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A COMPARATIVE STUDY EVALUATING THE DIAGNOSTIC ACCURACY OF WRIST ARTHROSCOPY USING THE NANOSCOPE COMPARED TO CONVENTIONAL ARTHROSCOPIC INSTRUMENTATION

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Statement of Compliance

This study will be conducted in accordance with the Code of Federal Regulations on the Protection of Human Subjects (45 CFR Part 46), 21 CFR Parts 50, 56, 312, and 812 as applicable, any other applicable US government research regulations, and institutional research policies and procedures. The International Conference on Harmonisation ("ICH") Guideline for Good Clinical Practice ("GCP") (sometimes referred to as "ICH-GCP" or "E6") will be applied only to the extent that it is compatible with FDA and DHHS regulations. The Principal Investigator will assure that no deviation from, or changes to the protocol will take place without prior agreement from the sponsor and documented approval from the Institutional Review Board (IRB), except where necessary to eliminate an immediate hazard(s) to the trial participants. All personnel involved in the conduct of this study have completed Human Subjects Protection Training.

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List of Abbreviations

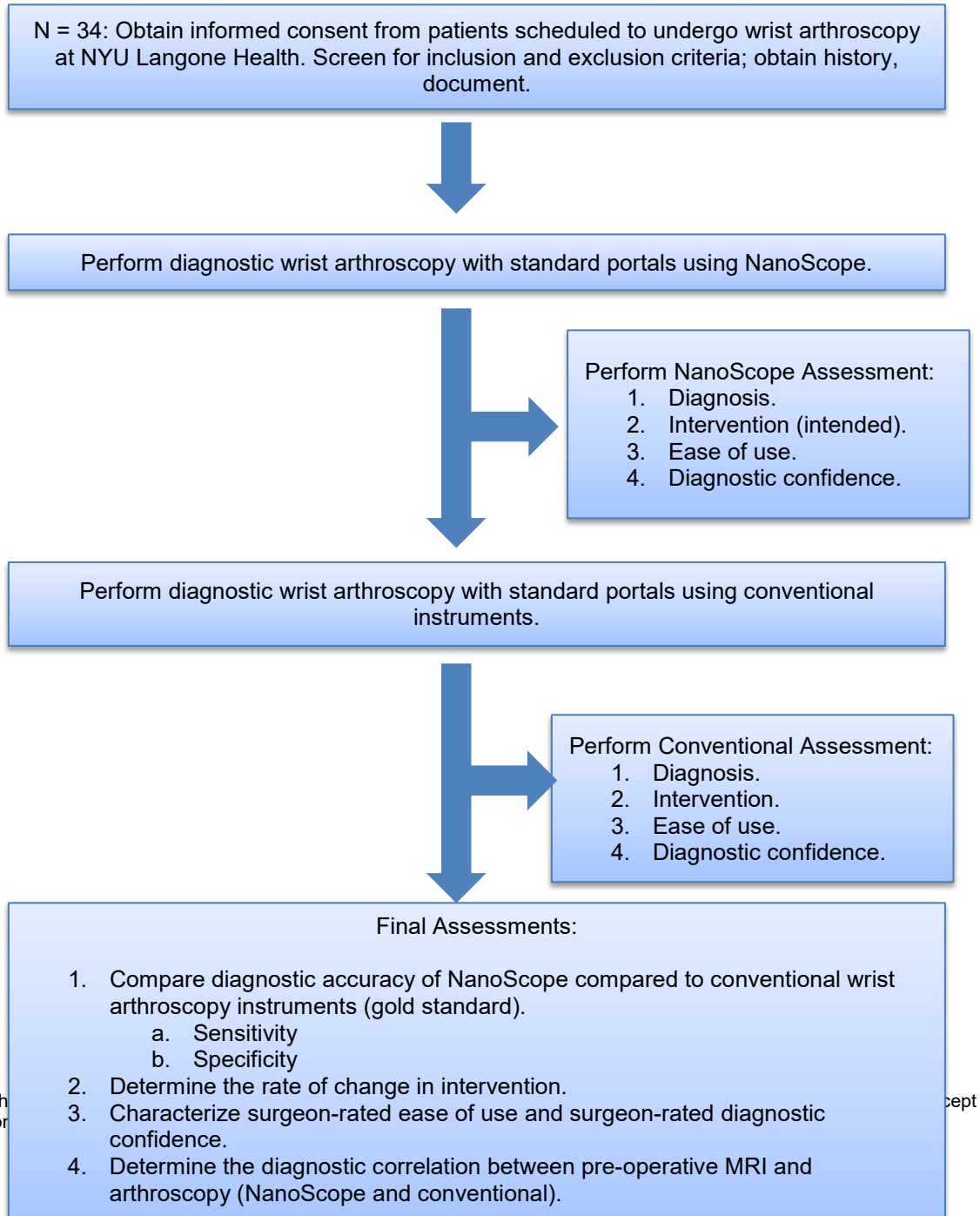
AE	Adverse Event/Adverse Experience
CFR	Code of Federal Regulations
CRF	Case Report Form
CSOC	Clinical Study Oversight Committee
DCC	Data Coordinating Center
DHHS	Department of Health and Human Services
DSMB	Data and Safety Monitoring Board
FFR	Federal Financial Report
FWA	Federalwide Assurance
GCP	Good Clinical Practice
HIPAA	Health Insurance Portability and Accountability Act
ICF	Informed Consent Form
ICH	International Conference on Harmonisation
IRB	Institutional Review Board
ISM	Independent Safety Monitor
MOP	Manual of Procedures
N	Number (typically refers to participants)
NIH	National Institutes of Health
OHRP	Office for Human Research Protections
OHSR	Office of Human Subjects Research
PI	Principal Investigator
QA	Quality Assurance
QC	Quality Control
SAE	Serious Adverse Event/Serious Adverse Experience
SOP	Standard Operating Procedure
US	United States

Protocol Summary

Title	A Comparative Study Evaluating the Diagnostic Accuracy of Wrist Arthroscopy Using the NanoScope Compared to Conventional Arthroscopic Instrumentation
Short Title	Wrist Arthroscopy Study
Brief Summary	*The purpose of this study is to evaluate the diagnostic efficacy of Arthrex NanoScope compared to conventional arthroscopic instruments. Patients with wrist pathology who are indicated for an arthroscopic procedure will be enrolled pre-operatively after a thorough discussion of the study aims, risks, and benefits. At the time of surgery, under standard conditions, using standard wrist arthroscopy portals, a diagnostic arthroscopy will be performed with the Arthrex Nanoscope. The diagnostic arthroscopy will be performed in a stepwise manner for consistency with notation of pathology and intended intervention. The diagnostic arthroscopy will then be performed with the standard arthroscopic equipment, again noting pathology and final intervention. Post-operatively, diagnostic accuracy, incidence of change in intervention, and surgeon rated ease of use and confidence will be determined.*
Phase	Not applicable
Objectives	Primary Outcome: To compare the diagnostic sensitivity and specificity of the NanoScope compared to conventional arthroscopic instruments. Secondary Outcome: To determine if the diagnostic variability between NanoScope and conventional arthroscopic instruments results in a change in intervention. Surgeon-rated ease of use. Surgeon-rated diagnostic confidence. Secondary Outcome: To determine the diagnostic correlation between pre-operative MRI and arthroscopy (NanoScope and conventional).
Methodology	Prospective Cohort Study, Diagnostic

