PROTOCOL TITLE:
Using Triamcinolone Acetonide to Reduce Pain after Scleral Buckle Surgery

PROTOCOL NUMBER:
IRB 19-377

PRINCIPAL INVESTIGATOR:
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This study does not require funding

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2.0 11.20.2019

REVISION HISTORY:
Use this table to keep track of changes. Add more rows as needed.

Revision #	Version Date	Brief Summary of Changes (i.e., the different sections)	Consent Change?
0	4/1/19		
1	6/4/19	Added compensation, pain protocol, 6 mo f/u, changed from WIRB to BRANY	Yes
2	11/20/19	Removed LGH study site	Yes

Table of Contents

1.0 Study Summary

Study Title	Using Triamcinolone Acetonide to Reduce Pain after Scleral Buckle Surgery
Study Design	*Simple Randomized Control Trial*
Primary Objective	*To assess pain reduction following scleral buckle surgery with sub-tenon irrigation of triamcinolone acetonide, as measured by 11-point Numerical Rating Scale at 24 hrs post-op*
Secondary Objective(s)	• *Pain at 1-2 week post-op visit (11 pt NRS scale)* • *Pain at 6 mo post-op phone call* • *Post-operative analgesic consumption* • *Post-operative nausea and vomiting score (0-6)*
Study Population	*Patients undergoing Scleral Buckle Surgery for rhegmatogenous retinal detachment at Vistar Eye Center*
Sample Size	*N = 48*
Research Intervention(s)/ Investigational Agent(s)	• *1 cc Triamcinolone sub-tenon irrigation* • *Self-report survey at 24-hrs post-operative including 11 pt pain scale, nausea and vomiting score* • *Pill Count at 24-hrs post-operative* • *Self-report survey at 1-2 week post-operative including 11 pt pain scale, analgesic consumption, nausea and vomiting score* • *Pill Count at 1-2 weeks post-operative* • *Intra-ocular pressure measurement at 24 hrs post-operative* • *Intra-ocular pressure measurement at 1-2 week post-operative*
Study Duration for Individual Participants	*90 mins for the surgery (standard medical procedure) + 30s for experimental procedure + 2 minutes for each survey* *Each pt. is enrolled for 2 weeks.*
Acronyms and Definitions	*IOP- Intraocular Pressure* *NRS- Numerical Rating Scale for Pain* *EMR- Electronic Medical Record* *TA- Triamcinolone Acetonide*

2.0 Objectives

2.1 The purpose of this study is to determine if sub-tenon irrigation with triamcinolone acetonide at the time of surgery for rhegmatogenous retinal detachment will reduce the pain and inflammation caused by scleral buckle surgery.

2.2 Primary Hypothesis: Sub-tenon irrigation with 1cc (40 mg) Triamcinolone Acetonide will significantly reduce post-operative pain at 24 hrs post-

operation in patients undergoing scleral buckle surgery for rhegmatogenous retinal detachment.

Secondary Hypotheses:

Peri-bulbar irrigation with 1cc (40 mg) Triamcinolone Acetonide will significantly reduce post-operative analgesic consumption at 24 hrs post-operation in patients undergoing scleral buckle surgery for rhegmatogenous retinal detachment

Peri-bulbar irrigation with 1cc (40 mg) Triamcinolone Acetonide will significantly reduce post-operative nausea and vomiting score at 24 hrs post-operation in patients undergoing scleral buckle surgery for rhegmatogenous retinal detachment

Peri-bulbar irrigation with 1cc (40 mg) Triamcinolone Acetonide will significantly reduce post-operative pain at 1-2 week post-operation in patients undergoing scleral buckle surgery for rhegmatogenous retinal detachment.

Peri-bulbar irrigation with 1cc (40 mg) Triamcinolone Acetonide will significantly reduce post-operative pain at 6 month post-operation in patients undergoing scleral buckle surgery for rhegmatogenous retinal detachment.

Peri-bulbar irrigation with 1cc (40 mg) Triamcinolone Acetonide will significantly reduce post-operative analgesic consumption at 1-2 week post-operation in patients undergoing scleral buckle surgery for rhegmatogenous retinal detachment

Peri-bulbar irrigation with 1cc (40 mg) Triamcinolone Acetonide will significantly reduce post-operative nausea and vomiting score at 1-2 week post-operation in patients undergoing scleral buckle surgery for rhegmatogenous retinal detachment

3.0 Background

3.1 Summarize the relevant prior research on this topic and gaps in current knowledge within the field of study.

Scleral buckle surgery is a widely used ophthalmic surgery for the correction of primary rhegmatogenous retinal detachment. Research suggests that it is of equal efficacy as pars plana vitrectomy and that most eyes retain visual acuity for 20 years after surgery. Studies also suggest that eye pain is a common and underestimated occurrence after vitreoretinal surgery for retinal detachment, with 56% of patients reporting intense pain post-operatively. Levels of post-operative nausea were also correlated to the level of pain experienced.[1] In a study on chronic pain following scleral buckle surgery, it was shown that all patients

