Subacromial Injection of Epinephrine Improves Visualization in Shoulder Arthroscopy

NCT05244525

Version Date: 09/02/2022

Study Protocol

Protocol Number: HSC-MS-21-1061

Protocol Title: Subacromial Injection of Epinephrine Improves Visualization in Shoulder Arthroscopy

Version: 1.1
Date: 11/22/2021

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General Information

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STUDY PROTOCOL

1. BACKGROUND AND RATIONALE

1.1. General Introduction

Arthroscopic technique is being utilized more to treat a wide variety of pathologic conditions of the shoulder. Adequate visual clarity is imperative to safely and effectively perform arthroscopic shoulder surgery. Addition of epinephrine to the arthroscopic irrigation can help to improve visual clarity [1-4].

References:

[1] D. Avery, et al., Arthroscopy 31(1) (2015) 12-8.
[2] D. van Montfoort, et al., Arthroscopy 32(3) (2016) 436-44.
[3] K Jensen, et al., Arthroscopy 17(6) (2001) 578-81.
[4] L. Kuo, et al. International Orthopaedics 42(12) (2018) 2881-9.

1.2. Rationale and justification for the Study

a. Rationale for the Study Purpose

Addition of epinephrine to arthroscopic irrigation raises the cost of the procedure and has the potential for rare, but serious, cardiovascular adverse events [5-9]. We have also used a subacromial injection of bupivacaine epinephrine prior to the initiation of the surgical procedure. This helps us limit the use of epinephrine to the first 6 liters of irrigation fluid. In this way, we limit the cost of the surgery as well as the total dose of epinephrine to decrease the likelihood of epinephrine-related adverse events, without sacrificing visual clarity. Additionally, when visualization is limited, surgeons may increase the pump pressure of arthroscopic fluid within the shoulder. This increases fluid extravasation into the surrounding soft tissues, and can cause difficulties with surgical exposure. We propose a double-blinded, randomized controlled trial to compare the use of subacromial injection of bupivacaine with and without epinephrine to determine the effectiveness in terms of visual clarity.

References:

[5] W. Stetson, et al. Arthroscopy Techniques 10(2) (2021) e411-8.
[6] T. Abdelrahman, et al. The Physician and Sports Medicine 12 (2021) 1-9.
[7] S. Cho, et al. Archives of Orthopaedic and Trauma Surgery 130(3) (2010) 353-6.
[8] J. Karns, et al. AANA Journal 67(5) (1999) 419-21.
[9] B. Gicquel-Schlemmer, et al. Orthopaedics & Traumatology: Surgery & Research 10(2) (2021) e411-8.

b. Rationale for Doses Selected

The dose of bupivacaine with epinephrine to be injected into the subacromial space prior to surgery will be the standard dose we have administered as part of our routine surgical protocol. The dose of epinephrine injected into the subacromial space will be 0.3 mg of epinephrine in 30mL of 0.5% bupivacaine for a dilution of 1:100. A total volume of 20 mL of the mixed solution will be injected into the subacromial space prior to the start of the surgery. The dose of epinephrine to be used in the arthroscopic irrigation fluid is 5 mL of epinephrine in 5 liters of sterile saline for a dilution of 1:1000. These doses of epinephrine in the subacromial injection as well as the arthroscopic irrigation fluid have been used for several years by the study investigators without any epinephrine-related cardiovascular adverse events. By limiting the use of epinephrine to the pre-operative injection and the first 10 liters of arthroscopic irrigation only as opposed to using epinephrine in the irrigation fluid throughout the surgery, we aim to limit the total dose of epinephrine, thereby limiting cost and minimizing the risk of epinephrine-related cardiovascular adverse events. Due to supply shortages, if 0.5% bupivacaine is unavailable then 0.25% bupivacaine will be substituted. All other dosing instructions will remain unchanged.

c. Rationale for Study Population

Our study population will be adult (18 years of age or older) patients undergoing arthroscopic shoulder surgery requiring visualization within the subacromial space. This includes primarily arthroscopic rotator cuff debridement or repair, arthroscopic subacromial decompression, arthroscopic subacromial bursectomy or bursal debridement, and arthroscopic distal clavicle resection, among other arthroscopic procedures. Only procedures performed in the seated, upright (ie, beach chair) position will be included as these cases present a unique challenge. The concept of "controlled hypotension" has been described as one technique for better visual clarity in the subacromial space, though this technique has been shown to affect cerebral blood flow and oxygenation [10]. Effective local hemostasis within the subacromial space to preserve visual clarity may obviate the need for controlled hypotension, thereby making surgery safer.