Primary	**Primary** 1. Diagnostic accuracy of Nanoscope compared to conventional arthroscope. **Secondary** 1. Incidence of change in intervention. 2. Surgeon rated ease of use. 3. Surgeon rated confidence of diagnosis. 4. Comparative correlation between pre-operative MRI and arthroscopy.
Study Duration	1 year
Participant Duration	1 day
Duration of IP administration	Not applicable
Population	N = 34, men and women, age ≥ 18 years, being treated at NYU Langone Health
Study Sites	1. NYU Langone Orthopedic Hospital 2. Tisch Hospital, NYU Langone Health 3. NYU Langone Orthopedic Center (38th Street) 4. Joan H. & Preston Robert Tisch Center at Essex Crossing, NYU Langone Health
Number of participants	34
Description of Study Agent/Procedure	The Arthrex NanoScope is a 1.9 mm wrist arthroscopy system.
Reference Therapy	Conventional wrist arthroscope
Key Procedures	Diagnostic wrist arthroscopy of wrists with clinical and imaging confirmation of internal derangement (ligament/articular/bony injury).
Statistical Analysis	Descriptive statistics will be used to provide a quantitative summary of the data in the study. Specifically, the analysis performed included measures of central tendency (mean, median, and mode) and measures of variability (range and standard deviation). Categorical data will be described in percentages and a Chi-squared test will be employed to detect if these categorical variables are related between the two treatment groups with a p value of < .05. Continuous data will be described in means with standard deviations. A two-tailed Student's T-test will be employed to compare the means between the two treatment groups with a p value of < .05.

Schematic of Study Design



1 Key Roles

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2 Introduction, Background Information and Scientific Rationale

2.1 Background Information and Relevant Literature

Arthroscopically assisted treatments continue to advance with regard to diagnostic efficacy and treatment capabilities. Arthroscopy affords surgical intervention through a minimally invasive approach, which translates into improved visualization, better outcomes, and decreased complications.[1] Initially developed for larger joints such as the shoulder and knee, arthroscopic technology has advanced to include instrumentation amenable to accessing smaller joints, including the wrist.[2] However, conventional instrumentation has inherent size limitations resulting in difficulty or inability to access smaller spaces (midcarpal joint, carpometacarpal joint, etc.). Innovations in instrumentation, including the Arthrex NanoScope, have focused on decreasing instrument size. The use of these smaller instruments have become commonplace for many surgeons for the diagnosis and treatment of wrist injuries. However, to our knowledge, there are no studies evaluating the diagnostic efficacy of these new arthroscopic visualization systems compared to conventional arthroscopic instruments.

The purpose of this study is to evaluate the diagnostic accuracy of the Arthrex NanoScope compared to conventional arthroscopic instruments. Additionally, we will analyze if there is difference in intended intervention, ease of use, and diagnostic confidence, and correlation between pre-operative MRI and arthroscopic findings.

2.2 Name and Description of the Investigational Agent

The Arthrex NanoScope is commonly used for joint arthroscopy. The instrument itself is not an investigational agent. We are evaluating the instruments diagnostic accuracy compared to conventional instruments.

The FDA-cleared Arthrex NanoScope System is intended to be used as an endoscopic video camera in a variety of endoscopic surgical procedures, including but not limited to: orthopedic, laparoscopic, urologic, sinuscopic, and plastic surgical procedures. The device is also intended to be used as an accessory for microscopic surgery.

Instrument: Arthrex NanoScope – Nano Operative Arthroscopy System

- *1.9 mm single-use, needle-size sterile camera.*
- *13" medical grade 3-in-1 camera control unit.*
- *This device is currently in use for wrist arthroscopy. The intended purpose of this research study is to compare this devices diagnostic accuracy to conventional larger arthroscopic equipment.*
- https://www.arthrex.com/hand-wrist/nano-arthroscopy-system-for-hand-and-wrist

2.3 Rationale

The use of these smaller arthroscopic instruments have become commonplace for many surgeons for the diagnosis and treatment of wrist injuries. However, to our knowledge, there are no studies evaluating the diagnostic efficacy of these new arthroscopic visualization systems compared to conventional arthroscopic instruments. The purpose of this study is to evaluate the diagnostic accuracy of the Arthrex Nanoscope compared to conventional arthroscopic instruments. Additionally, we will analyze if there is difference in intended intervention, ease of use, and diagnostic confidence.

2.4 Potential Risks & Benefits

2.4.1 Known Potential Risks

There are no additional potential risks pertaining to this study involving with the use of the Arthrex NanoScope compared to conventional wrist arthroscopy instruments. The NanoScope will be used with the standard extremity stabilization tower and arthroscopic portals as are used with conventional instruments. The diagnostic arthroscopy using the NanoScope will be performed immediately prior to the diagnostic arthroscopy with the conventional instrumentation. Estimated additional time to perform the diagnostic arthroscopy with the NanoScope is < 5 minutes, which will not result in subjects exposure to risks associated with prolonged anesthesia or surgery. There is also no additional wrist of passing a second device (NanoScope) into the wrist joint, in addition to the conventional arthroscope.

2.4.2 Known Potential Benefits

There are no potential benefits to the participants of this study by virtue of participation.

3 Objectives and Purpose

3.1 Primary Objective

To evaluate the diagnostic accuracy of the Arthrex NanoScope compared to conventional arthroscopic instruments.

3.2 Secondary Objectives (if applicable)

To determine if the diagnostic accuracy of the Arthrex NanoScope compared to conventional arthroscopic instruments results in a change in intended intervention.

To determine the surgeon-rated ease of use and diagnostic confidence of the Arthrex NanoScope.

To determine the diagnostic correlation between pre-operative MRI and arthroscopy (NanoScope and conventional). The MRI is standard of care for evaluation of ligamentous wrist pathology. It will not be mandated as part of the protocol.