experienced pain following the surgery, with a wide range of subject pain scores. 18% of these patients experienced chronic pain for >6 months following surgery. Patients who experienced chronic pain showed higher pain scores in the immediate post-operative period.[2] Local inflammation has been shown to be associated with eye pain in the first few days after surgery.[1] It has also been shown that reduction of swelling following scleral buckle surgery reduces pain following surgery.[3] Triamcinolone acetonide is a corticosteroid that is used extensively in ophthalmology for many indications including uveitis, vasculitis, proliferative vitreoretinopathy, macular degeneration, and macular edema. Triamcinolone works by inhibiting phospholipase A_2 induction, and thereby downregulating inflammatory mediators including interleukins, prostaglandins and tumor necrosis factor. Corticosteroids also have been shown to have profound anti-angiogenic effects, vasoconstrictive effects, anti-permeability effects, ability to help maintain blood-retinal barrier, and facilitation of exudate reabsorption. Furthermore, triamcinolone has relatively small particles, allowing it to be injected in or around the eye, and has a duration of action of several months.[4] Surgery in and around the eye has been shown to cause intraocular inflammation, called uveitis. Corticosteroids are currently the cornerstone of treatment for uveitis. A study of perioperative intravitreal injection of triamcinolone during pars plana vitrectomy for open globe trauma demonstrated a improvement in visual acuity, likely due to the anti-inflammatory effects of triamcinolone.[5] Another study using triamcinolone with bupivacaine as a peribulbar injection at the conclusion of surgery for retinal detachment demonstrated a reduction in the use of hydrocodone following surgery, and demonstrated a trend of reduced pain, though it did not reach full significance.[6] As of yet, there is no definitive management method for reducing pain and swelling following scleral buckle surgery. We will be employing a sub-tenon irrigation approach to deliver 1cc of 40 mg / mL triamcinolone directly on the sutured area to reduce pain following surgery to try to address this gap.

3.2 Describe any relevant preliminary data

The use of Triamcinolone Acetonide sub-tenon irrigation has been done as standard at Vistar for scleral buckle surgeries for the last 2 years by Dr. Vishak John and Dr. Michael McClintock. Observations by the two surgeons suggest that there is a great analgesic effect for patients 24 hours post-surgically when compared to patients not given TA. There have been no noted adverse effects resulting from this use.

3.3 Based on the existing literature, provide the scientific or scholarly rationale for and significance of your research and how will it add to existing knowledge.

Currently, there does not appear to be any definitive standard of care for reduction of post-operative pain and swelling following scleral buckle surgery, as demonstrated by the wide variety of techniques employed.[7] Multiple Vistar surgeons currently use Triamcinolone Acetonide for all scleral buckle surgeries within the system, but this practice has not yet been proven in a randomized control trial. Some physicians are prescribing opioids to control pain following scleral buckle surgery[6]; in today's environment of opioid crises, this is something we would like to avoid. The significance of this study is that if the outcome is positive, it will help to determine a definitive standard of care for reducing pain and swelling following scleral buckle surgery that will allow reduced prescription of narcotics.

4.0 Study Endpoints

*4.1 Describe the primary and secondary **study** endpoints*

Primary Endpoint:

- Statistically significant reduction in pain as measured by 11-point Numerical Rating Scale at 1-day post-op. We are powered to detect a reduction in 2 points on the NRS scale.

Secondary Endpoints:

- Statistically significant reduction in pain as measured by 11-point Numerical Rating Scale at 1-2 weeks post-op.
- Statistically significant reduction in pain as measured by 11-point Verbal Rating Scale at 6 months post-op.
- Significant reduction in analgesics consumed post-operatively (self-reported pill count) at 1-day post op
- Significant reduction in analgesics consumed post-operatively (self-reported pill count) at 1-2 weeks post op
- Significant reduction in Nausea and Vomiting Score at 1 day post-op.
- Significant reduction in Nausea and Vomiting Score at 1-2 weeks post-op.

*4.2 Describe any primary or secondary **safety** endpoints. These should be included for all studies that are greater than minimal risk.*

- Primary: No significant difference in ocular hypertension 1-2 weeks post-operatively, defined as IOP of >5mmHg above baseline
- Secondary:
  - No significant difference in infections following surgery
  - No significant difference in hypersensitivity following surgery

5.0 Study Design and Statistical Analysis Plan

5.1 Describe the basic study design/approach

Simple randomized controlled trial comparing two groups in reducing post-operative pain from scleral buckle surgery -
1. Peribulbar irrigation of triamcinolone acetonide (Experimental Group)
2. Balanced Salt Solution (Control Group)

5.2 Describe corresponding data analysis plan/approach

Parametric analysis of experimental and control groups using students' t-test for primary endpoint, secondary endpoint of pain and analgesic consumption will be analyzed similarly. Secondary endpoints of nausea and vomiting score will be analyzed via non-parametric analysis (Mann-Whitney U test)

6.0 Setting

6.1 Describe the sites or locations where your research team will conduct the research.

- *Identify where your research team will identify and recruit potential subjects.*
- Vistar Eye Centers of VA:
    - 5296 Peters Creek Rd, Roanoke VA 24019
    - 2154 McVitty Rd, Roanoke VA 24018
    - 2617 Sheffield Dr, Blacksburg VA 24060
    - 749A East Church St, Martinsville VA 24112
    - 710 West Ridge Rd, Wytheville VA 24382
    - 280 Westlake Rd Bldg 2, Hardy VA 24101

- *Identify where the team will perform the research procedures.*

    - Vistar Eye Surgery Center
      2154 McVitty Rd SW, Roanoke, VA 24018

7.0 Study Intervention(s)/Investigational Agent(s)

7.1 Describe the study interventions (including behavioral interventions) and/or investigational agents (e.g., drugs or devices) to be used in this study.

