# Evaluation of Angle Kappa and Different Intraocular Lens Calculation Formulas in Acrysof® IQ Panoptix Intraocular Lens Outcomes, Visual Disturbances and Patient Satisfaction

**Sponsor:**

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**Study Product:**

AcrySof® IQ PanOptix (TFNT00 and TFNTx0) intraocular lenses

**Protocol Number:**

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**Investigator Agreement:**

I have read the clinical study described herein, recognize its confidentiality and agree to conduct the described trial in compliance with Good Clinical Practices (GCP), the Declaration of Helsinki, this protocol and all applicable regulatory requirements. Additionally, I will comply with all procedures for obtaining informed consent, data recording and reporting, will permit monitoring, auditing, and inspection of my research center, and will retain all records until notified by the sponsor.

Name of the Investigator: _____
Name of the Institution: _____
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**Principal Investigator:** _____
Signature Date

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## INTRODUCTION

Current visual outcomes expectations of cataract patients are similar to those of refractive surgery patients. Their desire is to be spectacle independent for far, intermediate and near vision activities. Some may have already enjoyed freedom from glasses and would like to continue after the cataracts are removed. Different options are available. These options include: mono-vision and presbyopia correcting intraocular lenses (IOL).

Mono-vision can be achieved by setting the non-dominant eye to -1.75 (range may vary according to patient's preference -1.25 to -2.50 D) and the dominant eye to plano at time of cataract surgery, or postoperatively using contact lenses, or undergoing LASIK.
Presbyopia correcting IOLs include accommodative, multifocals, extended depth of focus (EDOF) and the recently approved trifocal IOLs.

Accommodative IOLs are design to expand the range of vision by emulating accommodation. The lens is designed to allow the lens optic to move slightly forward with the contraction of the ciliary muscle. The only accommodative IOL approved in the USA is the Crystalens (Bausch and Lomb). In addition to the non-toric model, there is a toric version (Trulign) that is ideal for patients who also have astigmatism. Different studies have shown limited accommodation (0.25 to 0.75 D), which is not optimal, leading surgeons to target slight residual myopia (-0.50 to -0.75) in the non-dominant eye. Tilting and decentration of the IOL due to contraction and fibrosis of the capsular bag have also been reported.

Multifocal IOLs (MIOL) have evolved since they were initially approved by the FDA in 1997 (Array SA40N, Abbott Medical Optics). MIOL have been classified based on their design as refractive or diffractive. Refractive MIOL (i.e ReZoom, Abbot Medical Optics) reportedly provided better intermediate vision compared to a diffractive MIOL (i.e ReSTOR, Alcon Laboratories) that provides better near visual acuity. Mixing and matching these 2 lenses was an option to overcome the limitations that each one presented providing patients with improved intermediate and near acuities. The ReSTOR has been modified while the ReZoom IOL was discontinued 2 - 3 years ago. The original ReSTOR had a +4.0 D add delivering good uncorrected distance and uncorrected near visual acuities (UCDVA and UCNVA) with a reading distance of 33 cm but with limited intermediate acuity. Two additional ReSTOR models are currently available in the market, a +3.0 D add to enhance the intermediate distance vision with a reading distance of 40 cm, and a +2.5 D add ideal for people who are interested in distance and intermediate vision (50 - 60 cm) activities. One potential disadvantage of the low add multifocal IOLs is the visual performance at near. Similarly, to mixing and matching, the use of a ReSTOR +3.0 in one eye and

the +2.5 in the fellow eye, known as blended vision, is an option to improve patients' vision at the different distances reducing their dependence on glasses.

Trifocal IOLs (a type of MIOL), specifically the PanOptix IOL, have been widely use in Europe, Canada and South America and was approved in the USA by the U.S. Food and Drug Administration (FDA) on August 27, 2019. Since its approval, it is becoming the presbyopia correcting lens of choice in the US. Because of the way the lens is designed, it provides good intermediate vision without compromising the near or the distance visions overcoming the limitation that previous multifocal lenses presented.