4 Study Design and Endpoints

4.1 Description of Study Design

- *Prospective cohort study, Diagnostic*
- *Single cohort*
  - *Step 1: NanoScope*
  - *Step 2: Conventional wrist arthroscopy instruments*
  - *A single cohort study, comparing the diagnostic accuracy of the Arthrex NanoScope to conventional instruments (gold standard).*
- *Single center*
- *Instrument: Arthrex NanoScope*

4.2 Study Endpoints

4.2.1 Primary Study Endpoints

The primary endpoint will be diagnostic accuracy (%) compared to the gold standard of conventional wrist arthroscopy instruments.

The primary endpoint was chosen to determine if smaller instrumentation provides adequate visualization for the diagnosis of wrist pathology and can therefore be used as the sole means of evaluation.

4.2.2 Secondary Study Endpoints

Secondary endpoints will be a incidence of change in intended intervention and surgeon-rated ease of use and diagnostic confidence.

These secondary endpoints were chosen to determine if a difference in diagnostic accuracy results in a change in intervention as well as to determine the number of uses required for surgeon familiarity with the instruments.

4.2.3 Exploratory Endpoints

An exploratory end point will be evaluation of diagnostic accuracy relative to surgeon-rated ease of use and diagnostic confidence to determine if there is a learning curve.

5 Study Enrollment and Withdrawal

5.1 Inclusion Criteria

In order to be eligible to participate in this study, an individual must meet all of the following criteria:

1. Age > 18 years.
2. Wrist pathology based on clinical examination/imaging studies undergoing wrist arthroscopy for further evaluation/treatment.
3. Willingness to participate in the study

5.2 Exclusion Criteria

An individual who meets any of the following criteria will be excluded from participation in this study:

1. Age < 18 years.

5.3 Vulnerable Subjects

Vulnerable populations will not be included.

5.4 Strategies for Recruitment and Retention

Patients will be recruited from investigator clinical practices. The recruitment plan does not propose to use any NYULMC media services or social media. Patients with clinically diagnosed wrist pathology undergoing wrist arthroscopy will be identified by the attending physician and recruited for the study in the office visit when surgery is indicated/scheduled or in the pre-operative area on the day of surgery. The nature of the information the subjects will be asked to give about themselves will include objective information relevant to their wrist injury. Only the individuals listed in the protocol will have access to the patients study.

As this study does not require long-term patient participation, there are no relevant modalities necessary to enhance participant retention.

The target sample size is 34 patients, recruited from the investigators clinical practice.

5.4.1 Use of DataCore/Epic Information for Recruitment Purposes

We will not be using DataCore/Epic for recruitment purposes.

5.5 Duration of Study Participation

The duration of the study participants' participation will be one day.

5.6 Total Number of Participants and Sites

Recruitment will end when approximately 34 participants are enrolled. It is expected that approximately 34 participants will be enrolled in order to produce 34 evaluable participants. Participants will be enrolled at four 4 NYU study sites:

1. NYU Langone Orthopedic Hospital
2. Tisch Hospital, NYU Langone Health
3. NYU Langone Orthopedic Center (38th Street)
4. Joan H. & Preston Robert Tisch Center at Essex Crossing, NYU Langone Health

5.7 Participant Withdrawal or Termination

5.7.1 Reasons for Withdrawal or Termination

Participants are free to withdraw from participation in the study at any time upon request. An investigator may terminate participation in the study if:

- Any clinical adverse event (AE), laboratory abnormality, or other medical condition or situation occurs such that participation in the study would not be in the best interest of the participant.
- The participant meets an exclusion criterion (either newly developed or not previously recognized) that precludes study participation.

5.7.2 Handling of Participant Withdrawals or Termination

Participants who withdraw from the study will continue routine post-operative follow up with the PI for wrist injury. Their continued care will not be affected by their enrollment in this study.

5.8 Premature Termination or Suspension of Study

Not applicable.

Study may resume once concerns about safety, protocol compliance, data quality are addressed and satisfy the sponsor, IRB and/or FDA.

6 Study Agent (Study drug, device, biologic, vaccine etc.) and/or Procedural Intervention

The procedural intervention will be a diagnostic wrist arthroscopy using the Arthrex NanoScope followed by a diagnostic wrist arthroscopy using conventional wrist arthroscopy equipment.

6.1.1 Device Specific Considerations

Instrument: Arthrex NanoScope – Nano Operative Arthroscopy System

- *1.9 mm single-use, needle-size sterile camera.*
- *13" medical grade 3-in-1 camera control unit.*
- *This device is currently in use for wrist arthroscopy. The intended purpose of this research study is to compare this devices diagnostic accuracy to conventional larger arthroscopic equipment.*
- https://www.arthrex.com/hand-wrist/nano-arthroscopy-system-for-hand-and-wrist

6.2 Study Behavioral or Social Intervention(s)

6.2.1 Administration of Intervention

The attending physician will perform the diagnostic arthroscopy.

6.2.2 Procedures for Training Interventionalists and Monitoring Intervention Fidelity

The use of conventional arthroscopic instruments and the Arthrex NanoScope are considered standard of care, and clinicians do not require additional training for either.

6.2.3 Assessment of Subject Compliance with Study Intervention

Not applicable.

6.3 Study Procedural Intervention(s) Description

Diagnostic arthroscopy is a well-established procedure. The procedure itself is not considered the study intervention. Use of the NanoScope using standard extremity stabilization tower and standard wrist arthroscopy portals will be employed. The instrumentation is similar to conventional arthroscopic instrumentation with exception of size, therefore additional training is not required for its use.

- https://www.arthrex.com/hand-wrist/nano-arthroscopy-system-for-hand-and-wrist

6.3.1 Administration of Procedural Intervention

The attending physician will perform the diagnostic arthroscopy.

6.3.2 Procedures for Training of Clinicians on Procedural Intervention

The intervention will be standardized by having a single operator (attending) perform the diagnostic arthroscopy with the Arthrex NanoScope and conventional instruments. The diagnostic arthroscopy will be performed in a stepwise manner evaluating the ligaments and articular surfaces of the wrist.

6.3.3 Assessment of Clinician and/or Participant Compliance with Study Procedural Intervention

Physician compliance with procedural intervention will be through review of the medical record/operative report.