- *Drug/Device Handling:*
  Triamcinolone will be stored in the operating facility according to package instructions: at controlled room temperature, 20° to 25°C (68° to 77°F. Vial will be stored in carton to protect from light, and will be stored upright. In the operating room, the vial will be opened according to sterile procedure by a nurse and prepared for injection by the surgeon.

7.2 List the name of all drugs (including any vitamins, supplements, herbs, or nicotine) to be used in the study. Indicate whether they have FDA approval, and list any limitations for their use.

Triamcinolone Acetonide injectable suspension. FDA Approved.

Marcaine (Bupivacaine Hydrochloride .75%). FDA Approved.

7.3 List all devices, how they will be used, their purpose in the study, and if they will be used in a manner consistent with their approved uses. If they will be used in ways that are not yet FDA approved, indicate whether they need an IDE or a determination that they are exempt from the IDE Determination. If a determination of significant risk or non-significant risk is needed for any of the devices, include the researcher's recommendation for each of those devices.

N/A

7.4 If the drug is investigational (has an IND) or the device has an IDE or a claim of abbreviated IDE (non-significant risk device), include the following information:

N/A

8.0 Procedures Involved

8.1 Describe and explain the study design.

Randomized Control Trial. Subjects will be patients at Vistar Eye Center who are undergoing scleral buckle surgery for rhegmatogenous retinal detachment. Patients of this indication will be consented and enrolled in the trial as detailed in section 24, and randomized (by coin-flip) into one of two arms, the control or the experimental. Patients in both arms of the study will be screened for IOP via handheld digital tonometry (tonopen) and will undergo standard scleral buckle procedures, including irrigation with 1 ml .75% Marcaine for local anesthesia (as is standard for all surgeries). At time of surgery, patients in the experimental group will receive irrigation of 1 ml (40 mg/mL) triamcinolone around the bed of applied scleral buckle distributed equally in all 4 quadrants (.25 ml per quadrant) under the tenon layer of the eye. Patients in the control group will be given irrigation around the applied scleral buckle of 1 ml balanced salt solution instead of triamcinolone. Patients will be masked to the treatment group assignment. The surgeon cannot be masked, as the triamcinolone solution is white and the balanced salt solution is clear. Intraoperative details will be recorded in the EMR about the surgery in both groups, including duration of surgery, time of irrigation, any additional pharmaceuticals or anesthesia applied, procedures performed, and placement of the buckle. Patient will receive a pill-count form at the end of the visit to keep track of rescue analgesic consumption. All patients

will be given appointments for post-operative day 1, and 1-2 weeks post-operative as is standard practice.

On post-operative day one, primary outcome data will be obtained by a blinded examiner who will be giving the patient a form which asks about the patient's pain score by reference to an 11-point numbered rating scale (0-10). On the same form, patients will also be asked about post-operative nausea and vomiting for secondary endpoint, which will be scored from 0-6 by adding the points for question II and question III from the pain and nausea survery[8]. The form will be collected by the same examiner when completed. Pill count sheet will be collected and additional sheet will be given for patient to track analgesic use between first and second visit. Patient will then have regularly scheduled visit with the surgeon who will be screening the patient for success of surgery, adverse events, and will examine pain and nausea scores to ensure both are well controlled. The physician will be ensuring the patient's safety, and will be allowed to prescribe any medications deemed medically necessary for control of side effects, nausea, and pain. IOP of all patients will also be measured at this visit.

At second post-operative visit (1-2 weeks), patients' IOP will be measured again for safety endpoint. Patient pill count sheet will be collected. Patients will be filling out 11-point NRS pain score and post-operative nausea and vomiting sheet again during office visit and it will be collected by blinded examiner. Patient will then be examined by surgeon again for success of surgery, adverse events, and control of pain and nausea.

	Before Surgery	Day of Surgery	Between Surgery and First Follow-Up Visit	First Follow-Up Visit (1 day after surgery)	Between 1st and 2nd Follow-Up Visits	Second Follow-Up Visit (1-2 weeks after surgery)	Long-Term Follow-Up (6 months)
Location	Clinic	Surgery Center	Home	Clinic	Home	Clinic	Phone
Procedures	The doctor will explain the study to patient	Everyone: Scleral Buckle Surgery. Experimental Group: Triamcinolone (steroid) will be applied during surgery. Control Group: Saline solution will		Everyone: will be examined by the doctor for safety		Everyone: will be examined by the doctor for safety	

		be applied during surgery.					
What Patient will do	Review and sign the consent document	Receive pill count form	Keep track of pain medications taken on pill-count form	Fill out pain and nausea form. Turn in pill-count and receive second pill-count	Keep track of pain medications taken on pill-count form	Fill out pain and nausea form. Turn in pill-count	Report pain level from 0-10

8.2 Describe:

- *Procedures or safeguards intended to reduce the probability and magnitude of risks.*

  Patients will be screened twice for IOP (measured by tonometer) post-surgically to check for ocular hypertension. Patients eyes will also be examined at both visits by the primary surgeon via slit-lamp to determine any adverse events as a result of surgery or the intervention. The surgeon is responsible for the medical safety of all patients and may prescribe any medications deemed necessary for control of side effects of surgery or intervention, including nausea and vomiting.

- *Be sure to describe all drugs and devices used in the research, when they will be administered or used, and their purpose.*
  See 7.1

  Methods used to collect data about subjects. Please upload all data collection forms to Protocol Management
- Pain and Nausea Survey
- Pill-Count
- IOP (tonometry)

8.3 What data will you collect during the study and how you will obtain them? Please include descriptions of electronic data collection, database matching, and app-based data collection.