The main complaint of patients who received a MIOL (regardless of the design) are visual disturbances such as glare, halos (rings around lights), starbursts (rays around light sources), mainly at night. The degree of limitation or how bothered patients are varies from patient to patient. To explain these symptoms different theories have been proposed including splitting the light into different focal points which decreases the intensity of the light reaching the retina. Most factors are common to all patients who received the lens; however, patients are not equally affected by these symptoms. Angle kappa has been considered a factor. Angle κ is the angle between the visual axis (straight line that passes through both the center of the pupil and the center of the fovea) and the pupillary axis (perpendicular line to the surface of the cornea that passes through the center of the pupil), figure 1. The larger the angle kappa the more symptoms.

## 1. OBJECTIVE:

The purpose of this study is to evaluate the effect of angle kappa in outcomes, patient satisfaction and visual disturbances in patients with and without astigmatism implanted bilaterally with the PanOptix toric and non-toric IOL after routine cataract surgery as well as to evaluate intraocular (IOL) calculation formulas.

## 2. STUDY DESIGN AND METHODS:

**2.1. Test article:** AcrySof® IQ PanOptix IOL (TFNT00 and TFNTx0 – Alcon Laboratories).

**2.2. Study Design:** Prospective, single center, bilateral eye study.

### 2.3. Subjects:

#### 1. Inclusion Criteria:

Subjects MUST fulfill the following conditions to qualify for enrollment into the trial

1. Subject is undergoing bilateral lens extraction with intraocular lens implantation.
2. Gender: Males and Females.
3. Age: 40 years and older.
4. Willing and able to provide written informed consent for participation in the study

5. Willing and able to comply with scheduled visits and other study procedures.
6. Scheduled to undergo standard cataract surgery with topical anesthesia in both eyes within 6 to 30 days between surgeries.
7. Subjects who require an IOL power in the range of +6.0 D to +30.0 D only.
8. Subjects who require a TFNT00 or TFNT30 to TFNT60 IOL.
9. Potential postoperative visual acuity of 0.2 logMAR (20/32 Snellen) or better in both eyes.

## 2. Exclusion Criteria:

Subjects with ANY of the following conditions on the eligibility exam may NOT be enrolled into the trial.

1. Severe preoperative ocular pathology: amblyopia, rubella cataract, proliferative diabetic retinopathy, shallow anterior chamber, macular edema, retinal detachment, aniridia or iris atrophy, uveitis, history of iritis, iris neovascularization, medically uncontrolled glaucoma, microphthalmos or macrophthalmos, optic nerve atrophy, macular degeneration (with anticipated best postoperative visual acuity less than 20/30), advanced glaucomatous damage, etc.
2. Subjects who require a higher toric power than the one available (TFNT60).
3. Uncontrolled diabetes.
4. Use of any systemic or topical drug known to interfere with visual performance.
5. Contact lens use during the active treatment portion of the trial.
6. Any concurrent infectious/non-infectious conjunctivitis, keratitis or uveitis.
7. Clinically significant corneal dystrophy
8. History of chronic intraocular inflammation.
9. History of retinal detachment.
10. Pseudoexfoliation syndrome or any other condition that has the potential to weaken the zonules.
11. Previous intraocular surgery.
12. Previous refractive surgery.
13. Previous keratoplasty
14. Severe dry eye
15. Pupil abnormalities
16. Anesthesia other than topical anesthesia (i.e. retrobulbar, general, etc).
17. Any clinically significant, serious or severe medical or psychiatric condition that may increase the risk associated with study participation or may interfere with the interpretation of study results.
18. Participation in (or current participation) any ophthalmic investigational drug or ophthalmic device trial within the previous 30 days prior to the start date of this trial.

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

### 3. Exclusion Criteria during surgery

If any of the following exclusion criteria are applicable to the study eye, the subject should not continue in the study.

1. Other ocular surgery procedures, i.e. iStent, anterior vitrectomy
2. Significant vitreous loss
3. Significant anterior chamber hyphema
4. Uncontrollable intraocular pressure
5. Zonular or capsular rupture
6. Bag-sulcus, sulcus-sulcus or unknown placement of the haptics
7. Suturing of incision required at time of surgery
8. Intraocular lens tilt or decentration
9. Significant sedation or retrobulbar block during surgery
10. Other procedure, such as pupil stretch, expanders, iris hooks during surgery

**Note:** Any subject in which surgery has been aborted for either eye should immediately be discontinued from the study and an exit form completed for that subject. These subjects will be followed up as per the clinic standard of care, monitored for safety, and their data will be excluded from the study efficacy analysis (obtained from FDA Database Research Results Feb, 05, 2009). All adverse events will be appropriately documented and reported.

