STU00213080

PROTOCOL TITLE: Anterior-segment OCT (AS-OCT) and intraoperative OCT (iOCT) for trans-conjunctival needle revision (TCNR) of trabeculectomy bleb

PRINCIPAL INVESTIGATOR:

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STUDY SUMMARY:

Investigational Agent(s) (Drugs or Devices)	N/A
IND / IDE / HDE #	
Indicate Special Population(s)	☐ Children ☐ Children who are wards of the state ☐ Adults Unable to Consent ☐ Cognitively Impaired Adults ☐ Neonates of Uncertain Viability ☐ Pregnant Women ☐ Prisoners (or other detained/paroled individuals) ☐ Students/Employees
Sample Size	Prospective study: 25 Subjects Retrospective study (historical controls): 25 subjects
Funding Source	Department of Ophthalmology Illinois Society for the Prevention of Blindness
Indicate the type of consent to be obtained	☒ Written ☐ Verbal/Waiver of Documentation of Informed Consent ☐ Waiver of HIPAA Authorization ☐ Waiver/Alteration of Consent Process

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Site	☐ Lead Site (For A Multiple Site Research Study) ☐ Data Coordinating Center (DCC)
Research Related Radiation Exposure	☐ Yes ☒ No
DSMB / DMC / IDMC	☐ Yes ☐ No

OBJECTIVES:

The aim of the research is to assess the surgical success, feasibility and utility of pre-operative Anterior Segment Optical Coherence Tomography (AS-OCT) and intraoperative Optical Coherence Tomography (iOCT) in trans-conjunctival needle revision (TCNR) of trabeculectomy bleb. Furthermore, we want to assess whether AS-OCT can be used to identify characteristics of trabeculectomy blebs that are associated with successful surgical outcomes.

To undergo this study, we will conduct a prospective study of patients who consent to AS-OCT and iOCT revision of TCNR. We will compare the outcomes of these patients with retrospectively identified, historical controls (i.e. patients who underwent TCNR by the same surgeon without AS-OCT or iOCT assistance).

We hypothesize that information gained from pre-operative AS-OCT and intraoperative OCT will aid with intraoperative decision-making for TCNR of trabeculectomy bleb and will thereby improve surgical outcomes. We also hypothesize that preoperative AS-OCT can be used to identify features of trabeculectomy bleb that can predict success with iOCT-assisted TCNR. More specifically, we hypothesize that filtering blebs with more extensive scarring as seen on pre-operative AS-OCT will benefit from iOCT.

BACKGROUND:

Trabeculectomy is one of the most commonly performed glaucoma procedures performed to control IOP with approximately 18,000 operations performed in US Medicare beneficiaries

alone in 2012.[1] One complication of trabeculectomy surgery is the formation of subconjunctival and episcleral fibrosis, which occurs as part of the wound healing process and can result in fibrosis of the filtering bleb and failure. Transconjunctival needle revision (TCNR) aims to lyse subconjunctival adhesions and reestablish adequate aqueous humor flow from the anterior chamber to the subconjunctival space. One study reported 17% of trabeculectomies require bleb-needling revision.[2] During TCNR the surgeon is able to visualize the trajectory of the needle or blade under the conjunctiva; however, detection of the fibrotic tissue and determination as to whether that tissue has been adequately lysed is difficult, limiting the success rate of the procedure.