Patients will be assigned an arbitrary patient ID at beginning of the study which is recorded in the EMR. Demographic data about patient age, gender, and ethnicity will be extracted from the electronic medical record. No patient identifying data including name, addresses, date of birth, or

SSN will be extracted from the electronic medical record for the purpose of the analysis. Details of surgery will be extracted from the EMR.

During the study, IOP will be collected at two time-points via tonometer. This data will be extracted from the electronic medical record for analysis. Pain level via 11-pt NRS will be collected at two time points by survey. Data about analgesic consumption will be collected via survey form at two time points by survey. Nausea and vomiting score will be collected at two time points by survey. This data will be matched to de-identified patient ID. Physical survey forms will then be confidentially discarded.

8.4 Who will transcribe or code audio and/or video recordings?

N/A

8.5 Include a description of any deception to be used in the study.

N/A

8.6 If the study involves long-term follow-up (once all research related procedures are complete), describe what data will be collected during the follow up period and when it will occur.

N/A

9.0 Data and Specimen Long Term Storage and Use

9.1 If you will store data or specimens for future use, describe where you will store the data or specimens, how long they will be stored, and how and by whom the data or specimens will be accessed.

Data from the study including IOP, procedure performed, and whether or not triamcinolone was applied will continue to remain as part of patient data within Vistar Electronic Medical Record for the purposes of medical care.

9.2 For specimens, list the data to be stored or associated with each specimen.

N/A

9.3 Describe the procedures to release data or specimens outside of the research team, including the process to request a release, approvals required for release, who can obtain data or specimens, and what data will be provided with specimens.

N/A

9.4 Describe the identifiers to be included with stored data or specimens, as well as any key or code that could be used to make them identifiable. Describe where the code will be stored, who will have access to it, and when it will be destroyed.

Data will be stored with arbitrary patient ID and will not be identifiable. A code to re-identify patients will be with the PI (Dr. John) and nobody else

will have access to it. It will be destroyed after publications of the results of the study

9.5 Please select the identifiers you will obtain (whether directly from participants or from another source), including but not limited to:

☐	*Name*
☐	*Geographical subdivisions smaller than a state, including street address, city, county, precinct, zip code, and equivalent geocodes (note, the initial three digits of a zip code are not considered identifiable)*
☐	*Elements of dates (except year) for dates directly related to an individual, including birth date, admission date, discharge date, date of death, and single year of age over 89 and all elements of dates (including year) indicative of such age (note, such ages and elements may be aggregated into a single category of age 90+)*
☒	*Phone numbers*
☐	*Fax numbers*
☐	*Electronic mail addresses (e-mail)*
☐	*Social Security numbers*
☐	*Medical record numbers*
☐	*Health plan beneficiary numbers*
☐	*Account numbers*
☐	*Certificate/license numbers*
☐	*Vehicle identifiers and serial numbers, including license plate numbers*
☐	*Device identifiers and serial numbers*
☐	*Web Universal Resource Locators (URLs)*
☐	*Internet protocol (IP) address numbers*
☐	*Biometric identifiers, including finger and voice prints (audio recording)*
☐	*Full face photographic images and any comparable images (including video recording)*
☐	*Student record number or identification number*
☐	*User name for online or computer accounts*
☐	*Any other unique identifying number, characteristic, or code (note this does not mean the unique code assigned by the investigator to code the data)**: (Explain)*

10.0 Sharing of Results with Subjects

10.1 Describe whether you will share results (study results or individual subject results, such as results of investigational diagnostic tests, genetic tests, or incidental findings) with subjects or others (e.g., the subject's primary care physician). If so, describe how you will share the results and

include this information as part of the consent document. Upload materials you will use to explain the results to subjects.

We will not be sharing results with subjects.

11.0 Study Timelines

11.1 Describe:

- *The duration of an individual subject's participation in the study (for example, 1 hour, 2-4 weeks, 3-5 years).*
- **6 months**
- *The amount of time expected to enroll all study subjects (weeks, months, years, etc.)*
- **Approximately 17-24 months**
- *The amount of time expected for the investigators to complete this study including primary data analyses.*

- **Approximately 2.5 years**

12.0 Inclusion and Exclusion Criteria

12.1 Describe how you will screen individuals for eligibility. When will screening occur and what procedures will you use? Upload any screening scripts or surveys to Protocol Management.

Individuals will be screened at time of diagnosis. All patients who are determined to need scleral buckle surgery for rhegmatogenous retinal detachment will be screened for eligibility. Screening for the trial will be done by the surgeon, who will be reviewing the medical history at time of visit via EMR. If patient does not fail the exclusion criteria, the patient will be consented for enrollment in the trial. There are no screening scripts or surveys that will be used.

12.2 Describe the eligibility criteria that define who will be included and who will be excluded from enrollment for each procedure of your study.

Inclusion Criteria: Patient must have rhegmatogenous retinal detachment and be scheduled to undergo scleral buckle surgery for correction.

Exclusion Criteria:

- Patient under 18 years old
- Advanced Glaucoma
- History of corticosteroid responsive elevation in IOP
- Allergy to Triamcinolone Acetonide or other corticosteroids
- Pre-existing chronic pain disorders
- Herpes zoster
- Prior corneal allograft
- Allergy to local anesthetic or penicillin

- Patients unable to consent on own behalf
- Patients unable to communicate pain and nausea levels
- Pregnancy
- Incarceration

12.3 Indicate specifically whether you will include or exclude each of the following special populations: (You may not include members of these populations as subjects in your research unless you indicate them in the description of your subject population.)