7 Study Procedures and Schedule

7.1 Study Procedures/Evaluations

7.1.1 Study Specific Procedures

- Patients undergoing wrist arthroscopy for diagnostic evaluation and treatment of a wrist injury will be enrolled pre-operatively following a discussion of the study, risks, benefits, and informed consent.
- All patients will be positioned supine and placed in an upper extremity traction tower with the shoulder abducted, elbow flexed to 90 degrees, forearm in neutral position.
- Standard arthroscopic portals will be made for viewing, instrumentation, inflow, and outflow: 3-4 portal, 6-R portal, midcarpal ulnar (MCU) portal, +/- midcarpal radial (MCR) portal, +/- 6-U portal.
- A diagnostic arthroscopy will be performed with the Arthrex NanoScope.
    - Structures evaluated:
        - Radial styloid
        - Proximal scaphoid articular cartilage
        - Scaphoid fossa
        - Radioscaphocapitate (RSC) ligament
        - Long radiolunate (LRL) ligament
        - Short radiolunate (SRL) ligament
        - Scapholunate (SL) ligament
        - Proximal lunate articular cartilage
        - Lunate fossa
        - Triangular fibrocartilage complex (TFCC)
    - The attending performing the diagnostic arthroscopy will make an initial diagnostic assessment based on the presence/location/severity of synovitis, articular cartilage integrity, ligament injury and determine the intended treatment.
- A diagnostic arthroscopy will then be performed with the standard arthroscopic instruments.
    - Structures evaluated:
        - Radial styloid
        - Proximal scaphoid articular cartilage
        - Scaphoid fossa
        - Radioscaphocapitate (RSC) ligament
        - Long radiolunate (LRL) ligament
        - Short radiolunate (SRL) ligament
        - Scapholunate (SL) ligament
        - Proximal lunate articular cartilage
        - Lunate fossa
        - Triangular fibrocartilage complex (TFCC)
    - The attending performing the diagnostic arthroscopy will make the final diagnostic assessment based on the presence/location/severity of synovitis, articular cartilage integrity, and ligament injury and determine the final treatment.

- Following the procedure the surgeon will perform a short questionnaire.
  - Surgeon rated visualization. (5 point scale)
  - Surgeon-rated ease of use. (5 point scale)
  - Surgeon-rated diagnostic confidence. (5 point scale)
- The initial diagnostic assessment and final diagnostic assessment will be compared to determine diagnostic accuracy of the Arthrex NanoScope.
- "Intended" treatment and "final" treatment will be compared to determine if diagnostic variability would result in potential treatment variability.
- Patients with pre-operative MRIs with a corresponding radiology report will be compared to arthroscopic findings to determination correlation between MRI and arthroscopy.
- No follow-up is required for the purposes of this study.

7.1.2 Standard of Care Study Procedures

Wrist arthroscopy will be performed with regional anesthesia or general anesthesia, determined by the anesthesia team pre-operatively. An upper arm tourniquet will be used. Standard wrist arthroscopy tower will be used. Access to the joint for visualization, instrumentation, inflow, and outflow will use standard portals (see above).

7.2 Study Schedule

7.2.1 Screening

Screening Visit (Day -28 to -1)

- During pre-operative clinical evaluation, the attending will determine potential study participants who are indicated for wrist arthroscopy and meet the inclusion criteria.

7.2.2 Enrollment/Baseline

Enrollment/Baseline Visit (Visit 1, Day 0)

- Obtain informed consent of potential participant verified by signature on study informed consent form.
- Verify inclusion/exclusion criteria.
- Patient then undergoes wrist arthroscopy with the Arthrex NanoScope followed by conventional instruments (See section 7.1.1).

7.2.3 Intermediate Visits

There will be no intermediate visits.

7.2.4 Final Study Visit

There will be no final study visit.

7.2.5 Withdrawal/Early Termination Visit

Following signing of the consent,, prior to the procedure, the patient is able to withdraw from the study..

7.2.6 Unscheduled Visit

As study participation takes place over a single day, unscheduled visit is not applicable.

7.3 Concomitant Medications, Treatments, and Procedures

All concomitant prescription medications taken during study participation will be recorded on the case report forms (CRFs). For this protocol, a prescription medication is defined as a medication that can be prescribed only by a properly authorized/licensed clinician. Medications to be reported in the CRF are concomitant prescription medications, over-the-counter medications and non-prescription medications.

7.4 Justification for Sensitive Procedures

The justification to for performing a diagnostic arthroscopy with the Arthrex NanoScope is to evaluate diagnostic accuracy as this device was intended for visualization of small joints and is currently in use and considered within standard of care.

7.4.1 Precautionary Medications, Treatments, and Procedures

Not applicable.

7.5 Prohibited Medications, Treatments, and Procedures

Treatment with additional upper extremity surgical procedures will not be permitted unless discussed with and approved by the principal investigator.

8 Assessment of Safety

8.1 Specification of Safety Parameters

8.1.1 Definition of Adverse Events (AE)

An ***adverse event*** (AE) is any symptom, sign, illness or experience that develops or worsens in severity during the course of the study. Intercurrent illnesses or injuries should be regarded as adverse events. Abnormal results of diagnostic procedures are considered to be adverse events if the abnormality:

- results in study withdrawal
- is associated with a serious adverse event
- is associated with clinical signs or symptoms
- leads to additional treatment or to further diagnostic tests

- is considered by the investigator to be of clinical significance

8.1.2 Definition of Serious Adverse Events (SAE)

Serious Adverse Event
Adverse events are classified as serious or non-serious. A ***serious adverse event*** is any AE that is:

- fatal
- life-threatening
- requires or prolongs hospital stay
- results in persistent or significant disability or incapacity
- a congenital anomaly or birth defect
- an important medical event

Important medical events are those that may not be immediately life threatening, but are clearly of major clinical significance. They may jeopardize the subject, and may require intervention to prevent one of the other serious outcomes noted above. For example, drug overdose or abuse, a seizure that did not result in in-patient hospitalization, or intensive treatment of bronchospasm in an emergency department would typically be considered serious.

All adverse events that do not meet any of the criteria for serious should be regarded as ***non-serious adverse events***.

8.1.3 Definition of Unanticipated Problems (UP)

Unanticipated Problems Involving Risk to Subjects or Others
Any incident, experience, or outcome that meets all of the following criteria:

- Unexpected in nature, severity, or frequency (i.e. not described in study-related documents such as the IRB-approved protocol or consent form, the investigators brochure, etc)
- Related or possibly related to participation in the research (i.e. possibly related means there is a reasonable possibility that the incident experience, or outcome may have been caused by the procedures involved in the research)
- Suggests that the research places subjects or others at greater risk of harm (including physical, psychological, economic, or social harm).

8.2 Classification of an Adverse Event

8.2.1 Severity of Event

For AEs not included in the protocol defined grading system, the following guidelines will be used to describe severity.

- **Mild** – Events require minimal or no treatment and do not interfere with the participant's daily activities.

- **Moderate** – Events result in a low level of inconvenience or concern with the therapeutic measures. Moderate events may cause some interference with functioning.
- **Severe** – Events interrupt a participant's usual daily activity and may require systemic drug therapy or other treatment. Severe events are usually potentially life-threatening or incapacitating.

8.2.2 Relationship to Study Agent

For all collected AEs, the clinician who examines and evaluates the participant will determine the AE's causality based on temporal relationship and his/her clinical judgment. The degree of certainty about causality will be graded using the categories below.

