse than (higher LogMAR) or equal to control)

$H_1: \mu_{\text{diff}} > 0$  (test is better (lower LogMAR) than control)

where

$\mu_{\text{diff}}$  = the mean difference in LogMAR DCIVA between control eyes and test eyes (control minus test)

Reject the null hypothesis if one-sided p-value  $\leq 0.025$ .

The success criterion is a statistically significantly lower mean DCIVA for test compared to control ( $p \leq 0.025$ ).

In addition, clinical significance will be achieved if the mean DCIVA for the test group is at least one line better than that for the control group.

## Secondary Endpoints

### MONOCULAR DISTANCE CORRECTED NEAR VISUAL ACUITY (DCNVA)

Mean monocular DCNVA at 40 cm will be reported by PresbyT-LASIK treatments (test) group versus iDesign CustomVue treatments (control) group and compared using a one-sided, paired t-test with an alpha level of 0.025. The null hypothesis is that the mean difference between eyes (control minus test) for logMAR DCNVA is less than or equal to zero. The alternative hypothesis is that the mean difference between eyes for DCNVA is greater than zero.

$H_0: \mu_{\text{diff}} \leq 0$  (test is worse than (higher logMAR) or equal to control)

$H_1: \mu_{\text{diff}} > 0$  (test is better (lower logMAR) than control)

where

$\mu_{\text{diff}}$  = the mean difference in logMAR DCNVA between control eyes and test eyes (control minus test)

Reject the null hypothesis if one-sided p-value  $\leq 0.025$ .

The success criterion is a statistically significantly lower mean logMAR value for test compared to control eyes ( $p \leq 0.025$ ).

Clinical significance is achieved if the mean DCNVA for the test group is at least 1.5 lines better than that for the control group.

## Safety Endpoints

### MONOCULAR BSCVA

Mean monocular BSCVA will be reported by test and control groups with the mean difference between postoperative and preoperative BSCVA evaluated using a two-sided, 90% confidence interval (CI). The null hypothesis is that the mean difference (postoperative minus preoperative) in logMAR BSCVA is greater than or equal to 0.1 logMAR. The alternative hypothesis is that the mean difference in BSCVA is less than 0.1 logMAR.

$H_0: \mu_{\text{diff}} \geq 0.1$

$H_1: \mu_{\text{diff}} < 0.1$

where

$\mu_{\text{diff}}$  = the mean difference in logMAR BSCVA between postoperative and preoperative eyes (postoperative minus preoperative).

The success criterion is achieved if the upper limit of the 90% CI of the differences in mean logMAR BSCVA for postoperative compared to preoperative eyes is  $< 0.1$  logMAR for both test and control groups.

Clinical significance is achieved if the mean postoperative BSCVA is no more than one line worse than preoperative BSCVA for both test and control groups.

#### INDUCED MANIFEST REFRACTIVE ASTIGMATISM

The frequency and proportion of eyes with induced manifest refractive astigmatism will be reported at each periodic study visit. The rate of eyes with induced manifest refractive astigmatism of greater than 2.00 diopters will be summarized.

#### SERIOUS AND DEVICE RELATED ADVERSE EVENTS

The number and proportion of eyes with serious and device-related adverse events (non-flap related) will be summarized.

### **20.3 ADDITIONAL ENDPOINTS**

The frequency, proportion and 95% confidence intervals of eyes with achieved MRSE within 0.50 D and 1.00 D of intended will be summarized over time. The intended MRSE is defined as “– Preop MRSE”. The achieved MRSE is defined as “Postop MRSE - Preop MRSE”.

Refractive stability will be evaluated for a consistent cohort (i.e., eyes with data at all periodic study visits). At the point of refractive stability, at least 95% of the eyes in the consistent cohort should have a change  $\leq 1.00$  D of MRSE between refractions performed at 1 month and 3 months after surgery or any two refractions performed at least 3 months apart. The mean change (paired differences) in MRSE between pairs of successive refractions will be calculated. The 95% confidence intervals of the mean changes should include zero.

The depth of focus curve data will be presented graphically and test and control groups will be compared by descriptive analysis. The mean and standard deviation of iDesign aberrometry measurements (HOA) and keratometry (mean and K cylinder) will be reported over time. Manifest cylinder will be analyzed as both non-vector and vector variables (Eydelman, et al, 2006). The frequency and proportion of eyes with

complications and slit-lamp findings, including corneal clarity, will also be reported over time. Other visual acuity endpoints (such as UCDVA, UCIVA, UCNVA and low contrast BSCVA) will also be reported by test versus control group with the mean difference between groups also determined. Results for visual symptoms from the PRVSQ for PRK/LASIK will be analyzed to compare differences between the test and control groups. The frequency and proportion of eyes with reported ocular visual symptoms (non-directed) will be presented. A listing of all serious and/or device-related adverse events will also be provided. Additionally, non-refractive retreatment procedures will be tabulated and summarized.

#### **20.4 VISUAL ACUITY CONVENTIONS AND GENERAL STATISTICS**

Visual acuity data will be converted to LogMAR values prior to analysis and adjusted for the test distance. Descriptive statistics will typically include sample size (N), mean, standard deviation (SD), median, minimum (Min) and maximum (Max) as appropriate for continuous variables. For continuous variables, statistical tests (e.g., t-test) assuming normality will generally be used. For categorical data, the frequency and proportion will be reported and Fisher's exact test or Chi-square test will generally be applied. For ordinal categorical data, the frequency and proportion will be reported with the Wilcoxon Rank-Sum test generally used.

#### **20.5 PERIODIC REPORTS**

Periodic analyses of data from all eyes completing the 3-month and 6-month visits to evaluate UCDVA, MRSE, BSCVA, DCIVA, DCNVA and safety outcomes including biomicroscopic findings and adverse events will be conducted.

#### **20.6 SAMPLE SIZE CALCULATIONS**

The sample size determination is based on intermediate visual acuity. There is over 80% power to detect a 0.7 line or greater difference in mean visual acuity between the test and control eyes with 34 subjects. This assumes a two-sided paired t-test with an alpha of 0.05 and standard deviation of 1.4 lines.