All of the following populations will be excluded from our study.

- *Minors, as defined by state law where the study is performed (infants, children, teenagers)*
- *Pregnant women*
- *Prisoners (including all incarcerated individuals)*
- *Adults not capable to consent on their own behalf*

13.0 Vulnerable Populations

13.1 If the research involves individuals who are vulnerable to coercion or undue influence, please describe additional safeguards you will include to protect their rights and welfare.

N/A

14.0 Number of Subjects

14.1 Indicate the total number of subjects to be enrolled and how this number was determined

Sample Size Calculation as performed by Dr. Allison Tegge of VT and VTCSOM

H_0= median post-operative pain equal in experimental and control groups

H_A= median post-operative pain not equal in experimental and control groups

Median Pain Score Experimental: 1. SD = 1, IQR = 0-2

Median Pain Score Control: 3. SD = 2.5, IQR = .5 – 5.5

Alpha = .01, Power = 0.8

Effect Size, d = 1.05

Sample Size: n = 48

14.2 If this is a multi-site study, indicate the number of subjects to be enrolled at this site and the total to be enrolled from all sites.

n/a

14.3 If applicable, indicate the number of potential subjects you expect to screen for enrollment, and the number of subjects you will need to complete the research procedures.

n/a

14.4 If the study has more than one procedure, indicate the total number of subjects to undergo each procedure separately.

n/a

15.0 Recruitment Methods

15.1 Describe when, where, and how you will recruit potential subjects.

Subjects will be recruited in the physician's office at Vistar Eye Center at time of surgery scheduling via the recruitment script attached. The surgeon (VJ, MM) or research coordinator (PV) will be recruiting the patients as they are the most familiar with the patient's medical history, potential drug complications, and have the best ability to address medical questions.

15.2 Describe the source of subjects (for example, clinic patients with specific conditions, students in the library, community members at a gathering, or members of a local gym).

Patients with rhegmatogenous retinal detachment with indication for scleral buckle surgery at Vistar Eye Center

15.3 Describe the methods that you will use to identify potential subjects.

All patients who present with indication for scleral buckle surgery are considered potential subjects.

15.4 Describe materials that you will be use to recruit subjects. Attach copies of these documents with this protocol in Protocol Management and be sure to include the IRB protocol number on each document.

Recruitment script can be found attached.

- *Describe any compensation to subjects. Separate compensation into appropriate categories, such as: reimbursement for expenses, time and effort, and additional incentives for study participation. For each category, specify the amount (including any pro-rated amount), schedule, and method of payment.*
- $20 total compensation for completion of the study (will be disbursed after 6 month follow-up phone call)

16.0 Withdrawal of Subjects

16.1 Describe circumstances under which you anticipate subjects could be withdrawn from the research without their consent.

- The research is canceled by the FDA or the sponsor
- Patient is unable to keep scheduled appointments
- A patient has a side effect that requires stopping the research

16.2 If applicable, describe any procedures for orderly termination (e.g., discontinuation of a study drug or debriefing after a behavioral intervention).

N/A

16.3 Describe procedures that you will follow when subjects withdraw from the research, including partial withdrawal from procedures with continued data collection (e.g., participant declines to continue with regular blood draws, but continues with periodic behavioral questionnaires).

If the patient withdraws consent to study before the time of surgery, the patient will not receive either the experimental or control treatments, and will receive standard surgical treatment. The patient's data will not be extracted from the EMR for study purposes, and the patient will not be given any of the survey materials. If a patient withdraws consent after the surgery, the patient's data will not be extracted from the EMR for analysis and the patient will be given no further survey materials. Existing survey materials will be destroyed. If patient partially withdraws from procedures after surgery, the data may be used except for that which is not completed.

17.0 Risks to Subjects

17.1 List the reasonably foreseeable risks, discomforts, hazards, or inconveniences to the subjects related the subjects' participation in the research.

Adverse event data was collected by the FDA from 300 published articles containing data from controlled and uncontrolled clinical trials which evaluated over 14,000 eyes treated with different concentrations of triamcinolone acetonide. The most common dose administered within these trials was triamcinolone acetonide 40 mg administered as primary or adjunctive therapy primarily as a single injection. The most common reported adverse events following administration of triamcinolone acetonide were elevated intraocular pressure and cataract progression. These events have been reported to occur in 20-60% of patients. Less common reactions occurring in up to 2% include endophthalmitis (infectious and non-infectious), hypopyon, injection site reactions (described as blurring and transient discomfort), glaucoma, vitreous floaters, and detachment of retinal pigment epithelium, optic disc vascular disorder, eye inflammation, conjunctival hemorrhage and visual acuity reduced. Cases of exophthalmos have also been reported.

Risk of infection: Corticosteroids may mask some signs of infection, and new infections may appear during their use. There may be decreased resistance and inability to localize infection when corticosteroids are

used. Corticosteroids may enhance the establishment of secondary ocular infections due to fungi or viruses. If an infection occurs during corticosteroid therapy, it will be promptly controlled by suitable antimicrobial therapy.

Elevated Intraocular Pressure: Increases in intraocular pressure associated with triamcinolone acetonide injection have been observed in 20-60% of patients. This may lead to glaucoma with possible damage to the optic nerve. Effects on intraocular pressure may last up to 6 months following injection and are usually managed by topical glaucoma therapy. A small percentage of patients may require aggressive non-topical treatment. Intraocular pressure as well as perfusion of the optic nerve head will be monitored and managed appropriately. As our study will be irrigating the peribulbar space rather than injecting into the posterior capsule of the eye, we expect our rate of elevated IOP to be much lower than that determined by the FDA.