- ***Definitely Related** – There is clear evidence to suggest a causal relationship, and other possible contributing factors can be ruled out. The clinical event, including an abnormal laboratory test result, occurs in a plausible time relationship to drug administration and cannot be explained by concurrent disease or other drugs or chemicals. The response to withdrawal of the drug (dechallenge) should be clinically plausible. The event must be pharmacologically or phenomenologically definitive, with use of a satisfactory rechallenge procedure if necessary.*
- ***Probably Related** – There is evidence to suggest a causal relationship, and the influence of other factors is unlikely. The clinical event, including an abnormal laboratory test result, occurs within a reasonable time after administration of the drug, is unlikely to be attributed to concurrent disease or other drugs or chemicals, and follows a clinically reasonable response on withdrawal (dechallenge). Rechallenge information is not required to fulfill this definition.*
- ***Possibly Related** – There is some evidence to suggest a causal relationship (e.g., the event occurred within a reasonable time after administration of the trial medication). However, other factors may have contributed to the event (e.g., the participant's clinical condition, other concomitant events). Although an AE may rate only as "possibly related" soon after discovery, it can be flagged as requiring more information and later be upgraded to "probably related" or "definitely related," as appropriate.*
- ***Unlikely to be related** – A clinical event, including an abnormal laboratory test result, whose temporal relationship to drug administration makes a causal relationship improbable (e.g., the event did not occur within a reasonable time after administration of the trial medication) and in which other drugs or chemicals or underlying disease provides plausible explanations (e.g., the participant's clinical condition, other concomitant treatments).*
- ***Not Related** – The AE is completely independent of study drug administration, and/or evidence exists that the event is definitely related to another etiology. There must be an alternative, definitive etiology documented by the clinician.*

8.2.3 Expectedness

Dr. Nader Paksima will be responsible for determining whether an AE is expected or unexpected. An AE will be considered unexpected if the nature, severity, or frequency of the event is not consistent with the risk information previously described for the study agent.

8.3 Time Period and Frequency for Event Assessment and Follow-Up

The occurrence of an AE or SAE may come to the attention of study personnel during study visits and interviews of a study participant presenting for medical care, or upon review by a study monitor. All AEs including local and systemic reactions not meeting the criteria for SAEs will be captured on the appropriate RF. Information to be collected includes event description, time of onset, clinician's assessment of severity,

relationship to study product (assessed only by those with the training and authority to make a diagnosis), and time of resolution/stabilization of the event. All AEs occurring while on study must be documented appropriately regardless of relationship. All AEs will be followed to adequate resolution.

Any medical condition that is present at the time that the participant is screened will be considered as baseline and not reported as an AE. However, if the study participant's condition deteriorates at any time during the study, it will be recorded as an AE. UPs will be recorded in the data collection system throughout the study.

Changes in the severity of an AE will be documented to allow an assessment of the duration of the event at each level of severity to be performed. AEs characterized as intermittent require documentation of onset and duration of each episode.

The PI will record all reportable events with start dates occurring any time after informed consent is obtained until 7 (for non-serious AEs) or 30 days (for SAEs) after the last day of study participation. At each study visit, the investigator will inquire about the occurrence of AE/SAEs since the last visit. Events will be followed for outcome information until resolution or stabilization.

All unresolved adverse events should be followed by the investigator until the events are resolved, the subject is lost to follow-up, or the adverse event is otherwise explained. At the last scheduled visit, the investigator should instruct each subject to report any subsequent event(s) that the subject, or the subject's personal physician, believes might reasonably be related to participation in this study. The investigator should notify the study sponsor of any death or adverse event occurring at any time after a subject has discontinued or terminated study participation that may reasonably be related to this study. The sponsor should also be notified if the investigator should become aware of the development of cancer or of a congenital anomaly in a subsequently conceived offspring of a subject that has participated in this study.

8.4 Reporting Procedures – Notifying the IRB

8.4.1 Adverse Event Reporting

Each adverse event will be reviewed on a case-by-case basis by the study physician and Principle Investigator to determine any risks to the participants' continued participation in the study.

There are no predefined stopping rules for the study. The following table will be used to document such adverse events:

Subject Name	Procedure Date	Signs of Adverse Event	Signature of Monitor	Date and Time

Adverse events will be reported to the IRB within 5 days of the event. Acute medical care will be provided as appropriately needed. The report will be submitted to the IRB on an adverse event CRF and an IRB reportable events form. If the subject reports their inability to continue the study, significant discomfort, or other negative effects, the procedure will terminate immediately, and any generated data will be destroyed. We do not anticipate any such adverse events as all pre-operative or post-operative assessments and interventions are standard of care.

The data of adverse events under this monitoring plan will be assessed by the PI quarterly, every 3 months. Results and all adverse outcomes will be communication to the IRB by the Investigator when required. Every 12 months a review of all subject records, the progress of the study, any safety issues and adverse events that have occurred will be conducted and a report will be included during the annual IRB continuation review.

8.4.2 Serious Adverse Event Reporting

If an event occurs and is determined to be a SAE, it will be documented and monitored as described for AE's, with the addition that the Investigator will notify the IRB directly within 1 business day. Appropriate acute medical care will be provided to the subject.

8.4.3 Unanticipated Problem Reporting

Incidents or events that meet the OHRP criteria for UPs require the creation and completion of an UP report form. It is the site investigator's responsibility to report UPs to their IRB The UP report will include the following information:

- Protocol identifying information: protocol title and number, PI's name, and the IRB project number;
- A detailed description of the event, incident, experience, or outcome;
- An explanation of the basis for determining that the event, incident, experience, or outcome represents an UP;
- A description of any changes to the protocol or other corrective actions that have been taken or are proposed in response to the UP.

To satisfy the requirement for prompt reporting, UPs will be reported using the following timeline:

- UPs that are SAEs will be reported to the IRB within 1 week of the investigator becoming aware of the event.
- Any other UP will be reported to the IRB within 1 week of the investigator becoming aware of the problem.
- All UPs should be reported to appropriate institutional officials (as required by an institution's written reporting procedures), the supporting agency head (or designee), and OHRP within 1 week of the IR's receipt of the report of the problem from the investigator.

8.4.4 Reporting of Pregnancy

Patients who are pregnant will not be included in this study.

8.5 Reporting Procedures – Participating Investigators

This is not a multi-center clinical trial.

8.6 Study Halting Rules

Not applicable.

8.7 Safety Oversight

It is the responsibility of the Principal Investigator to oversee the safety of the study at his/her site. This safety monitoring will include careful assessment and appropriate reporting of adverse events as noted above, as well as the construction and implementation of a site data and safety-monitoring plan. Medical monitoring will include a regular assessment of the number and type of serious adverse events.