Additionally, participants who are considered to be a vulnerable subject population are not to be enrolled into the study without prior written authorization from both the Sponsor and the IRB to ensure that a description of additional safeguards are in place during the consenting and enrollment processes. Vulnerable populations include, but are not limited to, the following:

1. Prisoners
2. Nursing home residents /institutionalized individuals
3. Mentally disabled /cognitively impaired individuals
4. Sponsor employees and their family members
5. Site employees and their family members that are directly and indirectly involved with the study
6. Students of the university or the principal investigator participating in the study
7. Economically and/or educationally disadvantaged individuals
8. Comatose individuals / traumatized individuals
9. Adults who do not read and/or write
10. Hearing impaired individuals
11. Terminally ill individuals / individuals with life-threatening conditions

# 3. Study Procedures

## 3.1. Informed Consent / Subject enrollment

Potential subjects will be identified from the patients presenting at the clinic. Additionally, a flyer will be placed in the check-in area of the different locations and on the practice website. Once identified as a study candidate, the patient will be asked if he/she would like to participate. The sub-investigator, study coordinator or an appropriately trained staff member will answer any and all questions and will obtain informed consent. A copy of the signed informed consent document will be given to the subject. The principal investigator will be available if the subject wants to discuss further details with him. Any testing that is part of the investigative site's standard preoperative cataract evaluation may be performed prior to the informed consent being signed, provided these tests are conducted within 90 days of surgery. The patient will understand that participation in the study, or declining to participate, will not affect his/her quality of care.

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

## 3.2. Surgery Procedures:

Patients will be received either a non-toric or toric PanOptix IOL based on the amount of astigmatism. Target refraction OU plano (±0.25 D).

## 3.3. Study Visit Schedule and Assessments (Table 1).

1. **Visit Schedule:** Subjects will be examined at the following intervals:

1. Visit 1: Screening and enrollment: Preoperative evaluation completed not more than eight weeks before surgery
2. Visit 2: Day of Surgery for each eye
3. Visit 3: Month 3: 90 ±15 days postoperative after second eye surgery

## 3.4. Measurements and evaluations

1. Visit 1: Informed consent process will be conducted at this visit. Assessments include best-corrected Snellen visual acuity, manifest refraction, intraocular pressure (IOP) using Goldman tonometer, slit lamp examination including dilated fundus exam,

cataract density and type, and angle kappa measured using OPD III scan, and visual symptoms, patient satisfaction and spectacle independence questionnaires. Any testing that is part of the site's preoperative cataract surgery standard of care evaluation may be performed prior to signing the informed consent provided these tests are conducted within 90 days of the surgery and notation of the date performed is entered onto the CRF. The surgeon's standard pre-cataract surgery treatment will be used in all patients

2. Visit 2: The surgeon may use his preferred cataract extraction technique (manual or laser). The lens will be implanted in the bag. The following information will be captured the day of surgery: phaco technique (manual or laser), lens implanted and power, target refraction for IOL power implanted using Barrett Universal II, Hill RBF, Holladay 2, Holladay 1 and SRK-T formulas, residual astigmatism and axis for Barrett Toric Calculator and Barrett TK for toric power calculation (if applicable), additional surgical procedures, intraoperative complications, and any device deficiencies. The surgeon's standard post cataract surgery treatment will be used in all patients.

3. Visit 3: Slit lamp examination, manifest refraction, UCVA, BCVA, UCIVA (at 60 cm), DCIVA (at 60 cm), UCNVA (at 40 cm) and DCNVA (at 40), and UCNVA at best distance, IOP, IOL orientation, dilated fundus exam (as deem necessary by the investigator), angle kappa measured using OPD III scan, visual symptoms, patient satisfaction and spectacle independence questionnaires, adverse events and any device deficiencies.

All adverse events and complaints will be monitored and recorded at all study visits.