## APPENDIX A SUMMARY OF PROCEDURES REQUIRED AT EACH VISIT

Examination	Preop Days -120 to -21 <sup>1</sup>	CL Disp Weeks -3 <sup>2</sup>	CL F/U Weeks -2 <sup>2</sup>	Op Day 0	1 Day Days 1-2	1 Wk Days 5-9	1 Mo Weeks 3-5	3 Mo Weeks 10-14	6 Mo Weeks 21-26	9 Mo Weeks 35-43	Unsched <sup>4</sup>
Informed consent	X										
Ocular and systemic medical history and concomitant medications	X			X	X	X	X	X	X	X	X
Inclusion/Exclusion criteria	X										
PRO questionnaire - PRVSQ	X						X	X	X	X	X <sup>4</sup>
iDesign System Measurement of refraction, aberrometry, topography, keratometry, pupilometry	X					X	X	X	X	X	X (after 1 week)
UCDVA - photopic, monocular, distance (logMAR)	X				X	X	X	X	X	X	X (after 1 week)
UCDVA - photopic, binocular, distance (logMAR)								X	X	X	
Manifest refraction (logMAR)	X					X	X	X	X	X	X
BSCVA - photopic, monocular, distance (logMAR)	X					X	X	X <sup>3</sup>	X <sup>3</sup>	X <sup>3</sup>	X <sup>3</sup>
BSCVA - photopic, binocular, distance (logMAR)								X	X	X	
BSCVA - photopic, monocular, distance low contrast (10%) (logMAR)	X							X	X	X	
DCNVA - mesopic, monocular at 40 cm (logMAR)								X	X	X	
Pupil size, mesopic, distance & near								X			
Pupil size, photopic, distance & near								X			
Minimum add power	X										
DCIVA - photopic, monocular at 67 cm (logMAR)	X							X	X	X	
DCIVA - photopic, binocular at 67 cm (logMAR)	X							X	X	X	
DCNVA - photopic, monocular at 40 cm (logMAR)	X							X	X	X	
DCNVA - photopic, binocular at 40 cm (logMAR)	X							X	X	X	
UCIVA - photopic, monocular at 67 cm (logMAR)								X	X	X	
UCIVA - photopic, binocular at 67 cm (logMAR)								X	X	X	
UCNVA - photopic, monocular at 40 cm (logMAR)								X	X	X	
UCNVA - photopic, binocular at 40 cm (logMAR)								X	X	X	
Defocus curve testing – photopic, monocular (logMAR)								X	X	X	
Keratometry (auto or manual)	X					X	X	X	X	X	X <sup>4</sup>
Corneal topography	X						X	X	X	X	X <sup>4</sup>
Anterior segment exam (biomicroscopic slit-lamp exam <sup>c</sup> )	X				X	X	X	X	X	X	X
Intraocular pressure (applanation tonometry)	X						X	X	X	X	X <sup>4</sup>
Pachymetry	X								X		
Cycloplegic refraction	X								X		X <sup>4</sup>
Dilated fundus exam	X								X		X <sup>4</sup>
Complications	X	X	X	X	X	X	X	X	X	X	X

Examination	Preop Days -120 to -21 <sup>1</sup>	CL Disp Weeks -3 <sup>2</sup>	CL F/U Weeks -2 <sup>2</sup>	Op Day 0	1 Day Days 1-2	1 Wk Days 5-9	1 Mo Weeks 3-5	3 Mo Weeks 10-14	6 Mo Weeks 21-26	9 Mo Weeks 35-43	Unsched <sup>4</sup>
Adverse events (Ocular/NonOcular)	X <sup>5</sup>	X	X	X	X	X	X	X	X	X	X
Device deficiencies/complaints	X			X		X	X	X	X	X	X
Contact lens trial		X	X								
Refractive stability assessment for contact lens wearers				X <sup>6</sup>							

<sup>1</sup> All screening assessments must be performed prior to surgery. The screening period is the 120 days before surgery, up to and including the day of surgery.

<sup>2</sup> The contact lens trial should occur after the preoperative exam at any time during the 120 days before the day of surgery. However, subjects must wear the trial contact lenses for a minimum of 1 week and remove the contact lenses for a minimum of 2 weeks prior to surgery.

<sup>3</sup> At 3 months or later, if there is a loss of 2 or more lines of BSCVA ( $\geq 10$  letters) compared to the preoperative visit, a rigid contact lens over refraction (or pin hole acuity if rigid contact lens over refraction is medically inadvisable) should be performed to estimate the best possible corrected visual acuity.

<sup>4</sup> At the investigator's discretion for unscheduled visits based on the reason for the unscheduled visit. Subject seen at an unscheduled visit due to an optical/visual symptom complaint should complete the PRVSQ.

<sup>5</sup> Adverse event collection begins after informed consent has been obtained.

<sup>6</sup> On operative day or other visit

**Note:** Patient reported outcome questionnaires are to be administered first, followed by the iDesign measurement before any other ocular examinations.

All non-contact procedures (e.g. topography and keratometry) are to be performed before contact assessments (e.g. IOP and pachymetry). Cycloplegic refraction/fundus exam are to be the final procedures.

**Note:** 1 month = 4 weeks, 1 week = 7 days

## APPENDIX B EQUIPMENT LIST

The following equipment will be supplied to an investigative site for the duration of the study provided that the site does not already have such equipment available for use. This equipment loan will be documented in the Clinical Trial Agreement, which indicates that the equipment is to be returned to Abbott Medical Optics at the completion of the study.

- One M&S Technologies CTS-1000 Smart System
- One Auto-Adjusting Monitor Calibration System
- Light meter
- DVD recorder (if necessary)
- Neutral density trial frame lenses for mesopic testing
- Tape measure (meters)
- NeurOptics Pupillometer
- AMO Laptop

## APPENDIX C      MANUAL OF TESTING PROCEDURES

**Anterior Segment Examination** shall be performed via biomicroscopic slit-lamp exam for determination of anterior segment medical findings including but not limited to the adnexa, conjunctiva, sclera, cornea, and iris. The corneal should be examined in detail and the following items graded on a scale of (0 to 4+, 0=clear): overall corneal clarity, any abnormalities such as corneal infiltrates, opacities in the lamellar bed, and density of the scar around the edge of the flap (for LASIK).

**BSCVA (Best Spectacle Corrected Visual Acuity)** shall be measured using the M & S Technologies CTS-1000 Smart System in logMAR format (100% contrast) at a test distance of 4 meters and calibrated to a photopic luminance of 85 cd/m<sup>2</sup> (80-110 cd/m<sup>2</sup>). BSCVA testing is to be performed with the 4.0-meter manifest refraction in place; no refractive adjustment is necessary for BSCVA measurement. Detailed instructions for performing BSCVA testing are provided in **Appendix G**.