9 Clinical Monitoring

Clinical site monitoring is conducted to ensure that the rights and well-being of human subjects are protected, that the reported trial data are accurate, complete, and verifiable, and that the conduct of the trial is in compliance with the currently approved protocol/amendment(s), with GCP, and with applicable regulatory requirement(s).

- The PI will conduct on-site monitoring for initial assessment with a comprehensive review of the data.
- Independent audits will be conducted by the sub-investigators to ensure monitoring practices are performed consistently across all participating sites.
- Each clinical site will perform internal quality management of study conduct, data collection, documentation and completion. An individualized quality management plan will be developed to describe a site's quality management.

10 Statistical Considerations

10.1 Statistical and Analytical Plans (SAP)

A formal SAP will be completed prior to database lock.

10.2 Statistical Hypotheses

We hypothesize that there will be no difference in the diagnostic accuracy of the Arthrex NanoScope compared to conventional arthroscopic instruments.

10.3 Description of Statistical Methods

10.3.1 General Approach

Descriptive statistics will be used to provide a quantitative summary of the data in the study. Specifically, the analysis performed included measures of central tendency (mean, median, and mode) and measures of variability (range and standard deviation). Categorical data will be described in percentages and a Chi-squared test will be employed to detect if these categorical variables are related between the two treatment groups with a p value of < .05. Continuous data will be described in means with standard deviations. A two -tailed Student's T-test will be employed to compare the means between the two treatment groups with a p value of < .05.

10.3.2 Analysis of the Primary Efficacy Endpoint(s)

Primary

1. Diagnostic accuracy of Nanoscope compared to conventional arthroscope.

Diagnostic accuracy of the Arthrex Nanoscope will be described as a incidence/percentage compared to the diagnosis determined by wrist arthroscopy with conventional instruments.

10.3.3 Analysis of the Secondary Endpoint(s)

Secondary

1. Incidence of change in intervention.
2. Surgeon rated ease of use.
3. Surgeon rated confidence of diagnosis.
4. Correlation between pre-operative MRI findings and arthroscopic findings.

Secondary endpoints will be described using incidence/percentage. A two-tailed Student's T-tests will be employed to compare the means of surgeon-rated outcomes between the Arthrex NanoScrope and conventional instruments groups with a p value of .05.

10.3.4 Safety Analyses

Safety endpoints will be analyzed as summary statistics during treatment. Adverse events will be PI reported. Adverse events leading to premature discontinuation from the study will be presented in a table.

10.3.5 Adherence and Retention Analyses

Not applicable.

10.3.6 Baseline Descriptive Statistics

Not applicable. Each patient will serve as an internal control.

10.3.7 Tabulation of Individual Response Data

Individual participant data will be listed by measure and time point.

10.3.8 Exploratory Analyses

Not applicable.

10.4 Sample Size

34 participants will be recruited to meet a goal of evaluable participants for the study.

- Outcome measure: diagnostic accuracy
- Test statistic: descriptive statistics

- Null hypothesis: We hypothesize that there will be no difference in the diagnostic accuracy of the Arthrex NanoScope compared to conventional arthroscopic instruments.
- Type I error rate (alpha): 0.95
- Power level: 0.819
- Dropout: Not applicable.
- Approach to handling withdrawals and protocol violations: Not applicable.

Statistical method used to calculate the sample size: At 90% prevalence, in order to detect a change in sensitivity (true-positive) between .70 (sensitivity of MRI) and .90 (sensitivity of arthroscopy), we would need a minimum of 34 subjects with a minimum of 31 who had a ligamentous wrist injury (see table below). This was determine with the guidance of the Center for Clinical Research.

Mohamad Adam Bujang and Tassha Hilda Adnan, Requirements for Minimum Sample Size for Sensitivity and Specificity Analysis www.jcdr.net

n (Sensitivity)							n (Specificity)						
Prev	H_0	H_a	Power	p-value	N1	N	Perv	H_0	H_a	Power	p-value	N1	N
70%	0.50	0.60	0.804	0.047	199	284	70%	0.50	0.60	0.804	0.047	464	663
70%	0.50	0.70	0.810	0.044	49	70	70%	0.50	0.70	0.810	0.044	114	163
70%	0.50	0.80	0.804	0.041	20	29	70%	0.50	0.80	0.804	0.041	47	67
70%	0.50	0.90	0.889	0.039	12	17	70%	0.50	0.90	0.889	0.039	28	40
70%	0.60	0.70	0.801	0.048	181	259	70%	0.60	0.70	0.801	0.048	422	603
70%	0.60	0.80	0.826	0.034	45	64	70%	0.60	0.80	0.826	0.034	105	150
70%	0.60	0.90	0.885	0.035	19	27	70%	0.60	0.90	0.885	0.035	44	63
70%	0.70	0.80	0.818	0.044	155	221	70%	0.70	0.80	0.818	0.044	362	517
70%	0.70	0.90	0.807	0.048	31	44	70%	0.70	0.90	0.807	0.048	72	103
70%	0.80	0.90	0.819	0.040	107	153	70%	0.80	0.90	0.819	0.040	250	357
70%	0.90	0.95	0.816	0.048	231	330	70%	0.90	0.95	0.816	0.048	539	770
80%	0.50	0.60	0.804	0.047	199	249	80%	0.50	0.60	0.804	0.047	796	995
80%	0.50	0.70	0.810	0.044	49	61	80%	0.50	0.70	0.810	0.044	196	245
80%	0.50	0.80	0.804	0.041	20	25	80%	0.50	0.80	0.804	0.041	80	100
80%	0.50	0.90	0.889	0.039	12	15	80%	0.50	0.90	0.889	0.039	48	60
80%	0.60	0.70	0.801	0.048	181	226	80%	0.60	0.70	0.801	0.048	724	905
80%	0.60	0.80	0.826	0.034	45	56	80%	0.60	0.80	0.826	0.034	180	225
80%	0.60	0.90	0.885	0.035	19	24	80%	0.60	0.90	0.885	0.035	76	95
80%	0.70	0.80	0.818	0.044	155	194	80%	0.70	0.80	0.818	0.044	620	775
80%	0.70	0.90	0.807	0.048	31	39	80%	0.70	0.90	0.807	0.048	124	155
80%	0.80	0.90	0.819	0.040	107	134	80%	0.80	0.90	0.819	0.040	428	535
80%	0.90	0.95	0.816	0.048	231	289	80%	0.90	0.95	0.816	0.048	924	1155
90%	0.50	0.60	0.804	0.047	199	221	90%	0.50	0.60	0.804	0.047	1791	1990
90%	0.50	0.70	0.810	0.044	49	54	90%	0.50	0.70	0.810	0.044	441	490
90%	0.50	0.80	0.804	0.041	20	22	90%	0.50	0.80	0.804	0.041	180	200
90%	0.50	0.90	0.889	0.039	12	13	90%	0.50	0.90	0.889	0.039	108	120
90%	0.60	0.70	0.801	0.048	181	201	90%	0.60	0.70	0.801	0.048	1629	1810
90%	0.60	0.80	0.826	0.034	45	50	90%	0.60	0.80	0.826	0.034	405	450
90%	0.60	0.90	0.885	0.035	19	21	90%	0.60	0.90	0.885	0.035	171	190
90%	0.70	0.80	0.818	0.044	155	172	90%	0.70	0.80	0.818	0.044	1395	1550
90%	0.70	0.90	0.807	0.048	31	34	90%	0.70	0.90	0.807	0.048	279	310
90%	0.80	0.90	0.819	0.040	107	119	90%	0.80	0.90	0.819	0.040	963	1070
90%	0.90	0.95	0.816	0.048	231	257	90%	0.90	0.95	0.816	0.048	2079	2310