Anterior segment optical coherence tomography (AS-OCT) allows for detailed assessment of the internal morphology of the bleb. Studies have utilized AS-OCT to assess morphological features of the bleb and correlate it with surgical success.[3,4,7] A small case series reported the utility of AS-OCT for pre-operative planning for bleb revision, in particular, identifying safe access sites and minimizing conjunctival dissection.[5]

More recently, real time OCT integrated with operative microscope has become available. Intraoperative OCT (iOCT) has been utilized extensively in retinal surgery and corneal surgery.[6] Dada et al., described performing iOCT-guided TCNR in 2 patients with failed trabeculectomy blebs without intraoperative or postoperative complications.[7] These authors report they were able to obtain a detailed view of the bleb wall and assess the depth and location of the needle, which permitted better lysis of adhesions. A pilot study by Kumar et al., reported one case of TCNR in which iOCT was used to demonstrate the extent of adhesions and loculations inside the bleb at the beginning of the procedure, and the lysis of these adhesions and formation of large single hyporeflective cavity inside the bleb at the end of the procedure.[8] These small case studies suggest a role of iOCT imaging for TCNR, however, further research is needed to assess its feasibility and utility for routine use.

STUDY ENDPOINTS:

Results from the following tests obtained as part of this study:

1. Spectralis Anterior-segment OCT (AS-OCT) (Heidelberg Engineering) available in Lavin 15th floor Ophthalmology clinic
2. Digital microscope integrated with Intraoperative OCT (Zeiss Artevo 800, Carl Zeiss Meditec AG) available in the Lavin 11th floor operating room

The primary outcome will be surgical success, defined as a 20% reduction in unmedicated IOP below the pre-operative baseline at the post-operative visits (POD1, POM1, POM3). The success rate will be compared to a cohort of historical controls comprised of a consecutive series of age- and race-matched subjects who underwent TCNR in the operating room by the same surgeon, with the same intraoperative anti-fibrotic therapy, without AS-OCT or iOCT imaging during a five-year time period from 6/1/2015 to 6/1/2020.

The secondary outcomes will be feasibility and utility of intraoperative OCT. Feasibility will be defined as the percentage of cases with successful imaging of the bleb with iOCT. Utility will be defined as the percentage of cases in which iOCT changed surgical decision-making. Intraoperative OCT will be used to determine whether adhesions have been completely lysed and/or whether further lysis of adhesions is necessary. A survey with set of questions based on prior literature[6] will be used to assess these parameters.

We will also assess whether findings seen with pre-operative AS-OCT can predict what type of blebs will benefit from iOCT-assisted TNCR. Features of AS-OCT and iOCT imaging that will be assessed include quality of image capture, visualization of surgical site, and characteristics of the bleb. Characteristics of the surgical site include bleb height, internal reflectivity, location and number of adhesions, and presence of cysts, cavities, and fistulas.

STUDY INTERVENTION(S) / INVESTIGATIONAL AGENT(S):

This prospective study will include approximately 25 patients with open-angle glaucoma who will undergo TCNR of trabeculectomy bleb by a glaucoma specialist at Northwestern Medicine. These patients will have a history of glaucoma and failed trabeculectomy bleb (as evidenced by clinical features and elevated IOP). During routine clinic visit, the patient will undergo lit lamp grading of bleb by Indiana Bleb Appearance Grading Score (IBAGS).[4,9] Subjects who agree to participate and provide written informed consent will undergo AS-OCT imaging (Spectralis OCT, Heidelberg) of the bleb. During their operation, the Zeiss Artevo digital microscope integrated with iOCT (Zeiss Artevo 800, Carl Zeiss Meditec AG), a commercially available device will be utilized to visualize and evaluate the morphology of the trabeculectomy bleb at the start and conclusion of the case.

PROCEDURES INVOLVED:

The devices used in the study are commercially available and have been used extensively in ophthalmology and intraocular surgery. Therefore, no experimental devices will be used. The AS-OCT is routinely obtained and is considered standard of care. The iOCT is commercially available and is also utilized routinely in ophthalmic surgery, particularly for retinal surgery.

The Zeiss Artevo digital microscopy integrated with intraoperative OCT will be used as an adjunct to TCNR. Published research[4,6] has not shown iOCT to increase risk of complications associated with routine TCNR and we believe injury from imaging is not biologically plausible. Surgery and iOCT will be recorded and saved to a secure NMH server. The surgical videos will only be used for research purposes.