**Table 1.** Visits and Study Assessments

| | Visit 1 Screening | Visit 2 and 2A DOS | Visit 3 3-Month 90 ±15 days |
|---|---|---|---|
| Informed Consent | X | | |
| Inclusion/Exclusion | X | X | |
| Demographics/PMH/Ocular history | X | | |
| Snellen BCVA | X | | |
| Snellen Manifest refraction | X | | |
| UCVA ETDRS (4m) | | | X* |
| Manifest refraction – Max Plus | | | X |
| BCVA ETDRS (4m) | | | X* |
| UCIVA ETDRS (60 cm) | | | X* |
| DCIVA ETDRS (60 cm) | | | X* |

| | | | |
|---|---|---|---|
| UCNVA ETDRS (40 cm) | | | X* |
| DCNVA ETDRS (40 cm) | | | X* |
| UCNVA at best distance | | | X* |
| Intraocular Pressure (Goldman) | X | | X |
| SLE | X | | X |
| Dilated fundus exam | X | | X† |
| Cataract density / type | X | | |
| OPD III scan | X | | X |
| IOL Power calculation using different formulas | X | | |
| Toric IOL calculation | X** | | |
| Intraoperative data | | X | |
| Toric IOL position | | X** | X† |
| Questionnaires | X | | X |
| AE/Device deficiencies | | X | X |

X To be performed as scheduled
* Monocular and binocular testing
** If a toric lens is used
† To be performed as deem necessary by the investigator

## 4. Study endpoint criteria

4.1. Patient Completion of Study: If a study patient has completed the final visit (Visit 3) of the study, he/she is considered to have completed the study.

4.2. Patient Discontinuation: Each study patient may voluntarily discontinue the study at any time they choose. Study patients who cannot complete the study for administrative reasons (e.g., non-compliance, failure to meet visit schedule, etc.) will be discontinued from the study. Study patients discontinued during the enrollment phase (prior to surgery) of the study will be replaced.

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

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

4.5. Study Completion: The study will be complete when all enrolled patients have completed Visit 3 or have been terminated from the study.

## 5. STATISTICAL CONSIDERATIONS

### 5.1. Sample size

A total of 30 subjects will be enrolled. In order to calculate the sample size, we need to know an accurate estimate of the standard deviation of the outcome measure which we do not know; therefore, we consider this study a pilot trial. When estimating the sample size for a pilot study, the simplest method is to apply a sample size rule of thumb. Browne suggests a general flat rule to 'use at least 30 subjects or greater to estimate a parameter'.

### 5.2. Statistical Analysis

All data will be collected by the site and entered into a database. Subjects will be assigned an ID number. Data analysis will be performed without patient identification. Statistical analysis will be performed using standard descriptive statistics. Analysis will include stratification based on the amount of preoperative angle kappa as follows: 0 to < 0.3 mm, 0.3 mm to < 0.4 mm and 0.4 mm or higher. Data analysis will be conducted by a third-party consultant.

### 5.3. Study Endpoints:

1. Primary Endpoint:
   a. Effect of angle kappa in visual disturbances and patient satisfaction

2. Secondary Endpoints:
   a. Proportion of eyes within ±0.50 D of intended target (plano) when using the Barrett Universal II formula for IOL power calculation
   b. Proportion of eyes within ±0.50 D of intended target (plano) when using the Hill RBF formula for IOL power calculation
   c. Proportion of eyes within ±0.50 D of intended target (plano) when using the Holladay 2 formula for IOL power calculation
   d. Proportion of eyes within ±0.50 D of intended target (plano) when using the Holladay 1 formula for IOL power calculation
   e. Proportion of eyes within ±0.50 D of intended target (plano) when using the SRK-T formula for IOL power calculation
   f. Proportion of eyes with residual astigmatism of 0.50 D or less when using the Barrett Toric Calculator
   g. Proportion of eyes with residual astigmatism of 0.50 D or less when using the Barrett TK for toric power calculation

### 5.4. Safety Analyses

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

## 6. DATA HANDLING AND RECORD KEEPING

### 6.1. Confidentiality

To ensure confidentiality in this study, records of the participants will be examined only by the principal investigator and research staff involved in the study. Study records will be kept on file. Any statistical analysis and publication will not include any subject identifiers. Medical records will be made available only for review by the investigators, Sponsor Company or Research Institution, the IRB, and other State or Federal Regulatory Agencies, if necessary. All information in these records will be kept confidential.