[Table/Fig-3]: Sample size calculation for sensitivity and specificity analysis for prevalence of disease from 70% to 90%.
Prev = prevalence of disease
H_0 = Hypothesis null
H_a = Hypothesis alternative
N1 = The minimum number of sample size for positive disease
N = The minimum number of sample size requirement for total

10.5 Measures to Minimize Bias

10.5.1 Enrollment/Randomization/Masking Procedures

Enrollment will not be randomized. Each patient will serve as an internal control.

10.5.2 Evaluation of Success of Blinding

Blinding is not possible and not indicated for this study design.

10.5.3 Breaking the Study Blind/Participant Code

Not applicable.

11 Source Documents and Access to Source Data/Documents

Access to study records will be limited to IRB-approved members of the study team. The investigator will permit study-related monitoring, audits, and inspections by the IRB/EC, the sponsor, government regulatory bodies, and University compliance and quality assurance groups of all study related documents (e.g. source documents, regulatory documents, data collection instruments, study data etc.). The investigator will ensure the capability for inspections of applicable study-related facilities (e.g. pharmacy, diagnostic laboratory, etc.).

Participation as an investigator in this study implies acceptance of potential inspection by government regulatory authorities and applicable University compliance and quality assurance offices.

12 Quality Assurance and Quality Control

QC procedures will be implemented beginning with the data entry system and data QC checks that will be run on the database will be generated. Any missing data or data anomalies will be communicated to the site(s) for clarification/resolution.

Following written SOPs, the monitors will verify that the clinical trial is conducted and data are generated, documented (recorded), and reported in compliance with the protocol, GCP, and the applicable regulatory requirements (e.g., Good Laboratory Practices (GLP), Good Manufacturing Practices (GMP)).

The investigational site will provide direct access to all trial related sites, source data/documents, and reports for the purpose of monitoring and auditing by the sponsor, and inspection by local and regulatory authorities.

13 Ethics/Protection of Human Subjects

13.1 Ethical Standard

The investigator will ensure that this study is conducted in full conformity with Regulations for the Protection of Human Subjects of Research codified in 45 CFR Part 46, 21 CFR Part 50, 21 CFR Part 56, and/or the ICH E6.

13.2 Institutional Review Board

The protocol, informed consent form(s), recruitment materials, and all participant materials will be submitted to the IRB for review and approval. Approval of both the protocol and the consent form must be obtained before any participant is enrolled. Any amendment to the protocol will require review and approval by the IRB before the changes are implemented to the study. All changes to the consent form will be IRB approved; a determination will be made regarding whether previously consented participants need to be re-consented.

13.3 Informed Consent Process

13.3.1 Consent and Other Informational Documents Provided to Participants

Consent forms describing in detail the study agent, study procedures, and risks are given to the participant and written documentation of informed consent is required prior to starting intervention/administering study product. The consent materials are submitted with this protocol.

13.3.2 Consent Procedures and Documentation

Informed consent is a process that is initiated prior to the individual's agreeing to participate in the study and continues throughout the individual's study participation. Informed consent will occur in the office visit when surgery is indicated/scheduled or in the pre-operative area on the day of surgery. If informed consent is obtained the day of surgery, it will occur in the pre-operative area where informed consent for the procedure occurs, providing a privacy. Patients will be given sufficient time to determine their involvement. Informed consent for surgery is obtained 30 minutes to 1 hour prior to the procedure. Discussion of the study will occur at the same time. If the patient does not feel that they have had enough time to contemplate involvement, they will not be included in the study. Only patients who are comfortable with involvement and express that they have had sufficient time to consider involvement will be asked to sign the consent. Extensive discussion of risks and possible benefits of participation will be provided to the participants and their families. Consent forms will be IRB-approved and the participant will be asked to read and review the document. The investigator will explain the research study to the participant and answer any questions that may arise. All participants will receive a verbal explanation in terms suited to their comprehension of the purposes, procedures, and potential risks of the study and of their rights as research participants. Participants will have the opportunity to carefully review the written consent form and ask questions prior to signing. The participants should have the opportunity to discuss the study with their doctor or relatives or think about it prior to agreeing to participate. The participant will sign the informed consent document prior to any procedures being done specifically for the study. The participants may withdraw consent at any time throughout the course of the trial. A copy of the signed informed consent document will be given to the participants for their records. The rights and welfare of the participants will be protected by emphasizing to them that the quality of their medical care will not be adversely affected if they decline to participate in this study.

A copy of the signed informed consent document will be stored in the subject's research record. The consent process, including the name of the individual obtaining consent, will be thoroughly documented in the subject's research record. Any alteration to the standard consent process (e.g. use of a translator, consent document presented orally, etc.) and the justification for such alteration will likewise be documented.

13.4 Posting of Clinical Trial Consent Form

Not applicable.

13.5 Participant and Data Confidentiality

Information about study subjects will be kept confidential and managed according to the requirements of the Health Insurance Portability and Accountability Act of 1996 (HIPAA). Those regulations require a signed subject authorization informing the subject of the following:

- What protected health information (PHI) will be collected from subjects in this study
- Who will have access to that information and why
- Who will use or disclose that information
- The rights of a research subject to revoke their authorization for use of their PHI.

In the event that a subject revokes authorization to collect or use PHI, the investigator, by regulation, retains the ability to use all information collected prior to the revocation of subject authorization. For subjects that have revoked authorization to collect or use PHI, attempts should be made to obtain permission to collect at least vital status (i.e. that the subject is alive) at the end of their scheduled study period.

Paper consent forms will be kept in a designated file box in the principal investigators locked office.

All study data will be collected, organized and stored on a safe, MCIT managed network drive. A “key” file will be created associating the MRN to a numerical value (1, 2, 3…). Once the data collection portion of the study is complete, all data sheets will be de-identified by permanently removing the “key” file containing identifiable information from the database (MRN).