Review of medical records will be performed for patients who agree to participate in the prospective study. Data gathered will include basic demographic information and clinical data relevant to glaucoma management (visual acuity, intraocular pressure, medications, disease

severity). Post-operative course including intraocular pressure, intraoperative or post-operative complications and repeat TCNR or additional surgery will also be collected.

Furthermore, a retrospective review of medical records will be performed for patients who underwent TCNR without iOCT or AS-OCT assistance by the same surgeon during the period from June 1, 2015 to June 1, 2020. This group of patients will serve as historical controls. These individuals will be identified using Enterprise Data Warehouse and billing data. We aim to identify approximately 25 controls. The selection criteria for controls are 1) age within 5 years of each study patient 2) same race as study patient 3) diagnosis of open angle glaucoma and 4) adequate follow up of at least 3 months.

DATA AND SPECIMEN BANKING

Participants will be assigned a study ID. The patient identifiers will be stored separately from the coded study data.

Data abstracted from the medical record will be collected on a secure sever, with computers only accessible with passwords. Only the research team will have access to the identified data.

SHARING RESULTS WITH PARTICIPANTS

The results are part of the standard glaucoma care for each participant and they will be discussed with participants as part of the management of the condition.

STUDY TIMELINES

The participant will be in the study for the duration of their office visit (with AS-OCT testing) and surgery. In the context of this research study, participants will also be followed for 12 months after surgery to assess their post-operative course.

It will likely take approximately 12 months to enroll all study participants. The estimated date for completion of primary analyses will be 6 months after enrollment of study.

INCLUSION AND EXCLUSION CRITERIA

Inclusion criteria

- Briefly, the diagnosis of glaucoma is based on the presence of 2 or more of the following findings: 1) glaucomatous optic disc damage, defined as the presence of optic disc excavation, diffuse or focal neuroretinal rim thinning or notching, localized or generalized RNFL thinning; 2) visual field defects consistent with glaucoma; and 3) IOP ≥ 22 mmHg.
- Patients with glaucoma who have been advised to undergo TCNR of a failed trabeculectomy bleb by a glaucoma specialist at Northwestern Medicine
- History of failed trabeculectomy (based on clinical features of the trabeculectomy bleb and elevated intraocular pressure)
- Patients can have history of other glaucoma surgery or cataract surgery
- The diagnosis of glaucoma is based on the presence of 2 or more of the following findings: 1) glaucomatous optic disc damage, defined as the presence of optic disc excavation, diffuse or focal neuroretinal rim thinning or notching, localized or generalized RNFL thinning; 2) visual field defects consistent with glaucoma; and 3) IOP ≥ 22 mmHg.

Exclusion criteria

- Age younger than 18 years;
- Secondary causes of glaucoma (e.g., iridocyclitis, trauma);

- Any evidence of corneal or conjunctival pathology adjacent to filtration bleb that could influence AS-OCT image
- Patients who did not undergo surgery or have adequate follow up
- Adults unable to consent, individuals who are not yet adults (infants, children, teenagers), pregnant women, prisoners and vulnerable populations

VULNERABLE POPULATIONS: NONE

PARTICIPANT POPULATION(S)

Prospective Study Population

Accrual Number:	Category/Group: (Adults/Children Special/Vulnerable Populations)	Consented: Maximum Number to be Consented or Reviewed/Collected/Screened	Enrolled: Number to Complete the Study or Needed to Address the Research Question
Local	25 adults	25 adults	25 eyes
Study-wide			
Total:	25 adults	25 adults	25 eyes

Age and race matched historical controls (identified via retrospective chart review)

Accrual Number:	Category/Group: (Adults/Children Special/Vulnerable Populations)	Consented: Maximum Number to be Consented or Reviewed/Collected/Screened	Enrolled: Number to Complete the Study or Needed to Address the Research Question

Local	25 adults	0	25 eyes
Study-wide			
Total:	25 adults	0	25 eyes

RECRUITMENT METHODS

Potential participants will be identified from the patients scheduled for follow up in the Glaucoma Service at Northwestern Medicine. Potential participants who are already scheduled for surgery may be called to gauge interest in the study. If they express interest, the patient will return to clinic prior to surgery to review and sign the informed consent and complete pre-surgery study imaging. Only patients who fit the inclusion/exclusion criteria will be asked to participate in the study.