References:

[10] J Aguirre, et al., Journal of Clinical Anesthesia 53 (2019) 40-8.

d. Rationale for Study Design
We propose a double-blinded randomized controlled trial to minimize bias and ensure similar baseline characteristics of the patients in each study group. Patients will be randomized to receive a pre-operative subacromial injection containing either bupivacaine with epinephrine, or bupivacaine alone. We will collect baseline characteristics of patients as well as potential confounding factors throughout and after the surgery to ensure that any difference in surgeon-rated visual clarity is a direct consequence of the intervention.

2. HYPOTHESIS AND OBJECTIVES

2.1. Purpose/Hypothesis
Purpose: The aim of this study is to investigate the effect of a pre-operative subacromial injection containing epinephrine on the visual clarity during subacromial arthroscopic shoulder surgery.
Hypothesis: Pre-operative injection of epinephrine into the subacromial space will result in improved surgeon-rated visual clarity as well as decrease the need for increased arthroscopic irrigation pump pressure throughout the arthroscopic shoulder surgery as compared to injection not containing epinephrine.

2.2. Primary Objectives
To evaluate surgeon-rated visual clarity and the need for increased irrigation pump pressure during arthroscopic shoulder surgery.

2.3. Secondary Objectives
To evaluate mean arterial pressure, operative time, and any adverse events that occur during arthroscopic shoulder surgery.

2.4. Potential Risks and Benefits:
a. End Points - Efficacy
The use of epinephrine injection into the subacromial space prior to surgery may improve surgeon-rated visual clarity throughout surgery and obviate the need for increased irrigation pump pressure increases. Limiting the total dose of epinephrine required for adequate visualization helps to limit both the total cost and the potential for cardiovascular adverse events related to the use of epinephrine. Improved visual clarity may also decrease total operative time, which would further decrease the cost of the surgery. Obviating the need for increasing the irrigation pump pressure decreases the extravasation of fluid from the subacromial space into the soft tissues, thereby decreasing intra-operative and post-operative swelling leading to improved pain post-operatively.

b. End Points - Safety
While there are several published case reports describing epinephrine-related cardiovascular adverse events during shoulder arthroscopic surgery, all of these have occurred with the use of epinephrine within the irrigation fluid throughout the case. By limiting the use of epinephrine to the pre-operative subacromial injection and only the first 6 liters of arthroscopic irrigation fluid rather than throughout the entirety of the surgery, we hope to decrease the risk of these uncommon adverse events.

3. STUDY POPULATION

3.1. List the number of subjects to be enrolled.
Thirty (n=30) subjects recruited from Texas will be sought for each group for a total enrollment of sixty (n=60). This is from a power analysis performed. The minimal clinically significant difference in visual acuity score (0-10) is 2 points, or 20%, as established in a prior study [1]. In order to ensure 80% power at an alpha of 0.05, a minimum of 26 patients are needed in each study group.
[1] D. Avery, et al., Arthroscopy 31(1) (2015) 12-8.

3.2. Criteria for Recruitment
Our study population will be adult (18 years of age or older) patients undergoing arthroscopic shoulder surgery requiring visualization within the subacromial space. This includes primarily arthroscopic rotator cuff debridement or repair, arthroscopic subacromial decompression, arthroscopic subacromial bursectomy or bursal debridement, and arthroscopic distal clavicle resection, among other arthroscopic procedures. Only procedures performed in the seated, upright (ie, beach chair) position will be included. Study participation will be contingent upon signed informed consent obtained prior to performing data collection or study procedures.

3.3. Inclusion Criteria
Patients will be included who:
- Are individuals 18 years of age or older
- Are able to provide informed consent
- Undergo arthroscopic shoulder surgery in the seated upright (beach-chair) position requiring visualization within the subacromial space

3.4. Exclusion Criteria
Subjects meeting any of the exclusion criteria at baseline will be excluded from participation. These criteria include those who:
- Are unable to provide informed consent
- Non-English speaker
- Have a history of adverse medication reaction to epinephrine
- Arthroscopic shoulder surgery not requiring visualization in the subacromial space or performed inthe lateral position

3.5. Withdrawal Criteria
Subject study participation will be discontinued upon patient request.

3.6. Subject Replacement
There is no intervention or required follow-up after the pre-operative subacromial injection, so patient drop-out will be minimal.