The study database will only be accessed by the principal investigator and sub-investigators.

Study data will be stored for no fewer than 3 years after completion of data collection to ensure appropriate time for data analysis, as well as need for re-review in analysis, write-up, publication and peer-review processes.

13.6 Future Use of Stored Specimens

Not applicable.

14 Data Handling and Record Keeping

14.1 Data Collection and Management Responsibilities

Data collection is the responsibility of the clinical trial staff at the site under the supervision of the site PI. The investigator is responsible for ensuring the accuracy, completeness, legibility, and timeliness of the data reported.

All source documents should be completed in a neat, legible manner to ensure accurate interpretation of data. Black ink is required to ensure clarity of reproduced copies. When making changes or corrections, cross out the original entry with a single line, and initial and date the change. DO NOT ERASE, OVERWRITE, OR USE CORRECTION FLUID OR TAPE ON THE ORIGINAL.

Copies of the electronic CRF (eCRF) will be provided for use as source documents and maintained for recording data for each participant enrolled in the study. Data reported in the eCRF derived from source documents should be consistent with the source documents or the discrepancies should be explained and captured in a progress note and maintained in the participant’s official electronic study record.

Clinical data (including AEs, concomitant medications, and expected adverse reactions data) and clinical laboratory data will be entered into a 21 CFR Part 11-compliant data capture system. The data system includes password protection and internal quality checks, such as automatic range checks, to identify data that appear inconsistent, incomplete, or inaccurate. Clinical data will be entered directly from the source documents.

14.2 Study Records Retention

Study documents will be retained for the longer of 3 years after close-out, 5 years after final reporting/publication, or 2 years after the last approval of a marketing application is approved for the drug for the indication for which it is being investigated or 2 years after the investigation is discontinued and FDA is notified if no application is to be filed or if the application has not been approved for such indication. No records will be destroyed without the written consent of the sponsor, if applicable. It is the responsibility of the sponsor to inform the investigator when these documents no longer need to be retained.

14.3 Protocol Deviations

A protocol deviation is any noncompliance with the clinical trial protocol, GCP, or Manual of Procedures (MOP) requirements. The noncompliance may be either on the part of the participant, the investigator, or the study site staff. As a result of deviations, corrective actions are to be developed by the site and implemented promptly.

These practices are consistent with ICH E6:

- 4.5 Compliance with Protocol, sections 4.5.1, 4.5.2, and 4.5.3
- 5.1 Quality Assurance and Quality Control, section 5.1.1
- 5.20 Noncompliance, sections 5.20.1, and 5.20.2.

It is the responsibility of the site PI/study staff to use continuous vigilance to identify and report deviations within 7 working days of identification of the protocol deviation, or within 7 working days of the scheduled protocol-required activity.

Protocol deviations must be reported to the local IRB per their guidelines. The site PI/study staff is responsible for knowing and adhering to their IRB requirements. Further details about the handling of protocol deviations will be included in the MOP.

14.4 Publication and Data Sharing Policy

This study will comply with the NIH Public Access Policy, which ensures that the public has access to the published results of NIH funded research. It requires scientists to submit final peer-reviewed journal manuscripts that arise from NIH funds to the digital archive PubMed Central upon acceptance for publication.

The International Committee of Medical Journal Editors (ICMJE) member journals have adopted a clinical trials registration policy as a condition for publication. The ICMJE defines a clinical trial as any research project that prospectively assigns human subjects to intervention or concurrent comparison or control groups to study the cause-and-effect relationship between a medical intervention and a health outcome. Medical interventions include drugs, surgical procedures, devices, behavioral treatments, process-of-care changes, and the like. Health outcomes include

any biomedical or health-related measures obtained in patients or participants, including pharmacokinetic measures and adverse events. The ICMJE policy, and the Section 801 of the Food and Drug Administration Amendments Act of 2007, requires that all clinical trials be registered in a public trials registry such as ClinicalTrials.gov, which is sponsored by the National Library of Medicine. Other biomedical journals are considering adopting similar policies. For interventional clinical trials performed under NIH IC grants and cooperative agreements, it is the grantee's responsibility to register the trial in an acceptable registry, so the research results may be considered for publication in ICMJE member journals. The ICMJE does not review specific studies to determine whether registration is necessary; instead, the committee recommends that researchers who have questions about the need to register err on the side of registration or consult the editorial office of the journal in which they wish to publish.

FDAAA mandates that a "responsible party" (i.e., the sponsor or designated principal investigator) register and report results of certain "applicable clinical trials":

- Trials of Drugs and Biologics: Controlled, clinical investigations, other than Phase I investigations of a product subject to FDA regulation;
- Trials of Devices: Controlled trials with health outcomes of a product subject to FDA regulation (other than small feasibility studies) and pediatric postmarket surveillance studies.
- NIH grantees must take specific steps to ensure compliance with NIH implementation of FDAAA.

15 Study Finances

15.1 Funding Source

There is no funding source.

15.2 Costs to the Participant

There will be no additional cost to the participant as a result of participating in the study.

15.3 Participant Reimbursements or Payments

Participants will not be compensated or provided with any incentives for study participation.

16 Study Administration

16.1 Study Leadership

The study leadership will consist of the principal investigator.

17 Conflict of Interest Policy

The independence of this study from any actual or perceived influence, such as by the pharmaceutical industry, is critical. Therefore any actual conflict of interest of persons who have a role in the design, conduct, analysis, publication, or any aspect of this trial will be disclosed and managed. Furthermore, persons who have a perceived conflict of interest will be required to have such conflicts managed in a way that is

appropriate to their participation in the trial. The study leadership has established policies and procedures for all study group members to disclose all conflicts of interest and will establish a mechanism for the management of all reported dualities of interest.

Any investigator who has a conflict of interest with this study (patent ownership, royalties, or financial gain greater than the minimum allowable by their institution, etc.) must have the conflict reviewed by the NYU Langone Conflict of Interest Management Unit (CIMU) with a Committee-sanctioned conflict management plan that has been reviewed and approved by the study sponsor prior to participation in this study. All NYULMC investigators will follow the applicable conflict of interest policies.

18 References

1. Bednar JM, Osterman AL. The role of arthroscopy in the treatment of traumatic triangular fibrocartilage injuries. *Hand Clin*. 1994;10(4):605-614.

2. Michelotti BF, Chung KC. Diagnostic Wrist Arthroscopy. *Hand Clin*. 2017;33(4):571-583. doi:10.1016/j.hcl.2017.06.004

19 Attachments

These documents are relevant to the protocol, but they are not considered part of the protocol. They are stored and modified separately. As such, modifications to these documents do not require protocol amendments.