COMPENSATION FOR PARTICIPATION IN RESEARCH ACTIVITIES

There is no additional cost for the patient to participate in this study. Patients and their insurance companies will be billed for office visits and procedures that are part of their usual medical care. There is no compensation made to the study subjects for participating in this study. Patients will have routine preoperative and postoperative follow up visits as necessary based on their clinical course. No extra visits will be required as a result of participation in this study.

WITHDRAWAL OF PARTICIPANTS

All the participants are free to withdraw at any point of the study. In case the participants are not willing to continue with the study protocol they will be removed from the analysis.

RISKS TO PARTICIPANTS

There is a risk of loss of confidentiality of the information that is used in this study. To minimize the risk of breach in confidentiality, the consent process for the prospective study will be done in a private room. Patient names will be replaced with arbitrary IDs. For the duration of the study, the patients will be referred by their ID. All data will be kept in a password-protected file.

POTENTIAL BENEFITS TO PARTICIPANTS

There may be no direct benefits of this study to the patient. Results of this study may provide important knowledge that will be generalizable to the care of other patients with glaucoma.

DATA MANAGEMENT AND CONFIDENTIALITY

PROVISIONS TO MONITOR THE DATA TO ENSURE THE SAFETY OF PARTICIPANTS

For the prospective study, the consent process and all the study procedures will be done in a private room/space. To protect participant's confidentiality, their information and study conduct will only be discussed with individuals listed in the study personnel.

In general, patients' data and all information pertaining to this study will remain confidential and all the study materials will be kept in a password protected computer a password-protected file and a secure server. Paper files will be kept in a locked drawer. In addition, the identifier list will be maintained separately from the study data. This identifier list will be kept in a password-protected file on a secure server.

PROVISIONS TO PROTECT THE PRIVACY INTERESTS OF PARTICIPANTS

The study is done in the same facility that glaucoma clinic is located and patients are imaged with the AS-OCT device on the same floor. The acquired data with AS-OCT are similar to images routinely taken for their glaucoma follow up. The iOCT is attached to the operating microscope in the same operating room that is routinely used for ocular surgery. The consent process and

all the study procedures for individuals enrolled in the prospective study will be done in a private room/space.

To protect participant's confidentiality, their information and study conduct will only be discussed with individuals listed in the study personnel. Patients' data and all information pertaining to this study will remain confidential and all the study materials will be kept in a password-protected computer a password-protected file and a secure server. Paper files will be kept in a locked drawer.

COMPENSATION FOR RESEARCH-RELATED INJURY

This study is minimal risk and therefore, there will be no anticipated research related injuries in this study or compensation for such injuries

ECONOMIC BURDEN TO PARTICIPANTS

Patients will be billed for the office visit as this was planned in advance. There will be no extra cost to patients as a result of this study. The AS-OCT or iOCT that will be performed as part of this study will not be billed to the patient or their insurance carrier.

CONSENT PROCESS

Potential participants in the prospective study will be identified from the patients scheduled for follow up or surgery in the Glaucoma Service at Northwestern Medicine. Patients will be approached verbally about the study during their visits or over the phone by study approved personnel. The informed consent process will take place in person in a private room. The research team will go over the consent forms with the patients to ensure they understand the nature of the research study, its procedures, potential risks and benefits, and their responsibilities as participants. The patients will be given as much time as needed to consider the study and address any questions or concerns. If patients need additional time to decide whether or not to enroll in the study, they will have the option of rescheduling for a later time.