4. TRIAL SCHEDULE
Based on historic clinic data for the principal investigator and co-investigators, we anticipate meeting our enrollment target around 12 weeks from opening enrollment. Once enrolled, subjects will be randomized into either the epinephrine or placebo group. Surgeon-rated visual clarity score will be obtained immediately post-operatively.

5. STUDY DESIGN
5.1. Summary of Study Design
The study utilizes parallel groups with randomized assignments. Randomization will be performed prior to surgery and group designation will be placed within an opaque envelope in the patient's chart. The circulating nurse will prepare the pre-operative injection: study patients will receive an injection containing a total volume of 20 mL of bupivacaine with epinephrine (0.3 mL epinephrine in 30 mL of 0.5% bupivacaine)whereas control patients will receive an injection containing 20mL of 0.5% bupivacaine alone. The syringe will not be labeled, and the contents of the injection will not be disclosed to the surgeon to preserve blinding. The injection will be performed with an 18-gauge needle into the subacromial space via a posterior or lateral approach after positioning the patient in the beach chair position, but prior to prepping and draping. The first 10 liters of arthroscopic irrigation used during the case will contain a total of 10 mg of epinephrine (dilution 1:1000), then saline without epinephrine will be used for the remainder of the surgical procedure. Throughout the case, the mean arterial pressure of the patient will be monitored. At the conclusion of the surgical procedure, the surgeon will rate visual clarity on a visual analog scale from 0 to 10. We will also record changes in pump pressure from the initial pressure of 35mmHg during the surgical procedure. Finally, we will note any adverse events during or after the surgical procedure. In the unlikely event of an intra-operative or early post-operative adverse event that may be related to epinephrine administration, the presence or lack of epinephrine will be revealed to the anesthesiology team to ensure optimal treatment of the adverse event.

6. METHODS AND ASSESSMENTS
6.1. Randomization and Blinding
Simple randomization of enrolled subjects will occur prior to surgical intervention. A certified random number generator will be accessed that will generate a number to assign to the enrolled patient. A research coordinator will bring the randomization envelopes on the day of surgery. Blinding of enrolled subjects will be performed to prevent bias from occurring based on patient expectations of the procedure. To reduce recall bias, group allocation will be kept concealed from the investigator until the completion of visual clarity scoring at the conclusion of each surgical procedure.

6.2. Contraception and Pregnancy Testing
Not Applicable

6.3. Study Visits and Procedures
a. Screening Visits and Procedures
After diagnosis and the decision to proceed with surgery has been made, patients will be screened for eligibility to participate in the study.
b. Study Visits and Procedures
If deemed appropriate for inclusion of the study after screening, informed consent will be obtained by a research coordinator prior to proceeding with surgery
c. Final Study Visit:
There is no post-operative visit required for this study.
d. Post Study Follow up and Procedures
None.
e. Discontinuation Visit and Procedures
Subjects who voluntarily wish to withdraw from the study will be asked to continue with all standard of care visits and procedures, and their removal from study participation will have no effect on the quality or level of care provided.

7. TRIAL MATERIALS
7.1. Trial Product (s)
Not Applicable

7.2. Storage and Drug Accountability
Not Applicable

8. TREATMENT
8.1. Rationale for Selection of Dose
The dose of epinephrine has been used by the investigators in this study for several years without any reported medication-related adverse events.

8.2. Study Drug Formulations
Not Applicable

8.3. Study Drug Administration
Not Applicable

8.4. Specific Restrictions / Requirements
No specific restrictions or requirements will be placed on the study patient except those indicated in accordance with the typical post-operative period following the specific surgical procedure that was performed.

8.5. Blinding
Blinding of enrolled subjects will be performed to prevent bias from occurring based on patient expectations of the procedure. If desired, patients may learn of their study designation after completion of the surgeon-rated visual clarity score immediately post-operatively.

8.6. Concomitant therapy
All medications (prescription and over the counter), vitamin and mineral supplements, and/or herbs taken by the participant will be documented.

9. SAFETY MEASUREMENTS
9.1. Definitions
An Adverse Event (AE) is defined as any untoward medical occurrence associated with the use of an investigational product in humans and that does not necessarily have a causal relation with the investigational product. AEs can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease

temporally associated with the use of an investigational procedure or product, whether or not related to the investigational procedure or product.
An adverse event is considered "serious" if, in the view of the investigator, it results in any of the following outcomes:

- Led to death
- Led to serious deterioration in health of the subject, that either resulted in
    - A life-threatening illness or injury, or
    - A permanent impairment of a body structure or function, or
    - Inpatient or prolonged hospitalization, or
    - Medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment to a body structure or a body function
- Led to fetal distress, fetal death or congenital abnormality or birth defect, or
- Required intervention to prevent permanent impairment or damage, or
- Other serious events that do not fit the other outcomes, but the event may jeopardize the subject and may require medical or surgical intervention (treatment) to prevent one of the other outcomes.