Endophthalmitis: The rate of infectious culture positive endophthalmitis is 0.5%. Proper aseptic techniques will always be used when administering triamcinolone acetonide. In addition, patients will be monitored following the injection to permit early treatment should an infection occur.

Cataracts: Use of corticosteroids may produce cataracts, particularly posterior subcapsular cataracts. As our study will be irrigating the sub-tenon's space rather than injecting into the posterior capsule of the eye, we expect our rate of cataracts to be much lower than that determined by the FDA.

Patients with Ocular Herpes Simplex: Corticosteroids should be used cautiously in patients with ocular herpes simplex because of possible corneal perforation. Corticosteroids should not be used in active ocular herpes simplex. We will be excluding all patients with ocular herpes simplex.

Systemic reactions are exceedingly rare in ophthalmic administration of corticosteroids but are included below for completeness:

Cardiovascular: Bradycardia, cardiac arrest, cardiac arrhythmias, cardiac enlargement, circulatory collapse, congestive heart failure, fat embolism, hypertrophic cardiomyopathy in premature infants, myocardial rupture following recent myocardial infarction, pulmonary edema, syncope, tachycardia, thromboembolism, thrombophlebitis, vasculitis

Dermatologic: Acne, allergic dermatitis, cutaneous and subcutaneous atrophy, dry scalp, edema, facial erythema, hyper or hypo-pigmentation, impaired wound healing, increased sweating, petechiae and ecchymoses, rash, sterile abscess, striae, suppressed reactions to skin tests, thin fragile skin, thinning scalp hair, urticaria

Endocrine: Abnormal fat deposits, decreased carbohydrate tolerance, development of Cushingoid state, hirsutism, manifestations of latent diabetes mellitus and increased requirements for insulin or oral hypoglycemic agents in diabetics, menstrual irregularities, moon facies, secondary adrenocortical and pituitary unresponsiveness (particularly in times of stress, as in trauma, surgery or illness), suppression of growth in children

Fluid and Electrolyte Disturbances: Potassium loss, hypokalemic alkalosis, sodium retention

Gastrointestinal: Abdominal distention, elevation in serum liver enzymes levels (usually reversible upon discontinuation), hepatomegaly, hiccups, malaise, nausea, pancreatitis, peptic ulcer with possible perforation and hemorrhage, ulcerative esophagitis

Metabolic: Negative nitrogen balance due to protein catabolism

Musculoskeletal: Aseptic necrosis of femoral and humeral heads, charcot-like arthropathy, loss of muscle mass, muscle weakness, osteoporosis, pathologic fracture of long bones, steroid myopathy, tendon rupture, vertebral compression fractures

Neurological: Arachnoiditis, convulsions, depression, emotional instability, euphoria, headache, increased intracranial pressure with papilledema (pseudo-tumor cerebri) usually following discontinuation of treatment, insomnia, meningitis, neuritis, neuropathy, paraparesis/paraplegia, paresthesia, sensory disturbances, vertigo

Reproductive: Alteration in motility and number of spermatozoa.

- *Privacy (e.g., potential for personal information being accessed, used, or disclosed without the subjects' knowledge or consent, breach of confidentiality/security)*

- In any clinical trial, there is a possibility for patient's personal information being accessed improperly. This has been minimized as much as possible through participation in CITI training by main investigators, as well as not extracting patient identifying information from the EHR for analysis purposes.

- *Economic (e.g., potential for individuals to lose access to economic services, employment, insurability)*
- There will be no additional charge for TA treatment to the patient.

17.2 If applicable, indicate which procedures might have risks to the subjects that are currently unforeseeable. This will be rare, and usually applicable when testing a new drug or device or a new use of an existing drug or device.

TA is a very well-studied drug that has been FDA approved since 1957 for ophthalmic application. It is unlikely there will be risks associated with the drug that have not been previously documented.

17.3 If applicable, indicate which procedures might have risks to an embryo or fetus should the subject be or become pregnant.

Triamcinolone is Pregnancy Category D, as it has been shown to increase rate of cleft lip in the first trimester when used systemically. It is unlikely to have this effect when applied locally to the eye, but some risk exists nonetheless.

17.4 If applicable, describe risks to others who are not subjects (e.g., collection of sensitive health data that might affect sexual partners if disclosed, mandatory reporting of abuse, DNA testing that might affect family members or relationships).

N/A

18.0 Potential Benefits to Subjects

18.1 Describe the potential benefits that individual subjects might experience from participating in the research. Include the probability, magnitude, and duration of the potential benefits, as this will be useful to the IRB's risk:benefit analysis. Do not include benefits to society or others. These should be included in section 2 or 3 of this document.

The largest benefit to subjects is the possibility to directly reduce pain following scleral buckle surgery. This is our primary outcome so the exact likelihood and magnitude are currently unknown, but likelihood is presumed to be high based on background literature. Magnitude is presumed to be around 50% reduction in pain. Subjects may also experience a decrease in intraocular inflammation, and post-operative nausea and vomiting. Furthermore, patients may have a reduced risk for addiction to pain medication, as we hope to demonstrate a reduced need for post-operative analgesics following surgery. All patients in the experimental group will also be receiving the treatment at no additional cost to them, which is a potential financial benefit.