**Corneal Topography** shall be measured with the iDesign System or any other Scheimpflug or Placido disk-based system and the same device should be used at every visit. Images will be retained by the Investigator.

**Cycloplegic Refraction** shall be performed following installation of 1 drop of tropicamide 1% at least 30 minutes prior to determine the subject's refraction without accommodation.

**Dilated Fundus Examination** shall be performed following installation of mydriatic agents at least 30 minutes prior to determine the status of the ocular media, retina and lens.

**iDesign Advanced WaveScan Studio™ System** measures the refractive error and wavefront aberrations of the human eye using a Hartmann-Shack wavefront sensor. Preoperatively, a minimum of three measurements shall be taken or until an exam is selected for treatment; a minimum wavefront diameter of 4.0 mm for preoperative measurements is required. Postoperatively, at least one measurement is required at designated study exams. Every effort shall be made to obtain measurements with the largest wavefront diameter possible at each visit.

**Intraocular pressure** is to be measured using applanation tonometry and is to be performed after manifest refraction, vision tests, keratometry, topography, aberrometry, biomicroscopy, and before pachymetry.

**Keratometry** (not simulated K) shall be conducted preoperatively using the iDesign System AND an auto or manual keratometer. The same additional keratometry method is to be used at each required visit, e.g., if auto keratometry was recorded at the preoperative exam, all postoperative keratometry readings should be auto K's. Do not use "sim K" from the corneal topography unit.



**Lighting levels and lane calibration** will be assessed by a representative of the Sponsor to ensure the lane length and lighting conditions are consistent across sites. The site or Sponsor designee will verify the M & S Technologies CTS-1000 Smart System luminance level of 85 cd/m<sup>2</sup> (80-110 cd/m<sup>2</sup>) with the auto-adjusting monitor calibration system at the start of each subject visit during the active enrollment and follow-up period. Verification of the screen luminance level will be recorded.

**Manifest Refraction** is to be performed using the phoropter and the M & S Technologies CTS-1000 Smart System in logMAR format (100% contrast) at a distance of 4.0 meters and calibrated to a photopic luminance of 85 cd/m<sup>2</sup> (80-110 cd/m<sup>2</sup>). Manifest refractions to be performed using the Maximum Plus refraction method as detailed in **Appendix E**. Because 4.0 meters is not optical infinity, refraction adjustments are necessary for some vision tests to ensure proper vision testing taking into account test distance and refraction distance. **Appendix F** lists the refraction adjustments required for the various different vision tests using the 4.0-meter refraction.

**Mesopic Luminance** is defined as 3 cd/m<sup>2</sup> (2.5-3.5 cd/m<sup>2</sup>).

**Mesopic Ambient Lighting** is defined as 30 – 50 lux.

**Mesopic Vision Testing** is to be performed using the 1.5 neutral density filters with the M & S Technologies CTS-1000 Smart System in ETDRS format (100% contrast).

**Mesopic Pupil Size Measurement** is to be performed under mesopic room lighting conditions of 30 – 50 lux. To set room lighting to 30 – 50 lux, turn off all the lights in the room, adjust the ambient light with the dimmer switch until the room lighting is dim to dark and verify with a light meter. Mesopic pupil size should be measured with the NeurOptics pupillometer.

**PRSVQ-Lasik Questionnaire** (2015 version) is a self-administered, validated assessment tool designed specifically for those who through correction of refractive error have normal visual acuity, but may still be experiencing problems in vision-related functioning and well-being. The PRSVQ questionnaire is to be administered preoperatively and at designated postoperative study exams.

**Pachymetry** to measure the corneal thickness shall be performed with an ultrasonic pachymeter preoperatively, intra-operatively (as applicable), and postoperatively.

**Photopic Luminance** is defined as 85 cd/m<sup>2</sup> (acceptable range of 80-110 cd/m<sup>2</sup>).

**Photopic Pupil Size** is to be performed under photopic room lighting conditions of 480 – 520 lux. Photopic pupil size should be measured using the NeurOptics pupillometer.

**Refractive Stability (preoperative)** is defined as a change of ≤1.00 D in sphere or cylinder (based on a previous exam, medical records, or prescription) at least 12 months prior to the preoperative manifest refraction. Additionally, the astigmatic axis must also

be within 15 degrees for eyes with  $>0.50$  D of preoperative and historical manifest cylinder.

**Refractive Stability Check for Contact Lens Wearers** is based on a change of not more than 0.50 D in MRS, MRC and as well as keratometric meridians on 2 separate occasions at least 7 days apart with readings following cessation of contact lens wear of 4 weeks for rigid contact lenses (toric or spherical) and 2 weeks for soft contact lenses (toric or spherical).

**Surgical Target** and planning is required prior to the operative exam. All eyes will be targeted for emmetropia. The iDesign 1.3-PRESBY TPS will be used to create a treatment shape for each eye that qualifies for the study. The TPS software used in this study is Version 1.3, which does not require any additional physician adjustments.

**UCVA (Uncorrected Visual Acuity)** shall be measured using the M & S Technologies CTS-1000 Smart System in logMAR format (100% contrast) at a test distance of 4 meters and calibrated to a photopic luminance ( $80\text{-}110\text{ cd/m}^2$ ). UCVA testing is to be performed through a  $+0.25$  D trial lens refractive adjustment to compensate for the 4 meter test distance. Detailed instructions for performing UCVA testing are provided in **Appendix G**.

## APPENDIX D MAXIMUM PLUS MANIFEST REFRACTION TECHNIQUE WITH CYLINDER REFINEMENT

Manifest refraction testing will be performed at 4 meters using the M&S Technologies CTS-1000 Smart System (M&S system) in logMAR format (100% contrast) and calibrated to a photopic luminance of 85 cd/m<sup>2</sup> (80-110 cd/m<sup>2</sup>). The ambient room lighting shall be set to mesopic. **NOTE: Objective refraction by iDesign measurement must be used as a starting point for the Manifest Refraction.**

Always ensure that the endpoint of refraction is maximum plus (or minimum minus) power that yields maximum visual acuity.