### 6.2. Records Retention

The PI is accountable for the integrity, retention and security of all study related data. The investigator must maintain accurate, complete and current records relating to the clinical study. The investigator must maintain the required records during the investigation and for a period of 2 years after the date on which the investigation is terminated or completed. Records will be scanned and kept electronically in a secured server.

## 7. STUDY MONITORING, AUDITING, AND INSPECTING

The nature and location of all source documents will be identified to ensure that original data required to complete the case report forms (CRFs) exist and are accessible for verification. If electronic source records are maintained, these records must be 21 CFR Part 11 compliant and will be printed and certified for verification as needed.

Required examination must be recorded on the CRFs. CRFs will be used as source document. All data reported must have corresponding entries in the source documents. The principal investigator or sub-investigator must review the reported data and certify that the CRFs are accurate and complete. No subject identifiers should be recorded on the CRFs beyond subject number, subject initials and study specific identifiers.

Data from CRFs will be entered into a database. Upon completion of the CRFs, the data will be reviewed by study designated personnel and statistician for accuracy and completeness. If corrections and/or any additions to the data are deemed necessary, queries will be generated. Designated research staff expected to respond to data queries in a timely manner and ensure that the corrections and changes made to the data in the database are reflected in the subjects' source documentation. Any changes will need to be initialed and dated by the authorized personnel making such changes.

Data will not be sold to third parties.

## 8. INVESTIGATIONAL PRODUCT

### 8.1. Description

Acrysof® IQ PanOptix Intraocular Lens is a non-apodized diffractive trifocal IOL that distributes light energy to three focal points in both small and large pupil conditions with a near focal point distance of 40 cm and intermediate focal point at 60 cm providing increased spectacle independence without compromising distance vision.

### 8.2. Treatment/Dosing Regimen

The IOL will be implanted at time of uncomplicated routine cataract surgery. Intraocular lenses are implantable medical devices and are intended for long term use over the lifetime of the patient.

### 8.3. Method for Assigning Subjects to Treatment/Dosing Groups

N/A

### 8.4. Subject Compliance Monitoring

Since the IOL is implanted at time of cataract surgery, subject compliance will not be an issue in this particular study.

### 8.5. Packaging, Receiving, Storage, Dispensing and Return

N/A

## 9. ETHICAL CONSIDERATIONS

This clinical trial will be conducted in accordance with the principles of the Declaration of Helsinki, and Good clinical practice. The Investigator and all clinical trial staff will conduct the clinical trial in compliance with this protocol. The Investigator will ensure that all personnel involved in the conduct of the clinical trial are qualified to perform their assigned duties through relevant education, training, and experience. Deviations from the clinical protocol must be documented in each subject's study records including the dates and reasons for each deviation. The PI must ensure that all aspects of the trial follow the applicable regulatory laws and conditions of approval imposed by the IRB.

## 10. IN CASE OF AN INJURY RELATED TO THIS RESEARCH STUDY

Every effort to prevent study-related injury will be taken by the study doctor and staff. In the event a patient is injured as a direct result of the study while following the study instructions and requirements, the patient will be instructed to immediately contact the principal investigator and/or study staff. Treatment will be provided as needed for those injuries caused directly by this research study. In the event of injury or illness caused by or occurring during the participation in this study, all charges for medical care provided will be billed to

the patient's insurance company. The medical care costs for injuries or illnesses that are not caused directly by the research study will not be covered.

## 11. CONFIDENTIALITY/PUBLICATION OF THE STUDY

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

## 12. REFERENCES

1. Walkow L, Klemen UM. Patient satisfaction after implantation of diffractive designed multifocal intraocular lenses in dependence on objective parameters. Graefes Arch Clin Exp Ophthalmol. 2001; 239:683-7.
2. Fu Y, Kou J, Chen D, et al. Influence of angle kappa and angle alpha on visual quality after implantation of multifocal intraocular lenses. J Cataract Refract Surg. 2019; 45:1258-1264
3. Qi Y, Lin J, Leng L, et al. Role of angle κ in visual quality in patients with a trifocal diffractive intraocular lens. J Cataract Refract Surg. 2018; 44:949-954

Figure 1. Angle kappa shown using the OPD - scan III (Nidek, Co)