Within 48 hours of becoming aware of a SAE, the investigator must complete the SAE report (providing as much information as is immediately available). The investigator must submit this SAE report to the study's DSMB. The investigator must also report all SAEs to the IRB, as is required by the IRB.

9.2. Collecting, Recording and Reporting of Adverse Events

Adverse Events (AEs) will be collected throughout the study and all AEs will be captured. The Investigator or designee will record all AEs on the appropriate CRFs. Investigators are responsible for reporting all AEs and SAEs. The investigator will assess subjects at each study visit for the occurrence of AEs. In order to avoid bias in eliciting AEs, subjects should be asked non-leading questions. All AEs, regardless of severity, reported by the subject or found on examination or report, must be recorded. All AEs must be followed until resolution is reached. All treatments and outcomes of the AE must be recorded. All AEs and SAEs must be followed until:

- AE is resolved (i.e., return to normal/baseline values)
- Subject is lost to follow-up or withdraws consent
- Subject completes study, including required follow-up visits
- Study closure

The investigator must, following GCP guidelines, continue to treat (or refer subject to an appropriate practitioner for continuing treatment of any AE that remains unresolved after the subject has completed study participation. The severity of all AEs will be categorized as mild, moderate, or severe based on the following definitions:

- Mild: The subject is aware of the sign or symptom, but finds it easily tolerated. The event is of little concern to the subject and/or little clinical significance. The event is not expected to have any effect on the subject's overall health or well-being.
- Moderate: The subject has discomfort enough to cause interference with or change in usual activities. The event is of some concern to the subject's health or well-being and may require medical intervention and/or close follow-up.
- Severe: The adverse event interferes considerably with the subject's usual activities. The event is of definite concern to the subject and/or poses substantial risk to the subject's health or well-being. The event is likely to require medical intervention and/or close follow-up and may be incapacitating or life threatening. Hospitalization and treatment may be required.

The investigator must assess causality of AE in relation to study procedure or using of the study product as: unrelated, possible, and definite based on the following definition:

- Unrelated: The AE is definitely not associated with the study procedure
- Possible: There is evidence to suggest the casual relationship between the study procedure and the AE
- Definite: The AE was caused by the study procedure

Reporting of Adverse Events · The principal investigator will report all AEs and SAEs occurring in clinical investigations to the IRB according to the UTHSC-Houston IRB policy.

9.3. Safety Monitoring Plan

Participants Safety

- The potential risks to study participants include very rare cardiovascular adverse events including arrhythmia and cardiomyopathy. There is a possibility for a breach of confidentiality.

- The potential benefits to study participants include improved visual clarity, shorter operative time, and less frequent need for increased arthroscopic irrigation pump pressure increases, which may result in less fluid extravasation into the surrounding soft tissue and less post-operative pain and analgesic use.
- Adverse Events (AEs), Serious Adverse Events (SAEs) and Unanticipated Problems (UPs) will be identified during clinical assessments by the principal investigator and medical team and reported to the study's safety monitor for review and the IRB. Protection against Study Risks
- Informed consent will be provided both verbally and in written form to subjects. The consent process informs a volunteer about the study, indicates the participation is voluntary and he/she has the right to stop at any time. Risks are enumerated in the informed consent form and described orally during the consent process.
- The procedures to protect against risks with participation in this study are minimized by a safe, hygienic environment for all medical procedures and an experienced, certified staff performing all procedures. The risk of breach of confidentiality is minimized by securing all study related data and PHI behind encrypted, password protected drives and servers.