- 1) Occlude the fellow eye.
- 2) Place the iDesign system (4 mm Rx Calc) sphere (adjusted to 4 meters) and cylinder power and axis from the iDesign exam (vertex distance at 12.5mm) selected for treatment in the phoropter or trial frame preoperatively and from the single exam acquired postoperatively.
- 3) SPHERE: Starting with the objective refraction, refine the sphere to yield best visual acuity.
- 4) CYLINDER AXIS: Refine cylinder with a cross-cylinder and the objective cylinder refraction as the starting point. Refine axis first and power second, since the correct axis can be found with an incorrect power, but the correct power cannot be found with an incorrect axis.
  - a. Direct the subject's attention to 1 line above (larger letters) the best visual acuity. With the trial cylinder (axis and power) in the phoropter, introduce cross-cylinder for axis refinement. When asking the subject which cross-cylinder axis position is better, "one or two?", remind the subject to look at different letters on the line and report preference based on the overall clarity of the letters.
  - b. Refine the axis based on the subject's responses, using small steps (less than five degrees), until the subject reports no difference in the two choices.
- 5) CYLINDER POWER: Set the cross cylinder to refine cylinder power and present choices to the subject, reminding the subject to look at different letters on the line and report preference based on overall clarity of the letters. Reduce or increase trial cylinder power accordingly.
  - a. Maintain the spherical equivalent throughout cylinder power refinement by adjusting the sphere once for every two clicks of cylinder power change.
- 6) SPHERE CHECK: Introduce fogging lens (typically +0.75D sphere) and reduce in 0.25D steps until visual acuity shows no improvement.

## APPENDIX E CYCLOPLEGIC REFRACTION TECHNIQUE

The baseline refraction and the amount of accommodation that the subject habitually employs can only be determined by refracting with and without cycloplegia. The chief benefit of cycloplegia, therefore, is that it eliminates accommodation so that the examiner can make an accurate measurement of the refraction in the un-accommodative state. By comparing this result with a manifest refraction, the true refractive state of the eye and the accommodative tone can be established.

There are two pieces of information that are available from the cycloplegic examination that cannot be deduced from the manifest refraction alone:

- the magnitude of the refractive error free from the influence of accommodation; and
- the extent to which the accommodative tone influences the refractive state.

The following cycloplegic refraction technique is to be used throughout the study:

1. Instill tropicamide 1% and wait 30 minutes to allow for a full cycloplegic effect.
2. Start with the Manifest Refraction (maximum plus; refined from the objective iDesign measurement).
3. **Refine only the sphere magnitude so the least minus yields the most letters.**  
Do not refine or adjust the cylinder axis or the magnitude of the cylinder power.

## APPENDIX F REFRACTION ADJUSTMENTS

Postoperative study manifest refractions are to be performed using the M & S Technologies CTS-1000 Smart System (M&S system) in logMAR format (100% contrast) at a distance of 4.0 meters. Because 4.0 meters is not optical infinity, refraction adjustments are necessary to ensure proper vision testing taking into account test distance and refraction distance. The adjustment required (in diopters) is  $1/\text{test distance}$  (in meters). To adjust a 4.0-meter refraction to optical infinity, -0.25 D is to be added to the sphere of the refraction to obtain a true distance (infinity) correction. When testing uncorrected visual acuity at 4.0-meters a +0.25 D sphere is required. In the case where the refraction distance (4.0 meters) and the vision test distance (4.0 meters) are the same, no adjustment is necessary. The following table lists the refraction adjustments required for the various vision tests in this study:

**Refraction Adjustments for Vision Testing**

<u>Vision Test</u>	<u>Test Distance</u>	<u>Correction/Adjustment</u>
Uncorrected distance visual acuity (UCDVA)	4.0 m	+0.25 D adjustment only
Best corrected distance visual acuity (BCDVA)	4.0 m	No adjustment; manifest refraction only
Best corrected distance defocus curve testing	4.0 m	No adjustment; manifest refraction only
Uncorrected intermediate visual acuity (UCIVA)	67 cm	No adjustment
Distance corrected intermediate visual acuity (DCIVA)	67 cm	-0.25 D added to manifest refraction sphere
Uncorrected near visual acuity (UCNVA)	40 cm	No adjustment
Distance corrected near visual acuity (DCNVA)	40 cm	-0.25 D added to manifest refraction sphere

## APPENDIX G INSTRUCTIONS FOR USE OF M&S DISTANCE VISUAL ACUITY CHARTS

Distance visual acuity testing will be performed using the M&S Technologies CTS-1000 Smart System® computerized vision testing system (M&S system). This system provides a descending logMAR chart with 100% contrast proportionally spaced SLOAN letters. Each presentation is randomized and is consistent and repeatable. The system is calibrated for both distance to subject and pixels/inch so that optotypes precisely follow ANSI Z80.21-2010 and ISO 8596:2000 in regard to size, spacing between optotypes and spacing between lines.

### Figure 1: Example of logMAR 4.0 meter chart screen

The M&S system background luminance is set to 85 cd/m<sup>2</sup> (range of 80 – 110 cd/m<sup>2</sup> is acceptable). Room lighting is to be set to a level lower than the illumination from the laptop screen. Ambient lighting should be mesopic (30-50 lux) to maximize pupil size. No surface (including reflective surfaces) within the subject's field of vision should be brighter than the chart background in luminance. The screen luminance will be verified at the start of each subject visit using the AMO-provided auto-adjusting monitor calibration system to ensure light levels are appropriate.

The M&S system laptop should be placed precisely at 4.0 meters (13 feet) from the subject for testing distance visual acuities. A laptop setting may be used to reverse charts for rooms that require "folding" via a mirror to reach a distance of 4.0 meters. Whether standard or "folded", measure and record the test distance accurately. If the room set-up does not allow the chart to be placed at precisely 4.0 meters, record the actual test distance used (e.g., 3.9 meters) and visual acuity measurements will be mathematically adjusted by AMO for the actual test distance used.

Subjects should be reminded prior to testing that squinting is not allowed. The technician is to observe the subject to ensure the subject is not squinting during visual acuity testing. If squinting is observed, the subject is to be reminded by the testing technician not to squint.

The right eye will be tested before the left eye; monocular testing should be completed for each measurement before binocular testing is done.

All subjects will be tested both uncorrected and best corrected, monocularly and binocularly. To test subjects monocularly, occlude the fellow eye in the phoropter or with an occluder (if trial lenses are used) and encourage subjects to read the smallest letters possible even if they have to guess. Visual acuity measurements are based on the total number of correctly read letters. Subjects should be instructed to start with the smallest line where they can read all of the letters. If they miss any letters, go up a line until they are able to read all the letters on a line, then continue to read each subsequently smaller line. The subject should be encouraged to read as many letters possible, even if they have to guess. Testing may be stopped when it is evident that no further readings can be made. Record the total number of letters read correctly on the chart. This will be displayed on the laptop screen along with the logMAR and Snellen acuity. Then begin testing for the fellow eye and repeat with both eyes together for binocular testing.