19.0 Data Management and Confidentiality

19.1 Describe procedures that you will use for quality control to ensure validity of collected data.

The surgeon will be including their subjective assessment of patient's pain on the EHR, which they may compare to the patients written assessment as a form of quality control.

19.2 Describe the steps that you will take to handle and secure study data during data collection, storage, use, and transmission. Include information about training of study staff, authorization of access,

password protection, encryption, physical controls, certificates of confidentiality, separation of identifiers and data, etc.

Patient data is stored securely in NextGen Electronic Medical Record at Vistar Eye Center according to HIPAA regulations. Data that will be extracted from the EMR will not contain any patient identifying information. The procedure by which it will be extracted is via CPT code records for scleral buckle surgery. De-identified data extracted will be stored in a dataset along with arbitrary patient ID within the Vistar Eye Center computer network so that it cannot be accessed without both physical access and log-in credentials. Access to study materials is granted only to 2 surgeons listed on this document (John, McClintock), and the research coordinator (Vaidya).

19.3 For multi-site studies, describe how data or specimens will be handled and secured for each site (e.g., central or disseminated data storage, data coordinating center).

19.4 Describe the plan for data disposition following the conclusion of the study (e.g., long term maintenance of data, data destruction methods).

Data will not be stored outside of that needed for medical care after the conclusion of the study. Medical information will continue to exist on the Electronic Medical Records at Vistar Eye Center, but all extracted data will be destroyed 3 years following publication of the results of this study as is standard protocol.

- *What information will be included in the long term storage of data or specimens?*
- *How long will the data or specimens be stored?*
- *Where and how data or specimens will be stored?*
- *Who will have access to the data or specimens during long term storage?*
- *Who is responsible for receipt or transmission of the data or specimens?*
- *How will data or specimens be shared or transported?*
- *When and how will personal identifiers be destroyed?*

20.0 Provisions to Protect the Privacy Interests of Subjects

20.1 Describe the steps that you will take to protect subjects' privacy interests. "Privacy interest" refers to a person's desire to place limits on with whom they interact or to whom they provide personal information (e.g., collecting the minimal amount of private information required to complete the study, protecting the data once it is obtained).

No patient identifying information will be extracted from the electronic medical records. The only people with access to this information is the medical care team of the patient. De-identified data will not be shared

beyond the two surgeons involved in the study design and research coordinator.

20.2 Describe steps that you will take to make subjects feel at ease with the research situation in terms of the questions being asked and the procedures being performed. "At ease" does not refer to physical discomfort, but the sense of intrusiveness a subject might experience in response to questions, examinations, and procedures (e.g., use of a same gender investigator to place sensors on the torso, a private changing area if clothing must be changed, sensitivity when discussing pregnancy testing with subjects, making it clear on surveys that participants can discontinue at any time, not asking questions about private or sensitive issues unless necessary for the research).

20.3 Describe how you plan to access existing sources of information about the subjects (e.g., medical records, grades) and how you will protect participant privacy through the data security plan.

Data extraction from the medical record will be done by one of the two surgeon members of the Vistar Eye Center team who would otherwise have access to the medical data anyway for patient care. The procedure by which it will be extracted is via CPT code records for scleral buckle surgery. De-identified data extracted will be stored in a dataset along with arbitrary patient ID within the Vistar Eye Center computer network.

20.4 Describe any required reporting that might occur as a result of your research questions, study populations, and data collection methods. Examples for Virginia and Virginia Tech include:

- ***Any*** *suspicions (e.g., circumstantial, disclosed) of child abuse (physical, emotional, sexual) and neglect*
- *Sexual discrimination and/or sexual violence that involves a student*
- *Disclosure or signs of intention to harm oneself (i.e., suicidal ideation and/or plan)*
- *Disclosure or signs of desire to harm others (i.e., homicidal ideation and/or plan)*
- *Suspected abuse, neglect or exploitation of vulnerable adults (e.g., individuals with a disability, elderly persons)*

21.0 Provisions to Monitor the Data to Ensure the Safety of Subjects

Safety monitoring is required when research involves greater than minimal risk and is sometimes appropriate for other studies.

21.1 Describe:

- *The plan to periodically evaluate the data collected regarding both harms and benefits to determine whether subjects remain safe (e.g., periodic reporting to the IRB, establishing a data monitoring*

committee, reporting data monitoring committee findings to the IRB and the sponsor).

The patient's IOP will be measured at baseline prior to the surgery, as well as 24 hrs post-op and 2 weeks post-op. This is done to monitor ocular hypertension, a potential side-effect of both the surgery and TA treatment. Patients will also have two normally scheduled follow-up visits with the surgeon who will be monitoring for any other adverse events such as hypersensitivity or infection. If adverse events occur that may be related to the intervention, they will be reported to the IRB promptly. The data will also be monitored after every 10^{th} patient completes the protocol for any statistically significant differences in the primary or secondary safety endpoints. If this occurs, it too will be reported to the IRB promptly.

22.0 Compensation for Research Related Injury

22.1 If the research involves more than minimal risk to subjects, describe the available compensation in the event of research-related injury, if any.

n/a

22.2 Provide a copy of contract language, if any, relevant to compensation for research-related injury. At Virginia Tech, this is most common for sponsored research.

n/a

23.0 Economic Burden to Subjects

23.1 Describe any costs that subjects might be responsible for because of participation in the research, including any uncompensated costs for items such as transportation, missed work, and childcare.