UTHealth CTRC DSMP Checklist

- Primary and secondary outcome measures
    - Primary: surgeon-rated visual clarity score (visual analog scale 0 to 10), changes in intra-operative arthroscopic pump pressure
    - Secondary: mean arterial pressure intra-operatively, total operative time, adverse events intra-operatively or post-operatively
    - Inclusion: patients 18 years of age or older who are able to provide informed consent and who are to undergo arthroscopic shoulder surgery in the seated upright (beach-chair) position requiring visualization of within the subacromial space.
    - Exclusion: Are unable to provide informed consent, non-English speaker, have a history of adverse medication reaction to epinephrine, and who are having arthroscopic shoulder surgery that does not require visualization within the subacromial space or performed in the lateral position.
    - Sample size: Thirty (n=30) subjects recruited from Texas will be sought for each group for a total enrollment of sixty (n=60). This is from a power analysis performed. The minimal clinically significant difference in visual acuity score (0-10) is 2 points, or 20%, as established in a prior study. In order to ensure 80% power at an alpha of 0.05, a minimum of 26 patients are needed in each study group.
- List of participating enrolling clinics or data collection centers
    - Memorial Hermann Memorial City Medical Center
    - Memorial Hermann Surgery Center West Houston
    - Memorial Hermann Orthopedic & Spine Hospital
    - Memorial Hermann Surgery Center
    - UT Physicians Orthopedics – Texas Medical Center
    - UT Physicians Orthopedics – Memorial City
- Projected timeline
    - Based on historic clinic data for the principal investigator and co-investigators, we anticipate meeting our enrollment target around 12 weeks from opening enrollment. Once enrolled, subjects will be randomized into either the epinephrine or placebo group. Surgeon-rated visual clarity score will be obtained immediately post-operatively.
- Target population distribution (e.g., women, minorities, etc.)
    - The target population distribution will be the typical patients that the principal investigator and co-investigators schedules and operates on here at the UT Health and Memorial Hermann Health systems. Randomization will ensure that both groups will have similar demographic backgrounds.
- Data acquisition and transmission
    - Clinical assessments and images will be uploaded and stored on Epic and Centricity as is standard. The recorded assessments and images will be stored for study use for at least six years, with all study related data stored in Redcap.
    - Demographic data (name, age, gender, weight, race) will be collected from medical records and stored in Redcap.
    - Surgical data (start and stop times for procedure, type of procedure performed, mean arterial pressure) will be recorded and stored in Redcap.

    - Objective clinical data (adverse events) will be collected during the post-operative period with information collected stored in Redcap.
    - Subjective clinical data (surgeon-rated visual clarity score, surgeon-requested increase in arthroscopic irrigation pump pressure) will be recorded and stored in Redcap.
    - Imaging data (none)
- Data entry methods
    - A linking log and data collection form will be used to protect subjects' PHI. All data will be entered and stored in a Redcap project drive to ensure maximal security and anonymity.
- Data analysis plan
    - Demographic variables and diagnostic outcomes will be compared using t-test for continuous variables and chi-square or Fisher exact test for categorical variables. A Mann-Whitney rank sum test will be used to compare median visual clarity scores.
- Quality assurance plan
    - To maintain accuracy, consistency and completeness of data, periodic audits and self-assessments will be conducted. The data will be cross-checked by the study coordinator and the PIs to maintain quality control.
- Reporting mechanisms of AEs/SAEs to the IRB, FDA, and NIDA
    - The principal investigator will report all AEs and SAEs occurring in clinical investigations to the IRB according to the UTHSC-Houston IRB policy. A definition of what constitutes an AE or SAE can be found below in this document as well as within the study protocol.
        - AEs will be complied and submitted on an annual basis to the IRB. Each AE will require review from the investigator as soon as identified.
        - SAEs will be reviewed by the investigator as soon as identified, and all SAEs will be reported to the IRB within 48 hours of identification.
- Reporting mechanisms of IRB actions to NIDA
    - No drugs are involved in this study, so reporting to the NIDA will not be necessary.
- Report of changes or amendments to the protocol
    - All requested changes or amendments to the protocol will be submitted for IRB approval prior to enacting on any subjects previously or to be enrolled. These amendments will be logged and a comprehensive record of all protocol versions and amendments will be maintained by the investigators.
- Trial stopping rules
    - Up to discretion of CTRC/IRB
- Conflict of interest
    - There are no conflicts of interest to report from any of the involved investigators on the study
- Potential risks and benefits for participants
    - The potential risks to study participants include very rare cardiovascular adverse events including arrhythmia and cardiomyopathy. There is a possibility for a breach of confidentiality.
    - The potential benefits to study participants include improved visual clarity, shorter operative time, and less frequent need for increased arthroscopic irrigation pump pressure increases, which may result in less fluid extravasation into the surrounding soft tissue and less post-operative pain and analgesic use.
- Collecting and reporting of AEs and SAEs
    - Adverse Events (AEs), Serious Adverse Events (SAEs) and Unanticipated Problems (UPs) will be identified during clinical assessments by the principal investigator and medical team and reported to the study's safety DSMB and the IRB for review.
        - An Adverse Event (AE) is defined as any untoward medical occurrence associated with the use of an investigational product in humans and that does not necessarily have a causal relation with the investigational product. AEs can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of an investigational procedure or product, whether or not related to the investigational procedure or product.
        - An adverse event is considered "serious" if, in the view of the investigator, it results in any of the following outcomes:
            - Led to death
            - Led to serious deterioration in health of the subject, that either resulted in