Perform monocular and binocular best corrected distance visual acuity testing in the same manner.

## APPENDIX H INSTRUCTIONS FOR USE OF M&S INTERMEDIATE VISUAL ACUITY CHART

Intermediate visual acuity will be measured using the M&S system intermediate charts designed for 67 cm.

The M&S system background luminance is set to 85 cd/m<sup>2</sup> (range of 80 – 110 cd/m<sup>2</sup> is acceptable). Room lighting is to be set at a level lower than the illumination from the laptop screen. Ambient lighting should be mesopic (30-50 lux) to maximize pupil size. No surface (including reflective surfaces) within the subject's field of vision should exceed the chart background in luminance.

The M&S system should be placed precisely at 67 cm from the subject for testing intermediate visual acuities.

Subjects should be reminded prior to testing that squinting is not allowed. Trial frames should be used for visual acuity testing with careful observation by the testing technician to ensure the subject is not squinting. If squinting is observed, the subject is to be reminded by the testing technician not to squint.

The right eye will be tested before the left eye; monocular testing will be completed for each measurement before binocular testing is done.

All subjects should be tested monocularly and binocularly, uncorrected and with distance correction in place. Visual acuity measurements are based on the total number of correctly read letters. Subjects should be persuaded to read the smallest letters possible even if they have to guess.

All subjects will be tested both uncorrected and best corrected, monocularly and binocularly. To test subjects monocularly, occlude the fellow eye in the phoropter or with an occluder (if trial lenses are used) and encourage subjects to read the smallest letters possible even if they have to guess. Visual acuity measurements are based on the total number of correctly read letters. Subjects should be instructed to start with the smallest line where they can read all of the letters. If they miss any letters, go up a line until they are able to read all the letters on a line, then continue to read each subsequently smaller line. The subject should be encouraged to read as many letters possible, even if they have to guess. Testing may be stopped when it is evident that no further readings can be made. Record the total number of letters read correctly on the chart. This will be displayed on the laptop screen along with the logMAR and Snellen acuity. Then begin testing for the fellow eye and repeat with both eyes together for binocular testing.



## APPENDIX I INSTRUCTIONS FOR USE OF M&S NEAR VISUAL ACUITY CHART

Near visual acuity will be measured using the M&S near charts designed for 40 cm. The M&S system background luminance is set to 85 cd/m<sup>2</sup> (range of 80 – 110 cd/m<sup>2</sup> is acceptable). Room lighting is to be set at a level lower than the illumination from the laptop screen. Ambient lighting should be mesopic (30-50 lux) to maximize pupil size. No surface (including reflective surfaces) within the subject's field of vision should exceed the chart background in luminance.

The M&S system should be placed precisely at 40 cm from the subject for testing near visual acuities.

Subjects should be reminded prior to testing that squinting is not allowed. Trial frames should be used for visual acuity testing with careful observation by the testing technician to ensure the subject is not squinting. If squinting is observed, the subject is to be reminded by the testing technician not to squint.

Monocular testing will be completed for each measurement before binocular testing is done. All subjects should be tested monocularly and binocularly, uncorrected and with distance correction in place. Visual acuity measurements are based on the total number of correctly read letters. Subjects should be persuaded to read the smallest letters possible even if they have to guess. Record the total number of letters read correctly for each near test on the case report form.

All subjects will be tested both uncorrected and best corrected, monocularly and binocularly. To test subjects monocularly, occlude the fellow eye in the phoropter or with an occluder (if trial lenses are used) and encourage subjects to read the smallest letters possible even if they have to guess. Visual acuity measurements are based on the total number of correctly read letters. Subjects should be instructed to start with the smallest line where they can read all of the letters. If they miss any letters, go up a line until they are able to read all the letters on a line, then continue to read each subsequently smaller line. The subject should be encouraged to read as many letters possible, even if they have to guess. Testing may be stopped when it is evident that no further readings can be made. Record the total number of letters read correctly on the chart. This will be displayed on the laptop screen along with the logMAR and Snellen acuity. Then begin testing for the fellow eye and repeat with both eyes together for binocular testing.

## APPENDIX J INSTRUCTIONS FOR DEFOCUS CURVE TESTING USING THE M&S SYSTEM

All defocus curve testing is to be performed using the M & S Technologies CTS-1000 Smart System in logMAR format (100% contrast) at a distance of 4.0 meters and calibrated to a photopic luminance of 85 cd/m<sup>2</sup> (range 80-110 cd/m<sup>2</sup> is acceptable).

The M&S system background luminance is set to 85 cd/m<sup>2</sup> (range of 80 – 110 cd/m<sup>2</sup> is acceptable). Room lighting is to be set at a level lower than the illumination from the laptop. Ambient lighting should be mesopic (30-50 lux) to maximize pupil size. No surface (including reflective surfaces) within the subject's field of vision should exceed the laptop in luminance.

Subjects should be reminded prior to testing that squinting is not allowed. During defocus curve testing, trial frames will be used to allow observation by the testing technician to ensure the subject is not squinting. If squinting is observed, the subject is to be reminded by the testing technician not to squint.

This test is to be done on all subjects.

Monocular Defocus Curve Testing: Starting with the subject's distance correction in place, begin testing by occluding the left eye and defocusing the image by +2.00 D over the manifest distance correction in the right eye. Subjects should be instructed to start with the smallest line where they can read all of the letters. If they miss any letters, go up a line until they are able to read all the letters on a line, then continue to read each subsequently smaller line. The subject should be encouraged to read as many letters possible, even if they have to guess. Testing may be stopped when it is evident that no further readings can be made. Record the total number of letters read correctly on the chart. This will be displayed on the laptop screen along with the logMAR and Snellen acuity. Then reduce the amount of defocus in the right eye by -0.50 D, to +1.50 D, and repeat the acuity test, recording the visual acuity LogMAR value. Continue to change the defocus in -0.50 D increments in the right eye, repeating the test and documenting the visual acuity LogMAR value at each level of defocus. Continue to change the defocus to -3.00 D over the subject's distance correction.

## APPENDIX K INSTRUCTIONS FOR PUPIL SIZE MEASUREMENTS

### PHOTOPIC PUPIL SIZE:

Pupil size for each eye should be measured under photopic ambient lighting conditions of 480 – 520 lux. Photopic pupil size should be measured using the NeurOptics pupillometer. To measure distance pupil size, have the subject focus the eye not being measured without glasses at a distance target (logMAR 0.4, unless this cannot be seen uncorrected) and record the pupil size measurements. To measure near pupil size, have the subject focus the eye not being measured without glasses at a near target at 40 cm (logMAR 0.4, unless this cannot be seen uncorrected) and record the pupil size measurements.