Throughout the consent process, the research team will stress that participation is completely voluntary and that participants may withdraw from the study at any point. Patients will be provided a copy of the fully executed, signed consent forms. An additional copy of the signed consent forms will be scanned into the patient's electronic medical record and hard copies will be maintained in the subject binder.

For the historical control data, a retrospective chart review of glaucoma patients who underwent TCNR surgery from June 1, 2015 to June 1, 2020, will be performed. Consent will not be obtained for these patients as they will not undergo any further testing or treatments.

NON-ENGLISH SPEAKING PARTICIPANTS

Only English-speaking patients will be included in this study

WAIVER OR ALTERATION OF CONSENT PROCESS

Written consent form will be required for all participants; except for patients in the control arm.

Waiver of consent is requested for subjects in the control arm.

This research involves no more than minimal risk of harm to the subjects and involves no procedure for which written consent is normally required outside the research context.

Given the retrospective nature of the data collection and de-identified reporting, the waiver should not adversely affect the rights or welfare of the participants. Protocols are in place to protect information and ensure minimal risk of identifiers being improperly used or disclosed.

The waiver or alteration will not adversely affect the rights and welfare of the participants

Process to Document Consent in Writing

For the prospective study, the consent process and all the study procedures will be done in a private room/space. To protect participant's confidentiality, their information and study conduct will only be discussed with individuals listed in the study personnel. The process will be documented using the department's standard consent documentation template. It may also be noted in Epic.

Waiver of HIPAA Authorization

Use of PHI described in the protocol is necessary to the research. The research could not practicably be conducted without access to and use of the protected health information. Protected health information will not be reused or disclosed to any other person or entity, except as required by law, for authorized oversight of the research project, or for other research for which the use or disclosure of protected health information would be permitted by the HIPAA Privacy Rule.

Given the retrospective nature of the data collection and de-identified reporting, the waiver should not adversely affect the rights or welfare of the participants. Protocols are in place to protect information and ensure minimal risk of identifiers being improperly used or disclosed. There is a plan to destroy the identifiers at the earliest opportunity consistent with conduct of the research as described in the Access Security and Management section, unless there is a health or research justification for retaining the identifiers.

PROTECTED HEALTH INFORMATION

Participant will be assigned a study ID. The patient identifiers will be stored separately from the coded study data.

Data abstracted from the medical record will be collected on a secure sever, with computers only accessible with passwords. Only the research team will have access to the identified data

ACCESS SECURITY AND MANAGEMENT

Subjects will be assigned a coded number and a coded identifier list with the corresponding name to an identification number will be kept in locked files in the ophthalmology department,

of which only authorized research personnel will have access to. The data recorded for the study will be kept as a password-protected file on a password protected computer, separate from the subject log key. Data will be recorded and analyzed in a coded manner, with only authorized research personnel having access to it. Health information collected during the study will be stored electronically in password-protected files in the Department of Ophthalmology and then will be deleted at the earliest opportunity at the close of the study and no later than 10 years.

QUALIFICATIONS TO CONDUCT RESEARCH AND RESOURCES AVAILABLE

We estimate that there are a few patients in each glaucoma clinic that qualify to be included in the prospective study. Patients are selected among the patients that are being followed for glaucoma in the glaucoma clinic. The clinical examination is done as part of the routine glaucoma follow up and imaging will be acquired at the same day. Imaging with devices will take few minutes and do not pose any risk to patients.

The eye clinic at Northwestern University has qualified and trained staff. Dr. Angelo Tanna is a Professor and Vice Chairman in the Department of Ophthalmology at Northwestern University and has 20 years of experience in Ophthalmology practice. He, along with his team of ophthalmologist colleagues and fellows will recruit, verbally consent, collect anonymous responses and analyze data.

In addition, Dr. Angelo Tanna and the other co investigators will ensure the proper adherence to this protocol and data reviewing. All IRB approved staff involved with the study will be given access to the protocol and trained on their roles/responsibilities.

REFERENCES

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