None. The TA irrigation will be done at no extra cost to the patient. Patients do not have to make any additional visits.

24.0 Consent Process

24.1 Indicate the process by which you will obtain consent for study participation. Please upload all consent, parental permission, and assent forms, documents, and scripts referenced in this section to Protocol Management.

Describe the following:

- *Where the consent process will take place (e.g., clinic waiting area, classroom, online)*

The patient will be consented in the clinic patient exam room, immediately following consultation with the doctor about the planned surgical procedure. The consultation will be done by the doctor who is well trained on the procedures and risks. The doctor will also be able to answer any more specific questions that the patient may have.

- *The time interval between sharing the consent information with the prospective subject and obtaining consent. For lab, interview, and focus group studies, the Virginia Tech IRB prefers that subjects have at least 24 hours to review the consent form and study information before the appointment where consent will be obtained. For simple online survey studies, you can typically present the consent information immediately before subjects begin participation.*

  The obtaining of consent will occur directly after the sharing of consent information. However, the patient will be given a copy of the consent forms and the surgery will not usually take place until the next day or longer still, giving the patient sufficient time to review the materials and change their decision to withdraw or provide consent by notifying any staff member up until the moment right before surgery.

- *If applicable, processes to ensure ongoing consent or assent (e.g., for multiple sessions; for research in which a minor will turn 18 during the study; for longitudinal research with minors who will later be asked to provide or affirm their assent).*

  As there is no more than minimal risk to the patient after the original intervention, we do not believe this is necessary.
- *Please review "SOP: Informed Consent Process for Research (HRP-090)" for recommended procedure. Describe your process, being sure to include:*
  - *The name and role of all study personnel who will be trained and certified by the PI to conduct the consent process*
    - Dr. Vishak John M.D. (PI)
    - Dr. Michael McClintock Jr. M.D.
    - Parth Vaidya, Medical Student, Research Coordinator
  - *The time that will be devoted to the consent discussion*
    The consent discussion will be given up to 15 minutes with the surgeon if the patient has questions or concerns about the study. The patient will also be given the phone number and email of the primary research coordinator to contact them with any additional questions after they leave. The patient also has as much time as they need to review the consent documents before the start of the surgery to decide to consent or not to.

- *Steps that you will take to minimize the possibility of coercion or undue influence*
- The patient will be given a copy of the consent documents and allowed to review them at home and change their minds about whether they will be consenting to the study up until time of surgery. Patients will also be asked teach-back questions to ensure adequate understanding as listed in the consent script document.
- *Steps that you will take to gauge or ensure the subjects' understanding*
- Patients will be asked 3 questions to gauge for understanding:
    a. What is the purpose of this study?
    b. What are the risks and benefits to participating?
    c. Are you required to participate in this study?

25.0 Process to Document Consent in Writing

25.1 Consult "SOP: Written Documentation of Consent (HRP-091)" for recommended procedures, and describe whether and how consent of the subject will be documented in writing.

25.2 If the research presents no more than minimal risk of harm to subjects and involves no procedures for which written documentation of consent is normally required outside of the research context, you can request that the IRB waive the requirement to obtain written documentation of consent (e.g., consent to participate is indicated by pressing a button for an online questionnaire – after the consent information is presented and before the questionnaire begins).

25.3 If you will document consent in writing, attach a consent document with places for signatures. If you will obtain consent, but not document consent in writing, please attach the consent script or text. Review "CHECKLIST: Waiver of Written Documentation of Consent (HRP-411)" to ensure that you have provided sufficient information. You should use "TEMPLATE CONSENT DOCUMENT (HRP-502)"to create the consent document or script.

26.0 Resources Available

26.1 Describe the resources available to conduct the research. For example, as appropriate:

- *Describe the PI's availability to supervise the research*
- The study was initiated by the PI (Vishak John) along with the research coordinator (Parth Vaidya) and another surgeon (Michael McClintock Jr), and the PI will take full responsibility for supervising the research. The PI will be fully available to answer any and all questions by both research team and patients. The PI will also

often be in the same physical location as the surgeons on the research team and the patients, ensuring access.

- *Justify the feasibility of recruiting the required number of suitable subjects within the agreed recruitment period. For example, how many potential subjects do you have access to? What percentage of those potential subjects do you need to recruit?*
- There are 4 scleral buckle surgeries done each month between the 4 surgeons who will be conducting the operations. We would need to recruit 50% of them into the study in order to meet the recruitment period of 2 years.
- *Describe the time that you will devote to conducting and completing the research.*
  This research project will not take much additional time as the majority of the time-consuming procedures are done anyway as standard of care. Additional time of 1 hour each week will be dedicated to consenting, answering questions, documentation, and statistical analysis.
- *Describe your process to ensure that all persons assisting with the research are adequately informed about the protocol, the research procedures, and their duties and functions (e.g., training plans, detailed study notebooks).*
- Each of the 2 surgeons are already well informed about the procedures, drugs, and risks involved due to routine retinal surgery training. There will be a meeting prior to beginning the study with the research coordinator, PI, Dr. McClintock, and all support staff that will be collecting the forms to ensure understanding of all protocols and procedures.

27.0 Multi-Site Research

Contact the HRPP for multi-site research (involving multiple institutions) and the details required for this section will be provided. Otherwise, indicate N/A.

N/A

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8. Myles PS, Wengritzky R. Simplified postoperative nausea and vomiting impact scale for audit and post-discharge review. *BJA Br J Anaesth*. 2012;108(3):423-429. doi:10.1093/bja/aer505