### MESOPIC PUPIL SIZE:

Pupil size for each eye should be measured under mesopic ambient lighting conditions of 30-50 lux. For mesopic measurements, the NeurOptics pupillometer should be used. To measure distance pupil size, have the subject focus the eye not being measured without glasses at a distance target (logMAR 0.4, unless this cannot be seen uncorrected) and record the pupil size measurements. To measure near pupil size, have the subject focus the eye not being measured without glasses at a near target at 40 cm (logMAR 0.4, unless this cannot be seen uncorrected) and record the pupil size measurements.

## APPENDIX L INSTRUCTIONS FOR KERATOMETRY

Keratometry must be performed prior to dilation and any contact with the cornea (e.g., tonometry or pachymetry) as follows:

1. Measure keratometry using the iDesign System AND an auto or manual keratometer using the same method at each required visit, e.g., if auto keratometry was recorded at the preoperative exam, all keratometry readings postoperatively should be auto K's.
2. **Do not use "sim K"s from the corneal topography unit.**
3. Always record the flat meridian (smaller number, e.g., 42.25) as K1. Record the steeper meridian (larger number, e.g., 43.00) as K2 along with the corresponding axis (e.g., 42.25 / 43.00 x 165).
4. Record spherical corneas by placing the corneal curvature values in both K1 and K2 and marking axes 180 attached to K2 (e.g., 44.00 / 44.00 x 180). **Spherical Ks will not be accepted with axes other than 180 (do not use 0).**

**APPENDIX M SLIT-LAMP EXAM RATINGS****A. Corneal Clarity**

Below is the grading scale to be used for corneal clarity.

<b>Grade</b>	<b>Description</b>
<b>0.0</b>	Clear
<b>0.5</b>	Faint / trace haze
<b>1.0</b>	Mild haze, not affecting refraction
<b>2.0</b>	Moderate haze, refraction possible
<b>3.0</b>	Haze / prevents refraction, AC visible
<b>4.0</b>	Haze / AC not visible

## APPENDIX N      CLINICAL WORKFLOW & LASIK SURGICAL PROCEDURE

### Clinical Workflow:

1. Patients will be measured on the iDesign 1.2 system.
2. The same iDesign system will be used for all measurements (in the event there is more than one iDesign in the center).
3. Preoperatively, iDesign exams will be acquired until an exam is selected for treatment. Postoperatively, a single iDesign exam will be acquired.
4. The iDesign 1.2 system database will be exported using the iDesign Export functionality on the Utilities Tab for all exams of the patient(s) being treated.
5. The exported patient database will be imported into the iDesign 1.3-PRESBY software (modified for this study) on the AMO provided laptop.
6. The treatments for the control and test eyes will be programmed and designed on the iDesign 1.3 PRESBY software. No Physician Adjustment or Percentage Nomogram adjustments will be used.
7. The treatments for the test eye (non-dominant eye) with presbyopia option turned **ON** and the control eye (dominant eye) with presbyopia option turned **OFF** will be calculated on iDesign 1.3-PRESBY software for the selected exams.
8. Treatments will be saved to USB and transferred to the STAR S4 IR laser.
9. Treatments will be executed on the STAR S4 IR laser.

### LASIK Surgical Procedure:

The following steps represent a typical LASIK surgical procedure and should be used as a standard model. Both eyes may be treated on the same day provided that treatment of the first eye is without an adverse event or clinically significant surgical complication. Any epithelial defect on the flap will preclude treatment of the fellow eye. However, placement of a bandage contact lens is at the discretion of the investigator does not preclude treatment of the fellow eye at the same time.

1. At the physician's discretion, administer a systemic medication (e.g., analgesic or sedative).
2. Apply topical ophthalmic anesthetic agent to the operative eye(s).
3. With the subject at the slit lamp and the eye anesthetized, ask the subject to fixate with both eyes on the letter chart at the end of the room. Use a sterile marking pen to mark the limbus at 3 and 9 o'clock. Marking may be facilitated by drying the area to be marked first with a sterile sponge. After marking the eye, ask the subject to close the eyes and keep the eyes closed until they are brought into the laser room.

4. Create a flap with the IntraLase® Femtosecond Laser.
5. Position the subject on the operating chair of the S4 IR Excimer Laser System.
6. Perform a lid scrub with a topical surgical disinfectant.
7. Shield the fellow eye and prepare the operative eye for the procedure.
8. Position chair underneath laser and lock. Turn on the fiducial line and align the subject. Make the adjustments to the surgeon chair and microscope to allow proper positioning and focus.
9. Instill topical ophthalmic anesthetic agent to the operative eye.
10. Place a lid speculum into position.
11. Activate the recording device(s) (e.g., DVD recorder), and begin video acquisition of the subject's procedure.
12. Align the eye with the appropriate hash marks on the reticle by moving the head prior to vacuum pillow deflation.
13. Remove fluid from the fornices with an ophthalmic surgical sponge.
14. Displace the flap toward the hinge.
15. Perform intra-operative pachymetry with an ultrasonic pachymeter if the estimated residual stromal bed depth is  $\leq 320$  microns.  
**NOTE: If the estimated residual stromal bed thickness is < 250 microns, the investigational treatment must not be performed.**
16. Ensure magnification on the operating microscope is 1.6X. Ensure the subject's pupil is centered in the reticle as the subject is fixating on the fixation LED. Focus on the anterior stromal surface.
17. Remind patient to fixate on flashing LED, then activate ActiveTrak and Iris Registration on the STAR S4 IR™ Excimer Laser System.
18. Confirm proper placement of OIB (outer iris boundary).
19. After ensuring that the reticle is centered over the subject's pupil and the subject is viewing the fixation light, fully depress the foot pedal to perform the laser treatment. If necessary, stop the laser and dry the cornea if there is fluid accumulation.
20. Replace the flap and irrigate as necessary. Assure flap is re-adhered.
21. Apply topical ophthalmic medications to the cornea and move the subject away from the laser.
22. Note the intended flap thickness setting used, the treatment time, whether the eye tracker lost track of the eye at any time during the procedure, and the environmental conditions (temperature and humidity).
23. Print the S4 IR Operative Report.
24. Note any adverse events or complications that occurred during treatment. Report any adverse events to the Sponsor.