        - A life-threatening illness or injury, or
        - A permanent impairment of a body structure or function, or
        - In-patient or prolonged hospitalization, or
        - Medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment to a body structure or a body function
    - Led to fetal distress, fetal death or congenital abnormality or birth defect, or
    - Required intervention to prevent permanent impairment or damage, or
    - Other serious events that do not fit the other outcomes, but the event may jeopardize the subject and may require medical or surgical intervention (treatment) to prevent one of the other outcomes.
- Management of SAEs or other study risks
    - Within 48 hours of becoming aware of a SAE, the investigator must complete the SAE report (providing as much information as is immediately available). The investigator must submit this SAE report to the study's safety monitor. The investigator must also report all SAEs to the IRB, as is required by the IRB.
    - Plans for Interim Analysis of efficacy data
    - In conjunction with the listed Safety Monitor patient reports will be sent once specific numbers of patients have been enrolled: 30 patients, 60 patients.
- Responsibility for data and safety monitoring
    - All investigators listed on the study will be responsible for upholding ethical and appropriate procedures and handling of subject data. Internal self-monitoring will be performed by the research team to ensure only data listed in the protocol is collected, and ensure the accuracy of the collected data. The principal investigator will ultimately be responsible for ensuring all safe handling of study related information.
- Frequency of DSM reviews
    - Up to discretion of CTRC/IRB
- Content of DSM report
    - Up to discretion of CTRC/IRB

10. DATA ANALYSIS

10.1. Data Quality Assurance

To maintain accuracy, consistency and completeness of data, periodic audits and self-assessments will be conducted. The data will be cross-checked by the study coordinator and the PIs to maintain quality control.

10.2. Data Entry and Storage

All data will be entered and stored into a Redcap project drive to ensure maximal security and anonymity.

11. SAMPLE SIZE AND STATISTICAL METHODS

11.1. Determination of Sample Size

Thirty (n=30) subjects recruited from Texas will be sought for each group for a total enrollment of sixty (n=60). This is from a power analysis performed. The minimal clinically significant difference in visual acuity score (0-10) is 2 points, or 20%, as established in a prior study. In order to ensure 80% power at an alpha of 0.05, 26 patients are needed in each study group. Minimal attrition is expected given that there is no routine follow-up necessary.

11.2. Statistical and Analytical Plans

Demographic variables and diagnostic outcomes will be compared using t-test for continuous variables and chi-square or Fisher exact test for categorical variables. A Mann-Whitney rank sum test will be used to compare median visual clarity scores. In the case where a serious medication-related adverse events occurs, we will also start an early analysis to determine the potential causes.

12. ETHICAL CONSIDERATIONS

12.1. Informed Consent

This study will obtain written informed consent prior to performing any study-related data collection. Research coordinators will obtain informed consent from the patient prior to administration of sedation. Consent will be obtained under the direction of Dr. James Gregory. In obtaining and documenting informed consent, we will ensure compliance with all GCP guidelines and standard ethical principles.

12.2. IRB review
This protocol and the associated informed consent documents will be submitted to the IRB for review and approval.

12.3. Confidentiality of Data and Patient Records
All study-related data will be de-identified and stored on a password-protected server within the Department of Orthopaedic Surgery, accessible only by study-specific personnel identified in this protocol. Records will be maintained for at least six years after study completion as per University Policy. Protected health information (PHI) will not be disclosed to any third party and will not be published in any research reports that result from their inclusion in the study.

13. PUBLICATIONS
We plan to publish the results of this study in the form of posters/abstracts for orthopedic-related organization meetings and manuscripts to orthopedic journals; however, no identify or personal information regarding the subjects will be reported. The results of this study will be submitted for publication and for coverage by scientific media. Dissemination to policy makers within the orthopedic community will be considered as well, pending results. Results will be returned to the research subjects upon request.

14. RETENTION OF TRIAL DOCUMENTS
Records for all participants and study-related documentation (consisting of evidence to study eligibility, history and physical findings, clinical data) as well as IRB records and other regulatory documentation will be retained by the PI in a secure fashion. These records will be made available for inspection and copying by authorized authorities upon request.