Clinical Protocol 2018-008
Effect of TrueTear use on anterior corneal surface imaging quality

PRINCIPAL INVESTIGATOR: Francis W. Price, Jr. MD
CO-INVESTIGATORS: Matthew T. Feng, MD; Kathleen Kelley, OD; Faye Peters, OD; Ashlyn Lynn, OD

Price Vision Group &
Cornea Research Foundation of America
9002 N. Meridian St.
Indianapolis, IN 46260

PURPOSE OF THE STUDY:
To evaluate the utility of TrueTear™ to improve anterior corneal surface imaging quality before cataract surgery, refractive lens exchange, or laser refractive surgery.

BACKGROUND:
Consistent and accurate mapping of the ocular surface is required to perform accurate preoperative calculations for a variety of "refractive" surgeries including cataract surgery, refractive lens exchange, and laser refractive surgery. Accurate mapping of the anterior surface of the eye is needed in order to obtain "keratometry" readings with a topographer (Tomey) and an optical biometer (LensStar™) to determine the appropriate intraocular lens power to implant in association with cataract surgery or refractive lens exchange. Likewise with new topography-directed laser refractive treatments using Contoura™ mapping of the cornea, it is essential that the mapping reflect the accurate contour of the ocular surface and not distortions caused by dry spots on the surface. If the imaging includes surface irregularities caused by dry spots, then the excimer laser treatment would transfer these irregularities onto the cornea, permanently distorting the optical system of the eye and causing poorer vision rather than improved vision.

The importance of a normal tear film for accurate corneal surface imaging has long been recognized,[1,2] and becomes particularly apparent when patients have dry eyes and/or low ambient humidity stresses patients' ocular surfaces causing the three imaging systems noted above to produce unusable images. During imaging, the eye may be open for a longer than normal interval between blinks, and the dryer the ambient air or the more stressed the ocular surface is from underlying disease, the more distorted these images can become. Using artificial tears, humidifiers, or having patients sit with their eyes closed for 20 to 30 minutes does not reliably improve the test results.

Because the TrueTear™ system uniquely improves all three layers of the tear film, we hypothesize that use of this device could be beneficial for obtaining more accurate imaging when the imaging is negatively impacted by the quality of the ocular surface.[3,4]

STUDY SPONSOR: Cornea Research Foundation of America
9002 N. Meridian St., Ste 212, Indianapolis, IN 46260

STUDY DESIGN:
This is a single-center cohort study.

CHARACTERISTICS OF THE RESEARCH POPULATION:

NUMBER OF SUBJECTS:
50 subjects scheduled to undergo cataract surgery or refractive lens exchange and 50 subjects scheduled to undergo laser refractive surgery will be enrolled for a total of 100 subjects.

GENDER OF SUBJECTS:
Males and females will be enrolled.

AGE OF SUBJECTS:
Age 18 years and older will be enrolled because that is typically the minimum age for these surgeries.

RACIAL AND ETHNIC ORIGIN:
Subjects can be of any racial and ethnic origin.

INCLUSION CRITERIA:
- Male or female of any racial or ethnic origin, age 18 years or older
- Able to provide written, informed consent
- Scheduled to undergo routine imaging for cataract surgery, refractive lens exchange, or laser refractive surgery

EXCLUSION CRITERIA:
- A cardiac pacemaker, implanted or wearable defibrillator, or other implanted metallic or electronic device (e.g. cochlear implant) in the head or neck
- Chronic or frequent nosebleeds, a bleeding disorder (e.g. hemophilia), or another condition that can lead to increased bleeding
- A known hypersensitivity (allergy) to the hydrogel material that comes into contact with the inside of the nose during use of the TrueTear™ device
- Pregnancy
- Presence of any ocular disease or condition which in the investigator's opinion would confound the study results

VULNERABLE SUBJECTS:
Most study subjects will be new patients, but it's possible that a few long-term patients might be interested in enrolling. To minimize coercion, the study consent clearly states that participation is voluntary and the decision whether to participate or not will not affect the patient's care.

METHODS AND PROCEDURES:

SCREENING: Prospective subjects who are scheduled to undergo imaging for cataract surgery, refractive lens exchange, or laser refractive surgery will be considered for enrollment into the study. Medical and ophthalmic histories will be recorded.

ENROLLMENT: Subjects who meet the inclusion and exclusion criteria will be informed about the opportunity to participate in the study. Subjects will be entered into the study after providing written informed consent. Each subject will be instructed that if they decide to participate, they may withdraw at any time.

EXAMINATION: Subjects are expected to complete the study in one visit.

Table 1. Visit Schedule	**Visit 1**
Informed Consent	X
Inclusion/Exclusion	X
Medical & Ophthalmic History	X
SPEED (dry eye symptom) Questionnaire	X
Ophthalmic Examination	X
Anterior corneal surface imaging	X
Use TrueTear™ device	X
Repeat anterior corneal surface imaging	X
Adverse Events	X

IMAGING:

- All subjects will have 3 images taken of the anterior corneal surface with the Tomey topographer.
- Cataract surgery and refractive lens exchange patients will have 5 LensStar™ images taken.
- Laser refractive surgery patients will have 10 Contoura™ images taken.
- The imaging will be done before and after use of the TrueTear™ device.

STUDY TREATMENT: Subjects will be carefully instructed regarding proper use of the TrueTear™ device. The device will be utilized for 3 sequential 1-minute cycles at the intensity level selected by the patient to provide a gentle tingling sensation.

PRECAUTIONS FOR MINIMIZING POTENTIAL RISKS

The study will use an FDA-approved device. Subjects assigned to TrueTear™ will be carefully instructed in proper use. The instructions for use note that the most frequently reported adverse events (≥2% incidence) were nasal pain, discomfort or burning, transient electrical discomfort, nosebleed, nasal congestion, headache, trace blood in nostril, and facial pain.

Subjects will be instructed to let the investigator or study coordinator know immediately if they notice any problems or discomfort. Any study subject who experiences an adverse event will receive appropriate treatment and be allowed to immediately withdraw from the study.

SAMPLE AND DATA ANALYSIS:

The primary outcome measure will be the change in the ocular surface asymmetry index (SAI) after use of the TrueTear™ device. The null hypothesis is that the mean SAI will not change significantly after TrueTear™ use. The research hypothesis is that SAI will decease significantly after TrueTear™ use. The hypothesis will be assessed using a one-sided paired t-test at a significance level of 0.05. Secondary outcome measures will include the change in the surface regularity index (SRI) measured with corneal topography and the variances of the keratometry readings obtained with the topographer, Lenstar, and Contoura imaging devices. The study participants will be scored on baseline signs and symptoms of ocular dryness and associations between the outcome measures and ocular dryness scores will be assessed.

This is a first-of-its-kind study. Considering the range of patients who undergo each type of surgery, we anticipate that enrollment of 50 subjects per treatment arm in each surgical cohort will provide adequate statistical power to detect clinically meaningful differences.

REFERENCES:

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4. Gumus K, Schuetzle KL, Pflugfelder SC. Randomized controlled crossover trial comparing the impact of sham or intranasal tear neurostimulation on conjunctival goblet cell degranulation. Am J Ophthalmol 2017;177:159-68.