**APPENDIX O      EXAMPLE PATIENT REPORTED OUTCOMES  
QUESTIONNAIRE****PRVSQ-LASIK/PRK**

**This questionnaire asks about your visual symptoms  
OVER THE LAST 7 DAYS.**

**For ALL questions, please mark an ☐ in the box or boxes  
that best describe your answer.**



The next few questions ask about halos.

**Halos** are bright circles or rings that appear around a source of light, such as oncoming car headlights.

Q1a. Over the last 7 days, how often did you experience halos?

- ☐ Never (**go to question Q2a**)
- ☐ Rarely
- ☐ Sometimes
- ☐ Often
- ☐ Always

If you experienced halos in the last 7 days, please answer the following questions.

Q1b. Did you experience halos... **Check all that apply.**

- ☐ When **not** wearing corrective glasses or contacts
- ☐ When wearing corrective glasses or contacts
- ☐ When wearing any type of sunglasses

Q1c. Did you experience halos... **Check all that apply.**

- ☐ During the day
- ☐ During the night
- ☐ During dawn or dusk

Q1d. Did you experience halos... **Check all that apply.**

- ☐ When driving during the day
- ☐ When driving at night
- ☐ When driving at dawn or dusk

Q1e. Overall, how much were you bothered by halos?

- ☐ Not at all bothered
- ☐ Slightly bothered
- ☐ Moderately bothered
- ☐ Very bothered
- ☐ Extremely bothered

Q1f. Is there anything you have a lot of difficulty with, or do not do, because of halos?

- ☐ No
- ☐ Yes. If Yes, please describe:

---

The next few questions ask about glare.

**Glare** is reflected light making it difficult to see. **Glare** may occur as light reflecting off of water, a window or pavement.

Q2a. Over the last 7 days, how often did you experience glare?

- ☐ Never (**go to question Q3a**)
- ☐ Rarely
- ☐ Sometimes
- ☐ Often
- ☐ Always

If you experienced glare in the last 7 days, please answer the following questions.

Q2b. Did you experience glare... **Check all that apply.**

- ☐ When **not** wearing corrective glasses or contacts
- ☐ When wearing corrective glasses or contacts
- ☐ When wearing any type of sunglasses

Q2c. Did you experience glare... **Check all that apply.**

- ☐ During the day
- ☐ During the night
- ☐ During dawn or dusk

Q2d. Did you experience glare... **Check all that apply.**

- ☐ When driving during the day
- ☐ When driving at night
- ☐ When driving at dawn or dusk

Q2e. Overall, how much were you bothered by glare?

- ☐ Not at all bothered
- ☐ Slightly bothered
- ☐ Moderately bothered
- ☐ Very bothered
- ☐ Extremely bothered

Q2f. Is there anything you have a lot of difficulty with, or do not do, because of glare?

- ☐ No
- ☐ Yes. If Yes, please describe:

---

The next few questions ask about starbursts.

**Starbursts** are lines or rays that appear to surround a source of light, such as oncoming car headlights.

Q3a. Over the last 7 days, how often did you experience starbursts?

- ☐ Never (**go to question Q4a**)
- ☐ Rarely
- ☐ Sometimes
- ☐ Often
- ☐ Always

If you experienced starbursts in the last 7 days, please answer the following questions.

Q3b. Did you experience starbursts... **Check all that apply.**

- ☐ When **not** wearing corrective glasses or contacts
- ☐ When wearing corrective glasses or contacts
- ☐ When wearing any type of sunglasses

Q3c. Did you experience starbursts... **Check all that apply.**

- ☐ During the day
- ☐ During the night
- ☐ During dawn or dusk

Q3d. Did you experience starbursts... **Check all that apply.**

- ☐ When driving during the day
- ☐ When driving at night
- ☐ When driving at dawn or dusk

Q3e. Overall, how much were you bothered by starbursts?

- ☐ Not at all bothered
- ☐ Slightly bothered
- ☐ Moderately bothered
- ☐ Very bothered
- ☐ Extremely bothered

Q3f. Is there anything you have a lot of difficulty with, or do not do, because of starbursts?

- ☐ No
- ☐ Yes. If Yes, please describe:

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The next few questions ask you about sensitivity to light.

**Sensitivity to light** is a decreased ability to tolerate light, such as sunlight, fluorescent light or incandescent light. Such sensitivity can cause discomfort resulting in a need to squint, close or shade your eyes.

Q4a. Over the last 7 days, how often did you experience sensitivity to light?

- ☐ Never (**go to question Q5a**)
- ☐ Rarely
- ☐ Sometimes
- ☐ Often
- ☐ Always

If you experienced sensitivity to light in the last 7 days, please answer the following questions.

Q4b. Did you experience sensitivity to light... **Check all that apply.**

- ☐ When **not** wearing corrective glasses or contacts
- ☐ When wearing corrective glasses or contacts
- ☐ When wearing any type of sunglasses

Q4c. Did you experience sensitivity to light... **Check all that apply.**

- ☐ During the day
- ☐ During the night
- ☐ During dawn or dusk

Q4d. Did you experience sensitivity to light... **Check all that apply.**

- ☐ When driving during the day
- ☐ When driving at night
- ☐ When driving at dawn or dusk

Q4e. Overall, how much were you bothered by sensitivity to light?

- ☐ Not at all bothered
- ☐ Slightly bothered
- ☐ Moderately bothered
- ☐ Very bothered
- ☐ Extremely bothered

Q4f. Is there anything you have a lot of difficulty with, or do not do, because of sensitivity to light?

- ☐ No
- ☐ Yes. If Yes, please describe:

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The next few questions ask you about multiple or double vision.

**Multiple or double vision** is when objects appear as separate or overlapping images.

Q5a. Over the last 7 days, how often did you experience multiple or double vision?

- ☐ Never (**go to question 6a**)
- ☐ Rarely
- ☐ Sometimes
- ☐ Often
- ☐ Always

If you experienced multiple or double vision in the last 7 days, please answer the following questions.

Q5b. Did you experience multiple or double vision... **Check all that apply.**

- ☐ When **not** wearing corrective glasses or contacts
- ☐ When wearing corrective glasses or contacts
- ☐ When wearing any type of sunglasses

Q5c. Did you experience multiple or double vision... **Check all that apply.**

- ☐ During the day
- ☐ During the night
- ☐ During dawn or dusk

Q5d. Did you experience multiple or double vision... **Check all that apply.**

- ☐ When driving during the day
- ☐ When driving at night
- ☐ When driving at dawn or dusk

Q5e. Overall, how much were you bothered by multiple or double vision?

- ☐ Not at all bothered
- ☐ Slightly bothered
- ☐ Moderately bothered
- ☐ Very bothered
- ☐ Extremely bothered

Q5f. Is there anything you have a lot of difficulty with, or do not do, because of multiple or double vision?

- ☐ No
  - ☐ Yes. If Yes, please describe:
-

The next few questions ask you about fluctuating vision.

**Fluctuating vision** is changes in how clearly you see throughout the day.

Q6a. Over the last 7 days, how often did you experience fluctuating vision?

- ☐ Never (**go to question 7**)
- ☐ Rarely
- ☐ Sometimes
- ☐ Often
- ☐ Always

If you experienced fluctuating vision in the last 7 days, please answer the following questions.

Q6b. Did you experience fluctuating vision... **Check all that apply.**

- ☐ When **not** wearing corrective glasses or contacts
- ☐ When wearing corrective glasses or contacts
- ☐ When wearing any type of sunglasses

Q6c. Did you experience fluctuating vision... **Check all that apply.**

- ☐ During the day
- ☐ During the night
- ☐ During dawn or dusk

Q6d. Did you experience fluctuating vision... **Check all that apply.**

- ☐ When driving during the day
- ☐ When driving at night
- ☐ When driving at dawn or dusk

Q6e. Overall, how much were you bothered by fluctuating vision?

- ☐ Not at all bothered
- ☐ Slightly bothered
- ☐ Moderately bothered
- ☐ Very bothered
- ☐ Extremely bothered

Q6f. Is there anything you have a lot of difficulty with, or do not do, because of fluctuating vision?

- ☐ No
- ☐ Yes. If Yes, please describe:

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The next question asks about any other visual symptoms.

Q7. Over the last 7 days, have you experienced any other **visual** **symptoms** not described above?

☐ No

☐ Yes. If Yes, please describe:

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## APPENDIX P CONTACT LENS STUDY PROCEDURES

### Study Materials

Subjects will wear a single vision distance contact lens in their dominant eye and a multifocal contact lens in their non-dominant eye. Details of the lenses are shown in the Table below. Subjects with astigmatism  $\geq 0.75\text{D}$  in the dominant eye and  $\geq 1.25\text{D}$  in the non-dominant eye must be fit with a toric lens in their respective eye. It is recommended that subjects wear their lenses daily for a minimum of 10 hours.

**TABLE 2: Study Lenses**

	<b>PROCLEAR SPHERE (DOMINANT EYE)</b>	<b>PROCLEAR TORIC (DOMINANT EYE)</b>	<b>PROCLEAR MULTIFOCAL D LENS (NON- DOMINANT EYE)</b>	<b>PROCLEAR MULTIFOCAL TORIC D LENS (NON- DOMINANT EYE)</b>
Base Curve (mm)	8.6	8.8	8.7	8.8
Lens Diameter (mm)	14.2	14.4	14.4	14.4
Sphere (D)	-1.00 to -6.00 (0.25 D steps)	-1.00 to -6.00 (0.25 D steps)	-1.00 to -6.00 (0.25 D steps)	-1.00 to -6.00 (0.25 D steps)
Cylinder (D)	N/A	-0.75 to -4.75 (0.50 D steps)	N/A	-0.75 to -4.75 (0.50 D steps)
Add (D)	None	None	+1.50D	+1.50D

### Contact Lens Care

Subjects will be provided with contact lenses as recommended above, and instructed to use a contact lens solution per the instruction of the investigator.

### Storage of Study Lenses

The study materials must be stored in a secure area and administered only by authorized study personnel. It is recommended that all lenses be stored at controlled room temperature (59-86 F).

### Ordering and Accountability of Study Materials



The contact lenses will be ordered by the investigator. The contact lens solutions will be provided by the clinical site.

**Disposal of Consumables**

Study lenses worn by the subject will be disposed of by either the subject or by the investigator.

**APPENDIX Q PATIENT QUESTIONNAIRE – CONTACT LENS STUDY**

Subject Name \_\_\_\_\_ Visit Date \_\_\_\_\_

**1. Please answer the following questions regarding your visual satisfaction and comfort while performing daily activities during the contact lens study.**

	Very Satisfied	Satisfied	Somewhat Satisfied	Somewhat Dissatisfied	Very Dissatisfied	Not Applicable
Driving during daylight	5	4	3	2	1	0
Driving at night	5	4	3	2	1	0
Working on a computer	5	4	3	2	1	0

**2. Please rate your overall experience with the contact lens study over the last 7 days.**

Very Satisfied	Satisfied	Somewhat Satisfied	Somewhat Dissatisfied	Very Dissatisfied	Not Applicable
5	4	3	2	1	0

**Comments:** \_\_\_\_\_

**Investigator Signature** \_\_\_\_\_

## APPENDIX R OCULAR DOMINANCE - DOLMAN TEST

### Hole-in-the-card test

1. Instruct the subject to hold a card with a hole in the middle with both hands at arm's length centered in front of themselves.
2. With both eyes open, view the examiner's nose standing on the other side of the room through the center hole.
3. The examiner is to look directly at the subject, and confirm which eye the subject is using for viewing i.e. the dominant eye.

## APPENDIX S ADVERSE EVENT AND COMPLAINT REPORTING INSTRUCTIONS

All adverse events and complaints related to using AMO products must be reported to AMO.


### ALL ADVERSE EVENTS AND COMPLAINTS:

For events that are not considered serious or related to the study device:

1. Record the event and/or complaint on the case report form that corresponds to the visit during which awareness of the event occurred. Additionally, a complaint may be reported via a telephone call to AMO.
2. Ensure the data are submitted to AMO electronically within a timely manner.

### SERIOUS ADVERSE EVENTS OR DEVICE DEFICIENCIES THAT MAY HAVE LED TO A SERIOUS EVENT

In the event of a serious event (i.e., life- or sight-threatening incident) whether or not related to the device, or a device deficiency that may have led to a serious event, the investigator shall:

1. Notify AMO immediately (no more than 48 hours after learning of the event) as follows:
  - a. Contact the following AMO personnel by phone:  

  - b. Complete a Detailed Adverse Event Form and submit electronically to AMO

### NON-SERIOUS, DEVICE-RELATED EVENTS:

For events that are not considered serious but are believed related to the study device (ADEs):

1. Complete a Detailed Adverse Event Form
2. Ensure the data are submitted to AMO electronically within a timely manner.